Department of Health and Human Services
Interagency Autism Coordinating Committee
Meeting Highlights
May 9, 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; Duane Alexander, M.D., National Institute of Child Health and Human Development; James Battey, M.D., Ph.D., National Institute on Deafness and Other Communication Disorders; Ellen Blackwell, M.S.W., (representing Mark McClellan, M.D., Ph.D.) Centers for Medicare and Medicaid Services; Kathryn Carbone, M.D., (representing Andrew von Eschenbach, M.D.), Food and Drug Administration; Judith Cooper, Ph.D., National Institute on Deafness and Other Communication Disorders; José Cordero, M.D., M.P.H., Centers for Disease Control and Prevention; Denise Dougherty, Ph.D., (representing Carolyn Clancy, M.D.), Agency for Healthcare Research and Quality; Lisa Gilotty, Ph.D., NIMH; Barry Gordon, M.D., Ph.D., Johns Hopkins University School of Medicine; Lee Grossman, Autism Society of America; James Hanson, M.D., National Institute of Child Health and Human Development (NICHD); Deborah Hirtz, M.D., (representing Story Landis, M.D.), National Institute of Neurological Disorders and Stroke (NINDS); Gail Houle, Ph.D., (representing John Hager, M.B.A.), Office of Special Education and Rehabilitative Services; Larke Nahme Huang, Ph.D., Substance Abuse and Mental Health Services Administration; Alice Kau, Ph.D., NICHD; Cindy Lawler, Ph.D., (representing David Schwartz, Ph.D.), National Institute of Environmental Health Sciences; Audrey Penn, M.D., NINDS; Celia Rosenquist, Ph.D., U.S. Department of Education; Jon Shestack, Cure Autism Now; Bonnie Strickland, Ph.D., (representing Elizabeth Duke, Ph.D.) Health Resources and Services Administration; Susan Swedo, M.D., NIMH; Lucille Zeph, Ed.D., Center for Community Inclusion and Disability Studies.

Dr. Thomas Insel, Director of the National Institute of Mental Health (NIMH) and chair of the Interagency Autism Coordinating Committee (IACC), called the committee’s eighth meeting to order. After the other members introduced themselves, Dr. Insel noted that, in November 2006, it will have been three years since the Autism Research Matrix was developed. Dr. Insel suggested that November would be an opportune time to review what has been accomplished and to discuss whether mid-course corrections are needed for the subsequent goals.

Mr. Shestack suggested that the original panel, along with additional stakeholders, reconvene in late summer or fall to evaluate progress made on the Autism Research Matrix and to make suggestions for the reevaluation or restating of goals; these discussions would be summarized in a brief report. He further suggested that a “long frank discussion" of the report should take place at the November IACC meeting. Hearing no dissent, Dr. Insel agreed to carry out Mr. Shestack's suggestions.

I: UPDATE OF FEDERAL PROGRAMS

Health Resources and Services Administration (HRSA)

The update from HRSA was given by Dr. Bonnie Strickland, who reported that Dr. Merle McPherson, the HRSA representative to the IACC, has accepted a detail to the HHS Office on Disability. Between May and December, Dr. Strickland will represent HRSA on the IACC, and Dr. McPherson will represent the Office on Disability, which is being added to the IACC. Dr. Strickland is representing both Federal groups at this meeting.

She reminded the committee that during the first two years, Dr. McPherson and Sybil Goldman, M.S.W., representing the Substance Abuse and Mental Health Services Administration (SAMHSA), had served as co-chairs of the Services Subcommittee. Ms. Goldman has since moved on and Dr. Larke Huang has taken her place. Leadership of the subcommittee will be shared by Dr. Gail Houle and Mr. Lee Grossman for the next year.

A year ago the subcommittee completed a comprehensive services roadmap, which is now on the IACC website for review. Given limited resources, each agency identified a part of the roadmap that it could undertake.

Dr. Strickland said that HRSA, had agreed to convene an expert work group to review the provision of health care services to children and youth with autism spectrum disorders (ASD). Over the past year the work group has worked toward developing a set of service guidelines to foster cooperation among the health care system, schools, social services, and subspecialty providers. That document is now in its preliminary draft, and it is anticipated that a near final draft will be completed by the November 2006 IACC meeting.

Dr. Strickland said that HRSA, through its Maternal and Child Health Bureau, also provides funding for the National Survey of Children's Health and the National Survey of Children with Special Health Care Needs. Both surveys are cosponsored by the Centers for Disease Control and Prevention (CDC). Data from the latter survey, which is expected to be available next spring, includes prevalence estimates for every two-year period, along with a description of the impact of the system on children with ASD and other special health care needs.

Agency for Healthcare Research and Quality (AHRQ)

Dr. Denise Dougherty reported that with the new Effective Health Care Program, AHRQ welcomes ideas for research on comparative effectiveness of different treatments and clinical practices. She explained that effectiveness research is done after a drug, device, or behavioral intervention has been shown to be efficacious in randomized controlled trials (RCT) with carefully selected patient subjects. Effectiveness studies are aimed at determining whether those treatments work in a broader population and in a different or broader array of settings than is typical of RCTs. In the new program, research will be informed by the needs of the Medicare, Medicaid, and State Children's Health Insurance Program (SCHIP). Research may include strategies for how these items and services are organized, managed, and delivered. The new program has issued a report providing guidance on setting up registries to facilitate effectiveness research. Dr. Dougherty said that registries should be useful for tracking children with autism and conducting effectiveness research on their care.

Department of Education

Dr. Gail Houle reported that the Department of Education had been maintaining its autism efforts and putting new resources into technical assistance initiatives funded through its Office of Special Education Programs, within the Office of Special Education and Rehabilitative Services. Although technical assistance is primarily provided to the States, the agency is developing interactive web tools that will facilitate access to a comprehensive matrix of Federal technical assistance resources in education available to all Web users. Dr. Houle proposed that the services subcommittee address the linking of training and technical assistance with practitioner needs. She said the Department would, in the near future, be making announcements to continue the professional development work it is funding in autism.

Dr. Houle explained that the 2004 reauthorization of the Individuals with Disabilities Education Act, provided for the establishment of the National Center for Special Education Research, to be housed within the Institute of Education Sciences (IES). Effective July, 2005 the special education research authority was administratively separated from the Department’s special education services and training programs.

Dr. Celia Rosenquist, IES associate research scientist, said that the National Center for Special Education Research is the newest center within IES. In April it announced a grant competition to fund a center in autism spectrum disorders that is aimed at identifying, developing, and establishing the efficacy of interventions for children with autism. The Request for Proposals has a deadline of November 16, 2006. Information is available at http://ies.ed.gov/ncser/funding/autism/autism.asp.

Centers for Medicare and Medicaid Services (CMS)

Ellen Blackwell, M.S.W, reminded the group of the scope of CMS activities by noting that 44 percent of the total Medicaid expenditures go to 8.4 million people with disabilities; in 2003, those payments totaled $102 billion. At present, CMS is occupied with the Deficit Reduction Act (DRA) of 2005. Ms. Blackwell outlined the many provisions that may affect individuals with autism:

- Sections 6041, 42, and 43 allow States to impose premiums and cost-sharing on certain groups, including prescription drugs and emergency room co-pays.
- Section 6044, the benchmark provision, permits States to provide comprehensive medical coverage to certain groups of beneficiaries (individuals with disabilities may not be compelled to join in the coverage). If States elect to exercise this option, they still must provide Early, Periodic, Screening, Diagnostic, and Treatment "wraparound" coverage for children ages 0 to 19, although Medicaid covers services for this group up to age 21. So far, three States have been approved to provide Medicaid services through benchmark coverage.
- Section 6052 redefines Medicaid case management, which allows people to gain access to needed medical, social, educational, and other services. Regulations will clarify past confusion over the definition of Medicaid case management, especially its distinction from case management provided through other agencies or entities.
- Section 6062 allows families with incomes up to 300 percent of the Federal poverty level to purchase Medicaid insurance for their disabled children.
- Section 6063 is a $218 million five-year demonstration project that will allow ten States to provide services in psychiatric residential treatment facilities. Costs associated with institutionalization will be compared with those of helping children remain in the community with their families.
- Section 6071, the "Money Follows the Person Rebalancing Demonstration," is a $1.75 billion five-year program that will facilitate the transition of individuals from institutions to community settings.
- Section 6201 addresses additional Federal payments for hurricane-related demonstrations.
- Section 6086 is a new provision that expands access through the Medicaid State plan option to provide home and community services through the regular Medicaid State plan. The 1915(c) waiver program measures individuals against an institutional level of care, and must be renewed every five years. Regulations for the new program, which will begin operating in January 2007, are now being written.

In her discussion of other CMS programs, Ms. Blackwell said that since the Real Choice Systems Change Grants for Community Living began in 2001, the program has awarded 297 grants totaling $240 million to facilitate life in the community for persons with disabilities.

A CMS-funded long-term care study is examining how eight States are rebalancing their long-term care programs to help people stay in the community. Information about promising practices served through the CMS 1915(c) waiver program will be posted on the CMS web site. At present, 294 waivers have been issued in 50 States; four of them—in Wisconsin, Indiana, Maryland, and Maine—are specific to autism, although the many other waivers for people with developmental disabilities, mental retardation, and other conditions may also cover individuals with autism. Ms. Blackwell said that under the 1915(c) waiver program, CMS can offer respite care, enhanced personal care, environmental modifications, and habilitative services that it cannot offer under the regular State plan or section 6086.

Ms. Blackwell said that another mechanism, the 1115 Waiver, has been used to provide emergency services to hurricane evacuees. Under that program, 32 demonstrations were approved for Katrina relief and four for Hurricane Rita relief. CMS also granted eight States the authority to activate uncompensated care pools for payment to providers of last resort that assisted people affected by the two hurricanes.

In answer to a question, Ms. Blackwell explained that coverage for services depends to some extent on where one lives. Although Medicaid does guarantee a basic set of benefits under the State plan option, States may also elect optional benefits, such as mental health benefits that could affect children with autism. The 6086 provision is such an optional benefit. Different States choose to operate different waivers that contain a variety of services based on the population served. Advocates can always go to State Medicaid Agencies to find out what is available. The Promising Practices web site will also make it possible to judge which States are doing a good job.

Mr. Lee Grossman asked about the availability of CMS data. Ms. Blackwell said that CMS collects data based on services provided rather than on diagnoses. It can, however, provide data on how much a State spends under specific Medicaid waivers, including autism waivers.

Dr. Insel said that an NIMH grantee at the University of Pennsylvania, who has been using local Medicaid data, learned that national data would only be available by combining data from individual States. He suggested that developing a national database could be useful. How services are rendered and how the money is deployed in different places are of great interest. He said that one study of Philadelphia Medicaid recipients showed a profound difference in ethnicity in the age at which autism was diagnosed. Dr. Insel said that a repeated concern among IACC participants is that even when payment sources are available providers often are not.

Later in the meeting, Ms. Blackwell elaborated on the role of CMS in serving children with autism in the schools. Medicaid pays for many costs associated with the special supports and services provided as part of a child’s special education. For example, a child with autism who has behavioral challenges may benefit from covered Medicaid mental health services.

Food and Drug Administration (FDA)

In her report on FDA activities, Dr. Kathryn Carbone said that the agency would like to see more applications for treatments for autism, including prophylactic treatments.

Within the FDA, an unfunded initiative called the "Critical Path" is underway to address critical issues that hold up development of drugs and other treatments. A description of the initiative can be found at http://www.fda.gov/oc/initiatives/criticalpath/. The list of priority research projects that could advance innovation in medical products is evolving, which provides an opportunity to give greater priority to concerns related to autism spectrum disorders. For example, biomarkers, clinical trials, endpoint improvements, and case definitions would help to expedite the development of better therapies. Dr. Carbone said that FDA has mechanisms to foster collaboration with scientists developing new treatments.

National Institutes of Health (NIH)

Dr. Susan Swedo pointed out that several current NIH-funded projects are basic neuroscience investigations that have direct relevance to autism. Clinical trials and studies of etiology and pathophysiology are also being funded. She and other NIH representatives described some of the programs:

Genetic Studies

Dr. James Battey, Director of the National Institute on Deafness and Other Communication Disorders, noted that data from twin studies provide compelling evidence that autism spectrum disorders are hereditary, although genetically complex. In the past, it has been difficult to identify the genes contributing to ASD because they make up a relatively small fraction of the risk. Only by understanding these genes will it be possible to know which molecules to target for potential therapeutic interventions. Dr. Battey said that whole-genome association is an emerging strategy that has promise to find genes contributing to ASD. These studies, which are done on hundreds of cases and controls, are now cost-effective because of the advances in understanding the human genome, a relatively dense map of single nucleotide polymorphisms, and a dramatically reduced cost to genotype the single nucleotide polymorphisms. He asked whether a whole-genome association study of autism spectrum disorders could be done in the near future.

Dr. Insel said that NIMH is currently funding one such study, which is being conducted by Aravinda Chakravanti at Johns Hopkins University. The Genetic Association Information Network (GAIN) Initiative, a public-private partnership through the Foundation for the National Institutes of Health, provides another opportunity. He agreed with Dr. Battey that drug development will depend on identifying the molecular target. At present, the rate-limiting step for most complex genetic disorders is having enough DNA available from cases and controls. The Autism Genetic Resource Exchange (AGRE) project sponsored by Cure Autism Now had the foresight to start collecting DNA several years ago so that a significant repository is available. Potentially, a whole genome association study of 1,000 patients and 1,000 controls could be done in a couple of weeks.

National Database for Autism Research

Dr. Swedo provided an update on development of the National Database for Autism Research (NDAR). The past year has been spent erecting the NDAR infrastructure. One key area of activity is acquiring the technology architecture, which was modified from the Biomedical Informatics Research Network (BIRN) grid (http://www.nbirn.net), a cyber-infrastructure that facilitates data-sharing and comparison. The NDAR infrastructure is now housed on the NIH campus. The clinical assessment module, Open Clinica, was chosen and installed, and staff have been hired to modify it specifically for autism; that process includes incorporating tools that are part of the Internet System for Assessing Autistic Children (ISAAC) and other major systems that have been integral to research to date. Dr. Swedo said that the incorporation of neuroimaging data into NDAR will be facilitated by the choice of the BIRN system, because it was developed to support multi-site, large-scale neuroimaging projects.

The NDAR team is currently working to render neuroimaging scans anonymous, ensuring that there is no capacity to reconstruct individual images. Contract negotiations are underway to develop an ontology system for autism research, the dictionary that will allow researchers around the world to speak and understand the same language. NDAR will be integrated with other critical community databases, for example, the Autism Tissue Bank, the NIMH Genetics Repository, the AGRE database, and the Autism Speaks Registry.

Dr. Swedo asked for help in developing data-sharing policies. Information needs to be made publicly available as soon as possible, but that need must be balanced by the need to assure that the data are clean and accurate. The general NIH data-sharing policy does not address the specific issues relevant to sharing of data within NDAR. The NDAR web site, www.ndar.nih.gov, contains a link by which individuals can offer opinions about when the data should be made public.

NIH Intramural Research Programs (IRP)

Dr. Swedo noted that several research protocols are being reviewed by the IRP Science Committee and the NIMH Institutional Review Board. Recruitment has begun for children between the ages of 12 months and 4 years for a screening protocol and a large-scale investigation of clinical and immunological factors involved in regressive autism. A new trial of riluzole, a glutamate-modulating agent, will begin in older children as soon as an open trial is completed among typically developing children with obsessive-compulsive disorder. Another protocol involves a study of the treatment of childhood regressive autism with minocycline, a tetracycline derivative that has effects on the immune system.

The NIMH intramural research program will also conduct a pilot feasibility study for the

Phenome Project, in collaboration with the M.I.N.D. Institute. Additionally, NIH autism coordinating committee members have met regularly with staff from the CDC to discuss a larger effort to describe the autism phenome. This effort will be made up of several components including both prospective data collections and retrospective data analyses. Possibilities being discussed include using the NIMH and AGRE repositories to examine genes and phenotypes associated with specific genetic abnormalities, as well as genetic evaluations of specific behavioral characteristics. Also under discussion is the use of the retrospective data from the STAART centers, and the Collaborative Programs of Excellence in Autism (CPEA) centers, as well as ongoing prospective studies in Norway or Denmark.

Dr. Swedo said the IRP web page is being updated and will be linked to the IACC web site (http://www.nimh.nih.gov/autismiacc).

Autism Centers of Excellence

Dr. Swedo said that the National Institute of Child Health and Human Development (NICHD), in collaboration with NIMH, NINDS, NIEHS, and NIDCD, issued a request for applications for the centers. NICHD will have the applications reviewed in late fall, and the first of the centers and networks are expected to be funded next spring. The STAART and CPEA centers will be ending over the next 18 months to 2 years, with the CPEAs closing at about the same time as the ACEs are fully funded.

Environmental Factors

In May, the National Institute of Environmental Health Sciences (NIEHS), together with the CDC, hosted a meeting of independent science experts to discuss the Vaccine Safety Data Link, a large administrative database maintained by several managed care organizations with more than 2.3 million children enrolled. The meeting is an effort to determine whether this database can provide a means for studying the potential association between thimerosal in childhood vaccinations and the risk of autism. While the database has a wealth of information, the panel members identified tremendous hurdles to overcome if the data are to be used in this way. NIEHS and CDC will be working hard to determine how this information might be informative for questions about autism risk.

Annual CPEA and STAART Meeting

The annual CPEA and STAART meeting will be held November 8th and 9th in Bethesda, Maryland. Since this will be the last meeting of the CPEA network, the focus of the meeting will be on each center's most significant findings from the past 10 years of funding, and the STAART Centers will also be presenting a progress report.

In answer to Mr. Shestack’s concerns, Dr. Swedo said that there is a public commitment to spend at least as much on the ACE centers as was spent on the STAART and CPEA centers. Whether the funding will be increased depends on the applications that come in and the budgets of the NIH institutes. Together with the funding for NDAR, the overall investment will be greater than in the past. The same STAART investigators may serve as principal investigators of the ACE centers or networks if they submit new applications.

Substance Abuse and Mental Health Services Administration (SAMHSA)

Dr. Larke Huang said that SAMHSA has no autism-specific programs at this time, but it does have two programs that are particularly relevant to individuals with autism spectrum disorders. The first is the $105 million program that supports comprehensive community mental health services for children and their families; that program has served some 93 grantees in the past 10 years. The money is given to States or other political entities to develop comprehensive, coordinated systems of care primarily for children with serious emotional disorders, although some of the children served also have developmental disorders or disabilities. Individuals with autism spectrum disorders constitute a very small percentage of the children and youth served. A large-scale national evaluation is being done across these sites. One secondary analysis of the data on approximately 65,000 children, for example, is exploring the characteristics and service referrals and utilization patterns of children with autism. The number of children with autism in the database is uncertain, but the database is accessible for further secondary analyses.

Another relevant SAMHSA activity is the National Registry of Effective Programs and Practices, which is undergoing a redesign and will be available on the SAMHSA web site. This is an online searchable database of programs and practices, the effectiveness of which is evidence-based. Developers of interventions are encouraged to submit to the database, which will be open to end users, such as consumers, families, providers, and sources of payment for services..

Ms. Ellen Blackwell noted that CMS is working with SAMHSA on provisions related to the Children's Health Act of 2000. Her agency issued a rule to protect children under the age of 21 from being improperly restrained and secluded.

Centers for Disease Control and Prevention (CDC)

Dr. José Cordero reported on several CDC activities related to autism:

- Centers funded under the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) Program, which are completing their first five years, have produced several publications and developed a case-cohort study. For the next five-year cycle, CDC expects to fund the centers by September and will begin recruiting participants for the case-cohort study in October.

- The Surveillance Network will be submitting a paper for publication later this year that compares autism prevalence in six areas of the US. A second report on the prevalence of autism in 14 areas is also being prepared. A study comparing the Atlanta data from 1996, 2000 and 2002 will also be published. An RFA announcing the next cycle of autism surveillance activities has been announced, and 10 sites are expected to be funded in June 2006. At present the surveillance data identify children at age eight. An RFA was issued for new methodologies for looking at the prevalence of autism or ASD, especially among children younger then four years of age. It is hoped that at least one pilot study will be funded for a study of the younger group (As of Sept 2006, three sites were funded for a one year development grant).
- In a recent publication, the National Health Interview Survey and the National Survey of Children's Health, showed that the prevalence of parent reported rates of health care provider-diagnosed autism was 5.5 and 5.7, similar to rates that have been previously reported. Thus, an estimated 300,000 children from the age of 4 to 17 have autism in this country. The surveys were done with nationally representative samples. An article resulting from these surveys indicates that, among Hispanics, parental reports of autism are significantly lower than in other groups, a finding that probably represents an under-diagnosis of autism in the Hispanic community. *(Schieve LA, Rice C, Boyle C, Visser SN, Blumberg SJ. Parental report of diagnosed autism in children aged 4-17 years—United States, 2003-2004. MMWR 2006; 55:481-486*). Another recent article, which is based on the 2000 Atlanta data when the children were eight years old, shows that the first professional's notation suggesting the need for an evaluation of autism was made at about 48 months, but it was not until 13 months later that a diagnosis was made *(Wiggins L, Baio J, Rice C. Examination of the time between first evaluation and first autism spectrum diagnosis in a population-based sample. J Dev Behav Pediatr. 2006 Apr; 27 (2 Suppl): S79-87)*.
- The "Learn the Signs. Act Early." campaign is continuing, through a public-private collaboration with Autism Speaks and other national partners. At present, CDC is emphasizing outreach to health care professionals, particularly pediatricians, as well as childcare providers and special-need populations such as Hispanics. Survey measures have shown increased knowledge and changes in reported behavior; a case-control study of the campaign will be done in two counties in Georgia to measure impact of an intense local campaign on age of referral. The campaign as a whole, as well as some of its components, has received several prestigious communication, social marketing, and public relations awards.
- During Autism Awareness Month in April, CDC placed a four-page insert in the newsletter of the American Academy of Pediatrics (AAP), which is sent to every AAP member. Millions of e-mails and other forms of electronic messages have been sent to other professional organizations. The message reminds health care providers that early diagnosis is important. In collaboration with Autism Speaks, the CDC also held a series of video teleconferences.
- CDC is also working with the AAP to develop an autism tool kit to support

appropriate awareness, screening, referral, diagnosis, and treatment. CDC and AAP, in collaboration with the Maternal and Child Health Bureau, are developing new guidelines on the management and diagnosis of autism; those guidelines should be coming out in July.

- CDC, in collaboration with the Association of University Centers on Disabilities (AUCD) is hiring a full-time post-doctoral fellow to conduct continuing education/training for physicians and other health care professionals, promote the use of validated screening tools, and promote the study and application of evidence-based interventions.

Dr. Gail Houle mentioned that the Department of Education had been asked to participate with the CDC and AAP in developing the autism tool kit. The objective is to increase the referrals of infants and toddlers to the Individuals with Disabilities Education Improvement Act (IDEA) Part C formula grant awards program, which provides services to infants and toddlers throughout the States.

II. SUBCOMMITTEE REPORTS

Update on Early Screening Subcommittee

Dr. Deborah Hirtz reported that at the previous day's meeting of the early-screening subcommittee, a representative of the American Academy of Pediatrics said that a policy statement on developmental screening would be released in July. The statement contains specific recommendations for autism screening with a variety of instruments. Other presentations at the subcommittee meeting concerned the Autism Speaks public awareness campaign; CADDRE investigators who are looking into the obstacles encountered when early screening is implemented; an update from the services subcommittee; and the latest version of the early-screening roadmap. A draft of the early screening roadmap has been distributed to IACC members. Dr. Hirtz asked committee members to send her their comments.

III. COMMUNITY INITIATIVES

Building National Autism Awareness: Ad Council Initiative of Autism Speaks

Dr. Insel introduced Ms. Alison Singer, senior vice president for communication and strategy at Autism Speaks. Before she joined that organization at its inception, Ms. Singer produced the CNBC award-winning series *Autism: Paying the Price*. She has a daughter and an older brother with autism.

Ms. Singer said the awareness campaign was created by the Ad Council, a consortium of advertising agencies and media groups that donate their time and media spots to run public service announcements. Although the formal commitment is to a three-year campaign, Ms. Singer said that the relationship with the Ad Council is likely to extend beyond that.

The autism awareness campaign, which is aimed at the general public, focuses on the prevalence of autism. It stresses the importance of parents recognizing the early signs of autism and seeking early intervention services. In addition to CDC, other advocacy groups, the scientific community, and governmental agencies have collaborated on the campaign.

The effectiveness of the campaign has been tracked through focus groups. Initially, those groups showed there was little awareness of autism and that parents demonstrated a disabling fear at the mention of the word. Parents became most motivated to learn more about autism when its prevalence was mentioned. That is why the message became "autism is more common than you think," rather than one that focused on early warning signs and developmental and physical milestones.

In brief, the supportive message is that one in 166 children is now diagnosed with autism. The call to action in the campaign is to visit www.autismspeaks.org, which describes the developmental milestones and encourages parents to talk with the child's doctor. The campaign title, "The Odds," was chosen because it juxtaposes the odds of activities that parents are concerned with or dream about with the odds of a child being diagnosed with autism. The messages are being delivered across multiple media platforms, including TV, print, radio, the Internet, and other nontraditional media.

Ms. Singer demonstrated a number of the video messages. One 15-second video messages (available in English and Spanish) contrasted the odds of a child being in a fatal automobile accident—one in 23,000—with the odds of a child being diagnosed with autism—one in 166. Concerned viewers are then directed to visit www.autismspeaks.org. The campaign also includes radio messages and print brochures.

She said that a second round of focus groups showed that the creative concepts were attention-getting. The mothers said that as a result of this ad, they would be likely to seek more information about autism and to talk to their children's doctors.

The television, radio, and print materials have been very widely distributed and press coverage has been extensive. Ms. Singer said that she and her colleagues will measure the campaign's success by the shift in attitudes or changes in behavior. They will also track when, where, and how often the spots are run. A pre-campaign tracking study has been completed, and a post-campaign tracking study will be conducted in six months. In addition to awareness and changes in attitudes and behavior, the study will track the volume and subject of calls to the 800 number; the number of web visits (already increased by 700 percent); the total number of donated media dollars; and press coverage.

In closing, Ms. Singer acknowledged the work of the campaign's advisory committee, particularly Mr. Peter Bell, chief executive officer of Cure Autism Now.

Dr. Huang asked whether the campaign's short messages would be placed in such settings as pediatricians' waiting rooms. Parents want pediatricians to address this and other harder issues, and the print material might serve as a stimulus for these discussions. Dr. Cordero said that CDC has a set of materials specifically meant for pediatricians' waiting rooms. The materials include key developmental milestones at different ages and questions to ask the pediatrician. Ms. Singer said that as part of the Autism Speaks campaign, the print media will be reproduced as posters for doctors' waiting rooms.

Autism Tissue Program: How Brain Donation Advances Autism Research

Dr. Insel introduced Dr. Jane Pickett, director of the Autism Tissue Program, a parent-led post-mortem brain tissue donation program. He said that Dr. Pickett's background is a combination of basic molecular biology and neuroscience research and clinical experience. She coordinated the development of the Autism Tissue Program in 1998.

Dr. Pickett noted that the Autism Tissue Program (ATP) was started by the National Alliance for Autism Research (NAAR) as a joint project with the Autism Society of America and later partnered with the M.I.N.D. Institute at the University of California at Davis. The ATP became an initiative of Autism Speaks through a merger with NAAR in early 2006. The ATP has an outreach project with the Cure Autism Now genetic program, AGRE, and is undertaking international brain bank activity. She said that data from the brain neuropathology studies will be shared with the National Database for Autism Research.

Per the Autism Research Matrix, NIH-funded brain banks constitute an infrastructure for enhanced brain acquisition, with the Harvard Brain Tissue Resource Center as the main repository for the ATP. A major effort of the ATP is outreach to encourage everyone—individuals affected by autism spectrum disorders or those unaffected—to register for brain donation to address the need for comparative studies. There are 112 who have donated tissue to the ATP.

Dr. Pickett described several projects and studies now underway:

- The Brain Atlas Project provides comprehensive quantitative analysis of morphological features at the cellular level, with images and 3D representations of entire brain hemispheres of approximately 12 autism and control subjects. Dr. Pickett showed a slide of a 3D structure of a 23-year-old man with autism with largely intact brain stem structures. Autism has not been associated with gross abnormalities in the brain.
- In 2003, it was reported that mini-columns in the cortex are greater in number, packed more closely together, and more regularly spaced in individuals with

autism. This research has been duplicated in a double-blind study and has been noted in small case cohorts in several labs. Dr. Pickett said that these columns are considered units of function in the cortex and are comprised of about 60 to 80 cells. The number of mini-columns is determined very early after conception, at about seven weeks of gestation. Current studies are aimed at learning more about how this neurodevelopmental structural anomaly affects functioning.

- In addition to trying to understand how cellular morphometric changes affect brain circuitry, researchers are exploring neurotransmitter pathways as well as intracellular neurochemistry and genetics.
- Diffusion tensor imaging studies have found evidence of new pathways in the brain connecting the fusiform gyrus to the amygdala and to the hippocampus; these connections appear to be atypical in autism. Using Brain Atlas slices, data collected via diffusion tracking is being verified at the cellular level.
- Autism researchers are also interested in finding and evaluating the human equivalent of ‘mirror’ neurons. In animals, mirror neurons fire not only when an animal is doing a particular task, but also when the animal observes another doing the same task. These cells could be important in imitation, a key part of early learning that is impaired in autism spectrum disorders.
- Other scientists are studying the function of neuropeptides that could be implicated in autism, notably, oxytocin and its role in social behavior.

The ATP web site portal at www.atpportal.org includes brain information for researchers related to tissue quality and fixation; donor information including perinatal data,; immunization reports; information about genetic disorders (e.g., Fragile X syndrome); tissue postmortem MRI data; and digital images. Information about the RNA quality of banked tissue is also included. The brain bank is responsible for obtaining the written consent for donation, arranges for the tissue recovery, and gathers basic donor information. Harvard processes the tissue, conducts a neuropathology exam, and stores the tissue. Tissue recovery protocols are on the McLean/Harvard web site. The ATP solicits tissue requests (proposals) and allocates tissue to researchers according to ATP’s 11-member Tissue Advisory Board’s (TAB) approval and recommendations.

Dr. Pickett and colleagues have conducted three mortality studies, finding an elevated mortality ratio (observed/expected deaths) among individuals with autism, especially in girls. She said that autism donors often have sudden and unexplained deaths. Epilepsy-related deaths are of particular interest, as are channelopathies—disorders caused by pathology of ion channel function—which seem to be linked with autism, and a recently characterized childhood onset seizure disorder. The causes of many of the deaths remains unknown.

Individuals may register to be a brain donor at the ATP web site www.memoriesofhope.org and call the 24-hour answering service (1-877-333-0999) for information; in the event of a death, this number will reach the Harvard Brain Bank, the designated autism bank supported by NIMH and the National Institute of Neurological

Disorders and Stroke (NINDS). Family bereavement support is provided after a donation is made. A home visit is arranged to obtain further donor and family information; the Autism Diagnostic Interview-Revised is administered as a diagnostic measure.

Dr. Pickett concluded her talk by acknowledging the gift of brain donation by all of the families in the ATP and citing the need for all IACC members to help promote increased brain donation in order to answer some of the important questions that only this resource can address.

IV. SCIENCE UPDATES

Early Indicators and Developmental Trajectories in Autism

Dr. Insel introduced Dr. Rebecca Landa, who is the director of the Kennedy Krieger Institute Center for Autism and Related Disorders and associate professor of psychiatry at the Johns Hopkins School of Medicine. Dr. Landa reported on an NIMH-funded study of infants at risk for autism because they have an older sibling with autism. . Dr. Landa said that the study has led to theoretical and scientific insights into infant learning mechanisms and clues to brain development. It has also yielded practical applications, such as identification of developmental characteristics that might be an early sign of autism spectrum disorders and should be considered in the development of efficacious treatments.

Like other presenters, Dr. Landa emphasized the urgent need to identify autism as early in life as possible, since it appears to have its neurobiological onset as early as pregnancy. Parents typically see that something is wrong by the time their child is 24 months of age. Some retrospective studies of autism indicate decreased social orienting, babbling, and imitation. No medical tests or diagnostic criteria exist for children under three. Yet, because neuroplasticity depends to some extent on experience, the goal is to begin early intervention during sensitive periods of development for social and communication skills.

To learn the early signs and progression of autism, Dr. Landa and her colleagues used a prospective longitudinal design to study the infant siblings, 4 to 10 percent of whom are likely to develop autism themselves. Dr. Landa presented data on 128 infants who have reached 30 or 36 months in age. Thirty of the infants had autism spectrum disorders, 22 had language and/or social developmental disruptions characteristic of the so-called *broader autism phenotype*, and 66 were essentially unaffected. The infants were tested about every 6 months from 6 to 36 months of age for social, language, motor, cognitive, temperament, and adaptive functioning. In her presentation, Dr. Landa reported on the results on the Mullen Scales of Early Learning, the communication and symbolic behavior skills, and the Autism Diagnostic Observation Schedule (ADOS).

The most noticeable signs at six months of age were passivity and motor disruptions; a somewhat late onset of milestones; some hypotonicities; atypical movements; and problems with motor coordination.

Dr. Landa said that the study results also suggest that there are aspects of behavior at 14 months of age that seem to predict whether a child will have autism at 36 months.. Dr. Landa supplemented her presentation with slides and a video illustrating behavioral differences between children whose development was typical with those who were judged to have an autism spectrum disorder.

Dr. Landa cautioned that diagnosing autism at 14 months is difficult. Not all children who eventually are diagnosed as having an autism spectrum disorder show clear manifestations of the disorder at this young age, even in the judgment of a highly experienced observer. The children might show only some of the manifestations or subtle signs that development is not proceeding normally. They may smile, communicate, and make eye contact, but those behaviors are not integrated. Because of normal variation, observers have to consider several systems and, when they are not sure, they have to monitor the children’s development carefully, she said.

Dr. Insel asked how refined the recognition would be if all the measures were considered together. Dr. Landa said that she believes it is possible to develop a diagnostic algorithm for autism at 14 months. She reiterated her earlier point that children who appear to be developing atypically at 14 months require treatment, even if they ultimately are not diagnosed with autism. Infant siblings of children with autism should all be followed, she said.

Dr. James Battey asked whether it is possible to distinguish children who will benefit from intervention strategies, to understand predictors of good outcomes. Dr. Landa said her team is trying to develop such predictors, although the children in the present study receive little treatment. Dr. Landa’s NIH-funded early intervention study, on the other hand, involves children who entered treatment between 24 and 33 months of age and are treated for 10 hours a week with parent training for 6 months. Those who are not showing robust changes with that intervention have significant attention difficulties and tend to have quite low developmental levels. However, even some of those children do respond to treatment.

Behavioral and Neuroimaging Investigations of Social and Communication Impairments in Autism

Dr. Insel introduced Dr. Helen Tager-Flusberg, professor in the Department of Anatomy and Neurobiology and Pediatrics at Boston University, where she is also professor of psychology. With more than 25 years of experience in autism research, Dr. Tager-Flusberg is principal investigator of one of the CPEA Centers and director of a STAART

Autism Center at Boston University.

Dr. Tager-Flusberg presented research done by a large group of investigators in the Boston area and the University of Wisconsin-Madison, all of whom are part of a STAART Center and/or a CPEA Center. Her focus during this presentation was on the affective impairments in social communication. The research, which ranges from studies of the single cell to the family, demonstrates the importance of multidisciplinary centers, she said. The work has been stimulated by investigators collaborating at the two sites.

Facial Recognition Studies

Dr. Tager-Flusberg said that for human beings, faces are the key social stimulus and the core of social relationships. Her interest in language and communication led to her interest in faces, she said, because facial expressions are the counterpoint to voices and language. Thus, face processing provides clues to the mechanisms of social impairment in autism. Her colleague at Boston University found that the atypical processing of faces in children with autism is specific to recognizing the eyes. When children with autism are cued to look at the eyes, their performance improved, but they were still unable to process the faces holistically. Dr. Tager-Flusberg investigated face processing in children with autism using an eye-tracking methodology developed by Dr. Ami Klin at Yale and showed the same pattern of not looking at the eyes.

Subsequent research showed that arousal, measured by skin conductance, was increased in children with autism when eyes were directed at them. Children who showed less arousal were better able to recognize faces.

Brain Imaging Studies

Brain imaging studies in individuals with autism have shown a lack of activation in the fusiform gyrus, which is the specialized face processing area. To further study this phenomenon, Dr. Tager-Flusberg and her colleagues placed a cross on a screen depicting a face, directly between the eyes. When participants were directed to look at that area all the time, they did so compliantly. With this method, no differences were found in fusiform activation in individuals with autism, but there was significantly less activation in other cortical areas that are related to face processing. Those regions crucial for social information processing also showed cortical thinning, which was related to social symptoms in the study sample. This finding has been replicated by her colleagues in Wisconsin using a different method for analyzing cortical thickness in similar regions, the superior temporal sulcus and the orbital frontal cortical regions. They also demonstrated that cortical thinning in these areas was related to deficits in face emotion recognition.

Dr. Tager-Flusberg said that the Wisconsin investigators have been pioneers in neuroimaging studies of behavioral performance, reaction time, functional activation, and eye tracking—all in the same participants. Their studies showed that subjects with autism were not as good as controls at recognizing whether a face is showing an emotional expression, and their reaction time was slower. The eye-tracking experiments produced findings that were similar to those found by the Boston group. Brain fusiform activation was somewhat less in participants with autism than in the controls, but the activation was greater in the orbital frontal cortex and the amygdala—part of the limbic system involved in processing memory of emotion and particularly important in recognizing potential dangers in the environment. Brain activation correlated directly with tracking time.

Dr. Tager-Flusberg said that, together, these studies suggest that the brain is not “broken” in terms of face processing; the pattern of activation is complicated. The Wisconsin researchers are now using a large sample of individuals with autism to compare the size of the amygdala in those who have gone through puberty with those who have not. In typically developing children, the amygdala continues to grow during adolescence, but that growth was not observed in the adolescents with autism. The size of the amygdala predicted slower judgment in recognizing faces and avoidance of eye gaze. Amygdala volume also predicted social reciprocity and nonverbal communication, but it was not related to repetitive behaviors and interests and verbal communication.

In more recent studies, the Wisconsin group has followed unaffected siblings of individuals with autism. The siblings also showed reduced amygdala size and the same relationship between eye tracking and fusiform gyrus activation during face processing. Those results were not found among control participants. The siblings did not show the same relationship between amygdala activation and fixation time as their siblings with autism—that is, their arousal pattern was not atypical. Thus, the siblings show some components of the neurocognitive phenotype for the social impairments, but not all of them.

Studies of Cells

The Boston group has studied the anterior cingulate cortex, which until recently was the only area in the cortex that had shown histological abnormalities, decreased cell size, and increased packing density in individuals with autism. Dr. Tager-Flusberg said that her colleagues have been focusing on serotonin receptors and uptake sites in the cingulate cortex. Previous research has shown that serotonin appears to be implicated in autism. The Boston researchers found no differences between cases and controls in the serotonin uptake sites in any of the areas of Broadman's 24, part of the anterior cingulate cortex. They did, however, find a significant reduction in receptor density in two serotonin receptors (5HT 1a and 5HT 2a), particularly in the deep layers of the anterior cingulate.

Effect of Social Affective Impairments on Families

Dr. Tager-Flusberg said that her group is conducting a large-scale longitudinal study of toddlers with ASD that is examining the children's development, that of their families, and the effect they have on each other. Both mothers and fathers have heightened levels of stress. Mothers are, however, at greater risk for depression. The child's IQ, adaptive behavior skills, and language are not related to stress in the parents. What is related to parental stress is the degree of social impairment in the children. Mothers are also stressed by behavioral dysregulation, affective issues, and eating and sleeping problems. Fathers are stressed by externalizing behavior, such as aggressiveness and self-injurious behavior.

These findings should inform intervention programs, Dr. Tager-Flusberg said. Support is needed by the families as well as the child. Parental well-being is critical to treatment efficacy.

Meeting participants and Dr. Tager-Flusberg discussed the phenomenon that children with autism find looking at eyes arousing or aversive. Dr. Tager-Flusberg said that the data thus far, although incomplete, suggest that an abnormal pattern of development in brain circuitry leads to the avoidance of eye contact because it is experienced as aversive. Longitudinal data from the same children will probably provide more robust findings about how these networks originate in very early in life and how they might be influenced by interventions.

Dr. Tager-Flusberg said that when children with autism avoid eye contact because it is too arousing, they miss a great deal of critical information, and missing that information, in turn, interferes with the formation of social relationships.

V. PUBLIC COMMENT

Ms. Vickie Debold, representing the Coalition for Safe Minds, Sensible Action for Ending Mercury-Induced Neurological Disorders, and the National Autism Association (NAA), gave an update on the groups' ongoing research and analysis activities, all of which she provided in written form. She noted that the August 2005 symposium on environmental factors and neurodevelopmental disorders had been sponsored by the two groups, with support from the National Institute for Environmental Health Sciences. A summary of the proceedings, which is now being prepared, identifies suggestions for future research. The report will document the latest environmental research on autism, identify unanswered questions, and suggest next steps needed in environmental research.

Ms. Debold raised concerns about the prevalence data reported in *Morbidity and Mortality Weekly* and cited by Dr. Cordero. She said her organizations suspect that the overall prevalence rates given in the report may be too low. If further analysis shows that the older age groups have a lower prevalence than the younger age groups, it would suggest that environmental mechanisms may be involved.

Dr. Cordero noted that the lower rates in the youngest group may also reflect the fact that children had not yet been diagnosed. Increased rates in the older group may reflect the narrower diagnostic criteria used before the DSM-IV was published in 1994.

Dr. Catherine Rice of CDC and one of the authors of the prevalence report cautioned that the data should not be used to infer trends. Population studies are needed for an accurate analysis of trends. Dr. Rice said she would be happy to provide participants with more details about the statistical analyses if they request such information.

Dr. Rice said that CDC is trying to collect more detailed population-based information on previous diagnoses as well as symptoms within the population. Reports on these data, which are expected to be published this year, will provide information on both diagnosed and undiagnosed autism spectrum disorders.

Dr. Insel noted that a discussion of environmental factors will be held at the November IACC meeting. Dr. David Schwartz, director of the National Institute of Environmental Health Sciences, will comment on last August's meeting and give a much fuller explanation of how the institute is working on several aspects of environmental factors.

Ms. Cheri Chafeman, the mother of a boy with autism and a representative for Unlocking Autism, asked Dr. Pickett if methods for measuring heavy metal in the brain are available and if research is being done on that topic. Dr. Pickett noted that she has helped potential investigators find experts with knowledge about measuring heavy metals, but so far no such proposals have been approved.

Ms. Chafeman said that her son was poisoned by arsenic, and that there is a need for better guidance for parents seeking treatment, information that would outline different types of procedures, and interventions that can be followed. Dr. Insel mentioned that many parents have used the Autism Sourcebook by Karen Siff Exkorn as a guide to where they can find the next best intervention. He said another useful resource is the Autism Treatment Network (ATN), which has a helpful web site (www.autismtreatmentnetwork.org). Along with other activities, the ATN focuses on helping families locate physicians who provide good medical care. The web sites of advocacy groups and governmental agencies also contain a great deal of information.

Ms. Cheryl Trapanier, who said she works in autism research and is the mother of a 30-year-old son with autism, said that the resources to provide adequate treatment are not available. She noted that currently the best supported treatment for autism is applied behavioral analysis (ABA), but that ABA is either being inadequately provided or not provided at all—even when claims are made that it is.

Dr. Insel said that in addition to the gaps in awareness and access, there is a gap in quality, which has not received as much attention as the other two issues. Committee members and attendees discussed the need for the field to address issues of treatment and services, including their effectiveness, access, and quality. It was noted that information about Medicaid funding is not widely known.

Mr. Shestack stated that the Federal response is out of proportion to the size and cost of the pain associated with autism. He expressed frustration at what he sees as lack of performance on the part of the IACC. He said he would like the committee to advise Congress to recommend how legislation should be shaped and what Administration policy should be. He noted that there has not been a substantial increase in federal funding for autism in the three years that the research matrix has been in existence.

Ms. Blackwell said that Medicaid provides many opportunities in its waiver programs to serve children and adults with autism. Yet, out of 300 waivers, only 3 or 4 are targeted to children with autism. Medicaid does not initiate such waivers; they must be requested by the States. She asked members of advocacy groups to approach their State Medicaid directors to start crafting such waivers. CMS approves an immense array of services that can benefit people with autism, she said. Certain income requirements can be waived. She said she is puzzled as to why more States have not approached Medicaid to provide services specifically targeted to children and adults with autism.

In his remarks before closing the meeting, Dr. Insel said he believed that most of the participants probably shared Mr. Shestack's frustration that more is not being done to serve individuals with autism through research and improved treatment and services. Available treatments do not measure up to interventions used in most other medical fields. There is hope, he said, but it is not just around the corner. Additional discussion about treatments and services will be part of the November's discussion of the IACC Autism Research Matrix.