Department of Health and Human Services
Interagency Autism Coordinating Committee
Meeting Highlights
November 17, 2006
National Institutes of Health
Bethesda, Maryland

IACC Members in attendance: Thomas Insel, M.D., National Institute of Mental Health (NIMH), chair; Ann Wagner, Ph.D., NIMH, Executive Secretary; James Battey, M.D., Ph.D., National Institute on Deafness and Other Communication Disorders (NIDCD); Ellen Blackwell, M.S.W. (representing Leslie V. Norwalk, Esq.), Centers for Medicare and Medicaid Services (CMS); Coleen Boyle, Ph.D., Centers for Disease Control and Prevention (CDC); Barry Gordon, M.D., Ph.D., Johns Hopkins University School of Medicine; Lee Grossman, Autism Society of America; Gail Houle, Ph.D. (representing John Hager, M.B.A.), U.S. Department of Education (ED); Larke Nahme Huang, Ph.D., Substance Abuse and Mental Health Services Administration (SAMHSA); Alice Kau, Ph.D., National Institute of Child Health and Human Development (NICHD); Story Landis, M.D., National Institute of Neurological Disorders and Stroke (NINDS); Cindy Lawler, Ph.D., National Institute of Environmental Health Sciences (NIEHS); Elizabeth Lopez, Ph.D., SAMHSA; Merle McPherson, Ph.D., DHHS Office on Disability; Patricia Morrissey, Ph.D., Administration on Children and Families; Audrey Penn, M.D., NINDS; Celia Rosenquist, Ph.D., ED; David Schwartz, Ph.D., NIEHS; Jon Shestack, Cure Autism Now; Bonnie Strickland, Ph.D. (representing Elizabeth Duke, Ph.D.), Health Resources and Services Administration (HRSA); Susan Swedo, M.D., NIMH; Lucille Zeph, Ed.D., University of Maine Center for Community Inclusion and Disability Studies.

Dr. Thomas Insel, Director of the National Institute of Mental Health and chair of the Interagency Autism Coordinating Committee (IACC), called the committee's ninth meeting to order.

I. AUTISM SERVICE GUIDELINES FOR PRIMARY CARE/MEDICAL HOME PRACTICES

Dr. Insel introduced Chris Plauché Johnson, M.Ed., M.D., Medical Director of the Village of Hope Center for Children with Disabilities at the University of Texas Health Science Center in San Antonio. Dr. Johnson has served on the American Academy of Pediatrics (AAP) National Committee on Children with Disabilities since 1997 and has chaired the AAP Autism Expert Panel since 2002. She represents the AAP on the services subcommittee of the IACC.

Dr. Johnson reported on a workgroup that was convened by HRSA to develop autism services guidelines, including developmental and general pediatricians, psychologists, school systems, parents, parent advocates, and facilitators. The workgroup was charged with three tasks: developing guidelines for the medical home/primary care (MH/PC) practice in pediatrics in collaboration with the AAP panel; identifying actions needed to help the primary care/medical home pediatrician in carrying out the

guidelines; and suggesting steps for implementing those actions. The workgroup's guidelines are based on the 2001 AAP guidelines, which are being revised and will be published in 2007.

The suggested guidelines address five goals:

1. General principles of MH/PC related to autism spectrum disorders (ASD). Dr. Johnson said the following are fundamental to all of the workgroup's goals: primary care pediatricians need to understand the principles of the *medical home*; every staff member needs to be involved in caring for children with ASD; provide appropriate information to parents and value parents as partners and decision makers; and deliver services in a culturally competent manner. The pediatrician needs the support of funders to reimburse the extra time required and, perhaps, provide a portion of the cost for training and other suggested activities. The workgroup emphasized the importance of training programs for primary care providers to screen for ASDs and for specialists to decrease the amount of time a child must wait to be seen by an autism team.

2. Surveillance, screening, and definitive diagnosis of ASD. The workgroup reaffirmed the importance of surveillance of all children at every well-child visit, as well as screening at select age intervals and at any visit when a parent raises concerns. A new AAP policy published in July 2006 provides an algorithm and standardized tool to conduct general developmental screening during every well child visit at 9, 18, 24, or 30 months and autism-specific screening at 18 months (*Pediatrics* 2006;118:405-420). The policy highlights the value and importance of screening younger siblings of children with autism and educating parents about the increased risks in subsequent children. The AAP Autism Expert Panel responded to the statement with a commentary (*Pediatrics* 2007;119:152-153). The IACC workgroup agreed with the policy guideline for immediate referral to an ASD team, and, if one is not available in the community, to a pediatric subspecialist who is experienced in such evaluations. A *simultaneous* referral should also be made to an early intervention program if the child is less than three, or if older than three to a special education program so that intervention can begin immediately. The workgroup emphasized that a definitive ASD diagnosis is not necessary to begin services. Referrals to audiology specialists and local family support groups were also suggested. The workgroup noted the need for funding and/or insurance reimbursements for medical homes to engage in these activities.

3. Ongoing medical care after diagnosis. These services include medical, behavioral, and mental health care, as well as complementary and alternative medicine options. Dr. Johnson noted that the need for the primary care pediatrician to continue to treat the child after the diagnosis is made was also among the guidelines. She underscored the importance of evaluating the child for underlying medical causes of maladaptive behavior and highlighted the need for more effective, well-staffed, and well-funded intervention programs.

4. Community services and coordination of care. The workgroup proposed that the medical home be comprehensive in collaborating with specialty care providers, develop a plan with them, and seek to achieve an integrated system of care.

5. Youth transition to adult services. The workgroup suggested developing an individualized transition plan by the time the child is 14 years old, identifying adult resources and providers, involving youth with ASD in their own care to prepare for transition, facilitating access to services in life skills, and ensuring that planning includes insurance and finance matters.

In concluding her comments, Dr. Johnson underscored that these suggested guidelines would require significant changes in pediatrician behavior and noted that barriers to these changes include funding constraints, lack of training, and lack of time and reimbursement. She also emphasized the need for the support of professional organizations; public and private funders; Federal, State, and local governments; early intervention and education systems; and community agencies. The workgroup plans to pilot test the guidelines in medical home practices through the Medical Home Autism Initiative, in conjunction with AAP and other organizations. It may also explore promoting the guidelines with the autism toolkit, which now includes screening tools, surveillance tools, algorithms for pediatricians, handouts for parents, web sites, and information on vaccines. The toolkit is expected to be sent to a sample of pediatricians; funds are now being sought to send the toolkit to every pediatrician and to family practice residency programs.

In answer to questions from IACC committee members about implementation of the guidelines, Dr. Johnson said that the workgroup sent draft guidelines to professional psychiatric and psychological organizations for feedback. She noted that the AAP is also trying to raise awareness of the need for early detection by encouraging practitioners to distribute its pamphlet--"Is Your One-Year-Old Child Communicating with You?"--to all families at their child's one-year-old checkup. Dr. Johnson said that a subcommittee is working on insurance coding and funding issues, which are major barriers to implementation. She also noted that draft guidelines were sent to Cure Autism Now and the members of the Autism Treatment Network (ATN), both of which made valuable suggestions. Dr. Johnson said that she will send the draft guidelines to IACC members following today's meeting and would appreciate their comments.

II. UPDATES ON FEDERAL ACTIVITIES

Health Resources and Services Administration (HRSA)

Dr. Bonnie Strickland noted that HRSA had been assigned to develop the practice guidelines for primary care providers for the Autism Services Roadmap, which was presented to the IACC at a prior meeting (http://www.nimh.nih.gov/autismiacc/). She said that the draft guidelines will be posted on the National Medical Home Autism Initiative web site (www.waisman.wisc.edu). She reminded the group that because HRSA has no designated appropriation for autism, it depends on partnerships with other agencies. Thus, collaboration is essential for HRSA's autism activities.

Dr. Strickland reported that the National Survey of Children's Health, http://www.cdc.gov/nchs/about/major/slaits/nsch.htm, which HRSA supports with the Centers for Disease Control and Prevention, would be launched in early 2007. In addition to screening for children with special health care needs in general, the survey asks if a doctor or other health care provider has ever told the respondent that the child had autism, Asperger's Disorder, pervasive developmental disorder, or other autism spectrum disorder. The second round of data from the National Survey of Children with Special Healthcare Needs is expected to be available in the fall of 2007. That dataset will include information on how the health care system affects children with ASD and their families.

Office on Disability

Dr. Merle McPherson said that the DHHS Office on Disability, like HRSA, has no funds designated for autism activities. Working within the services roadmap framework, the agency develops and supports the system of care for all children with disabilities, including those with autism. The Office will sponsor an international conference on community systems of services for children, youth, and families with special health care needs. More than 60 countries will be represented.

Centers for Medicare and Medicaid Services (CMS)

Ellen Blackwell, M.S.W., noted that several CMS departments and partners participate in discussions of the medical home. She then gave the following update on Medicare and Medicaid provisions that potentially benefit children with ASD.

- In 1995 Medicaid spent $50 billion on long-term care, $40 billion on institutional care, and $4.6 billion on home- and community-based care. In 2005, these numbers essentially doubled: $94.2 billion on long-term care, $59.3 billion on institutional care, and $22.7 billion on home- and community-based services (HCBS). In addition, it spent $12.2 billion on regular State plan services. In all, Medicaid spends about $300 billion a year. Ms. Blackwell said that the growth in spending represents a trend away from institutional services and toward home- and community-based services. "There is a huge focus in Medicaid on serving people with autism, people with disabilities, and older adults in the community," she said.
- The 1915(c) waivers are the backbone of these services. As of November 2006, the agency is currently operating 295 waivers in 48 States. Waivers that "target" people with autism operate in Wisconsin, Indiana, Maryland, and Maine. A waiver in Colorado serves children with autism. Ms. Blackwell reminded the group that to obtain Medicaid funds, States must approach CMS. To expedite the process, an electronic-based 1915(c) waiver application became operational on November 17, 2006.
- Deficit Reduction Act (DRA). New authorities in the act build on the success of home- and community-based (c) waivers. Ms. Blackwell reported on the experience so far with some of these provisions:
- Section 6044 of the Act, the benchmark coverage, allows States to provide

coverage to specific groups. Although experience with this coverage is limited, four State plans have been approved, in West Virginia, Kentucky, Idaho, and Kansas. Information on these plans can be found on the CMS web site (www.cms.hhs.gov).

- The Family Opportunity Act (Section 6062): CMS is about to issue guidance on this provision, which allows families whose income level reaches 300 percent of the Federal poverty line to purchase Medicaid coverage. As of January 1, 2007, States could elect to add this provision to their State plans.
- A new demonstration project allows States to provide services to children who would typically be in institutional psychiatric facilities. CMS received 17 applications from States, and will be making awards by the end of the year.
- The "Money-Follows-the-Person" rebalancing demonstration program seeks to move individuals from institutions into the community. This $1.75 billion, five-year program has drawn considerable interest from the States, which will receive an enhanced "match" for the necessary funds. By November 1, 2006, 38 proposals had been received, and the awards are expected to be made by early January. The vehicle for implementing this program is the 1915(c) waiver.
- The home- and community-based services are also altered by the DRA. These services, which must be renewed every five years, can now be put directly into the State plan so the States can expand their HCBS programs. One issue with this provision is that States cannot target individuals with autism or other disabilities as they can with the (c) waiver programs, although Congress did specify that people with chronic mental illness can be served. Services are limited to nine statutory services in the "c" authority.
- Section 6087 (Section 1915(j)) allows for "Self-directed personal care and related services and home and community-based services." States could implement the provision beginning January 2007. A couple of States are getting ready to work with CMS on the HCBS State plan benefit option. As of this meeting, no State had indicated an immediate interest in providing self-directed personal care through the (j) authority. The DRA provisions and the medical home concept were discussed by CMS at the National Association of State Medicaid Directors, which met in Washington in November 2006.
- A paper that will inform guidance on promising practices that States are using with children and adults with autism is expected in the future.
- The Direct Service Worker demonstration program, an effort to allay the shortage of providers who work with people with disabilities, is underway. Information on the program can be found at www.dswresourcecenter.org.
- Although not yet ready to be presented, some Medicaid data on autism have been collected. However, physicians don't always code autism as the primary diagnosis, and it is unclear whether the data will be complete.

Food and Drug Administration (FDA)

In the absence of an FDA representative, Dr. Insel reported that at the end of October 2006, FDA issued the first indication for a medication for autism. The drug, risperidone,

will be used to treat behaviors associated with autism, including irritability, aggression, and deliberate self-injury. He said that NIMH has had further discussions with FDA about drug development for the core symptoms of autism.

National Institutes of Health (NIH)

Dr. Susan Swedo highlighted recent autism-related activities at NIH, starting with programs that are moving towards their completion.

- Centers and networks: Studies to Advance Autism Research and Treatment (STAART) and Collaborative Programs of Excellence in Autism (CPEA) networks. As reported at their November 2006 annual meeting, these centers have made remarkable progress, particularly in the 10 years that the CPEAs have been in existence. The CPEAs are near the end of their grant cycle and are planning to publish a summary of their research accomplishments. The STAART centers are continuing to progress and are exploring new projects that they might do together.
- The annual meeting of the Baby Sibs Research Network Consortium, a product of both the STAART and the CPEA centers, also was held in November 2006. These researchers are studying the infant siblings of children diagnosed with autism, who themselves have an elevated risk of autism, particularly the diagnostic signs and symptoms that would aid diagnosis at the youngest age possible. They are also interested in recurrence rates in a population large enough to yield meaningful data.
- A great many applications were received for the Autism Centers of Excellence (ACE) grants. Topics of interest are diverse, reflecting all areas of the research matrix, and they are well distributed geographically. Initial reviews have been completed and the first group of ACEs is expected to be funded in summer of 2007, with the remainder expected to come on line in the fall.
- The National Database for Autism Research (NDAR) is being developed and will initially support the ACEs. Data-sharing policies are also being developed by NIH staff with input from scientists in the field. The NDAR was beta-tested in January 2007, and will provide full support for the ACE centers in April 2007.
- The phenome project: A workshop at the end of October 2006 addressed the merging of data from existing datasets, such as the STAART/CPEA shared data, and ongoing large-scale studies--the Childhood Autism Risks from Genetics and the Environment study (CHARGE), the Center for Autism and Developmental Disabilities Research and Epidemiology (CADRE) Program, the Norway and Denmark epidemiologic studies, and the Autism Genetic Resource Exchange (AGRE) sample. One goal is to identify subtypes, or syndromes, within the autism spectrum so that with greater homogeneity of subjects it will be possible to discover etiology. The workshop concluded that merging datasets is feasible, although it did not address issues of cost and logistics.
- The NIMH Intramural Research Program on autism is proceeding with the subtyping and regression studies; on average, one subject a week is being recruited. Two intervention protocols are planned.

During discussion, it was clarified that the STAART and CPEA data will be made publicly available through NDAR. The importance of common measures across studies, including other agencies and private funding groups, was also emphasized.

Department of Education (ED)

Dr. Gail Houle said that the ED-funded Professional Development in Autism Center, a collaborative initiative of training and technical assistance sites throughout the country, is in its fifth year and will be ending in the summer of 2007. A similar new initiative has been announced with the goal of training geographically diverse teams to increase the capacity to improve service delivery. An award is expected to be made in the spring of 2007. Dr. Houle said that at the next meeting she will update the group on the new center and the training and technical assistance funded by the Office of Special Education Programs (OSEP) to build the capacity for serving children with autism in the States and local school districts.

John H. Hager, Assistant Secretary for Special Education and Rehabilitation Services, will be conducting sessions throughout the country to roll out the Part B final regulations for the Individuals with Disabilities Education Improvement Act (IDEA), which was reauthorized in 2004. If anyone wishes to attend, a schedule of those meetings can be found on the web site (http://www.ed.gov/policy/speced/guid/idea/cbpm/index.html). Dr. Houle said her department has toolkits available to help parents of children with disabilities understand the reauthorized IDEA and its regulations. These are available at the National Technical Assistance Parent Training Center (www.taalliance.org).

Administration for Children and Families (ACF)

Dr. Patricia Morrissey gave an overview of a June 2006 conference on assisting the disabled and elderly during emergencies and disasters. The conference, which was largely sponsored by the Administration on Developmental Disabilities (ADD), included representatives from 45 States. The objective was to establish lines of communication among the various entities represented. Expert speakers addressed topics such as what to do during an evacuation, whether to keep registries, the elements of response and recovery operations, and the role of case management. Each State delegation developed ideas to be pursued. By October 1, 2006, 35 of the 45 States had reported back to ADD on what they had been doing since the conference. Many of the plans were incorporated into larger State initiatives, many were catalysts for State initiatives, and many had not only dealt with State-level activities but had replicated the June conference at the local level.

A web site has been set up to encourage further interaction with the delegations (www.add-em-conf.com). Some 30,000 local emergency management groups have used the web site as a resource.

One autism-related product, available through the web site, is a laminated booklet that emergency responders can wear on their belts. It explains how to interact with individuals with specific functional limitations, including those who are disoriented, have

trouble communicating, or find a change in routine difficult to tolerate. Another product used in shelters is a communication board for individuals who have impaired language, including individuals with autism. The individual can point to pictures on the board as a way of communicating wants and needs..

Substance Abuse and Mental Health Services Administration (SAMHSA)

Dr. Elizabeth Lopez said that although none of SAMHSA's activities specifically target autism, many of them involve providers who treat ASD. She reported on two such activities. First, over the past several years SAMHSA has been developing the National Registry of Evidence-Based Programs and Practices (NREP). This voluntary rating and classification system is designed to provide the public with reliable information on the scientific basis of interventions that prevent and/or treat mental and substance abuse disorders. The agency is now in the process of receiving and reviewing submissions of new programs to include in the registry. A recent major improvement is a database that can be searched for outcomes.

The second activity Dr. Lopez described is a workshop involving other Federal partners focused on developing an overall plan on the proposed integration of mental health and substance abuse services in various primary care contexts. This is an opportunity to bring services for children with all disabilities into the discussion.

Institute of Educational Sciences (IES)

Dr. Celia Rosenquist summarized the ASD grant program offered in 2006 by the Institute of Education Sciences through its National Center for Special Education Research. The purpose of the grant program is to identify, develop, modify, or establish the efficacy of comprehensive preschool and school-based interventions that improve the academic, communication, social, and behavior outcomes of children identified with ASD in preschool through middle school. Another purpose is to develop and validate measures to monitor progress and evaluate outcomes for these children.

Centers of Disease Control and Prevention (CDC)

Dr. Coleen Boyle reported on three major CDC activities--epidemiology, surveillance, and the health communication campaign.

- The major focus of the epidemiology activities is the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADRE) program. The first five years of funding for this program focused on surveillance, a national collaborative case-cohort study, and special studies that grew from the collaborative study. The centers began their new cycle of funding in October 2006. The new protocol for the CADRE is complete and is awaiting approval from the Office of Management and Budget. It is scaled back and is now focusing on the national collaborative case-cohort study.
- In 2006, the CDC funded a second round of the Autism and Developmental

Disabilities Monitoring Network (ADDM). Two reports from the first round, reporting on autism rates in 8 year-olds, were published in February 2007 in CDC's *Morbidity and Mortality Weekly Report (MMWR*); one presents the findings from six areas of the United States for the prevalence year 2000, and the second updates the prevalence for 14 areas within the United States. Eight sites are completing data analysis for the year 2004, and that report is expected by the end of 2007.

- A parallel activity is an attempt to develop a method to determine prevalence of autism in younger age populations, that is, in children under the age of four. Something similar will be attempted for adolescent and young adult populations. Three one-year developmental cooperative agreements, with the Florida State University, the California State Health Department, and the University of Utah, are aimed at developing the methodology to examine prevalence among very young children. Depending on the success of those programs, at least one of them will be funded to go forward and to develop surveillance capacity for young children. The ADDM program includes children at age eight.
- The Learn the Signs Act Early campaign is into its third and final phase, which focuses on childcare providers. The campaign was launched in November 2006 at the National Association of Educators of Young Children (NAEYC) conference. To prepare for the launch, CDC conducted interviews with childcare providers and directors to get their insight into the materials and messages needed for the early identification of children with developmental problems. Among the key findings of those interviews was that familiarity with milestones and early warning signs of developmental problems varies tremendously among childcare providers and directors, even though they recognized their role in early identification and the importance of early intervention. With the exception of Head Start and Early Head Start, few providers knew of specialists in the area to which they could refer children. They pointed out that they needed materials and training to help them have these difficult conversations with concerned parents. As a result, CDC developed a resource toolkit that includes the campaign messages, a CD-ROM, and other resource tips for parents and childcare providers. This childcare component will be rolled out in early 2007.

During discussion of the importance of disseminating information about evidence-based treatments, Dr. Insel announced that the American Speech-Language-Hearing Association issued a new document of evidence-based practices for speech pathologists that can be used in the treatment of autism spectrum disorders across the life span. This document has been published on paper and on the web (www.asha.org).

National Database for Autism Research (NDAR)

Dr. Swedo introduced Dr. Matthew McAuliffe, technical manager of NDAR, who reported on the status of the NDAR system. Dr. McAuliffe and John White, NDAR's project manager, are responsible for building the infrastructure to access the different types of information that will be generated by the Autism Centers of Excellence. The NDAR mission is to help accelerate autism research by creating a collaborative

infrastructure that will integrate heterogeneous datasets in a logical way so that researchers can combine their data, extract information, and query the databases. The main components of NDAR, Dr. McAuliffe explained, are *clinical assessments*, *neuroimaging*, and *genomics.*

The infrastructure is modeled after the Biomedical Informatics Research Network (BIRN), which had already built structures for doing collaborative research and grid computing and data-migration tools. As part of this cooperative arrangement, some tools developed for NDAR have already been installed back into the BIRN infrastructure. NDAR version 1.1 should become available at the end of fiscal year 2007.

Recently the group has turned its attention to clinical assessments. After evaluating several tools, Dr. McAuliffe and his colleagues concluded that the open-source tool, OpenClinica from Akaza Research, was the best. They are now building extensions to the OpenClinica tool to include such features as scoring skip patterns.

OpenClinica allows the user to enter and manage clinical data that has been incorporated into NDAR. The tool has an instrument or forms library, subject tracking, study management, querying, and reporting components. A total of 40 forms have been developed and integrated into OpenClinica. In addition to the standard assessment instruments used in autism, the library will include new forms developed in conjunction with the ACE centers. Dr. McAuliffe then demonstrated the use of OpenClinica and invited IACC members to participate in a more extensive demonstration during the lunch hour.

Discussion followed about the implementation of NDAR. Dr. Swedo said that training would be available, and the training module is now being developed for the database builders and for data entry. Another important issue that the NDAR team is working on is data migration and importation so that the data from the CPEA/STAART centers and other databases can be incorporated. Dr. McAuliffe said the NDAR system can be accessed by registered users from any computer that has an installed copy of a web browser (i.e., Explorer, Firefox, Netscape, etc.); that includes Apple computers.

III. GIRLS WITH AUTISM: CPEA/STAART NETWORK COLLABORATION

Dr. Insel introduced Katherine Loveland, Ph.D., professor of psychiatry and behavioral sciences and pediatrics at the University of Texas Health Sciences Center in Houston. Her work is on the neurodevelopment of communication and social behavior in persons with autism. She also is principal investigator on one of the CPEA-affiliated program projects and has served as the chair of the CPEA/STAART data-sharing and common measures subcommittee.

Dr. Loveland spoke to the committee about her group's cross-network study of girls with autism. The work illustrates many of the challenges that investigators face when

attempting to combine data across centers when the original studies did not share a common protocol.

Dr. Loveland said that although girls are included in research on autism in proportion to their prevalence in the population, their numbers are usually too small to do gender-related analyses. Many clinicians suspect, however, that girls who have autism differ from boys in their intellectual disability level, adaptive and social skills, and possibly in the way they present clinically. Since the CPEA/STAART networks have been collecting a large amount of phenotypic data on a well-characterized sample over 10 years, Dr. Loveland and her colleagues saw a unique opportunity to study girls with autism. They were interested in exploring the possible reasons for the sex-ratio difference and whether girls may present differently and be identified later than boys. If there are phenotypic differences between boys and girls, it could affect how to detect and treat autism spectrum disorders in girls.

The goal of Dr. Loveland's study is to compare participant characteristics and common measures in males and females, and to identify hypotheses that might need further investigation. She cautioned that the study suggests hypotheses to explore further, but the results cannot be generalized to the entire population of children with autism. Dr. Loveland explained that her sample, though large, does not necessarily represent the autism population because different centers had different inclusion and exclusion criteria and followed different protocols in other respects. There might be an atypical distribution of certain characteristics (such as age, IQ, or other characteristics) in this sample. In addition, data were combined across different measures and, in effect, are constructs rather than specific measures. To avoid distortions in combining data from different measures, DM-STAT did extensive data "cleaning" and created algorithms. No amount of databasing will solve this nontrivial problem, she said. Solutions must be grounded in an understanding of the measures and their modifications.

The sample comprised 298 girls and 942 boys for whom data from most or all of the measures were available. The subjects were heterogeneous, ranging in age from preschoolers through adults of all IQ levels. Dr. Loveland limited the analysis she reported on at the meeting to individuals 18 years of age or younger. Research questions included whether there were differences between males and females in the relationship of IQ and age to measures of everyday skills and autistic symptoms.

Findings

IQ. The data from this sample of children, showed that males, on average, have higher verbal and nonverbal IQs than girls do. Both groups, on average, have IQs in the below-average to moderately impaired range. Sex differences favoring males are also present for nonverbal IQ. Males are somewhat older than females in this sample. The relationship of age to IQ is not very different between boys and girls in this sample. Higher IQs are overrepresented at older ages in both groups.

Adaptive Behavior. The majority of the participants in both groups have adaptive delays, although the girls score lower than the boys. Higher adaptive communication,

daily living, and socialization scores were associated with higher IQs in both boys and girls in this sample. The relationship between IQ and communication and socialization scores is stronger for females than it is for males. However, the scores for adaptive behavior showed a different relationship to age than would usually be expected: adaptive skills did not increase significantly with age. Dr. Loveland finds that result interesting because children with high IQs are overrepresented among older children in this sample. The finding suggests that older and brighter individuals with autism may not necessarily show the expected advantage in adaptive skills over younger and less able individuals. The finding deserves further investigation since it may have implications for the developmental pathway of these children.

Autism Diagnostic Interview (ADI) and IQ. Both girls and boys with higher IQ tend to score better than those of lower IQ on the social subscale of this standard diagnostic instrument. Communication scores, however, are better in males with higher IQ, but not in females with higher IQ. Repetitive behavior scores tend to be worse in females but not males who have higher IQ, another finding that requires further exploration. No relationships were found between the ADI and age.

Dr. Loveland said these preliminary findings suggest hypotheses that should be followed up in larger and prospective studies on possible phenotypic differences between young males and females with autism, in particular that adaptive behavior is more strongly (positively) related to IQ in females than in males and that higher IQ is associated with lower autism symptom scores on the ADI-R for males but not for females. Additional studies are needed to determine whether these findings can be confirmed in a population-based sample.

Discussion about these findings included suggestions that there might be differences in the types of services received by younger versus older children, and this could account for different developmental profiles. There might also be innate differences in boys and girls that could affect their development over time. Dr. Loveland noted that it may be necessary to study little girls around the time of diagnosis to determine if they present differently. She reiterated that the findings from the current study are not definitive, but could help investigators to form hypotheses to be tested further.

Dr. Insel observed that recent findings show a striking male-female difference in autism in children born to fathers who are over 40, with girls at a much higher risk than boys. These children may constitute a subgroup with some form of genomic instability, perhaps an X-linked disorder, and could be an interesting cohort to study.

IV. STEREOLOGICAL ANALYSIS OF POSTMORTEM BRAIN TISSUE IN AUTISM

Dr. Insel introduced Dr. David Amaral, director of research at the M.I.N.D. Institute at the University of California, Davis. The M.I.N.D. Institute is dedicated to understanding the biological bases of autism and other neurodevelopmental disorders. Dr. Amaral studies brain structure and function in nonhuman primates and the neuroanatomy of the human brain. At this meeting he presented both MRI findings and the findings from the

first quantitative neuroanatomic study in autism, which were published in the summer of 2006 (Schumann CM and Amaral DG: Stereological analysis of amygdala neuron number in autism. *J Neurosci.* 2006 Jul 19;26(29):7674-7679).

Dr. Amaral reminded the group that no obvious neuropathological defect has been found in the brains of individuals with autism--no atrophy and no frank lesions. Yet, several imaging and histological studies have shown that there appear to be neuroanatomical abnormalities in the amygdala, an almond-shaped structure that lies deep within the temporal lobes of the brain, in front of the hippocampal formation. Numerous studies in animals and in normal populations have shown that the amygdala plays a role in detecting danger signals in the environment and generating a fear response. Of particular importance to the study of autism, the amygdala appears to be important in social and emotional development. Because dysfunction of social behavior is a hallmark feature of autism, the amygdala became the focus of studies Dr. Amaral and his colleagues have conducted over several years in their attempt to understand the etiology of the disorder.

Previous studies of the amygdala in autism had produced contradictory findings, partly because their samples were small and heterogeneous. Therefore, Dr. Amaral's team conducted a more comprehensive MRI study using a subject population that was as homogeneous as possible. Four groups of male subjects were compared: those with low- or high-functioning autism, those with Asperger's syndrome, and normal controls. Those with seizure disorders or Fragile X syndrome were excluded.

The researchers found that between the ages of 8 and 18, the amygdalae of typically developing boys grew by about 40 percent. Among the ASD groups, however, the amygdala appears to have achieved an adult size early and then plateaued. This pattern may account for the contradictory findings of earlier studies: the size of the amygdala in autistic subjects depends on their age.

During the next phase of their research, Dr. Amaral and his colleagues explored what might account for the abnormal growth pattern of the amygdala in autism. They carried out a postmortem histological analysis of the number of neurons using a quantitative technology, *stereology*. The brains used in the study were retrieved through the Autism Tissue Program, the NIH banks, and the Harvard Brain Bank. Unlike previous studies, none of the brains were from individuals who had comorbid features, such as epilepsy. Nine samples were studied in the autism group, with ages ranging from 10 to 44; the ten samples from the control group were age-matched, with ages ranging from 11 to 44.

Dr. Amaral and his team found no difference between the autism and control groups in the volume of these adult amygdalae, as the MRI studies had suggested, and there was no difference in neuron cross-sectional area. They did, however, find a reduced number of neurons in the autistic amygdala, both in the lateral nucleus and in the total amygdala. Most typical brains have on average about 12.5 million neurons in the total amygdala, but the amygdalae of individuals with autism had about 10.5 million neurons. That is a significant and substantial loss of neurons in the amygdala of these mature brains, Dr. Amaral said.

He concluded that although there is substantial pathology in the amygdala of individuals with autism, he cannot explain the reduced number of neurons. In the paper published in the summer of 2006, he and his colleagues hypothesized that there may be an ongoing process with the amygdala hyperactive at an early stage in development. That hyperactivity may actually be detrimental to the amygdala over the long range, perhaps because the hyperactivity drives the hypothalamic-pituitary-adrenal axis, which in turn would potentially result in dysregulated cortisol levels in the system. As has been shown, those dysregulated cortisol levels are able to feed back on the amygdala and cause neuronal damage.

Dr. Amaral said his team's research does not support the hypothesis that the amygdala is central to the etiology of autism. In the group's monkey studies, elimination of the amygdala bilaterally did not result in perturbations in social behavior; animals without an amygdala were actually more social than those with an intact amygdala. Rather than dysregulating social behavior, Dr. Amaral hypothesized that the abnormality of the amygdala in autism dysregulates fear behavior, and dysregulated fear behavior is an important feature of autism.

During discussion of his findings, Dr. Amaral noted a more fundamental question: What leads to increasing amygdala volume in typically developing children during the preadolescent and adolescent phase? To learn about the effect of amygdala lesions in developing animals, his group is doing ongoing studies of bilateral amygdala lesions in two-week-old monkeys, an age when social interaction is minimal. Those animals are now three and a half and are completely socially competent, although their fear behaviors are different from controls. They probably do have dysregulation of their fear system. They have shown paradoxical behavior, making more approaches to other animals and interacting more, and yet acting more fearful while they're making those approaches. If individuals with autism have an enhanced fear system and a social deficit, it could lead to an exacerbation of the core symptom of autism. Dr. Amaral reiterated, however, that he does not think the amygdala abnormalities lead to the core deficit in autism.

V. EVALUATION OF THE IACC AUTISM RESEARCH MATRIX

Dr. Insel began this session by noting that the original 10-year autism matrix was voted on by the IACC in November of 2003. On September 25, 2006, progress on the matrix was evaluated by 22 participants, who addressed eight themes and identified gap areas and opportunities for future research. Because environmental issues were not well represented, a second meeting on the role of the environment was held as a conference call. The presentations at the present meeting, together with copies of the draft research matrix evaluation report, were intended to elicit comments from the IACC and from a broader community as well. Dr. Insel said that the most important component of the presentations is the action plan. He proposed the formation of three workgroups: (1) etiology and pathogenesis, (2) diagnosis and detection, and (3) interventions. The workgroups would take the suggestions and turn them into plans, with set priorities,

goals, responsibilities, and accountability. Dr. Insel said the matrix should be a living document that gets continually renewed and becomes a basis for setting priorities and for moving forward.

Overview of the Matrix Discussions

Dr. David Amaral likened the process of continual evaluation to a research protocol that begins with pilot experiments and then proceeds to studies that address the goal of the research. He said the 2003 matrix and the recent evaluation reflect agreement that there is no single correct approach in determining the causes of autism. The evaluation panel concluded that for the foreseeable future, several parallel pathways of investigation will need to be pursued, and that progress currently depends on a loose confederation of public and private initiatives. Dr. Amaral said that his own belief is that brainstorming about critical research should be an ongoing process with increased effort to integrate across levels.

Quoting from the draft research matrix evaluation report, Dr. Amaral said “While progress is being made at the three-year mark, the overall autism research matrix represents at least a ten-year effort to best understand the disorder and identify the best treatments.” He said the panel agreed that significant progress and capacity building had been accomplished in the last three years and that opportunities and resources are now available to autism researchers that didn't exist three years ago. Much of that progress was the building of a research infrastructure.

The discussions also focused on the need for further research on the environment and the possibility that multiple types of autism exist that might have variable contributions of either genetics, genetic and environmental interactions, or simply environmental factors. The genetic contribution, as is evidenced by the high concordance rates in monozygotic twins, is indisputable, at least in some forms of autism. But other factors may also contribute.

Eight subject areas are covered by the matrix: epidemiology, characterization of autism, role of the environment, neuroscience, screening, early intervention, specific treatments, and school and community interventions. Although each was discussed at the evaluation meeting, Dr. Amaral focused on the characterization of autism spectrum disorders and associated genetics. Progress has been made in the autism phenome project, but the broader autism community is not sufficiently knowledgeable about the work that is being done to define the autism phenotype. More communication is needed. Progress has been lacking in developing good animal models and determining susceptibility genes; both areas may depend on better definition of the autism phenome. A realistic animal model of autism, one that is based on known clinical features, could be enormously helpful in understanding the mechanisms underlying the pathology of the disorder and in developing interventions. The matrix does not have a separate element on the development of animal models; rather, it was embedded in some of the genetic aspects.

Substantial progress has been made toward the matrix's goal of defining the impairments in neurocircuitry and neurochemistry in autism, such as that which underlies social behavior or repetitive movements. Other issues, such as defining the neuropathology of autism, have progressed relatively slowly, in part because of the need for an effective process for acquiring high-quality postmortem brains. Compared with other fields, such as Alzheimer's disease where tens of thousands of brains have been studied, less than 100 brains of individuals diagnosed with autism are now available to researchers. This shortage is a great impediment to future progress.

Advancing the Matrix

Dr. Insel introduced Denise D. Resnik, co-founder and board chair of the Southwest Autism Research and Resource Center (SARRC) in Arizona. Her presentation was prepared in collaboration with Autism Speaks, the Autism Society of American, Cure Autism Now, and SARRC. Ms. Resnik acknowledged that these organizations represent families and share a sense of urgency and commitment to finding answers from research. These groups want accountability. They want research that is actionable, integrated, and most promising for improving the quality of life for individuals with autism and their families.

To advance the matrix, Ms. Resnik said, it is necessary to articulate specific measurable goals; set priorities and align resources accordingly; define better outcome metrics; improve accountability; explore best practices; and promote evidence-based practices for autism.

Ms. Resnik noted that everyone recognizes the value of the autism tissue program, but families need to understand what can be learned from donated brains. The more specific researchers are in articulating the goals of their work the more cooperation they are likely to get from advocacy and parent organizations. Furthermore, the stated goals for obtaining and studying brains should be spelled out in phases.

She and her fellow advocates would also like to see a more cross-disciplinary, well-integrated approach to matrix goals and to understand where that integration takes place and at what points. They want to know what will have the greatest impact now and in the future. A comprehensive strategic plan is needed that extends beyond the matrix format. However, should the IACC continue with the matrix format, it will be necessary to consider "priority" versus "risk" along the Y-axis.

At present, progress is measured by the number of grants, the dollars awarded, and the number of publications. What is more pertinent, Ms. Resnik said, is how the work will affect individuals and families living with autism. What, for example, is the direct impact of effective treatment approaches and interventions? Also needed are more specific metrics to measure progress in infrastructure and capacity-building that will support future discoveries and advances toward identifying the causes and cures.

Evidence-based interventions should be tested in both the clinic and the community. The focus on early childhood and early intervention is understandable, but interventions

for adolescents and adults should not be neglected. Learning cannot stop when the children age out of the school system.

Ms. Resnik said it is possible that the IACC has outgrown a research matrix, which only provides a snapshot of what's taking place. What is needed is a comprehensive strategic plan that sets out specific goals consistent with stated priorities; aligns priorities with review processes and funding; identifies short-, mid-, and long-term objectives; assigns roles and responsibilities; and enforces accountability. She suggested reducing the current eight categories to three: detection/diagnosis, etiology/pathophysiology, and intervention/treatment. Ms. Resnik said that one major benefit of this strategic plan, together with a corresponding action plan, is that measurable progress can then be reported to families and further engage them to participate in the research. They will better understand the advancements being made and will want to be part of the enterprise.

Discussion of the Matrix

Dr. Insel asked participants to address two questions: Is something missing? And, how shall the IACC proceed from here?

Mr. Grossman said that he had requested the review, not to learn of the general progress in autism, but to learn how Federal efforts were directed toward the effort. That is, had the Federal government done anything to help realize the goals as set out in the roadmap? Mr. Grossman said that he believes that the question is not answered in the report. Instead, it appears that the matrix did not change the NIH funding pattern. In the absence of actual progress for children with ASD, a proxy is to measure progress by dollars spent, new projects undertaken, and papers published. The report lacks a rating card for those measures. Dr. Ann Wagner clarified that those who conducted the evaluation were provided lists of new projects, grants, initiatives, and some related publications as background, although the discussions did not focus on these lists.

Dr. Insel noted that the Congressional language specifically says that the matrix covers both public and private efforts, working collaboratively. It is now imperative to bring together the public and private efforts when planning for the future. For example, it makes little sense to have a meeting discussing the means to fund genetics research without having the Simons Foundation involved, since it has pledged $100 million to study genetics in autism. Workshops and implementation planning should involve all partners.

Dr. Houle suggested that a revised matrix or strategic plan should include research on services, perhaps under a heading of services epidemiology: who is getting services, what are the services preferences, how can the service needs of the future be predicted. Mr. Grossman agreed that services research has not been given enough emphasis in the matrix. He speculated that if such research were given high priority in the matrix it would attract money from private foundations.

Mr. Grossman said that he was still unsatisfied with the responses about Federal resources that support the matrix. It is hard to understand what is being funded and what is not being funded. He also said he would like to see more priority given to environmental health issues because it is a mechanism for achieving effective interventions and treatments.

Dr. Insel noted that research on services epidemiology would help to inform practice. For example, knowing what services most Medicaid recipients were actually receiving is a scientific question, an approach used in other areas of medicine.

Mr. Grossman added that during the lunch hour the services subcommittee had discussed the need for research that would show autism's true economic burden. Although the incidence of the disorder is relatively low, the economic and social impact constitutes a true national emergency.

Summing up the discussion to this point, Dr. Insel said that the IACC is suggesting two additions to the current draft document. One focuses on dollars, so that it will be possible to measure whether the amount of resources has changed over the last three years and determine how those resources have been deployed. The second addition is to emphasize services research as part of the intervention components.

Dr. Zeph said another issue is training, determining what physicians and educators know, what it will take to move forward, how to improve residency and other professional training in autism. Mr. Shestack suggested that economics should be part of the evaluation process; that is, how much money is being spent by private groups and how much is being spent by Federal agencies.

Dr. Insel noted that the draft research matrix evaluation report will be posted on the IACC web site, and comments solicited from the broader community. He again emphasized that the matrix should be a living document and planning should be an iterative process with each new discovery leading to changes in the plan.

VI. NIH GENES AND THE ENVIRONMENT INITIATIVE

Dr. Insel introduced Dr. David Schwartz, director of the National Institute of Environmental Health Sciences (NIEHS) and head of the National Toxicology Program, which is an interagency program to test chemicals and other agents of public health concern. In addition, Dr. Schwartz is the co-chair of the committee overseeing the NIH Genes and Environment Initiative, along with Dr. Francis Collins, director of the National Human Genome Research Institute (NHGRI).

Dr. Schwartz began his presentation by enumerating three critical questions related to the environmental contributions to the disorder:

1. What are the relevant exposures and genes associated with autism?
2. How do these genes and environmental exposures interact with each other?

3. Does this relationship of genes and the environment to autism tell us something about the biology or phenotype of this disease process?

As more is learned about the etiology of a complex disease, it often becomes apparent that several different phenotypes exist and the biology of the disease becomes clearer. Autism is a very good example of a complex disease that is likely caused by multiple environmental and genetic factors interacting in different ways, and those interacting factors may be causing different subtypes of the disease process.

NIEHS supports a range of research, from very basic studies in animals to epidemiologic studies. Funding was just approved for the CHARGE study, which began as a pilot developmental study in 2001 and is now a large population-based epidemiological study of the environmental etiology and the genetics of autism. About $7 million will go to support the study over the next five years.

Dr. Schwartz devoted most of his talk to the Genes and Environment Initiative http://www.gei.nih.gov/, a trans-NIH undertaking that began in 2006 and will continue for the subsequent four years. It is funded by all the institutes for a total of $192 million and has two basic components: a genetics component that will cost approximately $104 million and an exposure-biology component will be funded at about $88 million over the four-year period.

Genetics

The genetics program has several components. The largest of these, the genome-wide association studies, are directed at identifying loci in the genome and genes that might be involved in these complex diseases. Once a locus is identified, sequence variations related to a disease can quickly be identified. Then functional studies and translational studies aimed at understanding the biology that underlies the association between genes and genetic variations and complex diseases will be done.

The genome-wide association studies will focus on several specific diseases, one of which could be autism. Which diseases will be studied will depend on which proposals represent the strongest application of this technology to the study of a particular complex disease.

The data-analysis and sequencing component of the genetics program will begin subsequent to the genome-wide association studies. Issues of data analysis arise from the difficulty of looking at 500,000 markers across the genome for a particular disease and then sorting out which genes or loci are associated with the specific genetic disorder. Likewise, databasing problems will be addressed as part of the genetics program.

Environmental Exposure Biology Program

NIEHS is taking the lead on the environmental exposure biology program, which focuses on developing personalized measures of exposure that may be related to the risk of developing disease. The measures will be precise, sensitive, specific, and individualized so that scientists can discern differences in diet, physical activity, environmental exposures, psychosocial stress, and addictive substances from one individual to the next. The goal is to have the same degree of precision in the measurement of environmental exposures as that of genetic studies. Current exposure measurements are either area-based studies, not personalized, or retrospective assessments of what study subjects think they might have been exposed to.

Exposure to a possible etiological environmental agent or stress can be measured at various points. For instance, the CDC has already developed a series of body-burden measures of exposure to toxins and toxicants in the environment. Nearly 150 different measurements have been developed that clearly reflect body-burden measures of exposure. But those measures are problematic: they have to be caught at the right point; they may vary substantially from one individual to the next; and they may vary in the rapidity of the deposit of the substance and where it is deposited--in blood, serum, urine, or fat.

The exposure-biology program focuses on two measurements. The first is development of personalized, wearable environmental sensors, which will record diet, physical activity, psychological stress, intake of addictive substances, and exposure to chemicals and biologics. It is likely that very small devices will be developed to give discreet detail and accurate measurement that will allow assessment of a variety of different exposures.

The secondary development is in biomarkers, biological responses, or biological fingerprints that notify investigators that a perturbation has occurred in a system known to be potentially important in disease development. For example, the response may be inflammation, oxidative stress, program cell death, or even epigenetic markers that tell investigators that something has gone awry in a system; that perturbation may place an individual at risk of developing disease, or it may relate to an environmental exposure or an endogenous form of stress. The deployable devices to be developed will allow investigators to measure biological responses so that they can be incorporated into epidemiological studies. Ultimately, these environmental sensors and biological responses will be used in the genome-wide association studies to look at gene-by-environment interactions in developing complex diseases.

Implications for Autism

The genes and environment initiative relates to autism in several ways, Dr. Schwartz said. First, autism could be chosen as one of the diseases studied in the genome-wide association studies if the proposals focusing on autism are sufficiently scientifically rigorous. The second way the initiative relates to autism is the array of biomarkers of response that are developed; they could easily be applied to ongoing studies by using

biosamples that have already been collected and stored in autism studies. The third approach is to use these new environmental sensors in future studies to determine whether diet, physical activity, psychosocial stressors, and a variety of environmental stressors could alter the risk of developing autism. Finally, a variety of new tools are going to be developed to analyze and categorize gene and environment interactions that could be very relevant to studying autism.

During the discussion, Dr. Schwartz clarified that the identification of biomarkers and development of more rapid and field-deployable approaches to epigenetic markers are goals of the RFA. In response to a question about whether the technology being developed can be applied to interventions, Dr. Schwartz noted that if you understand the etiology of a disease, it will be possible to develop very specific interventions and identify which patients might benefit from them. For example, exposure to etiologic agents could be reduced in individuals who might be genetically more susceptible or in the population in general if the risks were shown to be general.

VII. THE ROLE OF ENVIRONMENTAL FACTORS IN THE PATHOGENESIS OF AUTISM

Dr. Insel introduced Dr. Jeffrey Bradstreet, founder of the International Child Development Resource Center in Florida, a fellow of the American Academy of Family Physicians, and a member of the American College of Toxicology. He is actively involved in treating children with autism.

Dr. Bradstreet noted that the proceedings from the 2005 symposium on environmental factors in neurodevelopmental disorders had been distributed to committee members, along with a recent review of many of the environmental factors that were discussed at that meeting, and a video about children who are recovering from autism, a disease that is supposed to have no recovery. The review, by Janet K. Kern and Anne M. Jones, was published in 2006 (Kern JK, Jones AM. Evidence of toxicity, oxidative stress, and neuronal insult in autism. *J Toxicol Environ Health B Crit Rev*. 2006 Nov-Dec;9(6):485-99).

The NIEHS-supported symposium was organized by SafeMinds and the National Autism Association. It brought together scientists and clinicians, who reviewed new findings, made recommendations, and designed a roadmap for future research into the role of environmental factors in the pathogenesis of autism.

The symposium largely concerned mercury as a model of a neurotoxicant that has been well described and well understood. Dr. Bradstreet said that one in six children currently are born at risk for mercury intoxication, but no plan exists for screening and reducing that exposure. Dr. Bradstreet then enumerated the topics covered at the symposium. Among them were a time-trend analysis of autism, a mouse model of the postnatal effects of thimerosal, the effects of very small doses of thimerosal on brain chemistry, the excretion of mercury in children with autism, immunotoxicology, neuroinflammation, mercury and autoimmunity, the correlation of release of mercury

into the environment and the prevalence of autism, relative mercury burden in autism, excretion of mercury-related porphyrins in children with autism, the long-term effects of exposure to methyl mercury on neurobehavioral problems, the possible deficiency among individuals with autism in mechanisms to defend against oxidative stress, and other biochemical and genetic vulnerabilities to toxic stress.

Dr. Bradstreet emphasized the need for translational medicine to be a collaboration between clinicians and scientists. He noted that clinicians are developing helpful intervention models around a combined neuroimmunotoxicological theory of autism. His own clinical experience suggests that such an approach yields favorable results. Dr. Bradstreet noted that his group's strategic plan overlaps the efforts of the NIH genes and environment initiative. He is interested, he said, in the ways in which the developmental process influences gene expression and the critical mechanisms of interactions among toxins and genes. There is a need to expand the biomarkers being studied and to validate them both for intervention and safety, and then enhance the bidirectional effort between clinicians and researchers.

The most fruitful areas for research, in Dr. Bradstreet's opinion, is rigorous investigation of the predictive value of the biomarkers and endophenotypic characteristics in autism and other neurodevelopmental diseases to identify causal pathways. The next step would be to develop safe and effective treatment options and then to validate those treatments in controlled investigations, with documentation of pre- and post-treatment behavior and biochemical, physiological, and immunological response s. Specific investigations into candidate environmental exposures should also be undertaken. In closing, he encouraged the NIH to make such activities a priority.

VIII. PUBLIC COMMENTS

Mr. Mark Corrales, with the U.S. Environmental Protection Agency, said that his comments were not made as a representative of that agency. He urged the group to keep in mind that fairly ubiquitous common environmental factors, such as toxins, might "hide" in the heritability estimates. He also suggested that the matrix categories be truly comprehensive and, ideally, mutually exclusive and parallel in structure. That way, he said, priorities and gaps could more readily be identified. The current organization tends to perpetuate the "silos" of approaches. Cross-cutting approaches could be specific substantive areas or avenues of investigation.

Ms. Wendy Fournier, president of the National Autism Association, suggested that autism be officially declared a national emergency. She asked the group to endorse that idea. She said she was particularly concerned about the treatment and education of today's individuals with autism, and noted that investigation of environmental factors could lead to effective treatments. She also urged advocacy groups to stand together in urging Congress to mandate the support of environmental research. She cited James Moody, J.D., of SafeMinds, who has said that the paradigm of autism needs to change from thinking it is an inheritable, untreatable disease to a triggered and therefore preventable and treatable disorder. Ms. Fournier also suggested that experts in

toxicology, immunology, and gastroenterology be added to the panels advising the committee.

Ms. Patricia Schissel, L.M.S.W., a parent of an autistic child, said that she agrees with the advocates of more environmental research, although the genetic contribution to autism has been clearly established and the subject should not be underemphasized in future studies. She said she believes the most urgent need is for better training of medical personnel and educators.

Laura Bono, of the National Autism Association, said that she sees the need for more money for all types of research and services in autism. She also urged the group to declare autism a national emergency.

At the close of public comments, Dr. Insel concluded the meeting.