Interagency Autism Coordinating Committee
November 19, 2001 Meeting Highlights

Introductions and Overview

Dr. Steven E. Hyman, Director of the National Institute of Mental Health (NIMH) and chair of the Interagency Autism Coordinating Committee (IACC), opened this inaugural meeting, with introductions around the table. Dr. Yvonne Maddox, Acting Deputy Director, National Institutes of Health (NIH), welcomed the IACC on behalf of Dr. Ruth Kirschstein, NIH Acting Director. She briefly highlighted the Children's Health Act of 2000 (P.L. 106-310), Title I, Section 104, which mandated the establishment of an Interagency Autism Coordinating Committee (IACC) to coordinate autism research and other efforts within the Department of Health and Human Services (DHHS) and with other agencies. In April 2001, Secretary Thompson delegated the authority to establish the IACC to the NIH. NIMH was designated the NIH lead for this activity. This committee is comprised of Federal members and representatives from the public.

Dr. Hyman established the purpose of this first meeting, which was to inform members about the various activities on autism across DHHS and in other departments. Dr. Hyman noted that the goal of this committee is to enhance both effective collaboration among agencies conducting autism-related activities and constructive dialogue with public members and a broader array of relevant stakeholders. He reminded the IACC that there are many other committees performing related functions. For example, there remains an NIH staff-level committee--the NIH Autism Coordinating Committee (NIH/ACC)--that will continue to meet regularly to discuss the mechanics of how different NIH Institutes do business. The issue of how this committee will interface with the IACC is under discussion.

Collaborative Research Programs

Collaborative Programs of Excellence in Autism (CPEAs)

Dr. Duane Alexander provided a brief historical background to the establishment of the CPEAs. The network came about as a result of a congressionally mandated conference entitled the "State of the Science in Autism," which took place in April 1995, to identify gaps in the knowledge of autism and directions for future research. This effort resulted in the National Institute of Child Health and Human Development (NICHD)/National Institute on Deafness and Other Communication Disorders (NIDCD) Network on the Neurobiology and Genetics of Autism. This network consists of 10 CPEAs that link together more than 75 researchers in 26 universities and more than 2500 families of people with autism. It requires each CPEA site both to conduct a cohesive, site-specific, multidisciplinary research program on the causes, brain structure and function, and clinical development in autism disorders and to participate in some trans-network collaborative studies that no one project has the needed expertise and/or subject population to investigate individually. The CPEA Network is now studying the world's largest group of well-diagnosed people with autism for whom both genotype and extensive phenotype data will be available. In addition, because of their combined clinical and scientific resources, the CPEAs address urgent public health questions when appropriate, including neuroimaging studies, genetic studies, a study of the neuropeptide secretin for treatment of autism, and a study of regression or late onset autism.

NIH has solicited applications from these sites for competitive review for consideration for an additional 5 years of funding. NICHD and NIDCD plan to allocate approximately $11.8 million a year through U19 cooperative agreement grants. Applications are due December 12, and awards are anticipated next summer. Dr. Alexander noted that this competition is a closed one (limited to existing sites) because the studies are meant to build upon the existing cohort of individuals with autism. Dr. Alexander noted that one of the things that will be featured in phase 2 of the CPEAs, with additional funding ($1 million) from the Centers for Disease Control and Prevention (CDC), is the study of the relationship between autism and the Measles-Mumps-Rubella (MMR) vaccine and other vaccines. This research will examine people diagnosed with regression autism, that is, those who seemed to develop normally but then started to show autistic symptoms. Researchers will compare them with people who do not have autism and those who have autistic symptoms from birth, called classic autism. CPEA researchers will compare vaccine records to determine if the onset of autism was associated with the receipt of MMR and other vaccines. Lab tests will be conducted to assess for evidence of persistent infections that could be related to the vaccine. In addition to the sites that are competitively renewed, a data-coordinating center, designed specifically to expedite and maximize analysis of the data generated by the CPEA research projects, will be established.

Studies to Advance Autism Research and Treatment (STAART)

Dr. Hyman updated the committee about the STAART Centers. The Children's Health Act calls for NIH to establish at least five Centers of Excellence in Autism Research. The comprehensive centers required by the Children's Health Act will be called STAART Centers. NIH took several steps in 2001 to begin implementing a centers program that will meet all of the specifications of the Act regarding the organization, scientific goals, and other activities of these centers. Dr. Hyman noted that the key role of the STARRT Centers is to facilitate translation of basic research into clinical research. At NIMH, such translational activities have been a strong focus. The goal is to create centers that will bring together experts in separate scientific areas, some of whom may be new to autism, to work together on solving the problems of autism. Since the idea is to foster cooperation and collaboration, these will be cooperative agreements; Dr. Deborah Hirtz from the National Institute of Neurological Disorders and Stroke (NINDS) will be working collaboratively with Dr. Stephen Foote at NIMH to staff them. The role of NIH/ACC is to coordinate the portfolio across the Institutes. The inclusion of members of the public is being considered as part of the review panels for the STAART Center applications.

As a first step, NIH took measures to help interested groups of investigators prepare to submit high-quality applications to become autism centers by issuing a request for applications (RFA)[1] on Developmental Grants for Autism Centers of Excellence (http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-01-013.html), jointly sponsored by NIMH, NICHD, NINDS, NIDCD and the National Institute of Environmental Health Sciences (NIEHS). This RFA, issued in April 2001, was designed to provide developmental grants to teams of investigators to enhance their ability to plan, organize, and demonstrate the feasibility of their

[1] A Request for Applications (RFA) is a formal statement that invites grant or cooperative agreement applications in a well-defined scientific area to accomplish specific program objectives. The RFA indicates the estimated amount of funds set aside for the competition, the estimated number of awards to be made, and the application receipt date(s). Applications submitted in response to an RFA usually are reviewed by an initial review group convened by the Institute that issued the RFA.

autism research efforts as they prepared applications for comprehensive center support over the following year. The deadline for developmental grant applications submitted in response to this RFA was July 12, 2001. Each award under this RFA was for 1 year and a maximum of $100,000 for direct costs ($125,000 if multiple institutions are involved; thus, the total cost of each grant--direct and facilities and administration costs--would range from about $150,000 to $175,000). It is anticipated that the developmental grants RFA will be a one-time solicitation. These developmental grants are intended for investigators who plan to apply for full STAART Center support for an August 2002 deadline, with anticipated funding of successful applications in FY 2003. Under this RFA, six developmental grants were awarded by the targeted funding date of October 1, 2001.

NIH also implemented a parallel funding initiative intended for applicants who wished to apply for center support on an earlier timeline, without participating in the developmental grant process. To this end, NIH released, in mid-June 2001, an RFA (http://grants.nih.gov/grants/guide/rfa-files/RFA-MH-02-001.html) that formally solicited proposals for comprehensive centers of excellence in autism research, with a deadline for applications of November 29, 2001. It is anticipated that funding of successful STAART applications under this RFA will begin in June 2002, with planned contributions from NIMH, NICHD, NINDS, NIDCD and NIEHS. In addition, applicants who submitted a developmental grant application for the July 12, 2001, deadline or who submit a comprehensive center application for the November 29, 2001, deadline and who are not successful may submit a revised application for STAART Center support for the August 2002 deadline, as may new applicants who have not previously responded to either of these solicitations. A new RFA will be issued for the second receipt date. Thus, applicants can compete for STAART support in one of three ways: (1) applying for a developmental grant in July 2001, with the intention of then applying for a comprehensive center grant in August 2002; (2) applying for a comprehensive center grant in November 2001, with the option to re-apply in August 2002 if unsuccessful; or (3) applying for a comprehensive center grant in August 2002.

The estimated total funds (direct and facilities and administration costs) available for support for all awards made under these and subsequent RFAs for the STAART Centers Program are anticipated to be $12 million per year. This total amount will be used to fund a complement of at least 5 centers, a data coordination center, and collaborative projects among the centers. Whether there are subsequent rounds of competition will depend on the number of centers funded in these first two rounds. The ultimate number of centers funded will be at least five and will depend upon the merit of the applications received and the funds available. The majority of the $12 million pool of funds will be distributed to successful center applicants to support the activities specific to each center. A separate portion of this pool of funds will be distributed to centers to fund specific cooperative projects among the centers, and another portion of the pool will be used to fund a data coordination center for which there will be a separate RFA in the future. The exact nature of the cooperative studies will be determined by the Steering Committee of the STAART Centers Program. The earliest awards for the STAART Centers are anticipated for July 2002.

Discussion
Dr. Hyman and Dr. Alexander clarified that these autism programs are not meant to create competition or to detract from one another. Rather, they are aimed to enhance current activities in autism research.

Mr. Jon Shestack suggested that the new STAART data coordination center and the CPEA data coordination center be closely coordinated to reduce overlap or duplication and facilitate research in this area.

Dr. Barry Gordon asked about the role of public members on the review committee. Dr. Hyman explained the role of public members on NIMH review groups, where public members provide input regarding the public health relevance of an application and help scientists view the research problem in a broader context. Public members are not expected to critique the science aspects of the applications.

NIH/ACC: Highlights on Autism Activities
Led by Dr. Stephen Foote

Dr. Foote described activities within NIH through the Autism Coordinating Committee (ACC). The five member Institutes include NIMH, NICHD, NINDS, NIDCD, and NIEHS. The NIH/ACC is intensively involved in both the STAART Centers and the CPEA Network. This committee meets regularly to communicate and coordinate about autism related activities.

Some highlights of recent activities include:

Request for Applications (RFA) on Innovative Treatments in Autism
As part of a special funding initiative, seven grants were awarded in September 2001 to support the development and/or refinement of treatments for core and secondary symptoms of autism. The grants were funded through the NIH/ACC, with four Institutes contributing funds to this effort: NIMH, NICHD, NINDS, and NIDCD. The grants are for 3 years each, totaling $2.9 million dollars over 3 years. These grants were solicited by an RFA on Innovative Treatments in Autism that was issued in 2000 and was part of an initiative that grew from a meeting on autism treatment methods held by the NIH/ACC in 1999. The grants address psychosocial treatments for teaching speech, imitation, and joint attention skills; psychopharmacology for behavioral problems, emotional dysregulation, and cognitive deficits; and testing of an animal model of self-injurious behavior.

Tissue resource
NIH has undertaken several activities to increase the quality and availability of genetic and tissue resources to the autism research community. The NIMH Genetics Repository has expanded its activities in the domain of collecting blood samples, creating cell lines, and distributing genetic materials to be used in autism research. This is a national resource that collects, stores, and distributes such materials very broadly across the scientific community. Also, the RFA for the STAART Centers Program is constructed so that these centers, when funded, will become a national resource for genetics studies, greatly expanding available resources. The CPEA

program, also, will continue its ongoing, extensive activities in the collection of its genetic data within its research network.

In the area of tissue resources, NIH Institutes have continued and expanded their support of existing tissue collection and distribution resources at several sites. NIMH also has just issued an RFA to enhance activities in this arena for several disorders, including autism. It also is anticipated that the STAART Centers Program will provide enhanced resources for tissue-based research in autism.

Database on Normal Brain Development

Co-sponsored among NIMH, NINDS and NICHD, this NIH MRI Study of Normal Brain Development will catalog brain development by age and sex, scanning more than 500 infants, children and adolescents, creating the world's first such large-scale database on normal brain development of children. This database will be critical in facilitating comparison of data being collected from individuals with autism.

Annual Conference on Autism

Each year, the NIH/ACC organizes a conference to focus attention on a selected topic in autism. This year's conference was held September 6-7, 2001, in Bethesda, Maryland, and was sponsored by NICHD and NIEHS, with co-sponsorship by NIMH, NINDS and NIDCD. The overall objective was to discuss possible cellular and molecular mechanisms for autism and related disorders, as well as new animal models and methodologies to study autism. The meeting included a special session on potential environmental factors that may be relevant to autism. Over 140 individuals attended the meeting, including scientists from the United States and abroad who study autism and related disorders and representatives from many of the major autism advocacy groups. A meeting report is being prepared that summarizes the findings presented and that identifies needs and opportunities for future research. The final report will be available on the NICHD Web site.

Discussion

Mr. Shestack asked for concrete ways to facilitate tissue resource efforts. Dr. Foote suggested that the committee discuss the types of coordination feasible at the next committee meeting by bringing relevant individuals to the table. Dr. Gordon indicated that there have been many prior group efforts to examine the phenotypic and genotypic manifestations of autism. Many questions are being asked. Perhaps what is needed is some consensus on the most important questions. Mr. Lee Grossman offered the Autism Society of America's (ASA) network of resources to publicize the need for tissues.

Institute specific activities were highlighted by representatives from the Institutes

NIDCD Activities

Dr. Judith Cooper noted that NIDCD supports research and research training in the areas of hearing, balance, smell, taste, voice, speech and language. It is within the areas of voice, speech and language that NIDCD forges a strong tie to NIH autism efforts. The communication limitations and disabilities of children and adults with autism are of great interest to NIDCD, and the Institute has long been committed to supporting research and research training in this area.

NIDCD supports scientists as they receive training in development of skills and knowledge that will allow them to become productive, cutting edge researchers in autism. One NIDCD fellowship award is doing just that by allowing an investigator to develop skills in genetics to explore a possible subtype of autism, a subtype specifically related to difficulty in coordinating and sequencing the oral-motor movements necessary to produce and combine speech sounds (developmental verbal dyspraxia).

Facilitating the development of language in autistic individuals and the treatment of language deficits and disabilities are two areas of research that are of high priority to NIDCD. Several projects are examining the efficacy of varied treatment approaches in the development of expressive communication in autistic children. Picture Exchange Communication System, Prelinguistic Milieu Teaching, a treatment that focuses on oral motor control, and the Denver Model are all being examined in carefully designed efficacy studies.

Since its inception, NIDCD has supported autism research, and the portfolio on autism has broadened and grown. NIDCD is strongly committed to continuing its participation in this critical effort.

NIEHS activities

Dr. Cindy Lawler reported that the NIEHS is a relative newcomer to the field of autism research. As part of the NIH/ACC for the last 18 months, NIEHS has participated in activities described above, and has set aside funds to support one full STAART Center. Beyond the NIH/ACC, NIEHS and the Environmental Protection Agency (EPA) jointly funded two Children's Centers for Environmental Health and Disease Prevention in August 2001. These centers will focus research on potential environmental inputs to autism. The centers each will be funded at $5 million, or approximately $1 million per year for 5 years beginning in August 2001. The new Children's Center at the University of California at Davis will investigate how environmental risk factors may contribute to childhood autism. There has been speculation among both parents and health professionals that prenatal or early postnatal exposure to various metals or chemicals or even vaccines may trigger autism. To help address this concern, the center's research will include a large case-control epidemiological study of various exposures and the development of autism. This center will also conduct research to develop new animal models for studying social interaction and the impact of neurotoxicants on social behavior. Additional studies will focus on elucidating the cellular and molecular mechanisms by which specific neurotoxicants can perturb critical neuronal functions during development. The work will be carried out within the infrastructure of the UC Davis M.I.N.D. (Medical Investigation of Neurodevelopmental Disorders) Institute.

The other recently funded Children's Center at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey, will seek to determine the possible influence of mercury, lead and valproic acid (a drug commonly used to control seizures) on autism, learning disabilities and regression. Studies to be conducted will look at critical windows for brain development in the forebrain and hindbrain and will attempt to link exposures or disturbances at these times to subsequent behavior. Researchers will also look for differences in genetic susceptibility of children to environmental toxicants. Brain imaging will be used to determine whether children with higher exposures to environmental toxicants have different patterns of brain growth and development.

NINDS Activities

Dr. Audrey Penn reiterated NINDS' special interest and long standing commitment to autism as a neurodevelopmental disorder. She noted that better understanding of the etiology and pathophysiology of autism is essential to the development of strategies for prevention and treatment. The identification of biological markers, functional and behavioral measures, and neuroanatomical correlates for the disorder would enable progress toward this understanding. In March 2001, NINDS assembled a small group of extramural and NINDS intramural researchers with expertise in autism or brain growth factors and brain anatomy for an exploratory discussion of current understanding in these areas. The Institute is considering information from this meeting in charting future research directions.

In addition, NINDS intramural researchers are working to study the biology of autism, using neonatal bloodspot specimens for microassays and several new techniques for their analysis, and biomarkers in conjunction with longitudinal studies of volumetric MRI brain imaging and to pursue questions about immune function in autism.

Discussion on the link between vaccines and autism

Mr. Albert Enayati, a meeting attendee, asked about the association between vaccines and autism. He noted that an overwhelming majority of parents at a recent meeting felt strongly that thimerosal (a preservative used in vaccines that contains ethyl mercury) caused autism in their children.

Dr. Alexander acknowledged that this is a topic that has received a tremendous amount of attention. He cited several separate and independent efforts--including those by the Institute of Medicine (IOM) and the United Kingdom's Committee on Safety of Medicine--that have pointed to the lack of support for an association between autism and the MMR vaccine. At the same time, a number of groups are trying to address this issue. These include the CPEAs' work in conjunction with the CDC discussed above. Another effort involves the National Children's Study (NCS), a longitudinal cohort study of environmental effects on child health and development, which was mandated when the Children's Health Act of 2000 was signed into law, laying the groundwork for a 30-year study to follow 100,000 children from before birth to adulthood. This effort, led by the NICHD, CDC, and EPA, together with other NIH Institutes and Federal agencies, will include data on environmental exposures during pregnancy and postnatally to examine environmental agents including vaccines. This study might be able to address this question of the link between MMR vaccine and autism as well.

Concerns about the ability of the NCS to answer the vaccine-autism link were raised. Dr. José Cordero clarified that the MMR vaccine does not contain thimerosal. Studies can only be done in a retrospective fashion because currently available vaccines do not contain or contain only trace amounts of thimerosal. Thus, the NCS with its prospective, longitudinal design may not be able to definitively address the vaccine-autism link. Ms. Barbara Loe Fisher, a meeting attendee and President of the National Vaccine Information Center, stated that the epidemiological design of the NCS is insufficient to address the vaccine-autism link and asked if more in-depth studies are planned. Dr. Alexander noted that up to 10-20 percent of children do not receive vaccines; the size of the study may allow for adequate comparisons of the impact of vaccines. He also said that the NCS is an observational study and plans for in-depth studies such as brain imaging have not been determined.

Dr. Gordon cautioned against an over-focus on vaccines. The cause or causes of autism have yet to be determined, and there is an extremely large number of possibilities. He suggested that the public needs to be educated about the plausibility of reported findings and about how much investigative weight to apply to such findings. Perhaps criteria can be agreed upon, by public groups as well as by scientific ones, by which reported findings could be evaluated.

Update from Other Federal Agencies and Public Members on Autism Activities

Administration on Children and Families (ACF)

Dr. Patricia Morrissey indicated that she is new to the issue of autism and relatively new to her position as Commissioner of Administration on Developmental Disabilities at ACF. She suggested that NIH needs a translator in disseminating scientific findings to the community. She offered the assistance of the University Centers on Developmental Disabilities (which work directly with families and communities and are funded by ACF) in helping to translate research information. Dr. Morrissey suggested that the IACC offer guidance on when or how scientific information is released to the public, particularly how conflicting information may be presented in a balanced manner. Dr. Morrissey also offered her own expertise and experience with legislation to the committee.

Agency for Toxic Substances and Disease Registry (ATSDR)

Dr. Henry Falk provided a brief background on the inception of ATSDR, an agency directed by congressional mandate (the "Superfund" Act) to perform specific functions concerning the effect on public health of hazardous substances in the environment. These functions include public health assessments of waste sites, health consultations concerning specific hazardous substances, health surveillance and registries, response to emergency of hazardous substances, applied research in support of public health assessments, information development and dissemination, and education and training concerning hazardous substances. The ATSDR works with states and other Federal agencies to prevent exposure to hazardous substances from waste sites on the EPA's National Priorities List.

ATSDR's involvement in autism is related to the Brick Township Study in New Jersey. This a community-based prevalence study designed in response to the concern of parents regarding a possibly larger than expected number of children with autism spectrum disorder in Brick Township. The study found 6.7 cases of autism spectrum disorders (ASD) per 1000 children, a

relatively high rate compared with a recent population based study in Atlanta that found rates of 3.4 per 1000 children. Such state surveillance projects and centers surveillance activities will provide vital background data for evaluating potential clusters of autism.

ATSDR, under the mandate of the superfund program, has worked with other agencies to address the issue of mercury in vaccines.

National Center on Birth Defects and Developmental Disabilities (NCBDDD)
Dr. Cordero noted that the NCBDDD at the CDC was created as part of the Children's Health Act on April 16, 2001. The NCBDDD seeks to promote optimal fetal, infant, and child development; prevent birth defects and childhood developmental disabilities; and enhance the quality of life and prevent secondary conditions among children, adolescents, and adults who are living with a disability. The agency comprises two divisions--the Division of Birth Defects and Developmental Disabilities and the Division of Child and Adult Disability and Health. He went on to describe autism-related activities conducted at the CDC.

National Autism and Pervasive Developmental Disabilities Surveillance Program
In 1998, CDC initiated one of the few programs in the world that conducts active, ongoing monitoring of the prevalence of ASD in children in Atlanta, Georgia. Rates of ASD in this population-based study were found to be 3.4 per 1000.

In 2000, CDC funded six states--Arizona, New Jersey, Delaware and Maryland (joint), South Carolina, and West Virginia--to monitor the prevalence of ASD. These states are adapting the model developed in CDC's Atlanta-based monitoring program for their local area. In the first year, activities focused on hiring staff, developing protocols, establishing collaborations with education agencies and clinical providers, and obtaining institutional review board and other approvals. In September 2001, CDC provided additional funding to four of the states (Arizona, New Jersey, South Carolina, and West Virginia) to continue their surveillance projects. New Jersey received increased funding that will allow expansion of surveillance activities from four to eight counties, along with training for community service providers. In addition to conducting surveillance on the prevalence of autism, West Virginia uses part of its grant funds for dissemination and evaluation of a family-focused model program for preventing secondary conditions of autism. In 2001, Maryland/Delaware received funding as one of the newly established Centers of Excellence (see below) and will continue their autism monitoring activities under that mechanism. Data collection in these states is expected to begin in 2002.

Centers of Excellence in Autism and Pervasive Developmental Disabilities Epidemiology
In September 2001, CDC funded four Centers of Excellence in Autism and Pervasive Developmental Disabilities Epidemiology to conduct collaborative studies on the number, incidence, and causes of autism and related developmental disabilities. The four centers include: (1) Johns Hopkins University, which will identify children with autism in northeastern Maryland and the entire state of Delaware; (2) the University of Pennsylvania, which will cover the Philadelphia metropolitan area; (3) the Colorado Department of Public Health, which will concentrate on identifying children with autism in the Denver area; and (4) the California Department of Health Services, which will ascertain autism cases statewide, with more intensive monitoring in the San Francisco Bay area. In addition to conducting surveillance of autism in their areas, the centers will also participate in collaborative case-control studies of factors that

may cause autism and related developmental disabilities. Each center also will conduct center-specific special studies focusing on areas of particular expertise, such as genetics, immunology, biological markers, and screening. The first meeting of the centers' investigators is scheduled for November 27-29, 2001, in Atlanta, Georgia.

Clearinghouse

As part of the Centers of Excellence in Autism and Pervasive Developmental Disabilities Epidemiology, CDC will establish a clearinghouse on policies and research methods that can be used to facilitate the establishment and operation of surveillance projects and epidemiological studies of autism and related pervasive developmental disabilities. The clearinghouse will serve as the central repository of data generated from the autism monitoring activities of the Centers of Excellence in Autism and Pervasive Developmental Disabilities Epidemiology. Any materials or information developed by the centers that may be useful for the public or other researchers will be made available through the clearinghouse (for example, results of surveillance and other epidemiological studies; publications; research protocols, including questionnaires and other instruments; guidelines on accessing educational and clinical records, including privacy and confidentiality of records and databases; community outreach strategies; and educational materials for professionals, families, schools and the general public).

Dr. Cordero also noted that promoting wellness in individuals with disabilities is an area of interest for his agency. Such individuals have difficulties in accessing good health care and NCBDDD is trying to focus not only on primary prevention and on preventing secondary conditions but also on access to important health care and preventive care. He alerted the audience to the Surgeon General's initiative on mental retardation.

Discussion

Mr. Grossman was struck by the differences in the prevalence rates documented in Atlanta vs. Brick Township. He emphasized the pressing need to get accurate numbers in light of significant variations in reported incidence of autism. Mr. Shestack further highlighted the need to obtain cost of illness estimates to help maintain funding in this area. Dr. Cordero noted that the CDC is looking at the direct cost of autism; indirect cost is difficult to establish. He stated that CDC would be happy to update the autism congressional caucus about the recent prevalence data, as suggested by Mr. Shestack. Dr. Hyman agreed, with the caveats noted by Mr. Grossman on the varying rates, that updated information on prevalence data is needed, and one step would be to update NIH information sheets.

Ms. Loe Fisher relayed a message on behalf of Mr. Rick Rollens, co-founder of the M.I.N.D. Institute, who was not able to be present. In this message, Mr. Rollens wanted to emphasize the dramatic increase in the number of new cases of classic autism, as reported by the California Department of Developmental Services. According to this recent report, the state of California has documented the largest increase in new cases of classic autism in its history--record number of 705 new cases between July and October 2001. Ms. Loe Fisher noted that the $12 million for the new centers that NIH has dedicated to autism does not come close to what in her opinion is an epidemic of autism, at least in California.

Food and Drug Administration (FDA)

Dr. Kathryn Carbone highlighted three major areas of activities at the FDA related to autism: clinical therapeutic trials, clinical surveillance of the regressive subtype of autism and its link to vaccines, and basic science investigations. With respect to clinical trials, Dr. Carbone reported that the more objective the clinical trials, the less evidence there is on the efficacy of secretin for treating autism. One of the difficulties conducting clinical trials in this area is the huge placebo effect (parents of children who receive placebo report positive effects, upwards of 70 percent), necessitating rigorous study design to determine efficacy. Dr. Carbone described a couple of studies under formulation, on the link between the regressive subtype of autism to vaccines. The first part of the study concerns the medical aspects of autism following vaccination using a questionnaire and medical record review. The goals of this study are to gather information about the clinical features of the cases to look for patterns that might provide clues into the etiology of autism and whether there is a possible connection with vaccination, especially the regressive subtype. This study is not designed to determine whether vaccination causes autism. However, it may result in the generation of hypotheses that could be evaluated in subsequent controlled epidemiological studies. Another proposed study focuses on evaluation of home videotapes to improve the researchers' ability to identify cases of the regressive subtype of autism. The second part of the study concerns parental risk perception. The questionnaire addresses such issues as parental concerns about vaccination, how parents came to believe their child's autism was related to vaccination, where parents obtain information about vaccines, and what factors (e.g., race, socioeconomic status, education) might influence risk perception. The results of this portion of the study might be used to help improve the Government's ability to communicate the risks and benefits of vaccination to the public. With respect to basic science investigations, the Center for Biologics Evaluation and Research at the FDA continues to develop and assess neurovirulence assays in vaccines to determine the safety of vaccines for the developing nervous system. She noted that a combination of basic pathogenesis and clinical information can lead to illuminate interesting findings and theories.

Discussion

A brief discussion regarding current diagnostic criteria and endpoints for clinical trials followed. Dr. Hyman noted that current diagnostic criteria, while helpful for epidemiology, could be limiting because the boundaries of the disorder are not clear. There is a need to address both the clinical pathogenesis and the symptoms clusters. The goal is to find pathophysiologically related symptom clusters that could be targets for the development of therapeutics. Dr. Hyman noted that in some sense, the NIMH Research Units on Pediatric Psychopharmacology Studies are aimed at defining symptoms clusters that can be targeted by therapeutics.

A meeting attendee (name unrecorded) reported repeated attempts to contact Dr. Bernard Schwetz, Acting Principal Deputy Commissioner of the FDA, to inform him of parents' concerns about the safety of vaccines. He has yet to obtain a response and requested that Dr. Carbone address this with Dr. Schwetz. Dr. Carbone agreed to do so and reported that thimerosal-reduced (i.e., trace amounts) and thimerosal-free childhood vaccines are currently available.

Dr. Sprouse, a meeting attendee, urged the committee to consider the value of examining parent reports of change in light of the high placebo effects in clinical trials. Important data may be missed or dismissed as unscientific because current assessment tools are not adequately

sensitive. She noted that current tools may be too crude to capture early symptoms of autism, often missed by physicians but reported by parents.

Department of Education (DOE)
Dr. Gail Houle reported that autism related initiatives come primarily out of the Office of Special Education Programs (OSEP). She described Part B (for 3- to 21-year olds) and Part C (for 0- to 2-year olds) of the Individuals with Disabilities Education Act (IDEA) that help states carry out their responsibility to provide all children with a free appropriate public education, including related services designed to meet their unique needs. OSEP funds technical assistance, training, and interventions. Over the past 5 years, OSEP has been synthesizing the research base that can inform families about interventions. The Department of Education helped fund the recently released National Academy of Science's synthesis of an interdisciplinary approach to education for children with autism. The report, "Educating Children With Autism," explores what makes education effective for the child with autism and identifies specific characteristics of programs that work. Recommendations are offered for choosing educational content and strategies, introducing interaction with other children, and other key areas. Over the past 4 years, the department also funded a National Early Childhood Technical Assistance System--autism is one of the key foci.

Public Members

Mr. Lee Grossman
Mr. Grossman stated that the DHHS and the DOE are perhaps the most important players at the table. Both these agencies have a role in providing services, which are extremely difficult to access for autistic children and their families. Mr. Grossman noted that he has been pleased with dialogues he has had with the NIH, CDC and other DHHS agencies. He hopes to continue this relationship through the IACC, and offered the ASA's resources, with its 25,000 members and over 200 chapters across the United States, as a way for the IACC to get a sense of what is on the minds of the autism constituents. Based on current statistics, Mr. Grossman reported that it is the opinion of ASA that autism will become the largest group of individuals with disability in 10 years. He strongly urged a national agenda on autism to ensure that every child will have access to appropriate diagnosis, services, and supports necessary for autistic individuals to lead productive lives.

Dr. Barry Gordon
Dr. Gordon did not comment at this time, preferring to save his comments for later discussion. He did note the difficulties involved in translating research into practice. One example he gave was the problems faced by researchers who attempt to conduct research in schools and with school children.

Mr. Jon Shestack
Mr. Shestack pointed out that prevalence data from the CDC indicate that autism is a public health problem and that congressional interest on this topic will likely increase. He noted the uneven implementation history of Title I. For example, Section 103 of Title 1, which authorizes the Secretary to establish and implement a program of education and information for health professionals and the general public as well as a stipend program for health professionals, has not

yet been implemented. He noted that volunteer organizations have a lot to offer in helping move forward issues such as brain and gene banking through joint funding of projects and the dissemination of information. He questioned whether the DOE could play a role in physician and patient education.

Dr. Lucille Zeph

Dr. Zeph encouraged collaborations that have already begun--the interdepartmental and interdisciplinary activities. She noted that so much is not known about the neurology and pathogenesis of autism, and yet there are often preconceived notions about its deviance. In her personal experience in working with such children as a teacher and an administrator, she realized that there is much to gain by remaining open to various possibilities. For example, the development of a child with autism may not follow the normal developmental trajectory. In her experience, she found that she had to violate rules learned about normal child development in order to help children with developmental disabilities progress in their learning. She encouraged sharing of information and being open to data that may not make sense or fit into existing professional rubrics.

Opportunities for Collaboration: Interagency and Public-Private Partnerships

Other relevant agencies that could contribute to the IACC mission

Dr. Hyman noted that one key player that needs to be included at the table is the Health Resources and Services Administration (HRSA). Dr. Hyman questioned Ms. Rita Goodman, Chief Nurse at the Bureau of Primary Health Care in HRSA, who was in the audience at this meeting. Ms. Goodman indicated that HRSA funds approximately 750 organizations that deliver comprehensive primary care services in about 4000 sites to approximately 11 to 12 million people. Given that a significant number of people served likely have autism, there is a need for clinician training. Ms. Goodman noted that HRSA is interested in the translation of science into clinical practice and highlighted potential contributions of both the Bureau of Health Care and the Maternal Child Health Bureau of HRSA on this committee. HRSA will be invited to participate on the IACC.

Role of the IACC

Mr. Grossman asked for clarification of the ground rules for the IACC. Dr. Hyman described the purpose of the IACC as one of facilitating coordination across agencies. Dr. Hyman noted that this committee could have a creative role and a strong voice in pointing out potential collaborations but that the IACC cannot serve in an advisory capacity. Dr. Gordon also noted that the committee could provide information that might raise the profile of autism as well as that of developmental neuroscience as a whole.

Strategic Map to Guide IACC Efforts

Dr. Gordon noted that a vast amount of research relevant to autism may not be counted as autism research. He suggested that it might be helpful to outline the information and issues in autism visually, as has proven useful in other fields. Such a map could have a number of overlays, representing such information as the nature of the problem(s) in autism, the current state of knowledge about those problems, the availability of services for the problems, and the agencies responsible for various aspects of autism-related activities (both research and service). He noted

that autism should not be viewed as a condition in isolation. Instead, it is one part of the broader problem of developmental disorders, which in turn are part of the larger problems of such fields as genetics, neuroscience, education, and social services. What a committee such as the IACC could do is to provide evidence for some of the recommendations that might be ultimately made to Congress. Dr. Gordon views autism as an opportunity for all the communities involved, such as the educational one and the neuroscience one, to help demonstrate the utility of their efforts on a very tangible and very common problem. He offered to lead the initial efforts to draft the map he suggested to provide a target for organizing and presenting the issues and the work being done on autism. He cautioned that such a map could not be too detailed, or the overview it could offer would be lost. However, it might be possible with current technology to allow a viewer to drill down into the map for greater detail and also to zoom out for the bigger picture. Several members of the IACC concurred with Dr. Gordon's suggestion as a good starting point. Dr. Hyman agreed that such a map could be an educational document for Congress.

Dr. Zeph reiterated that a comprehensive status report of what exists is needed and further suggested that DHHS think about what other agencies need to be at the table (e.g., HRSA, Center for Medicaid and Medicare Services). Dr. Gordon cautioned that there would be information that will not show up on the map; he again offered to take a first step in developing a working map for the committee. Mr. Shestack asked if members of the IACC could review the congressional report, which summarizes activities across the department, prior to its submission to Congress. The report could serve as a useful starting point in the mapping effort. Ms. Gemma Weiblinger from NIMH will find out.

Coordination of current activities

Mr. Shestack questioned the effectiveness of coordination thus far (e.g., between NIH and CDC, NIH extramural and intramural programs), and asked for clarification of the FDA's role. Dr. Carbone described the FDA's role in reviewing data, working with industry to determine endpoints, measurement, etc., and approving or disapproving studies. For example, FDA can create opportunities for new pharmacotherapies. Dr. Foote noted that the STAART Center applications will have been reviewed in 6 months and would allow for more substantive discussions. As suggested by Mr. Shestack, one topic for discussion could be how to coordinate information from the CPEA Network and STAART Centers (e.g., common measurement/protocol). Dr. Hyman suggested that another topic for future meetings could be to invite the NIH intramural research program to update the committee about autism-related research.

Review of autism grants

Mr. Shestack also expressed concern about how autism grants fare in study sections where they are reviewed. Dr. Hyman agreed that the committee could invite individuals from the Center for Scientific Review at NIH to talk about the grant review structure and process.

Open Session for Public Comment

Sallie Bernard, Safe Minds, Cranford, New Jersey

Ms. Bernard represented Safe Minds, an organization involved in investigating the relationship between thimerosal and autism. This organization raises public awareness about the use of

mercury in medicines and its role in contributing to human disease. Ms. Bernard asked the committee to consider the recommendations of the recent IOM report on "Immunization Safety Review: Thimerosal--Containing Vaccines and Neurodevelopmental Disorders."

Agnes Cushing-Ruby, Parent
Ms. Cushing-Ruby is a parent with a 15-year-old daughter with autism, whose disorder is complicated by several comorbid conditions (e.g., gastrointestinal dysfunctions). She encouraged the IACC to look beyond core autistic symptoms and to address comorbid conditions that accompany autism.

Albert Enayati, Safe Minds & Cure Autism Now (NJ Chapter)
Mr. Enayati noted that many components in vaccines have not been tested. He cited a recent report funded by the CDC indicating that DPT and MMR vaccines may cause seizures. He noted that most children with autism suffer from seizures and that every symptom of autism mirrors the effects of mercury poisoning. He said the only way children were exposed to mercury poisoning is through childhood vaccination. He believes mercury poisoning caused his son's autism. He called for the IACC to initiate research regarding childhood vaccination and autism. He appealed to the committee to review the evidence on vaccines.

Raymond Gallup, President of Autism Autoimmunity Project
Mr. Gallup is another parent who believes that vaccine caused autism in his son. He reported abnormal titers and T-cell abnormalities in his son after receiving vaccinations. In addition to the evidence Mr. Enayati presented, Mr. Gallup also cited anecdotal evidence to support his contention that vaccines cause autism. He is concerned about what he termed an "epidemic" out there and called for more research on immunology and its relationship to autism.

Edward Wong, Safe Minds
Dr. Wong noted that he is a scientist and was Assistant Director of Research for a medical technology division of Pfizer. He has a 4½-year old grandson with autism. He described difficulties his family encountered in obtaining services for his grandson, including long wait lists at special schools. At this time, his grandson is enrolled in an intensive home program, costing the family $70,000 per year in services, which the school district refused to subsidize despite guidelines that advocate for early intervention for autism. He advanced his hypothesis about how to distinguish the environmental and/or genetic factors related to autism. He noted that the recent IOM report indicated that there is as yet insufficient evidence to support the link between thimerosal in vaccine and autism but recommended the removal of thimerosal from vaccines and other products administered to children. Dr. Wong encouraged studies to compare children who now receive thimerosal-free vaccines with those who did not. He called for the development of blood tests to determine those at risk for developing autism (similar to allergy testing) and studies to identify genetic and biologic factors that may be triggered by such environmental agents.

Discussion
Dr. Lawler noted that the common theme from these testimonies suggests a need to coordinate research efforts to evaluate safety of vaccine components. One of the children's centers funded through NIEHS is looking at the potential effects of thimerosal. Dr. Hyman assured Dr. Wong

that his written comments would be forwarded to NIEHS. Several studies are already in progress as described earlier by Dr. Alexander. Dr. Cordero also noted that the CDC is in the process of studying the prevalence of autism in children who receive thimerosal-free vaccines in Denmark. Mr. Shestack reported that the vaccine-autism link is a topic he hears from numerous families and suggested that the Government is doing a terrible job at educating families about the research on this topic and that the autism community feels that Government's actions are motivated by fear of litigation. Dr. Cordero reported that three advisory committees have been established to address vaccine safety issues: the National Vaccine Advisory Committee, the Advisory Committee on Immunization Practices and the Advisory Commission on Childhood Vaccines. He suggested that some efforts at coordination may be helpful.

Ms. Loe Fisher pointed out again that the data of the dramatic increase in numbers of autism cases in California suggests a public health crisis. She urged for good science to address and resolve the issue regarding the link between vaccines and autism.

Ron Oberleitner, Princeton, New Jersey
Mr. Oberleitner has an autistic son. He described substantial difficulties in accessing services despite connections in a community known to be one of the best in the Nation when it comes to providing for autistic children. His son travels 1½ hours each way to school daily. He urged the audience to recognize the gifts these children have and their awareness of their disorders, even if they may not be able to communicate them.

Discussion
Mr. Shestack pointed out that there is no safety net for children with autism. He highlighted his point by noting that if one suffers from a heart attack, every emergency room in the country would provide treatment regardless of insurance status. Yet, this is not so for autism. Service access is not guaranteed. He suggested that parents are counting on radical research findings that will help raise awareness and stimulate progress in this area.

Mr. Grossman again encouraged the IACC to view autism as public health crisis, to develop a national agenda on autism, and to focus on services needed by such children. Dr. Zeph noted that the Center for Medicare and Medicaid Services [CMS, previously Health Care Financing Administration (HCFA)] needs to be at the table if services are to be addressed

Next Steps

Drs. Hyman and Kimberly Hoagwood summarized tasks and follow-up topics.

Tasks

1. The committee agreed to develop a comprehensive map of the issues in autism, the efforts directed against those issues, and the agency and volunteer organizations behind those efforts. This map could be used both to summarize current activities as well as to guide future activities by identifying gaps and needs. Dr. Gordon volunteered to initiate this.

2. The committee suggested that a Listserv or e-mail list be created to aid communication among IACC members.

3. The committee suggested that additional members be invited onto the IACC: HRSA and CMS.

4. A list of topics for the next meeting will be circulated to the IACC for prioritization.

5. The committee recommended that a subcommittee be formed to address service needs for autistic individuals. Mr. Grossman and Dr. Houle indicated an interest in beginning a dialogue on this issue.

6. The committee requested that the IOM report on vaccines be made available to its members.

7. The committee suggested that the fact sheets sent out by agencies and volunteer organizations be updated to reflect the new prevalence figures from CDC.

Potential Topics for Next Meeting

1. Strategies to improve gene and tissue banking--ways to increase the availability of DNA material for analysis.

2. The comprehensive map: conceptual framework, content, gaps.

3. Optimal opportunities for data sharing and coordination among the agencies.

4. Progress reports on CPEA and STAART programs--how best to coordinate the science and maximize communication to increase efficiency and effectiveness.

5. Creating better partnerships between Federal agencies and associations.

6. Research application review: Invite the NIH Center for Scientific Review (CSR) to provide an overview of the NIH expert review process and structure.

7. The NIH intramural program: staff update on autism research.

8. Service needs for autistic individuals--suggestions forwarded by Dr. Houle (DOE) follows.

    a. Family involvement presentation on parent training and advocacy centers. The DOE (Office of Special Education) funds at least one such advocacy center in every state. It is run by parents of children with disabilities for parents of children with disabilities, ages birth-21, and assists parents in obtaining appropriate services for their children.

    b. Distance learning--model demonstration and training programs funded by DOE (special education) to provide training for teachers and school personnel who provide

services for children with autism via distance learning (University of Kansas and University of Alaska).

c. Examination of school records--a presentation on DOE's regulations and policies on release of school records. This would have to come through Secretary Paige.

d. Panel of State Directors of Special Education to speak about the provision of services and funding of services--how is this implemented and financed in their states (should include MD and VA). A focus on state-local collaboration models would be appropriate.

e. Department of Defense programs for children with autism: What are they doing? They have an annual conference and a representative on the DOE Federal Interagency Coordinating Council (FICC) established through the 1991 amendments of the IDEA. Request for Applications (RFA) for early childhood. Perhaps invite to join IACC?

f. Presentations by salient service delivery school models that are successfully practicing family-focused, interagency coordination.

| Agenda | Congressional Report (pdf format, 13 page) | Participant List |