

Department of Health and Human Services

Centers for Disease Control and Prevention

National Center on Birth Defects and Developmental Disabilities

Minutes of the Meeting of the

**National Task Force on
Fetal Alcohol Syndrome and Fetal Alcohol Effect**

September 26-27, 2006

**Meeting held at the
Doubletree Buckhead Hotel
Atlanta, Georgia**

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National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect**

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September 26-27, 2006**

A meeting of the National Task Force on Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effect (FAE) was convened on September 26-27, 2006, in Atlanta, Georgia by the Centers for Disease Control and Prevention's (CDC's) National Center on Birth Defects and Developmental Disabilities (NCBDDD).

Thursday, September 26, 2006

Call To Order

Dr. Louise Floyd, Acting Executive Secretary, called the meeting to order at 9:00 a.m. offering a warm welcome to those present. She reported that the flight of Dr. Jean A. Wright, Chair, had been delayed and that she would join the meeting as soon as possible. Dr. Floyd also announced that Mary Kate Weber would not be joining them due to the death of her brother, and indicated that an address would be provided for those who wished to send condolences. Dr. Floyd explained that the agenda for this meeting would predominantly direct the Task Force's attention to two areas of early identification of the conditions and those who are affected. Task Force members and liaisons then introduced themselves.

Introduction of Task Force Members, Liaisons, and Attendees:

Chair:	Jean A. Wright, MD, MBA, Backus Children's Hospital, Savannah, GA
Acting Executive Secretary:	R. Louise Floyd, DSN, RN, Fetal Alcohol Syndrome Prevention Team, DBDDD, NCBDDD, CDC
Acting Designated Federal Official:	Jacquelyn Bertrand, PhD, Fetal Alcohol Syndrome Prevention Team, DBDDD, NCBDDD, CDC
Standing Member:	Kenneth R. Warren, PhD, National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health (NIH) Washington, DC

Task Force Members Present:

Dr. James Berner, MD, Alaska Native Tribal Health Consortium, Anchorage, AK
Carole Brown, EdD, Catholic University of America, Washington, DC
Grace Chang, MD, MPH, Brigham and Women's Hospital, Boston, MA
Mary DeJoseph, DO, Philadelphia College of Osteopathic Medicine, Philadelphia, PA
Lisa Miller, MD, Department of Public Health and Environment, Denver, CO
Dr. Colleen Morris, MD, University of Nevada School of Medicine, Las Vegas, NV
Mary O'Connor, PhD, ABPP, David Geffen School of Medicine at the University of California, Los Angeles (UCLA), Los Angeles, CA
Melinda Ohlemiller, BA, MA, Saint Louis Arc and parent of a twelve-year-old with FAS, St. Louis, MO
Heather Carmichael-Olson, PhD, University of Washington FAS Diagnostic Clinic, Washington State FAS Diagnostic and Prevention Network, Seattle, WA
Jean Wright, MD, MBA

Task Force Members Absent:

Kristen Barry, PhD, Serious Mental Illness Treatment Research and Evaluation Center, Ann Arbor, MI
Raul Caetano, MD, PhD, MPH, The University of Texas School of Public Health, Dallas, TX

Liaison Representatives Present:

American College of Obstetrics and Gynecology (ACOG): Robert J. Sokol, MD, Department of Obstetrics and Gynecology, C.S. Mott Center for Human Growth and Development, School of Medicine, Wayne State University, Detroit, MI

March of Dimes (MOD) Karla Damus, RN, PhD

The Arc: Sharon Davis, PhD, Professional and Family Services, Silver Springs, MD

Center for Science in the Public Interest (CSPI): George A. Hacker, JD, Alcohol Policy Project, Washington, DC

National Organization on Fetal Alcohol Syndrome (NOFAS): Kathleen T. Mitchell, MHS, LCADC, Washington, DC

Liaison Representatives Absent:

American Academy of Pediatrics (AAP): George Brennehan, MD, FAAP

Guest Speakers:

Paul Connor, PhD, Fetal Alcohol and Drug Unit, University of Washington, Seattle, WA

Callie Gass, Substance Abuse and Mental Health Services (SAMHSA) FASD Center for Excellence, Washington, DC

Julie Kable, PhD, Departments of Psychiatry and Behavioral Sciences and Pediatrics, Emory University School of Medicine

Kimberly Leeks, PhD, RTI International, Atlanta, GA

Mary Ellen Lynch, PhD, Departments of Psychiatry and Behavioral Sciences and Pediatrics, Emory University School of Medicine

Elizabeth Sowell, PhD, Department of Neurology, University of California, Los Angeles School of Medicine

Scott F. Wetterhall, MD, MPH, RTI International, Atlanta, GA

Other Attendees:

Coleen Boyle, PhD, Director, DBDDD, NCBDDD, CDC

Sherry Ceperich, PhD, FAS Prevention Team, DBDDD, NCBDDD, CDC

Elizabeth Parra Dang, MPH, FAS Prevention Team, DBDDD, NCBDDD, CDC

Karen Howell, PhD, Emory University, Atlanta, GA

Maggie Kelly, NCBDDD, CDC

Alberta Mirambeau, Atlanta Alliance on Developmental Disabilities, Atlanta, GA

Patricia Price Green, MSPH, FAS Prevention Team, DBDDD, NCBDDD, CDC

Eileen Miles, MPH, Battelle

Jacqueline Vowell, FAS Prevention Team, DBDDD, NCBDDD, CDC

Stephanie Henry Wallace, Writer-Editor, Cambridge Communications

Continuing the Conversation of Diagnosis of Individuals with FASDs**Jacquelyn Bertrand, PhD, NCBDDD/CDC**

Dr. Bertrand reported that during this meeting they would spend some time addressing the issue of diagnosis of individuals with FASDs. In 2002, CDC was mandated by Congress to develop guidelines for diagnosis and referral of children with fetal alcohol syndrome (FAS) and other prenatal alcohol-related conditions. In developing the guidelines for FAS, it became clear early on that there was not enough data and information about children who did not meet all of the criteria for FAS, meaning that they did not have the facial features or they were not experiencing growth problems, but they were still having central nervous system deficits.

Therefore, the Task Force and the Guidelines Working Group decided to table the issue of alcohol-related neurodevelopmental disorder and work on it once there was more scientific data to contribute to the body

of evidence in this area. The FAS guidelines were published in 2004. Since this time, the conversation has continued regarding behavioral and neurocognitive problems and more is known about what those deficits are. However, gaps still remain in being able to determine a behavioral phenotype for diagnostic purposes. There has been a lot of work on brain imaging and possible underlying brain damage that accompanies prenatal alcohol exposure. With this in mind, CDC decided to invite guest speakers to educate the Task Force about making a diagnosis and consider the potential uses of these technologies for diagnostic purposes and what is needed to move these kinds of efforts forward as a Task Force (e.g., resources, developing a research agenda, writing a letter).

Kathleen T. Mitchell, MHS, LCADC, National Organization on Fetal Alcohol Syndrome

Kathleen Mitchell indicated that she is a birth mother, addictions therapist, and the Program Director and National Spokesperson for the National Organization on Fetal Alcohol Syndrome (NOFAS). Each day she receives numerous crisis calls from parents, many of whom tell her that because their child has no facial features and does not meet the FAS criteria, they cannot receive a diagnosis and subsequent services. The vision at NOFAS is to do a better job of identifying children who have problems due to prenatal exposure. She stressed that families do not have time to wait for the experts to convene repeatedly and argue over definitions. For years, dysmorphologists have said that pediatricians cannot diagnose ARND, while pediatricians insist that they know it when they see it and insist that it should be in the Diagnostic and Statistical Manual of Mental Disorders (DSM).

NOFAS wants to keep the momentum going. While she has heard repeatedly that ARND is not a diagnostic term and there is no code for it, physicians state that they use it. In order to collect data, NOFAS began with a survey of clinicians in an effort to find out what physicians are doing in practice. It is difficult to assess how many of these individuals there are, given that they are diagnosed with “depression” or other disorders in order to be connected to services. However, if they continue to be thrown in wherever, they will never have the numbers to support the fact that services and funding are needed and to convince the government to pay attention. Ms. Mitchell lamented that families are being passed from one clinician to another, particularly when they are continually misclassified. She stressed that they are not serving the individuals and their families by waiting for answers of “exact science.”

In conclusion, Ms. Mitchell indicated that subsequent to the survey, NOFAS plans to convene a group of clinicians in a focus group setting with a professional facilitator who would pose questions of the clinical community regarding how they are diagnosing individuals in the absence of facial features. Unfortunately, they lost the funding to do so. However, NOFAS is willing to host such an effort if someone is willing to provide the resources to do so.

Imaging the Impact of Prenatal Alcohol Exposure on the Developing Brain

Elizabeth R. Sowell, PhD

Associate Professor, Department of Neurology

UCLA Laboratory of Neuro Imaging

Dr. Sowell reported that new imaging technology has allowed the study of pediatric populations *in vivo*. Magnetic Resonance Imaging (MRI) is non-invasive; no sedation is required; and children can tolerate the procedure, even children with the cognitive impairment typically associated with FAS. It is important to stress that in most cases the types of brain morphological abnormalities seen in FAS are not diagnostic via neuroimaging methods. This is why researchers are exploring computer technology to quantify changes in brain structure.

Dr. Sowell indicated that most of the data she would discuss pertained to a group of 21 children with prenatal exposure and 21 normal control children. Of the 21 exposed children, 14 have the facial features and 7 do not. The first type of study the team in San Diego conducted was a volumetric study, in which they looked at the volumes of the different regions of the brain. Computer algorithms were used to

determine which tissues were which. Green reflects gray matter, black is white matter, and red represents cerebral spinal fluid (CSF). Once the images are tissue segmented, they go in on a slice-by-slice basis and define brain and non-brain matter. When different regions of the brain are defined on a slice-by-slice basis, they can determine volumes of tissues within different regions of the brain that they can identify based on focal boundaries that can be seen on the outside of the brain. This is important, given that different parts of the brain are responsible for different cognitive functions. For example, they can determine a volume measure for the frontal gray matter, parietal lobe gray matter, or white matter.

Children with fetal alcohol exposure have smaller brains overall, and many of them are microcephalic. While it is known that these children are microcephalic, the team wanted to know which regions, if any, were more affected than others. The parietal lobes appear to be the most affected as they are the most reduced of all the regions, and they are reduced above and beyond the generalized microcephaly. They are also interested in brain size reductions above and beyond the microcephaly. Looking at just volume per se does not offer regional information, but when they correct for the overall brain volume reduction, they see only the parietal lobes are still significantly reduced in FAS children. With respect to white matter, overall there is a highly significant reduction in white matter and even when they correct for the overall volume reduction, reductions are seen in frontal, parietal, and temporal lobes. In terms of gray matter, once volume is corrected for, only the frontal lobe is significantly reduced. Hence, they are beginning to get at regional patterns, which is important because these can help figure out how those relate to the cognitive deficits. With respect to volumetric results, Dr. Sowell stressed the following points: Within the cortex, only the parietal lobes are significantly reduced in total volume above and beyond the generalized microcephaly; white matter hypoplasia is more significant than gray matter hypoplasia overall; gray matter volume is reduced in all areas, most significantly in parietal lobes (and at trend level significance in temporal lobes); and white matter is reduced in all areas, most prominently in temporal and parietal lobes.

The problem with volumetric studies is that investigators are dependent on anatomical brain regions that can be visually identified. Regions are not exactly well-defined in the brain. The tectonic or cellular differences cannot be seen, which really tell which regions are different. Therefore, these investigators applied an approach to studying brain morphological differences that have typically been used in functional MRI studies. In these studies, they allow the computer to tell them where in the brain, throughout the entire brain, problems are seen in different tissue types. They begin with the original brain scan where they can see gray matter, white matter, and CSF and they add tissue segmenting. With Voxel-Based Morphometry (VBM), all brains are transformed into the same space making them the same size. This is based on the assumption that, within some level of accuracy, homologous coordinates in each volume are the same anatomical structure. VBM allows measurement, with greater spatial resolution, where abnormalities occur in patients versus controls. However, they preserve relative proportions of gray to white matter in the new transformed volume. Then they can run statistical tests at each anatomical point. While all of the brains are the same size because they transformed them, and a particular voxel within the coordinate system is generally the same anatomical region, the tissue within that region varies. They look at the value of each voxel, and run a statistical test by group to determine if one group has more 1s or 0s than another. If so, it means that one group has more or less gray matter at that location than another. This allows them to look at group differences. They separated the children with prenatal exposure without the face to determine whether they have the same anatomical problems. When looking at these children compared to the controls, they have too much gray matter in the same locations where the children with FAS have too much gray matter. Thus, even if it is not seen in the face, it is seen in the brain.

Pertaining to VBM, Dr. Sowell reiterated the following points: Gray matter density increase is observed bilaterally in posterior temporal and parietal perisylvian regions. The alcohol-exposed subjects have too much gray matter in this region; white matter density decrease is observed in the same regions where gray

matter density is increased; subjects with severe prenatal alcohol exposure (PEA) but without FAS show a similar, though less severe pattern of tissue density abnormalities; and white matter density decrease in posterior temporal and inferior parietal lobes may be consistent with volumetric results in the same individuals where white matter volume is reduced most prominently in parietal and temporal lobes.

Dr. Sowell reported that most of the work she has done in the last five years has involved very complex computer algorithms that allow her to match anatomy across subjects using surface-based analyses. The corpus callosum has been noted to be abnormal in FAS children. It also offers the advantage of being fairly easy to see and define on MRI. Corpus callosum dysmorphology has been shown to be more common in FAS than other developmental disorders. The first type of analysis is not really surface based, but measures the area of various regions of the corpus callosum. The most posterior region is disproportionately reduced in area. Anterior and inferior displacement of the more posterior splenium of the corpus callosum is more prominent than anterior displacement. Notably, the anterior corpus callosum and posterior corpus callosum are not displaced. Displacement of the corpus callosum is a better predictor of group membership than area measures. The splenium is the region that connects the posterior temporal lobes where the gray and white matter abnormalities are being seen in FASD children using the other methods. Again, they separate the children without the face, who lie somewhere in the middle between the abnormalities in the FAS children and the control children. Thus, even without the face, the brain does not look quite normal on average.

There is a correlation between the amount of dysmorphology and the amount of cognitive impairment. Thus, the team used a verbal learning method (e.g., The California Verbal Learning Test) to correlate children's scores with a measure that captures the amount of dysmorphology in the corpus callosum. In the FAS children, they found a highly significant correlation between dysmorphology in the brain and cognitive dysfunction on this verbal learning measure. They conducted a similar study in which they looked at the shape of the vermis of the cerebellum. Dysmorphology is very prominent in the anterior vermis of FAS children. The dysmorphology of children without the face falls somewhere between the children with the face and the controls with no exposure.

Having learned about tissue density abnormalities and callosal dysmorphology, the investigators became interested in anatomical differences in the overlying cortical surface by matching cortex across subjects over the entire cortical surface of the brain. There is a huge amount of difference in the superior frontal sulcus in each normal individual. It is in slightly different locations in everybody, which is also true with the posterior. Thus, transforming everybody into the same box does not result in getting the same anatomy, although it is close. Essentially, for each subject, they began with the 3-dimensional brain volume, remove the skull and other non-brain tissue, and create surface renderings based on the signal value that best differentiates sulcal CSF from cortical gray matter. They define upwards of 36 sulci (based on a standardized, reliable protocol), and then flatten out the anatomically defined brain surface renderings of each subject. The next step is to warp each individual's flattened image to a standard atlas of sulcal landmarks. This method allows them to measure gray matter at anatomically matched points which is a clear advantage to the voxel-based methods described earlier where brain anatomy was only "assumed" to be matched. The X, Y, and Z coordinates can vary because it is in a slightly different place in every brain, but the computer tells them that it is the same anatomy.

Now they can look at gray matter differences across subjects at the locations where they matched cortical anatomy across subjects. They take a region of interest from the statistical map in average standard space and transform it back to the native space of each individual subject. Then they can get a gray matter volume in the region where they saw increased gray matter density. In fact, they did see gray matter volume increases in the circumscribed region of the temporal lobe with volume reductions in the surrounding temporal lobe area. This suggests that they are improving the spatial resolution in their ability to detect differences between groups using surface-based analyses with cortical pattern matching.

Again, they are seeing too much gray matter in the FAS children. In fact, they see a lot more differences once they get rid of the variability across individuals.

Not only can they look at gray matter, but also they can look at localized differences in the size of the brain. They know the FAS children are microcephalic and their brains are too small, but they want to know *where* their brains are too small. She does not want to know where they are too small when she is confined to defining anatomical regions she can actually see and trace. She wants to know where their brain sizes are different over the entire brain. To do this, they take a point at the center coordinate of everybody's brain and draw a line to the surface to the brain, measuring the length of that line in millimeters. They do this in both the exposed and the control groups, essentially creating maps which show the difference between the two lines in millimeters. Here they are localizing where brain size is too small without being dependent on being able to trace different lobes. This is consistent with the volumetric results that show that the parietal lobes were the most reduced in the exposed children. They also observed anterior frontal size reductions.

The gray matter density difference between groups was more prominent in the left hemisphere than the right. This led investigators to speculate that there might be an asymmetry difference in gray matter density in the alcohol-exposed subjects. When they match the left hemisphere to the right, much the same as they are matching cortical structure across subjects, they can begin to get an idea of where asymmetries are. This is where they begin to see the differences in the alcohol exposed children. In both sets of control groups, there is a posterior temporal region where asymmetry is significant, but which is absent in the alcohol-exposed children. The difference in asymmetry is statistically significant between the two groups. Thus, the alcohol-exposed children are showing reductions in white matter, increases gray matter, and abnormal asymmetry patterns all localized in the posterior temporal and inferior parietal lobes. Hence, they are beginning to see convergence of evidence across the different methods they are using.

The gray matter that is measured within a sphere is the amount of gray matter—it is not very concrete. Therefore, the investigators developed new methods recently to look at gray matter thickness in millimeters using an Eikonal fire equation to map the distance between the inner and outer “layers” of tissue segmented gray matter. In terms of how they can use their methods to measure not just local brain size, but changes in the tissue that constitute the near-adult volume brain in children, after they have warped each individual's brain to the standard atlas, they can use the information in the warping fields to help map cortical thickness in the average child.

Dr. Sowell shared some information about normal development in order to help put what they were observing in the alcohol exposed children into perspective and helps to interpret what is being observed. She reminded the group that in the alcohol-exposed children, they see increases in gray matter in the posterior temporal regions. From longitudinal data, across a period of two years, in normal children between the ages of 5 to 11, they observe highly significant cortical thinning in dorsal frontal and parietal regions mostly in the right hemisphere, while cortical thickening occurs bilaterally in posterior temporal and in left inferior frontal regions. This has to be a productive change given that these are normally developing children. Cortical thinning patterns are related to cognitive function. For example, the correlation with change in vocabulary scores is seen predominantly in the left hemisphere. Therefore, there are relationships between the changes observed in cortical thickness in normal children and changes in cognitive function that co-occur. Over the lifespan, there is a dramatic thinning of cortex that occurs over dorsal, frontal, and parietal lobes. In the posterior temporal lobes, there are slight increases before there is a decline.

With respect to how this relates to alcohol-exposed children and the relationship between white matter and cortical thickness, they see that the cortex is too thick in the alcohol-exposed children. It turns out

that cortical thickness during development is impacted by myelination, a cellular process that occurs in the white matter where the fibers that connect different regions of the brain are insulated with a fatty substance that shows up differently on MRIs than the cell bodies in the gray matter. When an individual is less than 35 years old, there is a highly significant negative correlation between white matter volume and gray matter thickness. The more white matter one has, the thinner their cortex is. In normal individuals, thinner cortex goes along with more white matter or more myelination, so it is not that the thickness of one's cortex during development is completely dependent on the number of cell bodies or synapses in that region, but it is also impacted by the amount of insulation one has on their fibers. That is, the more insulation one has, the more efficient connections between different regions become. When an individual is over 35 years old, the relationship between cortical thickness and white matter is highly positive in some regions, so the thinner the cortex is, the more white matter one has. White matter volume peaks somewhere around 40.

Trying to find a way to interpret what is being observed in FAS children is dependent on understanding what is occurring in normal children. With that in mind, these investigators have recently created maps of cortical thickness in millimeters in the FAS children. Not surprising, they observed the same patterns they did with the other methods in that FAS children have thicker cortex in certain areas. They have increases of up to 1.2 millimeters. The thickness increase could be because of abnormal myelination patterns in the FAS children. Dr. Sowell's colleagues in San Diego have collected a new set of data and she said she wanted to point out that they are actually replicating, in an independent sample, cortical thickness increases in the posterior and anterior temporal regions. This is a small sample, so they have not done a lot with it to date (e.g., 10 FASD and 13 controls). However, in some other San Diego data (with 21 FASD and 21 control children) they are looking at the correlation between cortical thickness and performance on verbal learning measures. The patterns in FASD children and controls are very different, which they confirmed by carrying out statistical tests to prove that the patterns are actually different. These data highlight that brain behavior relationships are impacted by prenatal alcohol exposure.

Regarding surface analysis results, Dr. Sowell highlighted the following points: Callosal and vermal dysmorphology are prominent and greater dysmorphology within the FASD group is associated with greater impairment on verbal learning. Similar to the VBM results, increased gray matter thickness (up to 1.5mm) is observed over large lateral brain surface areas in FASD subjects. These thickness increases have been observed in 2 independent samples; given results in normals, it seems reasonable to hypothesize that the cortex in FASD subjects does not thin during childhood and adolescence as it does in normals, perhaps due to decreased myelination. Longitudinal studies in this area are underway at UCLA. Cortical thickness correlates of verbal and visual-spatial functioning are altered as a function of prenatal alcohol exposure.

In using fMRI, they can look at not only the structure of the brain, but also how the brain is working during different cognitive tasks. In this study at UCLA, they have a sample of 11 children with FASD and 16 controls. There are differences in IQ between groups. A paired associates learning (PAL) task is used. The child is in the MRI scanner and hears dog-paw, house-cat, et cetera. The child is asked to learn these words and the brain is being scanned while this is in progress. In another block of trials they ask, "What word went with paw?" "What word went with house?" There is a learning component and recall component. If they look at the difference between learning and recall and rest, they can get an idea what parts of the brain are performing what verbal learning example. Posterior temporal and inferior parietal regions are active when children are hearing words or recalling them versus when they are resting. In the alcohol-exposed children, the left medial temporal lobe region is not showing activation, or at least not to the extent that it is in the control groups, and this is confirmed with statistical tests. Dr. Sowell's colleagues in San Diego have shown that the medial temporal lobes in FASD children are actually too large, so they have too much gray matter in their medial temporal lobe, but they are activating it less and not using it in the same way. It is possible that the FASD children are over-reliant on the regions of the

brain in the frontal lobe than they are on the medial temporal lobe to perform the tasks. They are asking children to learn pairs of words. One important point is that perhaps the alcohol-exposed children are not doing this because perhaps they are not learning as well. The differences in the controls and the exposed children could represent global differences in intellectual function rather than the children doing the same thing. It is known that the IQs of FASD children are significantly lower than non-exposed children.

In an effort to correct for IQ and perhaps show that there is something different about the organization of the brain in alcohol-exposed children that is not just about their overall cognitive deficits, they knocked off the top 5 high IQ children, leaving them with 11 control children and 11 FASD children. IQ was not exactly matched given that the control children still had higher IQs, but they were not significantly different, particularly in the verbal IQ. They looked at the maps again, finding that even when they took out the higher IQ children, they observed the same thing—the FASD children still have less reliance on medial temporal and over reliance on dorsal frontal lobes to perform the tasks. In addition, they used post-test performance as a statistical control. So, even though they observed no statistical difference between post-test performance, meaning controls are performing the same statistically, still they see the decreased activation in the FASD children in the medial temporal lobe. Therefore, they are reasonably confident that these maps are showing them regions where brain activation is not working the same in FASD children as it is in controls.

In a summary of functional activation, Dr. Sowell stressed the following points: Their results show that FASD children may rely too heavily on frontal memory systems. The San Diego group has also shown increased frontal activation in FASD children during a response inhibition task (Fry, et al., Submitted). FASD children do not rely as much on medial temporal memory systems while learning verbal material. Other groups have shown increased medial temporal lobe volumes (Archibald et al., 2002). Despite the increased volume, the medial temporal lobe is not performing as it does in normal children. Increased cortical thickness is observed in posterior temporal language regions, yet functional activation is decreased in these regions. Again, more is not always better.

Regarding some interesting studies that they are trying to conduct on relationships between facial morphology and brain morphology, Dr. Sowell noted that when they do an MRI scan, frequently they have information about the face as well. So, just like they can create a surface rendering of the brain, they can create an automated surface rendering of the face. They can then use some of these same methods to define, for example, different anatomical structures on the face and compare them across subjects in an effort to quantify where abnormalities are seen over the entire face. They are beginning to work on methods to allow them to coordinate relationships between the brain and the face using these highly technical facial pattern matching techniques.

Dr. Sowell concluded that brain structure continues to be affected during adolescence. Myelination that would normally occur during adolescence may go awry in those with FAS. Individuals with prenatal exposure to alcohol but without facial dysmorphology for a diagnosis of FAS also show evidence for gross brain dysmorphology. Perhaps brain morphological variables eventually could be used as a better marker for prenatal exposure than facial dysmorphology. Parietal lobes and callosal fibers that connect them appear to be particularly vulnerable to alcohol. Parietal lobe functions should be further studied in neuropsychological and functional imaging paradigms. There may be evidence for myelination abnormalities and white matter may be a target of alcohol's teratogenic effects. Asymmetries in the posterior temporal lobes suggest there may be asymmetrical patterns to myelination deposition abnormalities. These studies show abnormalities in the frontal cortex, both functional and structural, which is perhaps consistent with the cognitive behavioral literature. Functional imaging studies will be useful in determining the significance of these abnormalities relative to the more robust dysmorphic changes observed in parietal cortices.

With respect to future directions, Dr. Sowell indicated that continued investigations are needed with larger samples to evaluate reproducibility of structural findings in children with FAS and other FASD disorders. Longitudinal studies are necessary to determine if cortical thickness abnormalities are resulting from abnormal developmental patterns during childhood and adolescence. Evaluation of function-structure relationships are needed to determine how structural dysmorphology impacts brain function. Examination of face-brain relationships is important. Currently, the face is used to diagnose, but obviously it is the brain that is resulting in the more debilitating cognitive sequelae. Questions needing further examination include: Can something grossly measurable in the face predict with any accuracy the extent of brain dysmorphology? Can neurocognitive measures predict brain dysmorphology allowing us to eventually bypass expensive imaging studies?

Discussion:

- Ms. Mitchell asked what the criteria were for the PEA children. Dr. Sowell responded that these data were collected by her colleagues in San Diego. PEA means they did not have the face but they had cognitive behavior deficits and a history of prenatal exposure. They did have a strong documented history of exposure, which is corroborated from various sources (e.g., medical, legal, et cetera). As far as how much alcohol, they do not know.
- Dr. O'Connor said she thought they were now calling them dysmorphic and non-dysmorphic prenatally exposed. They do not have the face, but they still have the brain damage.
- An inquiry was posed regarding whether Dr. Sowell knew how the sample was constructed. Dr. Sowell responded that she did not recruit the children herself. She indicated that Sarah Mattson and Edward P. Riley have an FAS clinic. It was based on the children who are able to tolerate scanning and the amount of money they had to scan. Dr. O'Connor added that the children are run through Ken Jones' teratology clinic. The sample from UCLA was a less selective sample. Many of them participated in the Social Skills groups (intervention funded by CDC) for children with prenatal alcohol exposure. They did not advertise to parents that their children must have prenatal exposure. These were parents whose children were having problems so they were still a clinical sample. They quantified the alcohol once the children arrived and selected for the heavily exposed children. It is different in that they were not presenting to an FAS clinic; they were there for another service. In Dr. O'Connor's sample the only criterion was social skills deficits. They were not selecting on alcohol exposure.
- Dr. Berner asked whether there was any interest in studying some of the other possibilities that could interact with alcohol, such as mercury, which is a neuronal migration agent. In Alaska, due to the large number of Alaskan natives who depend on the traditional diet, there are some interesting mercury data. His guess from looking at them for over 30 years is that the interaction of alcohol and mercury is worse than either one alone. It is very simple to measure an integrated mercury exposure in women in the prenatal clinic by obtaining a hair specimen. Thus, it seems to be a useful and cheap way to address that question. He was curious as to why this is not considered an issue, especially in coastal communities. When the Environmental Protection Agency developed their new benchmark reference dose of prenatal mercury, they estimated that probably 5% to 7% of U.S. women in the childbearing age range who are exposed to levels EPA considers possibly hazardous. That is at least as common as heavy alcohol intake. Dr. Sowell responded that it is known that mercury is a teratogen. They are studying methamphetamine exposure and how that differs from alcohol, although they do not yet have enough subjects in their methamphetamine group. It is not clear how specific the issue is. Perhaps it is not about alcohol, but could be about other substances. However, she did not think there was any reason to believe that mercury levels would vary as a function of alcohol intake.

- Dr. Bertrand reported that there is some interest in conducting a study in South Africa among women who drink homemade alcohol, which has a very high mercury levels, to determine if for some reason this accounts for the very high levels of FAS seen in the farm communities. Dr. Berner replied that this is a different type of mercury. It is not organic mercury. Metallic mercury and organic mercury exposures are fundamentally different, but there are populations in the U.S. where organic methyl mercury and alcohol exposure could be studied.
- To get to the central question of using this imaging for diagnostic purposes, given that these data are all based on averages and there is quite a bit of overlap, Dr. Bertrand asked whether Dr. Sowell had considered conducting studies in another sample where she picked a threshold of being able to use this predictively. Dr. Sowell responded that this is their ideal goal. While they are not there yet, there have been some studies published by the Washington group where there may be some specificity in some of the corpus callosum measures, but in her opinion, using these quantitative techniques will not be done in every city in the country. Most practices cannot do a brain scan to tell parents whether their child is affected. However, with large enough samples and sensitive enough methods with large groups, they can begin to pinpoint the most highly significant predictive differences of a group and then look in those places, however they do it—come up with a brain measures that correlates very highly with a face measure. Although, they do not know what part of the face it is yet. It may not be the measure already being done. Perhaps those endeavors will be fruitful down the line.
- Dr. Bertrand clarified that what Dr. Sowell was saying is needed are large sample sizes and longitudinal studies so that they could achieve a better mean difference and begin to work on variability. Dr. Sowell responded that working with neurocognitive deficits and facial patterns and correlating them to derive face measure (computer-generated or even the ruler and measurements that are used) is what they are interested in. The brain is what it is all about.
- Dr. O'Connor asked whether eventually Dr. Sowell would want to be secure enough that her measures of cognitive and neurobehavioral functioning were so highly correlated with brain function they would not need to look at the brain any longer. Dr. Sowell responded that this is exactly the goal, which is why they need large samples and correlations between the face and the neurocognitive and the brain to identify the areas so that they no longer need the brain scan and cortical pattern matching.
- With the fMRI, Dr. Morris wondered if they had any tests that looked at executive functioning. Dr. Sowell responded that they do, although they have not fully analyzed the data. They are conducting 6 different fMRI tests on these children.
- An inquiry was posed regarding the minimum age of a child who could be put in the MRI. Dr. Sowell indicated that with normal children, they go as low as 5 years old. Other groups such as National Institute of Mental Health are doing a lot of scanning of normal children down to 3 or 4 years old with structural MRI. They put them in during bedtime. The cost to Dr. Sowell's group is \$600 per hour to put the children in the scanner. They have two scanning sessions of 45 minutes each. If they put 10 5-year olds in, they might get 5 good scans. Those are normal, not impaired, 5-year olds. With their FAS methamphetamine study, they are starting at age 7. They have a mock scanner that they put the children in to get them used to the environment and sounds. That seems to help. If children could be sedated, they could use infants. People are doing that, but they do not want to sedate normal children.
- Dr. Wright reported that she sedates normal children for MRIs down to premature ages. However, if someone is going to sedate and try to do functional, that one is wiped out. They do 12 structural MRIs a day. The most common referral is parents who want to know whether their child has autism.

Dr. Sowell replied that their Institutional Review Board (IRB) will not allow them to recruit children who are normal for any clinical reason and sedate them.

- Dr. DeJoseph asked whether there was any follow-up testing beyond speaking to the children again once they got out of the scanner to determine what they retained (e.g., 12, 24, 48 months). Dr. Sowell responded that there is not. The post-test session is conducted within an hour of the children getting out of the scanner. They do not see the children again for two years.
- Many children seem to have disabilities that are related to deeper structures, Dr. DeJoseph wondered if Dr. Sowell's work gave them any information about that structure. Dr. Sowell responded that they know that the medial temporal lobe structures (which she stressed she was using loosely because it was not *the* hippocampus) are responsible. The functional MRI data are 4 x 4 millimeters, so when they get to structures within that, they are using resolution to make determinations. To look at activation in the amygdala, for example, they would probably need a task to tap that structure very well, which none of their tasks are really doing. Medial temporal lobe decreases in activation in the FASD children were prominent in the verbal learning paired associate learning task.

Neuroimaging Studies of Infants, Adolescents, and Adults with FASD:

Perspectives from the Far Northwest

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Dr. Connor reported on three studies that the University of Washington has been conducting since the mid 1990s, which include the: 1) Adolescent and Adult Structural MRI study with 60 FAS, 60 FAE, and 60 comparison subjects; 2) Adult Functional MRI with 16 FAS, 16 FAE, and 16 comparison subjects; and 3) Infant Ultrasound with 23 Exposed and 21 Unexposed subjects. The group in Seattle has been working for a while with adults and adolescents and they are just beginning to work again with early infancy as well. In the first two studies, the subjects with FAS and FAE were previously clinically diagnosed through the University of Washington clinic. For the third group, investigators prospectively sought babies whose mothers drank alcohol during pregnancy, and were not chosen based on cognitive problems with these infants. This was very much a systems-based approach to attempt to find these children and to obtain early information on structures of the brain.

These investigators have been studying the morphology of the brain by looking at the shapes of different regions. They do this with a relatively simple method of placing landmarks in different parts of the brain. They have studied the corpus callosum primarily. They basically find a mid-plane of the corpus callosum, though in their case it is not a strict mid-plane, which they get off of the scanner. They find the local mid-plane for every point. They find the point of left to right symmetry so they get a compilation image. Once they find the point of symmetry on every point around the corpus callosum, they then map that. These are then collapsed down to create a centralized corpus callosum. This is a relatively simple approach that can be fairly easily automated, although they need funding in order to do the computational power required to do that.

In the Adolescent and Adult Structural MRI Study, they used this technique with 180 individuals, those who had been diagnosed and the control subjects. They found that there is definitely a lot of variability in that margin of corpus callosum throughout. They also measured the size of the corpus callosum, and very much like the San Diego group found, they found, on average, a 7% decrement in the size of the corpus callosum. This is not new and has been reported on for many years; however, the Washington group wanted to determine whether there was a difference in the shape of the corpus callosum. To do this, they plotted the averages, upon which they found no difference, on average, between the shape of the corpus callosum in the controls and exposed individuals. There is some indication that FAE females may have

an arch to the corpus callosum that is slightly raised, but overall there is no statistically significant difference, on average. Therefore, they returned to the data to determine if there was something they could salvage out of this, and there was.

When psychologists discuss fetal alcohol spectrum disorders, they talk a lot about the variability in presentation. Some of these individuals are horrible at math, some are very good at math, some have high IQs but poor social skills, and others have low IQs with slightly higher social skills. Hence, it is very difficult to come up with a phenotype for fetal alcohol spectrum disorders. These researchers found this exact pattern when looking at the neuroimaging of the corpus callosum. The control subjects have fairly tightly packed corpus callosums despite any variability. There is no difference in the subjects with FAS and FAE. These are essentially intermingled with no statistical difference. However, the variability is incredibly high, so they had some FAS and FAE individuals with very thick corpus callosums very far advanced into the frontal lobe. Others had very thin corpus callosums or very far advanced into the posterior section, the parietal lobes. The variability went in multiple directions. There was no single direction that the variability went in.

With respect to impact in the real world, they believe this is something that can be used as a diagnostic tool, with the problem of specificity. There are many things that can cause the corpus callosum to be deranged, one of which is FASD. One of the 4-digit diagnostic codes is CNS disturbance. The MRI can offer a great deal in documenting CNS disturbance along with the alcohol exposure information that should be acquired. One particular example of a corpus callosum from an individual with FASD was shown. If a radiologist looks at a picture of somebody who was exposed to alcohol prenatally, he or she may not see this and may say it is within normal limits. However, compared to a control subject, it is clearly different. In this case, the alcohol-exposed individual has a much shorter corpus callosum without as much humping in the posterior section, the rostrum point is collapsed and there is a much thinner looking corpus callosum. This methodology has begun to be used in legal cases, though not in clinical cases. This is typically used in death penalty cases during the mitigation phase where exposure history is well-documented and they bring the developer of the technology in to testify. He can take the image of the brain, identify the corpus callosum, and create a probability map of how likely the person is to be considered within the normative group of 60 control subjects or the FAS or FAE group. This has been successful for commuting from a death penalty case to a life sentence case, for improving the possibility of getting treatment services for these individuals, and, in situations that are not death penalty cases, getting the individual into inpatient treatment rather than just into prison.

In terms of the correlation between the structure of the brain and neuropsychological effects, the Washington group looked at the relationships between their entire battery (5 or 6 hours) of neuropsychological functioning covering a number of realms, and the corpus callosum structure. They found that there was a very significant relationship between the structure of the corpus callosum and two patterns of neuropsychological functioning. If the individuals with fetal alcohol spectrum disorder had a corpus callosum that was too thin relative to control subjects and leaning forward, they found that these individuals had deficits in motor coordination function. This makes sense architecturally because the connections between the two hemispheres through the corpus callosum come through the posterior section of the corpus callosum. Issues of lack of myelination of white matter could come into play with this sort of thing. Conversely, the individuals who had corpus callosums that were too thick and leaning backwards, toward the parietal area, performed relatively well on these motor tasks. However, they had significant executive function deficits (e.g., working memory problems, problems with problem solving, planning their behaviors, inhibiting responses). Again, bigger is not better. Having more corpus callosum white matter is not helping these individuals. The increase in the white matter tends to be in the frontal areas of the corpus callosum, which is the conduit between frontal lobe structures. However, it is not entirely clear why the over-thickness of the corpus callosum could be related to the executive function issue. It is possibly a result of issues of apoptosis where possibly the process is not functioning

appropriately in the frontal part of the corpus callosum. Thus, there are a lot of interconnections between brain regions that are not supposed to have those connections anymore, which may cause some sort of derangement in a person's behavioral functioning. This sort of imaging cannot be done with structural MRI, although it might be possible to do this with diffusion tensor imaging to look at directions of pathways.

The team went back to the same 180-subject population to look at a different region of the brain. They decided that because the literature has been pretty strongly indicating it, they wanted to study the cerebellum in these individuals. They used the same types of methods used for the corpus callosum, except this time they mapped the exterior surface of the cerebellum by using the semi-landmark points. They used 328 semi-landmark points around each individual's cerebellum that were manually placed, although there was some semi-intelligent software involvement to work the landmark points so that they approximated where they should be, but they needed to be adjusted by hand. They were left with an overall surface rendering; however, this is not mapping directly onto the cerebellum or looking at patterns of the cerebellum, it was simply looking at the outward shape of the cerebellum overall. When they did this, they also looked at the vermis and measured the size, although they did not find a change in the size of the vermis of the cerebellum. They did not do a lot of parceling to look at anterior versus posterior, so they do need to go back and do this later. However, they did want to determine 3-dimensionally whether there was a difference between control subjects and exposed subjects. They found that overall, individuals with FAS or FAE on average had smaller cerebella. They also wanted to determine whether there was an easier way to measure this. Thus, they looked at the points on the outer silhouette of the cerebellum and then mapped them out. When they did this, they found an average size decrement of the cerebellum. There was definitely increased variability in their exposed subjects, but they also found an average difference in which the cerebellum in those who were alcohol damaged was pinched as it came around toward the front of the cerebellum. This is true with every single age and gender group assessed.

Trying to look at this diagnostically, structural neural imaging has great utility for assisting in this. There are issues with respect to the age of the person. They really do not want to image children under the age of 3 or so unless there is sedation, which is a problem. However, as individuals get older, this becomes a much simpler technique and is relatively inexpensive. In terms of being able to link this to the neuropsychological functioning, they can use the neuropsychological assessments as proxies for the decrements in shape and size of the brains.

Pertaining to the functional MRI study, the University of Washington investigators chose a subgroup of the individuals (all of whom now are adults over the age of 18) from the structural MRI study and gave them a series of 5 different cognitive tests while they were taking a functional MRI image acquisition. The tests included arithmetic skills (subtraction tasks), a working memory test, a motor coordination test (alternating finger tapping), a response inhibition test, and a general attention test (which did not work out very well at all). When doing functional MRI, the idea is to look at the aspect of the task that one is most interested in. If they were to take an image of the brain while a person is completing a math task, a lot of areas of the brain would be lighting up. While there may not be much concern about how much overall the brain is lighting up, they are concerned about whether there is something wrong with the way a person's brain is working on an arithmetic task versus some other type of task. Thus, basically they have to have subjects do two tasks and then subtract them out. They looked for all the tasks that are done in arithmetic that did not really concern them, such as visual processing, and they determine a way to get rid of that. They are not really concerned about motor coordination for being able to push buttons. In this study, the subjects were giving answers (pushing buttons to indicate their responses) while they were in the scanner. They did not want to know much about eye movement, so visually the images are set up the same way. Then based on this, they create a task.

In this case the control task was a letter matching task. They used a triangle of letters and the subjects were supposed to match the letter that showed up in the top with one of the two down below. They had two buttons with which to choose these. In the math task (the experimental task), subjects were asked to subtract the number that they saw in the top center from the number 11. They found that the regions which were activated for controls, FAS, and FAE subjects were essentially the same regions. There was some activation in the frontal region and there was a lot of activation in the intraparietal sulcus, which has been shown very much to be involved in arithmetic functioning. There was also activation in posterior parietal regions and the anterior cingulate. They noticed a decrease in activity in those regions. Control subjects had very robust activations, while FAE subjects had slightly less activity in those regions and the FAS subjects had the least level of activity in these regions. On average, the subjects with FAS and FAE did perform more poorly than the control subjects. Intellectual functioning was very much statistically different as well. When they did the averaging to look at differences between the groups, they found indications of control subjects having greater activity in particular regions of the brain than subjects with FAS. They found bilateral, in the intraparietal sulcus, very much involved in arithmetic functions, and also in the anterior cingulate region, which is a part of the brain that is involved in being able to direct attention—tell the brain where to focus next.

They did not find significant differences between the control and FAE subjects, except in the cingulated, an area that directs attention to the proper task. The FAE subjects had a decrease in activation in this region. However, when they continued looking, they found areas in the brain where the FAE subjects had increased activations relative to controls. They found that the left hippocampus in FAE subjects was significantly activated relative to control subjects. This is an unusual part of the brain to be lit up while a person is doing a math task. One possible explanation for this is that these people may have been trying to compensate for their poor math performances by trying to memorize the responses, resulting in increased activation in this region.

In terms of the executive functions with functional MRI, working memory tasks (N-Back), basically requires subjects to press a button when they see a letter that is the same as they saw two or three letters previously (e.g. A-L-A). This is a relatively difficult task because it requires the subjects to be able to maintain the information in their memories and keep constantly updating the information, because they are getting the letters at a reasonable clip and they are no longer seeing the letters from the past. Nevertheless, the FAS and FAE subjects performed equally well on this particular task. When looking at the averaged images for each group, again, basically the same areas (e.g., dorsal lateral prefrontal cortex (DLPFC) and posterior parietal regions) are active in all three groups—most robust in controls, a little less so in the FAE subjects, and still less in the FAS subjects. When they looked at the comparison between the groups, they found that in both cases, dorsal lateral prefrontal cortex (especially on the right dorsal lateral prefrontal cortex) there is a significantly decreased activation in FAS and FAE subjects relative to controls. For the FAS subjects, this was more bilateral. Also, especially in FAE subjects, there is decreased activation in the posterior parietal region. In all of these cases there was a trend where, the FAE subjects in this case, had decreased activation.

The third task pertained to motor coordination and involved alternating finger tapping (Alternating Motor). Subjects had to push a button in time to a tone. When they did this, they noticed that FAS and FAE subjects did significantly more poorly than the controls. If a subject is supposed to be pushing the right hand for high pitched tasks and the left hand for low pitched tasks, with it coming every half second, it is very easy to get off sequence. The control subjects did not get off sequence as often, so investigators wanted to determine whether the subjects with FAS/FAE did not tap as much and perhaps gave up because they were out of sequence. However, they found no significant difference in total taps between the groups. They are still all tapping, so they should be able to look at their brains for differences. They looked at the cerebellum, which is involved in the coordination of movements and found that three groups had activations in the cerebellum, but in slightly different regions for some reason. When they averaged

it, they found that both FAS and FAE subjects had significant decreases in activity in the right cerebellum region, with FAE subjects having a little more bilateral decreases in activity.

Dr. Connor said that, as a diagnostic tool, he did not believe fMRI was the way to go. However, he did think its major contribution was in the area of outcomes research; that is, looking at treatment approaches to determine whether there is a visualizable change in a person's neuroimaging and in the activity of the brain as a result of this treatment technique that is involved. Therefore, in the future he would like to look at some techniques like EEG neuro-biofeedback. This involves placing a couple of electrodes on the subject's head. As the person gets into a certain brain rhythm state, a little Pacman starts moving around on the screen in an effort to train the brain to get into a more relaxed state with the electrical patterns of the brain. That has a lot of impact, at least anecdotally, on improving attention, decreasing volatility, et cetera. It would be very interesting to approach this empirically in a research setting with fetal alcohol spectrum disorders and couple that with the neuroimaging studies of the fMRI in order to determine whether there is an alteration in brain patterns as a result of this treatment.

To summarize the findings of the second study, although the FASD group performed significantly more poorly in the arithmetic tasks compared to the controls, activation patterns were similar to the comparison group, but reduced. Activation of the hippocampus in FAE subjects was surprising and could indicate an attempt to compensate for poor subtraction skills by memorizing answers. In the N-Back tasks, FASD subjects' performance was similar to comparison peers on the 2-Back task. FASD subjects showed decreased activation relative to comparison subjects. They seemed to rely on regions other than the DLPFC to perform this task. With alternating motor tasks, FASD subjects demonstrated significantly reduced bilateral activation in cerebellar hemispheres and middle cerebral peduncles relative to controls despite similar motor performance.

The previous studies included adolescents and adults, but Dr. Connor stressed that it is very important to identify individuals as soon as possible after birth so that therapies can be offered in an attempt to ameliorate or minimize the risks of secondary disabilities. The best possible way to do this is to attempt to reach women when they are giving birth. They may not present for prenatal care, particularly high risk women, and they may not present for postnatal aftercare. However, they usually end up at the hospital at some point to deliver the baby. In this third study, investigators visited two hospitals and disseminated screening questionnaire that asked about alcohol and other drug use during pregnancy. The investigators interviewed those who they found to have significant exposure, with consent. In addition, they would add in a calendar follow-back during their pregnancy asking about alcohol and other drug use. In the hospital screening questionnaire, many women were willing to disclose their prenatal exposure history. However, upon interviewing the women and completing their calendar follow-back, they found the women were being conservative on the hospital screening questionnaire. They were able to obtain better data, and more of it, from the calendar follow-back. The screening worked fairly well, though it likely missed a few people who were underreporting significantly.

Upon completion of the interviews and follow-back, the women were enrolled in the study. They brought the baby in within the first three months, although if this were implemented, it would be preferable to do this during her current hospital stay. Fortunately, the fontanelle is still open for the first three months. Using a pediatric cephalic transducer from an ultrasound, they could obtain a reasonable image of the baby's brain and a very good image of the corpus callosum. The investigators took approximately 50 shots of each baby's corpus callosum and averaged them together. Just one image of the corpus callosum is fuzzy. However, if 50 images are averaged together, it becomes fairly clear. The border is relatively clear around the corpus callosum; however, this is not clear enough for the techniques described in the first two studies. Once they had the averaged image, they placed four points around the corpus callosum on each baby and measured the angle between the genu point in the front, the very bottom of the splenium, and a point that bisected the length of the splenium. They found that the control subjects had a

fairly smoothly arching corpus callosum, while the alcohol-exposed subjects has a fairly sharp hook in the corpus callosum. The angle is below 90 degrees and was found in over half of their subjects who were highly exposed. Only one subject who was not exposed to alcohol had an angle greater than 90 degrees. There were also a number of individuals who were highly exposed who did not have a hooked corpus callosum. The investigators did not expect that everybody would—they expected that about 50% of those exposed would be exposed and damaged, which is what they found. About 12 of the 23 had an angle greater than 90 degrees.

They also collected a lot of data on other substances used by these women who were also high alcohol users, the most common being marijuana and nicotine. However, when looking at marijuana across exposed subject versus the angle of the corpus callosum, they did not really see much to differentiate them. Increased nicotine also spanned the entire range of corpus callosum angles. Very few women were using crack or cocaine, but two of the three had the hooked angle in the corpus callosum, so there may be something there. Some mothers were on antidepressants, painkillers, and other drugs and one was on methamphetamines during their pregnancies, though no relationship was found to that and the corpus callosum angle.

The investigators also wanted to determine whether there really was a relationship between the hook of the corpus callosum and the facial features of fetal alcohol syndrome. Hence, they brought Ken Jones in to consider a small subset. When he saw these individuals, he definitely diagnosed one with full fetal alcohol syndrome, which was somebody who had a corpus callosum with an angle greater than 90 degrees. He deferred diagnosis on two others who were within the high angle, high exposed group. He said that four of them were not diagnosable with fetal alcohol syndrome. However, they all had heavy exposure, so they could have been ARND. Dr. Connor said that even though Dr. Jones was not identifying FAS, the facial features, they were definitely picking up individuals who when they do psychological evaluations later, they will be able to see that they have FASD. Dr. Jones did not diagnose anybody in the less than 90 degree angle, although he deferred one person who was unexposed to alcohol.

Discussion:

- With respect to the structural MRI, Dr. Bertrand pointed out that early on Dr. Conner stated that they did not find differences between the exposed and non-exposed subjects for the shape of the corpus callosum on average. She asked him to speak to how he reconciled that with the San Diego data that does find a difference in shape. Dr. Conner responded that what they found was non-significant, overall, on average change in shape. There was a trend toward a difference in shape; however, the variability washed that out. It is possible that because they are looking at older individuals, there are a lot more life chances of other things affecting the corpus callosum as well that increases the variability issue or makes the control subjects less tightly packed to give them more chances of the variability problem versus a mean shift.
- Dr. O'Connor asked whether there was a difference in time of diagnosis and the different organizations making the diagnosis. Dr. Conner replied that the difference in time of diagnosis was fairly great. They had individuals who were diagnosed at birth who were part of the study since 1973, some who were diagnosed in adolescence, while a couple who were diagnosed as adults. The majority of the subjects, with a couple of exceptions, were diagnosed by Sterling Clarren, David Smith or one of his associates. So, they were all diagnosed by the same school of diagnosis over the years. However, the age of diagnosis was quite variable.
- Dr. Berner inquired as to the subject's age of assessment in the third study. Dr. Conner replied that there was an age range because it took them a while to collect all of their data, but they were approximately 12 to 18 months old when Dr. Jones saw them.

- An inquiry was posed with regard to whether any developmental testing had been done. Dr. Conner responded that they have, but they have not been able to report the data because it is so small. They have been using the Baley Scales with these subjects at 18 months old and A-not-B, which is a task similar to the Wisconsin Card Sorting test of problem solving, rule change, and being able to adjust to those rules. They have not seen them differentiating groups at all, even exposed versus control at this point. He stressed that he says “control versus exposed” literally because none of these subjects have been diagnosed. They did not present because they have cognitive / social problems. They did not come in because they were diagnosed already. They were simply highly exposed. This is an attempt they hope can be replicated and increased, with additional funding, at very early identification and with the goal of very early intervention.
- Dr. Olson asked whether these were all high-risk families. Dr. Conner replied that they are not. They have another project in Seattle called *The Parent-Child Assistance Program*, which is a program that works with high risk alcohol and drug abusing women who have had a child who was exposed to one of these things. They did get a number of referrals from that source for the third study, so there would be high-risk cases; however, about half of them were obtained as intake referrals from hospitals when they were distributing the hospital screening questionnaires. Thus, these were not necessarily high-risk women. They were simply women who were delivering and filled out the questionnaire. They attempted to give the questionnaire broadly, but they were unable to “control” the charge nurse the entire time, so there were some selection issues in play. The charge nurse had ultimate veto. It was to be given to everybody unless the charge nurse declared someone too vulnerable. Hence, they may not have been getting some of the more sensitive people. Dr. Olson observed that it is not just a sample of clearly high risk, low socioeconomic, high social problem individuals. As they grow the sample, they may be able to make it more representative of the broader hospital nursery. Dr. Conner concurred, indicating that their goal within the consortium was to be able to spread this to different sites across the country and around the world. It is fairly simple to do and it can be fairly automated. In fact, it could be programmed straight into the computer that does the ultrasound scanning.
- Dr. Berner wondered whether the angle changed with age. Dr. Conner replied that he thought it must because they did not see the angle when looking at adults and adolescents, other than with the hints of the leaning back corpus callosum, which suggested that there was some angle still there. They conducted the initial pilot study with 8 versus 11 and they found this angle. When they increased the study size to 23 versus 21, the angle persisted and they got an even stronger signal. This surprise finding held its own.
- Dr. Bertrand asked for clarification about the surveys originally being done anonymously in the hospital. Dr. Conner replied that it was pseudo-anonymous. The nursing staff distributed them with some sort of ID marker that was kept from the investigators. When the investigators reviewed them and found those which looked significant, they would ask the nurse to connect them to the person. The nurse would ask the women to recruit into the study, not the investigators.
- In the exposed children, Dr. Bertrand wondered whether there were any kind of external things that could be used as a screening marker at birth. Dr. Conner replied that they have not yet really considered this aspect yet. APGAR probably would not help much. Time of delivery may with respect to whether the baby is a significant premie, but this study did not use significant premies, they used 37 weeks and above. Prenatally-exposed children can be premies.
- Other than the alcohol exposure, Dr. Bertrand wondered if there could be some other marker in their survey to be used down the line, noting that they should be able to obtain height and weight measures. Dr. Conner responded that this was possible. The initial screening itself is only a 5-minute screen. It

is not a significant burden on the woman other than the concern about reporting negative behaviors during pregnancy that has stigma attached to it. While they could obtain height and weight measures, they did not do so with this group because this was a super-pilot, followed by a pilot, followed hopefully by the main study where they will be able to collect a lot more data.

- Dr. O'Connor inquired as to whether they asked the women about drinking prior to pregnancy recognition and whether that showed a stronger effect. Dr. Conner responded that this is too small a group to be able to separate those types of things out. He did not recall that they observed any differences that may be pre-pregnancy or during pregnancy. With other studies that they have conducted over the years, they have found that drinking prior to knowledge of pregnancy has a pretty large impact during the first 6 to 8 weeks when facial features may be laid down, for example.
- With respect to only 50% having the hook, Dr. O'Connor noted that when the investigators looked at their cut point, 11 of 12 were positive, which meant a sensitivity of 92%, which is highly significant. At least they would capture those true positives, although they would miss some others. Nevertheless, these are very positive findings. Dr. Conner responded that whether the ones they missed would turn out to be the lucky few in the Russian roulette who were exposed but not damaged, or whether they were damaged in a way that the corpus callosum will not pick up is not clear. The corpus callosum is just one marker.
- Dr. Olson noted that Dr. Conner had high sensitivity and low specificity. Dr. Conner replied that their specificity is very confusing because they are not claiming that it is specific to prenatal alcohol exposure. They are claiming that it is specific to the difference between controls, or unexposed, and alcohol exposed also.
- Ms. Ohlemiller inquired as to where Dr. Conner's center is with the funding of this project and whether they are still adding to the sample and if there will be additional measures. Dr. Conner replied that they are currently stalled out. Their funding has ended for this piloting through the consortium. They are applying within the consortium for a full project that would allow them to increase their sample size to 150 to 200 babies and would open the possibility of doing that in multiple sites around the country, in South African, and possibly in Eastern Europe. They do plan for additional measures as well. They would like the study to be much broader than just an ultrasound, so they are considering looking at developmental measures, early cognitive functions, doing dysmorphological exams on all of the subjects, getting growth measurements, etc.
- Dr. Berner asked whether in the future they planned to consider other risk factors such as tobacco. Dr. Conner responded that they looked at nicotine already and found that there was no correlation. They will continue to do this. Another progression forward they hope to do is the same study adding in methamphetamine and combined methamphetamine and alcohol exposure so they can attempt to separate that out.
- Dr. DeJoseph wondered whether there was anything about the method of delivery that had any bearing. Dr. Conner replied that he did not know. Given that this was done on a tight budget, to get as many babies as they could, they had to sacrifice on some data collection. The method of delivery is not a piece of information that was collected. Dr. Sokol added that method of delivery would be acute and would not seem to have any bearing.
- Dr. Olson inquired as to whether there was the notion that if they did another measurement of the cerebellum and found a similar kind of noticeable anomaly, they could raise the specificity. Dr. Conner replied that it was possible.

- Referring back to Dr. Conner's earlier comment that many things can damage the corpus callosum, Dr. Bertrand wondered whether there was something they could do additively that might narrow it down further. She pointed out that one frustration in this area for the clinical field looking at the more basic science is the lack of differential diagnosis data. Perhaps one way to go forward would be in an additive manner. Dr. Conner responded that this would be possible. One of the greatest frustrations about fetal alcohol syndrome and fetal alcohol spectrum disorders is that it is such a diffuse damage. The alcohol is pretty non-specific in who it will affect, and is pretty non-specific in what parts of the brain are damaged. Moreover, there is the interaction of timing, dose, et cetera. Getting whacked up side the head with a baseball bat is simple in comparison. There is a big lump and bruising in specific locations. However, it will be more difficult to pin down a region of the brain that is related more exclusively to fetal alcohol syndrome and he did not think they would get to that level for a while. Perhaps by adding in some other methods, such as diffusion tensor, they might.
- Dr. Bertrand wondered if classifications such as FAS Type 1, ARND Type C, etc. could be mapped onto the neuropsychological data (e.g., an ARND individual with math deficits that is identifiable by this particular imaging pattern). Dr. Conner responded that this would give them a corpus callosum FAS versus a cerebellum FAS or a frontal lobe FAS versus a parietal FAS. He said he saw great value in this clinically because this would identify a person's strengths and weaknesses as well as the underlying etiology of that. From a research perspective it is difficult because it is parceling out so much that the subgroups get smaller and smaller.
- Dr. Bertrand pointed out that if someone presented with a child who has a math problem, alcohol exposure is not the only thing that would be responsible for this. However, a math problem with the additive value of imaging that is known to go with the FAS math problem could be beneficial. Dr. Conner responded that at the same time, a lot of the math problems he was talking about with functional imaging have been studied by their colleagues in France who have looked at control subjects to find the inner parietal sulcus being very much involved in subtraction. However, they also did this with Turner's syndrome, which has at its core a math dyscalculia. They had the same sort of pattern that Conner, et al had in their FAS subjects, so it is not specific. No neuropsych testing for almost any disorder can be specific to a particular etiology. A person with a memory deficit could be Alzheimer's, a head injury, a stroke, or fetal alcohol syndrome. That is why history becomes one of the biggest keys. Getting the prenatal exposure history, trauma history, genetic history, et cetera is very important. Then they can start ruling out things and what they are left with may or may not be alcohol exposure.
- Dr. Floyd found it interesting that in two of the three presentations they had heard so far, there were some convergent findings, but there were non-convergent findings as well. Over a period of time, what will have to build is a level of convergent findings to the point that they could act upon them in terms of translating to practice. She noted that they would later have time to discuss that and how to go in stagewise, logical sequence to be able to arrive at building a science that would take them eventually to a psychometric test battery that will help delineate those who do not have the face but have the brain damage from alcohol.

Implications of Diffusion Tensor Imaging for Diagnosis of FASDs

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Dr. Lynch reported on a study conducted by Dr. Claire Coles' group using diffusion tensor imaging (DTI) to examine the corpus callosum in alcohol affected individuals. This study was published about a year ago. It was a pilot study for a large ROI that Dr. Coles now has in progress. For the pilot, they did structural, functional, and DTIs. The full study includes the imaging protocol as well as a full scale neuropsych evaluation, a medical evaluation, and interviews concerning adaptive functioning. This is a collaborative project with Dr. Xiaoping Hu, Director of the Biomedical Imaging Technology Center, and Staff of the Wallace H. Coulter Department of Biomedical Engineering, a Joint Department of Emory University and Georgia Tech.

The Atlanta Fetal Alcohol Study began in the early 1980s and is made up of a low socioeconomic status (SES), predominantly African-American sample. The mothers were identified prenatally. An interview was done at approximately the 4th or 5th month of pregnancy, during which time the mothers were asked about their health habits during pregnancy, including their alcohol use. Mothers were invited to be in the study if they did not drink at all during pregnancy or if they reported drinking a minimum of 1 ounce of absolute alcohol per week. The mothers for the samples upon which Dr. Lynch reported for this study drank quite a lot more than that. Their average was 14 ounces of absolute alcohol per week. She also mentioned that when the recruiting was done, if during the interview the mothers stated that they drank, there was an intervention done by the interviewer explaining that there were problems involved with drinking and they were urged to stop.

This is a longitudinal study (1980 to 2008). With respect to the data collection, in the early 1980s, there were two cohorts recruited. The one recruited between 1980 and 1984 includes 325 participants, while the one recruited from 1984 to 1986 included 130 participants. There were some follow-ups done during the preschool years. There was a large follow-up done at age 7 and another one done at about age 15. They are currently doing the third large-scale follow-up and subjects are between 21 and 25 years of age right now. They are doing the MRI and the neuropsych components during this follow-up.

The team became interested in the effects of prenatal alcohol exposure on white matter due to some of the studies discussed earlier. Their hypotheses are that alcohol-affected individuals have specific functional neurobehavioral deficits relative to SES matched controls; therefore, they have posited that: 1) using MRI, alcohol-exposed individuals have measurable differences in brain volume and in microstructure of white matter; and 2) in alcohol-exposed, affected individuals, there is a significant relationship between structural and functional deficits. In terms of methods, they have 16 young adults in this sample. The average age was 20.56 years. They were all recruited prenatally. There are 9 alcohol-affected and 7 SES controls. There were 7 male and 9 female and they are 94% African American. The functional assessment data they used is from the WISC-III that was administered during their teen follow-up five years earlier. The particular measure that they plan to look at is Processing Speed.

In the alcohol-affected group, 7 of the 9 had a dysmorphia score of 10 or above, and the 2 who had a dysmorphia score under 10 had IQ scores lower than 70, suggesting that they had some cognitive effects of alcohol exposure. The imaging was done on a 3T Siemens Magnetom Trio Scanner. The sMRI-morphometric scan time was 7:18 minutes. The diffusion tensor imaging (DTI) scan time was 7:27 minutes. Imaging focused on the corpus callosum, a large midline, and highly myelinated structure. The protocol was to pick up the participant at his or her home and take him or her to their lab where training was done for the functional part of the protocol and then they were escorted to the hospital for their imaging session.

The team focused on white matter, looking at it in two different ways. The first way was to look at the volume of the white matter and the other was to look at the microstructure of the actual white matter. They are using DTI, which is a fairly new technique. It is a way to measure the integrity of the white matter tracts. The researchers measure diffusion characteristics of water in the brain tissue along at least six non-collinear directions in space to map direction dependence of water. They are attempting to look at the directional dependence of the diffusion. Diffusion in the direction of the nerve fibers is faster and direction perpendicular to the nerve fibers is slower, so they can look at the pattern of the diffusion along the nerve fibers to determine the integrity of the white matter. This actually enables investigators to study white matter tracts. There are two DTI indices: Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC). FA is an indicator of diffusion in the direction of the fibers. If there is high anisotropy, diffusion will go right along the fibers. It is linear, orderly, and the fibers are likely to be dense. In terms of myelination, fibers that are highly anisotropic are also likely to be well myelinated. ADC is an index of diffusion perpendicular to the fibers. High ADC suggests much less directionality in the diffusion and the fibers are likely to be much less well myelinated. In terms of these measures, they expected alcohol-affected participants to have higher ADC and lower FA than the control group. This would indicate less white matter integrity in the alcohol-affected group.

They are focusing on the corpus callosum because it is a large, white matter tract often associated with efficiency of information processing and, in prior research, agenesis of the corpus callosum has been found at higher rates in FAS patients. Previous studies also have identified corpus callosum abnormalities in terms of size, shape, or displacement, so they wanted to focus on that tract as being quite important (e.g., Riley et al, 1995, Johnson et al., 1996, Swayze et al, 1997, Sowell et al, 2001, Bookstein et al. 2001). With respect to the sample characteristics, they have 7 control participants and 9 alcohol affected. There are no significant differences in the age, sex, or ethnicity. There were significant differences in the dysmorphia scores, which would be expected, with the alcohol affected group at 17.22. There are also significant differences on IQ and processing speed, with the control group being higher than the alcohol affected group on both of these variables.

Based on a midsagittal slice of 3D T1 weighted image, demonstrating the scheme of corpus callosum as divided for volumetric measurement, they looked at the genu and the splenium in particular as areas that would be important. This was related to some prior research examining the relationship between chronic alcohol use in adult women and structure and microstructure in these areas (Pfefferbaum & Sullivan, 2002).

Regarding the results in this study for volumetric measurements, for each area the alcohol effect measurements were smaller, but the differences were not significant between the two groups although there is a trend there. However, the lack of effect also may be due to the small sample size and relatively large standard deviations. However, their volumetric measurements showed no difference between the two groups.

To illustrate the areas that they focused on for DTI measurements, Dr. Lynch showed a midsagittal slice of a FA map corresponding to the same slice for volumetric measurement, demonstrating the ROIs of the genu (CCg) and the splenium (CCs) of corpus callosum for FA and ADC measurement. Results of the DTI measures indicate that the alcohol affected group scored lower on FA and had higher scores on ADC when compared to the control group, which suggests some abnormality in their white matter. Dr. Lynch showed box graphs of the distributions of values for FA and ADC in the splenium and genu for each group. In line with their expectations was the result that the alcohol affected group had higher diffusion and lower FA in each area than the control group.. There is very little overlap between these distributions.

The team found significant differences in the microstructure of the corpus callosum. They found that there is more diffusion in alcohol affected individuals and lower FA, which does suggest some abnormalities to the corpus callosum that could be related to connectivity issues as well. It could affect other white matter tracts also, although they have not looked at this yet. They were also interested in knowing whether these findings correlate with functional outcomes in affected individuals, so they decided to look at processing speed because it has been shown to be impaired in other studies of individuals with white matter deficits. FA in the splenium and processing speed are highly correlated. For FA in the genu, there also is a very high correlation between FA—directionality of diffusion -- and the processing speed.

In summary, for the morphometric comparisons, they did not find any significant volume differences, but there was a trend in the predicted direction. Possibly, if they had a larger sample this might be significant. The DTI results showed significantly lower FA and higher ADC in alcohol affected as compared to control group participants, which suggests lower white matter integrity among the alcohol affected participants. Processing speed is related to FA. In terms of what can be concluded from these findings, Dr. Lynch stressed that this is an exposure versus clinical sample, which means that they interviewed the mothers during pregnancy and the exposure level and amount were documented at that time, so the amounts and exposure levels are known. The white matter deficits may be associated with processing inefficiencies in alcohol affected individuals. These deficits could impact other areas, such as arousal, attention, and learning accounting for the global as well as specific deficits observed. These may be observable earlier than adulthood. This methodology may be a possible way of identifying a “signature” of FASD. Dr. Lynch pointed out that there are some limitations to this study. The sample size is very small. They used extreme groups for exposure (current study includes exposed / nondysmorphic group). Groups are not matched by IQ. No other disability groups are included in the analysis.

Concerning diagnostic issues, if they wanted to use a test like this for diagnosis, it must predict an outcome and also needs to differentiate the predicted disorder from other similar disorders. Other possible disability groups for comparison study include: Down’s syndrome, Williams syndrome, unspecified MR, fragile X syndrome (Barnea-Goraly et al., 2003), temporal lobe epilepsy (Arfanakis et al., 2002), and white matter deficits associated with prematurity. DTI as a diagnostic tool has some potential practical problems. Children are uncomfortable in the scanner, which can cause movement artifacts. Eligibility for scanning can be problematic. Some people are claustrophobic, have metal in their body, have non-removable jewelry, et cetera. The cost of the scan can be an issue because it may not be covered by insurance.

Dr. Lynch concluded that additional research is needed to determine the feasibility of DTI as a diagnostic tool for FASD. This method holds promise for dealing with diagnostic problems (e.g., exposed, but not dysmorphic children; or children without documented exposure or growth problems).

Discussion:

- An inquiry was posed regarding whether they had data on what time during pregnancy the exposures occurred and whether there was any evidence of white matter damage related to timing of exposure. Dr. Kable responded that they would probably have to wait for this type of data from the larger study underway.
- Dr. Miller requested that the investigators further discuss the methodology, given that she was experiencing difficulty imagining how they could image diffusion. Dr. Lynch replied that diffusion has to do with the molecules in the water in the white matter, so they try to contrast the motion that is created when the molecules move. The motion that is in the direction of the fibers turns out brighter or looks more apparent. Dr. Kable added that what they are mapping is the flow of water through that tract. The hydrogen atoms have a certain orientation and the scanner actually makes all the hydrogen

atoms spin in a certain direction and as it is flowing through, they can watch as it changes over the course of that mapping. Dr. Bertrand added that it is closer to an fMRI in that what is being tracked is movement—how fast and efficiently the water molecules are moving. Dr. Wright added that they use diffusion all the time. This is just applying it to a special group of patients and seeing the diffusion cut or view.

- With respect to the subjects, Dr. Miller wondered about their own use of alcohol and whether researchers captured any information pertaining to this. Dr. Lynch responded that she did not know about these particular people. At the teen follow-up they did ask about alcohol use, which was not very high. It was not significantly different from the controls at that point.
- Dr. Wright said she was impressed with the investigators' ability to track these subjects for such a long time. Dr. Kable replied that they have an excellent outreach staff. Dr. Lynch added that one person has been with them for 15 years and that she knows everyone and has a relationship with these families.
- Dr. Bertrand requested that the investigators speak more about the speed of processing measure. Dr. Lynch responded that was from the WISC-III, which uses two scales: the Verbal Scale and the Performance Scale, each of which has several subsets. One scale they used is a coding measure where subjects are given numbers and matching symbols and they have to write this down. The other one is a symbol search where the symbols are shown on one side of the page and they have to match the symbols on the other side of the page.

Discussion Regarding Innovative Approaches to Identification of FASDs

Facilitator: Jacquelyn Bertrand, PhD

Dr. Bertrand then solicited comments from the Task Force with respect to innovative approaches to identification of FASDs presented during the morning session.

Discussion:

- Dr. Morris pointed out that availability of such testing posed a major limitation. In addition, other than the ultrasound findings, they really depend on older more cooperative children. However, a diagnosis should be made before that. In addition to the dysmorphology examination which picks up some of the children who have FAS, it seemed to her that the more sensitive measure might be that of neuropsychological evaluations and obtaining an appropriate history. The history in FAS, not just the history of the prenatal life, but the trajectory of the behavior is often as informative as anything else. It is very important to correlate it with the neurologic findings as well as the neuroimaging findings, but it does not seem that this science is at the stage where it will be as helpful diagnostically as some of the neuropsychological testing. Dr. Bertrand said she did not think anybody around the table thought that imaging was ready to go out into the doctors' offices; however, she wondered if there was a future for it. She also wondered why, if neuropsychological testing was working, were these children not being diagnosed.
- Dr. Warren said that what they had heard during this meeting were presentations that were at a very basic research level, which was one reason it was not ready to go into the clinic. He was not sure that it ever would go into the clinic. These technologies are very expensive and they are dealing with a problem that has a fairly high prevalence even in the U.S. He thought the advantage of these approaches was to give them clues to move in the direction of refining their knowledge base with respect to an understanding of the types of deficits, which are then translatable potentially into other neurodevelopmental measures which can be more cost-effectively evaluated and also to define the deficit for the purpose of intervention. He does not see that in the future a diagnosis of FASD is going to be made on the basis of a \$600 or \$1000 scan. It will have to be done in a more cost-

effective manner or they will only be subserving a very small part of the population who can meet those costs.

- Dr. O’Conner thought another advantage was that if they could show that this is truly a brain disorder that has fairly regular findings, this has significant implications for diagnosis and payment by insurance companies for treatment, which is a very important practical aspect. In autism, once they were able to show that there are brain deficits, genetic links, et cetera, insurance companies could be sued for not paying for services. It might also be helpful in getting agencies to think about this as a disability that should be funded for services.
- Dr. Berner thought that this was being picked up more often as a matter of access to the services where available. In Alaska, they have worked hard to make the diagnosis widely available all over the state, even in the remote parts of the state. However, practically speaking they did not make a major breakthrough in services until they convinced the state’s Department of Education that ARND deserved the special treatment that FAS did. The schools rapidly found out that if they dealt with that, it was much less expensive to do it early. On a population basis, he thought that was the most they could ask for at this point.
- Dr. Morris clarified that she did not mean to say she did not think studies should be done because one of the obvious applications is, in looking at these types of studies done in genetic disorders, when they are able to look at the similarities and differences, that gives them an idea of what genes may be impacted—what genes literally are affected by the prenatal exposure to alcohol and what pathways. She said she thought all of this work was very important to elucidate those pathways, so they could determine the genetic predispositions to the more severe effects of prenatal alcohol exposure, and why there is such variability. Diagnostically, this is probably not the answer in terms of the general population.
- Dr. Olson said that as one of the people who makes an effort on a regular basis to do the testing, to define the problem and then render a diagnosis using their process (e.g., the multi-disciplinary team process), she would like to see the Task Force take an action step of proposing a research agenda that focuses on moving forward their understanding of brain-behavior relationships. The data they saw during the day and that has been accumulating over the past couple of years is beginning to direct her, on a practical basis, to know what tests to give. Sometimes they are not the standard tests in her usual clinical battery. She has a huge number of tests she can use, but she might not think to do a computerized test of response inhibition or focus very clearly on steadiness in fine motor control. Yet, those might be the tasks that are most clearly tapping into the kinds of deficits that are apparent when alcohol affects a child prenatally. Therefore, she proposed the idea that the Task Force consider trying to encourage brain-behavior research to move forward, perhaps not with the ultimate goal of using MRIs for diagnosis, or maybe not even ultrasounds for detection, but to help find the neurocognitive tests needed to better pick up the non-dysmorphic children. She is having trouble convincing the schools and helping parents change their attitudes without a picture of the brain and a clear statement of the fact that this is a neurologically impaired individual even though it cannot be seen in their face and their IQ is fine. She thought the Task Force had the charge, based on the charter, to advise funding to move in that direction. She suggested that they create a workgroup to write a letter or a short action paper to encourage that kind of research.
- Dr. O’Connor said that in terms of funding agency priorities, if they thought about what they would have to do in terms of a comprehensive behavioral and functional assessment, that is much more expensive than a \$600 or \$1000 MRI. She agreed with Dr. Olson that if they could refine their tools based on brain and behavior research, they would have a much more efficient way of doing this and making recommendations for specific treatments.

- Dr. Olson indicated that the other place she would like to have this brain-behavior research direct her is once she has identified the children, she might begin to have some innovative ideas about what to do to ameliorate problems early and get a better grasp on what she could do in the early intervention period. She was the one who argued against that at the beginning because they were not finding children early enough, so it did not seem efficient to direct their intervention research to the younger children then. She said she completely took that back because at this point, she believes there are some neuroprotective kinds of agents, enrichment activities, and really great ideas for intervention. However, she needs the brain-behavior science to direct her in the right way for the interventions as well.
- Dr. Warren commented that when he heard a recommendation for funding for agencies that fund research, there were only two agencies at the table that fund research: CDC and NIAAA. In terms of getting into the basic research, most of that is NIAAA. He noted that later in the day he would be presenting on some of the work they are doing in this area, which would touch upon many of these themes. These areas are covered within NIAAA's strategic plan, and it is a major focus of their institute currently. One issue that had arisen was early intervention. It is known from animal models that this appears to make a difference. It is known from other behavioral disorders in humans that it makes a difference as well, such as with autism. Their hope is that it will make a difference for FAS. An important issue for them to address would be to improve the capability for recognition as early as possible and even prenatally. He wondered if others believed they really could have success with an early start. Dr. Olson responded that she absolutely thought they could make a difference. Dr. O'Connor responded that they have data that they do have success.
- Dr. Berner pointed out that another area that has been overlooked somewhat is one of the genetic issues that is addressable. There are a couple of cases of fraternal twins in Alaska, one of whom has clear FAS and the other which has been exposed, but who does not have FAS. Clearly, the environment for both was the same, but the genetics were not. This seemed to be a group to target and it would not matter whether they are adults or infants. Dr. O'Connor thought that some of the genetic studies that show protective effects, the amount of variance accounted for is not very high. There are some studies showing some protective effects based on the ability to metabolize alcohol during pregnancy.
- Dr. Warren indicated that at this point, there are two genes that appear to offer some protection: the ADH1B2 and the ADH1B3. While the reason is not known, it probably has to do with the fact that the dyphoric effect created by drinking too much if one carries either of those probably discourages alcohol consumption, so people who carry these do not drink as much as others. Basically it is a dose-response effect. In animal models there are variabilities dependent on genes, but there is no evidence for that at this point in humans, although they would expect this to be the case. More research is needed to know what that is. There are some pressing research questions from 30 years ago that remain today. He thinks in addition to all of the fundamental research they are doing, they have to be emphasizing some targets and moving forward. Developing a better understanding of the neurobehavioral profile or deficits and defining them so that even if children are identified earlier, then there is some indication of the direction in which to go. The imaging studies should help them get there, but it has to be coupled with brain-behavior. This must be done immediately. He came into NIAAA when this was emerging 30 years ago and the same issues remain. Also, one of the issues in terms of establishing FASD as a real brain disorder is establishing it on the basis of those agencies that pay for services so they understand that they are not just dealing with a badly behaving child. His hope would be that families could obtain services merely on the basis that a child is showing a particular characteristic profile, which is different from a child behaving in a deviant manner coupled with either the evidence of prenatal alcohol exposure or the probability of prenatal alcohol exposure.

He has seen a transition in some of the states and counties he deals with where at least FAS is accepted as a diagnosis to be eligible for services. This should be true in all states and counties. The same must be done for FASD. If the imaging knowledge can establish a knowledge base so that the appropriate agencies or the appropriate legislatures can basically make such a decision, it would greatly add to this field. Anything the Task Force, an advisory body to the Secretary of Health and Human Services, could do to facilitate this would be of great help in that direction.

- Ms. Ohlemiller said she could not agree more that it would be a beautiful world if they could just have services standing by for all children who were struggling. Unfortunately, that will not be the reality in the current funding climate. Even children who have identifiable disorders are fighting for services. It would be more difficult for individuals with FASDs. She thought they would do a disservice to the community by not providing some leadership around what FASDs are and that leaves out the prevention piece. They certainly will not be able to get preventive services for children who are not yet struggling, but who will be. They must get in early with children and anything they could do to advance that would be extremely helpful. The way she saw it, there was a triangle that needed to happen (three points which were all interrelated), one of which is the neuroimaging. The ultrasound work was particularly intriguing to her because every hospital in the U.S. has an ultrasound machine. They have the imaging, the behavioral phenotype (and the cognitive and neuropsychological information goes with that), and the third one they never talk about is clinical judgment and helping to provide guidance on that. Basically, that is what is occurring in the community currently. That is how they get the diagnosis of anything other than FAS; that is, a child without the face is being diagnosed through clinical judgment. With that in mind, she thought the Task Force should develop a plan or advisory statement to whoever needed to listen that involves all three of those concepts. They also should stress that one cannot wait for the other. These must move forward together.
- Dr. Sokol said that in terms of the utility of imaging, it was wrong to focus on its sensitivity and think about it as screening. There is nothing to say it would be valid. The real issue to him was specificity. While they might be able to document brain damage, they need the comparisons with other entities so they can do something with true specificity—not just that it is *some* damage, but that there is a pattern even if it is syndromic. This is work that still must be done before any kind of recommendation could be made. Dr. Bertrand responded that they could make a recommendation that this work should be encouraged and resources should be devoted toward it. It seemed to Dr. Sokol that this was a peer review issue for the institute. Unless they were going to earmark, not a good thing to do, if the investigators came up with something interesting and the institute makes a peer review, it will happen. He also suggested that imaging might be helpful as a metric. When there is a secondary prevention methodology or an intervention, if someone gets any change in behaviors, it would be nice to know whether changes could be induced that are seen either in structural or functional MRI. Some animal work has been done this way.
- Dr. Wright pointed out that in the world of child abuse, the phrase “shaken baby” did not have enough impact to change enough people’s behavior whether it was funders, caregivers, or parents. Therefore, that language is being changed to “non-accidental brain injury.” Imaging has led to a new articulation and strong, more serious, more scientific words were needed to get funders, scientists, and others to understand the global impact of that injury. Perhaps ARND is too squishy or has drifted into that type of category. Now that they have more precise imaging, frankly they may need to make up a new term that is more scientific and come out with something that helps to address the issue. They could probably write something to state that the emerging work of imaging is causing them to rethink screening tools, diagnostic architectural tools, mapping the changes in behavior after intervention, et cetera. If it has a mapping tool to say it is not a squishy diagnosis, it has a very different meaning.

- Ms. Mitchell said that if they are not identifying the first child, second child, or third child, when a woman has the 5th or 6th, she is suddenly a bad mother. This mother may have had no idea that her children, with a collection of problems, had anything to do with prenatal alcohol exposure. This is one reason NOFAS is convinced that they need to put a name to it. She said she believed a lot of the “soft petalling” was rooted in the stigma. Physicians do not want to deal with this issue with moms and no one wants to say what it is. Everybody seems petrified to talk about prenatal alcohol exposure. Therefore, it is much easier for clinicians to call it something else, especially if it does not connect anything to prenatal exposure. From a prevention standpoint, she thought they were making a mistake. If the Task Force does not take the power they have been given to move this forward, she thinks they will have themselves to thank when more children are born alcohol affected.
- Dr. Wright thought that by virtue of the studies currently underway that they heard about earlier, they are moving forward. She wondered whether the Task Force could be part of the definition of where they wanted to go. It seemed like the goal was to use technologies to define brain pathologies and associate those pathologies with functional deficits. It did not seem like they could make a practice recommendation at this point.
- Dr. Warren said he thought they knew the directions they had to go, but it would not be cheap and in the current funding climate with constrained health budgets, this posed problems. For the first time in the 30 years he has been with NIH, the President’s budget is calling for a decrease in actual dollars, not in inflation-adjusted dollars. He recently had a meeting with their institute director for one of the FAS related projects that is very relevant for the Task Force and he mapped out the direction they needed to go. The director looked at the list and declared that it would cost at least \$14 million, which is probably a factor of about four more than they have. They will simply have to make some difficult decisions, make the right investments, and hope that the peer review committees agree with them in those directions so they can try to have products that are available for the prevention and clinical communities to use as soon as possible.
- Dr. O’Connor cautioned the group in that they are out of the realm of the laboratory now, so that when they look at neuroimaging of children who are alcohol exposed compared to the neuroimaging of the adult alcoholics, there is separate independent damage for cigarette smoking, alcohol, other drugs, trauma, et cetera. So when they look at these children and declare them alcohol exposed, 80% of them are also tobacco exposed. The lifestyle that alcoholic women are living includes trauma, violence, other drugs, tobacco, mercury, other environmental toxins, etc. The challenge is that the general practitioner on the street cannot tell whether something is only from alcohol. Medicaid is going to start reimbursing screening and brief intervention, which is something the Task Force can and should support as a body. Half of their task is to add on the prenatal piece. They could make a difference immediately in just supporting those things.
- Dr. Warren noted that the reason this panel was known as the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effects and not the National Task Force on Smoking and Adverse Outcomes is due to a fair amount of epidemiological research conducted over the years that showed that as a potent teratogen, alcohol is in a league greater than many of the other substances frequently encountered. While that did not mean to say that smoking and pregnancy was not a problem, by and large when alcohol is present, it is the greatest of the risk factors. If they begin to focus on one as the lead in, alcohol is a good lead in. At the same time they could address the smoking and nutritional issues. They still cannot explain why SES is such a risk factor. His hypothesis is that it will turn out to be nutrition. This will be a major factor in why investigators who published this about 20 years ago found that given the same level of alcohol exposure, the outcome is so much worse in individuals who are in SES classes 4 and 5 than in SES classes 1 and 2. They should also consider this, but his

institute has experienced difficulty in getting applications through the peer review system. They are all risk factors.

- Dr. O’Conner indicated that in their WIC study of low SES women, once the providers had the tools to provide a brief intervention, they would do it with everything (e.g., smoking and other things unhealthy for the child). Providers need the tools and the confidence to talk to women about their drinking.
- Dr. DeJoseph pointed out that they must bridge the divide between the laboratory and the diagnostic studies.
- Ms. Ohlemiller said there seemed to be two issues arising in their deliberations. First was that the Task Force is charged with sitting in an advisory role for funding agencies and decision making arms. Second was that they needed to leave this to peer review. She asked for clarification about whether this was an either/or situation. She called attention to the current funding climate, which is predicated only to grow increasingly worse. Peer review sometimes breaks down as a mechanism to get what the community needs, particularly in a negative funding climate. Dr. Bertrand responded that it is not really an either/or because agencies do make decisions about how they will spend their dollars and what direction they will take by putting out RFAs. Congress may encourage that they pursue a particular topic, but if Congress mandates a particular study, those are earmarks, which are completely different. In all cases, studies go through the peer review process in an effort to get to the best science going forward. Dr. Floyd added that it also depends on where the agency is at a particular point. CDC is increasingly being encouraged to develop programs that are focused on prevention that demonstrate positive health impacts. Clearly, one of the important roles of the Task Force is to understand the balance of action and funding intent and moving forward on important fronts at the same time. Based on what they had heard during this meeting, there is a lot of interest and they would like to find a role for the Task Force to play in encouraging this work. CDC, NIAAA, SAMHSA, and a number of other agencies are very interested in primary prevention. In January 2007, Medicaid will begin paying for screening and brief interventions for Medicaid patients. These are women who could be delivering a child, so this is an opportunity. She thought they had a lot of diversity within the Task Force group, which would help them address the issues in a broad-based manner.
- Dr. Bertrand requested feedback regarding whether there was a concrete product that the Task Force was ready to recommend, or if it should go to a working group to discuss potential concrete product(s). She heard two things: 1) development of an advisory statement to somebody about this being a serious brain damage disorder; and 2) does the Task Force want to address the ARND issue? Do they want to leave it as a clinical diagnosis with practitioners using their own criteria, or do they want to do something else? There is an existing congressional mandate that the Task Force address this, which is their decision.
- Dr. Berner thought they could make a useful recommendation to the Department of Education, and he wondered whether this group had ever worked with them. Dr. Warren replied that the Department of Education has representation on the Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS). This is the internal government body that is the counterpart to the Task Force. The Department of Education is a major player on that committee and they came on board very enthusiastically. When ICCFAS first made contact with the Department of Education, they did not have any interest in FAS. They indicated that they focused on developmental disabilities. For example, if a child cannot read, they work on reading. If a child cannot do math, they work on math. They have now fully come around.

- Dr. Brown recommended that they work with the Department of Education in some different ways in addition to working with them through the ICCFAS. The Division of Research in Special Education has been moved out of Special Education. They still have funding for demonstration work; however, the research funding has been moved to the Institute for Educational Sciences, which has its own set of criteria. The Task Force is not working with them currently. Also, the diagnostic process in early intervention is not being addressed in a systematic way. The Center for Excellence and the State Early Intervention Coordinators around that need to be addressed systemically. Their proposal for changes in the IDEA regulations were minor, but were not accepted. She agreed that Department of Education involvement was extremely important. If they understood the cost benefits in terms of implementing more structured interventions, that would make a major difference. Dr. Bertrand added that the Department of Education's budget was limited, which factors into what they can and will do.
- Dr. O'Connor inquired as to whether there were data on the cost-benefits of making the diagnosis and treating children appropriately through education. Dr. Brown replied that if there is not, there should be research in this area. Dr. Warren added that this would be for an economist to determine. While there are data on the cost of an FAS case, he did not think there were data on the costs of not intervening. Dr. Berner added that they considered this in Alaska and it turned out that the same technology used to show efficacy for immunization could be used to show efficacy for FAS. This entails determining the cost for an event that does not happen. CDC worked out the method that Alaska used, which seemed to be perfectly applicable in Alaska.
- Based on what they hear from their regional centers in California, Dr. O'Connor pointed out that once they "open the flood gates" and make this an official category of development disability, they would be overwhelmed with requests.
- Dr. Olson requested further clarification regarding what the Task Force could and could not do. She understood that they could write advisory letters as they had to the Department of Education, which did not result in what they hoped for; that they could facilitate hearing from people trying to move other organizations forward on this issue; and that a monograph could be published following a major amount of effort (the *FAS Diagnostic Guidelines* took about 5 years). Beyond that, she wondered if the Task Force was allowed to make a consensus statement and publish it in an appropriate forum. She said she wanted to formulate a motion for the Task Force to convene a small working group to meet between this and the next meeting to propose a product of some sort regarding brain-behavioral relationships, early intervention, intervention for older affected individuals, and prevention. However, she wanted to be clear about the Task Force's allowed activities. Dr. Floyd responded that normally consensus statements come from NIH. However, they took on the publishing of the guidelines which was a consensus of opinions of from the Task Force and other experts.
- Ms. Mitchell inquired as to whether the Task Force could encourage CDC to move forward with ARND, perhaps by forming a committee. From NOFAS's perspective, research is great and they certainly supported on-going research. However, she stressed that they want to see the existing research move into practice. They do not want to wait another 20 years. Dr. Floyd responded that the Task Force could do so. They could consider reforming the ARND Working Group, although they still face the possible sunset of the Task Force. The ICCFAS used to conduct special sessions where they convened national experts to deliberate on the issue and consider future directions. The Task Force and the ICCFAS could work together to convene such a session and develop joint recommendations based on the findings. Ms. Mitchell pointed out that they needed to bring in clinicians as well as researchers. Many clinicians tell her that they know the difference between a child with ARND and a child with a variety of mental health and environmental issues. There are clinicians identifying ARND/FASD. They are all seeing the same things, but are using different language to describe it because they are being trained to use different diagnostic tools. The Task

Force and ICCFAS need to hear what is being done in the field. Dr. O'Connor agreed that while they do have to have a scientific base, when they get too scientific they can become immobilized. She herself has no problem diagnosing ARND and feels perfectly comfortable stating that a child has been exposed to alcohol and has neurobehavioral sequelae associated with that. Dr. Morris also agreed that, as a clinician, she could make an ARND diagnosis—it is a gestalt just like the facial features. With the guidelines published, she believed that the time was right to bring together all of the clinicians (including geneticists, psychologists, neuropsychologists, etc.) to develop a definition for ARND.

- The Task Force concurred that they were not ready to formulate any motions at this point in the deliberations. They agreed to hear further presentations and then reconsider the discussions on this issue.

Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS) Update

Kenneth R. Warren, PhD

Dr. Warren extended greetings to the Task Force from the entire ICCFAS Committee. Given that there were a number of members new to the Task Force, Dr. Warren began with a background of the ICCFAS. He reported that the ICCFAS was created in response to a recommendation from the Institute of Medicine (IOM) in their report in 1996 for the establishment of such a body to have coordination among all the agencies of the Department of Health and Human Services (DHHS), and to coordinate the federal response on FAS and related disorders. The IOM designated that NIAAA take responsibility just as legislation designated that CDC take responsibility for the FAS Task Force.

The purpose of the ICCFAS is to improve communication, cooperation, and collaboration among disciplines and federal agencies that address: health, education, developmental disabilities, alcohol research, and social service and justice issues related to prenatal alcohol exposure. Since its inception in October 1996, there have been three chairs of the group: Mary Dufour, Faye Calhoun, and Kenneth R. Warren.

The initial charge of the ICCFAS only called for the establishment of collaboration among the various agencies of DHHS. However, they subsequently expanded by inviting in the Department of Education and the Department of Justice because of the interest both have in FAS and FAS-related issues. Included within the DHHS are representatives from the Indian Health Services (IHS); CDC; Health Resources & Services Administration (HRSA); the Agency for Healthcare Research & Quality (AHRQ); National Institutes of Health (NIH) with 27 institutes and centers, 2 of which are active members currently: NIAAA and the National Institute on Child Health and Human Development (NICHD); and SAMHSA. The agency within the Department of Education that has a very active member is the Office of Special Education and Rehabilitation Services (OSERS). In the Department of Justice, the Office of Juvenile Justice and Delinquency Prevention (OJJDP) has been a very active member as well. The current membership includes the following: Ken Warren, NIAAA, Chair; Lynn Haverkos, NICHD; John McGovern, HRSA; Ammie Bonsu, SAMHSA; Charlotte Mullican, AHRQ; Paul Brounstein, SAMHSA; Ann Smith, ED; Tammy Clay, IHS; Karen Stern, DOJ; Louise Floyd, CDC; Judy Thierry, IHS; Laurie Foudin, NIAAA; Sally Anderson, NIAAA, Executive Secretary.

On the staff of NIAAA, they are fortunate to have recruited an appeals court judge who has visited Dr. Warren to say that the adult justice system has a large amount of problems associated with FAS. Therefore, the ICCFAS plans to make an effort to bring in the Adult Justice part of the Department of Justice as well.

The themes around which the ICCFAS bases the foundation of its work includes: prevention of drinking during pregnancy; intervening with children and families affected by prenatal alcohol exposure;

improving methods for diagnosis and case identification; increasing research on etiology and pathogenesis; and increasing information dissemination. That the goals sound identical to those of the Task Force is not a coincidence. The difference between the two bodies is that the ICCFAS is really a working body for agencies within the federal government, which gives them some freedoms that the Task Force does not have, but alternatively the Task Force has some capabilities that the ICCFAS does not have. The interaction in various activities with ICCFAS include: basic and clinical research, best practices & patient treatment, health care delivery, justice rehabilitation of persons with FASD, education of children with FASD, and data for public health policies. They basically produce the data that influence public health policy.

Some of the noteworthy federal actions in the fight against FASD include: publication of the Institute of Medicine's report: *Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment*, 1996; formation of the Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS), October 1996; establishment of the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect in 2000 and its inaugural meeting in December 2001; creation of the FASD Center for Excellence by SAMHSA in late 2001; re-issuance of the Surgeon General's Advisory on alcohol use during pregnancy in February 2005 (for which the Task Force played a major role by recommending that it should be issued); and the designation of September 9th as National Fetal Alcohol Spectrum Disorders Day, a day for formal annual recognition of and focus on alcohol-related birth defects, 2005.

Dr. Warren indicated that the information on noteworthy federal actions was compiled by Sally Anderson, but said if he had prepared the information he would have gone back to 1977 when the first health advisory was issued by the Department of Health, Education, and Welfare before it changed its name. That was the so-called famous "Two Drink Limit," which basically warned people not to drink more than two drinks per day. It was very conservative because prior to that point, the existing perspective was that alcohol was perfectly safe during pregnancy and they had just had their first national conference on FAS where they reviewed data and realized that there was a major problem here. They went forward with a very cautionary statement because they did not know what sort of reaction they would get from the field, but by 1981 there was already enough acceptance that the first health advisory had been published from the Surgeon General, followed with legislation in 1988 and 1989 that George Hacker had a role in helping to establish for the alcoholic beverage warning label. The U.S. was the first country, and may still be the only country, to have the warning label.

THE ICCFAS collaborated with the FAS Task Force on the Surgeon General's Advisory on Drinking and Pregnancy. NIAAA drafted the advisory, which SAMHSA and CDC reviewed. CDC coordinated document preparation and initiated correspondence. In January 2005, ICCFAS provided a list of 12 proposed venues for presentation of the advisory by the Surgeon General and six ideas on message promotion. In March 2005, six ICCFAS members and nine Task Force members participated in a brainstorming teleconference call on dissemination of the advisory. CDC and the SAMHSA FASD Center posted the advisory on their websites. NIAAA highlighted the advisory in its 2005 spring newsletter (printed and on their website). NIAAA and SAMHSA included the advisory in information packets for their media contacts on National Alcohol Screening Day, April 7th, this resulted in national and local press coverage, (e.g., HealthNewsDigest.com; Evansville Courier & Press).

Dr. Warren then offered highlights on those agencies represented on the ICCFAS, but who were not in attendance at the Task Force meeting.

Highlights of some recent OJJDP activities include the following: in FY2006, OJJDP funded the Marcus Institute to increase community outreach to educate parents, professional, and students about FASD; Spring solicitations for Field-Initiated Research and Evaluation projects resulted in 145 proposals (only one was FASD-related, so a repeat of this solicitation is planned for FY2007); OJJDP led the ICCFAS

Work Group on Juvenile Justice Issues; and OJJDP consults with SAMHSA and NIAAA on FASD-related justice issues.

Highlights of selected Department of Education activities include: chairing the ICCFAS Work Group on Education Issues, which will host a summer 2007 meeting to summarize the state of knowledge and identify gaps and opportunities to enhance the school experience of children with FASD; working with State Directors of Special Education Programs to summarize education experiences and current use of FASD-related resources to identify ways to help them and their teachers improve education for children with FASD; and evaluating existing FASD-related training and educational tools for teachers and other school system staff. The 2007 meeting will examine current educational approaches and recommendations on learning and behavioral issues, the latest developments from current research, and model systems from several state educational systems. The lead for this conference will come from ICCFAS representatives from ED, NIAAA, NICHD, CDC, and IHS, with assistance from other members of the ED Work Group.

Highlights of selected recent HRSA activities include: patients at the 96 HRSA Healthy Start sites screened for alcohol use, counseled and referred, as appropriate -- a recent HRSA meeting for Healthy Start staff included training about FASD; to reduce problems with reimbursement, three "in progress" studies are testing the effect of multiple risk assessment tools that combine identifying domestic violence, depression, substance abuse, and alcohol use; and a FY2006 grant to NOFAS which includes training staff at five HRSA Community Health Centers on screening for alcohol use, knowledge about FASD, and patient education.

Highlights on selected IHS activities include: expanding activities work with Canada to facilitate networking and cooperation among First Nations and American Indians and Inuit and Alaska Natives; beginning analysis of data from the National Survey on Children's Health and National Survey on Children with Special Health Care Needs; updating forms for use at health facilities to improve future data analyses and collection; and offering a spring conference with Canadian partners in Ottawa (about 100 attendees). One focus of the conference was to explore the use of the prevention techniques associated with mentorship programs.

Selected examples of NICHD FASD-related activities include: major program emphasis on understanding mechanisms of health risk behavior change in children and adolescence; a May 2006 conference on the effects of media on cognitive, social, and emotional development of children and adolescents; and co-funding with NIAAA projects on the relationship between alcohol consumption during pregnancy and SIDS; and creating an Infant Health Consortium in Northern Plains Indian communities. FASD-related research is found throughout the research portfolio of NICHD, including projects supported through the Child Development and Behavior Branch, the Perinatology Branch, and the Mental Retardation and Developmental Disabilities Branch. Projects include basic and applied research and support for scientific meetings with sessions on relevant topics. FY2006 funding for projects with direct relevance to FASD is \$4 million. Additional millions of dollars fund projects studying basic research on maternal health in general, overall childhood development and well being, and numerous projects on cognition and behavior.

In conclusion, Dr. Warren shared the ICCFAS website address with the Task Force, which is as follows: <http://www.niaaa.nih.gov/AboutNIAAA/Interagency/>

Discussion:

- An inquiry was posed regarding the date of the next ICCFAS meeting. Dr. Warren responded that the next meeting would be in November 2006. It will be a working group meeting of members, which

includes only federal agencies. However, they do convene other meetings to which they invite experts.

- Dr. Olson asked for a contact from whom to learn more about the Summer 2007 Teacher Conference, and she wondered whether it would be an open conference. Dr. Warren replied that the contact would be Sally Anderson and that it would be an open conference.

Federal Updates

National Institute on Alcohol Abuse and Alcoholism (NIAAA) Update

Kenneth R. Warren, PhD

Dr. Warren updated the Task Force on the activities of NIAAA. He first reported budget data pertaining to the alcohol and pregnancy budget for NIAAA over the course of the last five years. He clarified that the last year for which he included data was FY2005, given that FY2006 would not end until September 30th. Given the fact that the budgets within NIH have not been growing, he expected that the budget for 2007 would look about the same as the 2005 budget. They have about 97 FAS or alcohol and pregnancy related projects, with a cost of about \$27.5 million. This represents 7.7% of NIAAA's overall budget for the broad spectrum of alcohol related problems, which totaled \$438.3 million in 2005. The budget is projected to be \$435 million for 2006, an actual decrease in dollars. This is the first time in the 30 years that Dr. Warren has been with NIAAA/NIH that he has witnessed an absolute number decrease in the appropriation. This represents a half a percent decrease.

In 2006, NIAAA produced a new strategic plan. Dr. Warren highlighted the FAS and alcohol and pregnancy related components of that plan and explained how they are addressing some of the issues. For the new plan, NIAAA decided to adopt a lifespan perspective. This was developed from the perspective that the emergence and progression of alcohol-related health problems (including FASD) are influenced by many changes in biology, psychology, and exposure to environmental inputs over the life-time. Understanding these factors is key to prevention and treatment of these disorders. While the *fetal* period is one of the key phases of the lifespan, fetal alcohol exposure by itself will have repercussions throughout the life course: Pregnancy – Birth – Postnatal Development – Maturation.

The neurobehavioral profile is one of the highest priorities within the NIAAA strategic plan, with the continued emphasis on research leading to the identification and characterization of the neurobehavioral profile of FAS and ARND. This also includes determination of the extent to which the FASD neurobehavioral profile is unique from deficits observed in other disorders. Evidence to date suggests that no single attribute is likely to be solely unique to FAS, but similar to facial dysmorphism, the cluster of behavioral impairments may well be specific. Knowledge of the neurobehavioral profile is critical for development of interventions for FAS and ARND, and for diagnosis.

With respect to a neurobehavioral phenotype, in 2003, NIAAA established the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) to address research questions that were more effectively pursued with multiple investigators at diverse, international research sites. One of the key issues underlying the creation of CIFASD was the issue of the FAS and ARND neurobehavioral profile (or phenotype). Other key issues included improvements in diagnosis, prevention, behavioral, pharmacologic and nutritional interventions. Although research on neurobehavioral attributes of FAS had been pursued for many years prior to the creation of CIFASD, a major limitation was that different studies had used different, and not necessarily compatible, instruments. This impeded the ability to establish a common database for analysis of the neurobehavioral profile. In addition, each population sample was, in itself, relatively small. Pooling offered advantages. Therefore, a major objective of CIFASD was the development of a neurobehavioral database from FASD research studies around the world. CIFASD investigators agreed on common instruments to be used and employed them in multiple populations involving the U.S., Finland, Russia, and South Africa. Subject population ages range from approximately

4 years to 16 years. The research data is uploaded into a CIFASD database. Statistical analysis is underway to develop a “statement” of the neurobehavioral profile of FAS and ARND. It is anticipated that this profile will aid in future diagnostic efforts. As with other disorders, future research findings will likely contribute to and improve our understanding of the diagnostic profile. But this initial description will be supported by statistical analysis on a large, world-wide sample. With respect to non-invasive imaging to define structural deficits underlying FASD, another strategic plan goal is to “Refine and increase knowledge about specific brain structural alterations underlying the FASD neurobehavioral deficits through imaging technologies (e.g., fMRI, MEG).” Indeed, imaging research is also on-going in a number of research projects, including CIFASD. These projects seek to identify the functional and structural brain deficits that underlie the FASD neurobehavioral phenotypes.

Regarding treatment of individuals affected by prenatal alcohol exposure, one strategic plan goal is to “Use the knowledge from increased understanding of the neurobehavioral phenotype and underlying structural deficits to design and study interventions to improve functioning of children with FASD.” Within CIFASD, pilot trials have already been implemented in South Africa: metacognition and pre-literacy skill training have provided very promising results. In another approach, the plan encourages continued exploration and understanding of nutritional and pharmacological interventions (e.g., choline, maternal nutrition) and preliminary studies are underway.

Another strategic plan goal pertains to diagnosis. The facial dysmorphia of FAS is a very valuable “biomarker” for FAS. However, with a limited number of trained dysmorphologists, remote diagnosis (telemedicine) remains a challenge, particularly when diagnosis is based on two-dimensional pictures. The human face is three-dimensional (3-D) and 3-D cameras are becoming more available in medical settings. Within the strategic plan and CIFASD, several facial imaging opportunities present themselves: (1) establish the effectiveness of remote facial diagnosis by use of 3-D images sent to a trained clinician at a remote site; and (2) develop computer algorithms for analysis of 3-D photographic data by the computer itself. Two computer-based analysis approaches are underway in CIFASD, one of which is to define facial area for the computer to analyze. The other is to have the computer establish its own facial recognition algorithm based on comparison to normals or other disorders with “machine learning.” The application of findings would be to provide a diagnosis and to uncover dysmorphic features not recognized by the “human eye” and potentially improve the ability to recognize FAS and provide new insights on FASD. The combination of 3-D facial imaging, brain structural imaging, brain functional imaging, and neuropsychological performance measures may offer clues in the functional relationship between facial dysmorphology and the underlying brain structural and functional deficits.

Other potentially new diagnostic approaches include prenatal ultrasound and neo-natal transfontanelle ultrasound. These may aid in early case recognition through identification of structural deficits at an early point in life to permit early initiation of supportive interventions. A CIFASD prenatal ultrasound project with CIFASD in the Ukraine has provided valuable data related to the ability to diagnose FAS prenatally, and in identifying specific regions of the brain affected by prenatal alcohol (e.g., the volume of the frontal lobes). Also, new and emerging metabolomics technology may provide unique metabolic signatures that may serve as markers for FASD. Biomarker development continues for alcohol exposure in pregnancy (e.g., adducts of ethanol, fatty acid ethyl esters, ethyl glucuronide, etc.)

The NIAAA strategic plan also encourages the implementation and refinement of preventive interventions in concert with the IOM model, with emphasis on high-risk populations (*selected*) and individuals at high risk (*indicated*). Also encouraged is continued exploration of basic research on potential protective agents such as the neuropeptides NAP and SAL, cell-adhesion molecule L1, anti-oxidants, choline, and others. In terms of health service and prevention research, the strategic plan supports identification of barriers to implementing alcohol screening in primary care and obstetric practice, and exploration of the

acceptability of new screening technologies, such as computer assisted interviewing. NIAAA is working with the ICCFAS and HRSA on addressing barriers.

Pertaining to alcohol, genetics, and FASD, both animal and human research have demonstrated that genetic factors play a role in prenatal alcohol adverse events. In humans, ADH1B*2 and ADH1B*3 are protective for FAS and FASD (likely associated with decreased drinking from elevated acetaldehyde). There is evidence of alcohol-induced alterations in gene expression found in the early embryonic stage: Pax6, Otx6, Sox3, NCAM, TBX5, VAX2 + others. Disruption of several of these genes produces outcomes consistent with the types of deficits found in FAS (e.g., microcephaly, micro-ophthalmia). Mechanisms may also involve ROS and RNS as anti-oxidants provide some protection (ascorbic acid, catalase, peroxidoxin 5). The strategic plan recommends continued exploration of genetic risk factors in FASD.

A lifespan transcending theme is epigenetics. Epigenetics is a major alcohol-related theme throughout the lifespan, with critical importance for the prenatal period. Stable alteration in the genome that does not involve change in the DNA sequence itself is an additional source of biological variability. This involves chemical modification of DNA and histones, including those in response to environmental stimuli. Alcohol and its metabolites can be important factors in epigenetics, either directly or through its effects on metabolic events underlying epigenesis. An important potential site of epigenetic programming is the hypothalamic-pituitary adrenal (HPA) axis. Animal model research has shown that alcohol exposure during fetal development can reprogram the HPA axis to increase HPA tone throughout life. Sustained elevation of stress hormones can produce adverse effects on behavior, cognition, emotion, physiology, metabolic and immune function with implications for FASD and other adverse effects. The strategic plan encourages the application of genomic, proteomic, and “epigenomic” technologies to examine alcohol’s effects on gene expression patterns involved in development. Also encouraged is further examination of the interaction of alcohol with additional factors, such as maternal stress and nutrition, in altering epigenetic patterns and identification of sites where the interaction of these factors changes gene expression.

With respect to neuroscience, the NIAAA strategic plan encourages the further exploration of mechanisms through which alcohol impairs the functioning of various neurotransmitter systems (GABA, NMDA, serotonin, Ach), second messenger signaling, and cell adhesion communication systems. Also encouraged is applying knowledge gained in uncovering target sites for alcohol’s action on the embryonic and fetal stages of life to begin developing potential therapeutic or preventative interventions, including dietary supplements (e.g., antioxidants and choline) that may be safe for use in pregnant women.

Pertaining to outreach, NIAAA will continue to support the meetings and work of the ICCFAS, which has developed its own strategic plan with actions that involve the participation of alcohol researchers, and those engaged in treatment, prevention, and education. NIAAA will continue to communicate with the Secretary’s National Task Force on FAS/FAE coordinated by CDC. NIAAA and the ICCFAS are also partnering with HRSA and the National Organization on Fetal Alcohol Syndrome (NOFAS) in an effort to include alcohol screening in maternal care programs and beyond and to identify research-based interventions that can be implemented in a cost effective manner in health care facilities. NIAAA and the ICCFAS will seek to partner with other agencies on including screening of children from birth through early childhood for the disabilities that result from prenatal exposure to alcohol. NIAAA is co-sponsoring, with NIH’s NICHD, the National Cancer Institute, and the National Center for Complementary and Alternative Medicine (NCCAM), the Global Health Initiative on Maternal and Child Health. This is an initiative for a multi-center international research network designed to conduct randomized clinical trials of interventions to reduce the major risks to maternal, neonatal, infant, and early childhood health in resource-poor countries.

Discussion:

- Regarding the lifecourse perspective that NIAAA is adopting, Dr. Damus pointed out that the budget does not reflect this at all with only 8% of the budget allocated to pregnant women. She noted that the lifecourse perspective is usually from the perspective of a preventive model. She wondered if they would shift the budget to reflect that focus. Dr. Warren responded that given all the areas on which the Institute has to focus (including adolescents, all of the other pathologies derived from alcohol, alcoholism itself, alcoholism treatment, other preventions, drunk driving, et cetera) there is an enormous spectrum of activities. Certainly, he would like the budget to be larger. They have tried to maintain about 8% of the budget in the pregnancy-related area. They have a lot invested in the adolescent area as well. There is a lot of information that indicates that the earlier an individual starts to drink, the greater the probability that person will develop alcoholism or alcohol dependence in their lifetime. That appears to be independent of whether their mother drank during pregnancy. A lot of that has to do with the influence of peers and starting to drink early. There are many major challenges in the alcohol field. NIAAA's overall investment currently, in excess of \$25 million, still makes them the largest player in this area. They were fortunate in terms of the CIFASD, which basically is a prospective study of alcohol exposure during pregnancy that will give them a wealth of data on FAS and FASD. NICHD, a larger institute than NIAAA, is investing \$3 dollars for every \$1 dollar that NIAAA invests, so for NIAAA's investment of about \$1 million, NICHD is investing \$3 million. They will get a lot out of these investments, so this represents a stretching of the budget as much as they can.
- Dr. O'Connor asked whether Dr. Warren was saying that 8% was about right. Dr. Warren confirmed that he was saying that 8% was about right, given all of the issues with which they must deal. He indicated that they had various breakdowns he could share with Task Force members if they were interested.

Substance Abuse and Mental Health Services Administration (SAMHSA) Update Callie Gass, MPH, FASD Center for Excellence

Callie Gass reported on SAMHSA activities, given that Ammie Akyere Bonsu was unable to attend due to travel moratoriums. Ms. Gass indicated that the SAMHSA FASD Center for Excellence was authorized by the Children's Health Act of 2000 and was launched in September 2001. Congress gave five mandates to address, two of which Ms. Gass will highlight today. One was to build capacity in state and local communities and the other was dissemination of information focusing on FASD prevention and determining how to intervene with populations affected by FASD. The Center for Excellence has attempted to fulfill their mandates through: training and technical assistance, materials development, information dissemination, and funding for states and communities to test the integration of effective practices into their existing service programs. One of the biases that the Center of Excellence began with was that there was never going to be enough money to make stand alone programs to either support prevention or address the needs of people living with an FASD and their families. The only hope they had was to integrate into existing service delivery systems.

The Center's first effort was to build state capacity. They began by convening Building FASD State Systems (BFSS) Meetings. They convened four BFSS meetings between May 2003 and May 2006. The May 2006 meeting included representatives from 49 states, the District of Columbia, and the Navajo Nation. They have moved from basic discussions about what FASD is to more sophisticated discussion regarding how to integrate a parent/child assistance program into a juvenile justice system; how to conduct motivational interviewing; what policies need to be in place, etc. States continue to increase their level of activity related to FASD. Forty-two states have created a staff position that deals specifically with FASD issues, an increase of 36 since May 2003. This does not necessarily mean that there is an FASD State Coordinator, but there is somebody in the state, at the state level, that carries FASD in his/her position description. Five of the 36 states received technical assistance from the Center. Thirty-six states

offer resources and services to “FASD-affected” families. Fourteen states have a dedicated source of state revenue used to fund some form of FASD prevention, although this does not necessarily mean “effective” FASD prevention. Twenty-five states have targeted one or more information campaigns to women of childbearing age. This was ongoing activity that has spiked since there has been more policy pressure on the states. Fourteen states have explicit policies regarding pregnant women and alcohol misuse. These vary state by state; although some are quite punitive in nature.

The FASD Center continues to support the National Association of FASD State Coordinators (NAFSC). There were 6 coordinators when they began and there are currently 18. The NAFSC is seeking to establish and maintain a national identity for FASD by providing information and resources on FASD; and by providing mentorship and support to individuals involved in FASD efforts on the state level. Members are also taking steps to becoming incorporated as a 501(c)(3) nonprofit. The NAFSC have begun to work with manufacturers of home pregnancy testing kits to get a message on the box stating that if a woman is trying to become pregnant, thinks she is pregnant, or is pregnant, she should abstain from alcohol. They are also working on sharing relevant information with states about policies they can put in place. Of the 42 states with FASD-related staff, 18 have designated an FASD Coordinator who participates in NAFSC, an increase of 12 since the inception of the organization.

The Center also conducts training and offers technical assistance. Participation in the BFSS meetings often leads to follow-up training and technical assistance, which in turn generates a statewide response. Six States (Arizona, Illinois, Michigan, Mississippi, Pennsylvania, and Utah) have formed, or have taken steps to form, statewide FASD task forces. All of those task forces are beginning to look at policy on prevention and on services for school aged children, although that is where they are hung up. The Center provides technical assistance to all six states currently primarily by phone due to travel restrictions. Three States (California, Michigan, and Nevada) have developed statewide FASD strategic plans. In addition, Illinois has recently released their strategic plan. Three States (Hawaii, Arizona, and West Virginia) report increased legislative interest in FASD and have used Center trainings and presentations to help generate that interest.

The other component of capacity building has been the Center’s 33 community subcontracts. These have funded 18 local organizations to integrate promising FASD prevention or treatment practices into existing service delivery systems. Most of the prevention sites are working on identification of pregnant women engaged in high-risk drinking and are developing brief interventions, motivational interviewing, or referral to treatment. Some of these are closely modeled on Project CHOICES. Several locations are reaching out to their Maternal and Child Health (MCH) clinics. South Dakota is moving into the WIC program to screen women who they have reason to believe should be screened for drinking and also to talk to women who are at high risk for drinking during pregnancy. Most of the treatment programs are about identifying children and getting them referred for some type of intervention program. These programs have probably had the most difficult time, partly due to the fact that they do not have enough diagnostic centers. For example, Alabama wanted very much to get a diagnostic team in place, but were unable to do so. There is one residential facility in West Virginia among these centers, that is working on modifying residential treatment for adjudicated juveniles to make it more effective for children with FASD. They have now formed a network with similar facilities in Utah and Alaska where they are gearing up for a “Bring the Children Home” initiative to move children from out-of-state to in-state placements. That group has been meeting by conference call for several months sharing information on how to manage children with FASD who are in residential facilities for whatever reason. West Virginia thinks they have some very nice outcome data and they plan to work on a paper soon.

The juvenile justice subcontracts fund five juvenile courts to develop, implement, and evaluate policies and procedures to screen, refer for diagnosis, and intervene with juveniles with an FASD. The desired outcomes include reduced recidivism, reduced probation violations, and improved functioning of the

youth. In some ways, the juvenile justice contracts are the Center's most exciting because they have produced such good data. One challenge has been trying to provide an appropriate screening tool they can use in the juvenile court system. This is an example of the kind of problems that occur between the science (finding a scientifically accurate screen) and reality (something that can be answered in three minutes with a probation office sitting at a desk in public without a computer). Four of the sites use some variation of the facial features. They are primarily picking up children with FASDs and are then using that to make recommendation where they can in their court systems for diversion, sentencing, etc. They are all picking up larger numbers of youth than expected. Ms. Gass clarified that these are not designed as an epidemiological study. They were designed to determine whether integrating screening and referral into the court system will make a difference.

In terms of building capacity in Native communities, there has been some activity but recent budget cuts have prevented them from continuing. However, they had begun offering training and technical assistance. An American Indian, Alaska Native, and Native Hawaiian stakeholder group was developed and began meeting this year to provide advice on addressing FASD in Indian Country. Train-the-trainer sessions were given for American Indian, Alaska Native, and Native Hawaiian trainers. Technical assistance and training were given to the Crow, Alabama-Coushatta Tribe of Texas, Navajo, Winnebago Tribe of Nebraska, Dakota Sioux, and Yaqui. The first FASD Institute for Native Professionals was conducted at the IHS/SAMHSA Behavioral Health Conference. The piece that remains is that they are completing a *Resource Kit for Native Communities* that will include posters, templates for print materials, brochures, and booklets. This replaces the previous IHS toolkit. Field training ended in June 2006; however, up to that point, 87 trainings were delivered to 4,054 participants in 27 states, including Washington, DC. Most trainings were aimed at professionals who work with either children, pregnant women, and/or women who drink.

The Center launched an improved, updated website. They also launched the Spanish-language companion site. They also received a 5-star rating from the Tufts University Child and Family WebGuide. Their fact sheets continue to be available both on-line and in hard copy. The two top items are: (1) Understanding Fetal Alcohol Spectrum Disorders: Getting a Diagnosis (13,752 copies); and (2) Independent Living For People with Fetal Alcohol Spectrum Disorders (11,914 copies). New "What You Need To Know" facts sheets FASD and the Criminal Justice System; How FASD Co-Occurs With Mental Illness; Independent Living for Persons with FASD; FASD—The Basics (online and mini-CD); and the FASD Center brochure. Two new downloadable reports and proceedings are out: (1) Building FASD State Systems: Proceedings, 2006; and (2) FASD Legislation by State--Spring 2006. This is a chart with links to give people an idea of where states are headed in the legislative arena. They have been quite surprised by some of the punitive legislation that exists.

The Center has a new curriculum for training professionals in the juvenile justice system that is now winding its way through clearance. This was developed in partnership with the Minnesota Organization on FAS (MOFAS) as a follow-up on their NIAAA funded work for juvenile courts. The Center trained eight teams of trainers in April 2006, although there is a fee now for those who are trained to go to other sites for training due to funding issues. At some point the curriculum will be finalized and available to the public. Coming out soon is *FASD—The Course* on-line, which is also in the clearance process. This is an interactive basic course for professionals. It is set up so that professionals can take it through their various bodies in order to receive certification. Also coming soon is the *Curriculum for Addiction Professionals Levels I and II*. *Level I* will be on-line, while *Level II* is a face-to-face course. This has been a challenge to pull together, but it should turn out to be a really great product. Two booklets for families are currently in clearance.

Ms. Gass clarified that the FASD Center for Excellence is not actually SAMHSA. SAMHSA contracted the Center to a contractor for whom the entire Center staff works. This contract is technically due to end

on November 30, 2006. However, they do expect a no-cost extension that will take them into the Spring 2007. They are now working with a reduced scope of work, they are no longer conducting training and technical assistance unless it is local, they are completing the products that are in clearance, and they are operating the subcontractors. Once the funding is exhausted, the Center contract will end. The Center's Steering Committee developed a set of recommendations for SAMHSA to consider based on some of the information from the Center evaluation. The Steering Committee supports the continuation of the Center, particularly to fill the niche they have been filling, which is science to services and piloting how to get information out into the field, how it needs to be adapted for courts and schools, etc. They recommended that the work of the Center should continue, including: the website, training and technical assistance, information dissemination and materials development, efforts to improve and integrate screening (they particularly talked about continue to work with CDC and NIAAA to move these things as they are out to the various service fields), capacity building, and evaluation activities. The Steering Committee recommended that the subcontracts be converted to regular grants that would be directly administered by SAMHSA.

Discussion:

- Dr. Warren wondered if the Center's funding ended whether the products would continue to be maintained. Ms. Gass replied that this would be up to SAMHSA and she does not know their plans.
- Ms. Ohlemiller inquired as to what was happening to the funding that has been appropriated for the Center in the past. Besides the subcontracts, she wondered if the funding was going away or being re-appropriated. Ms. Gass replied that funding was requested in SAMHSA's Office of Management and Budget (OMB) package that went forward in the approximate amount that was requested for FY2006. However, if SAMHSA has a stated plan for the funding, they have not shared it with the contractor.
- Speaking for NOFAS, Ms. Mitchell stressed that having the resources that were created by the Center disappear and not be maintained would be a shame. SAMHSA should share what their vision is and what they plan to do. Ms. Gass suggested that questions and/or requests for dialogue should go directly to SAMHSA, perhaps to Dennis Romero. She offered to take back any information and/or recommendations those present wished to share. Dr. Wright added that the Task Force may want to do something as a committee, so she urged participants to give some thought to this between then and the end of the meeting the next day. Dr. Olson requested that ample time be set aside prior to the end of the meeting in order to craft a motion.

Centers for Disease Control and Prevention Update

R. Louise Floyd, DSN, RN

Jacquelyn Bertrand, PhD

Louise Floyd highlighted a number of CDC's FAS activities. In 2003, CDC funded 7 states (Michigan, Wisconsin, Missouri, North Dakota, South Dakota, Minnesota, Colorado, and Oregon) to develop comprehensive FAS prevention programs that include FAS surveillance and the development of individual and community level interventions, focusing on women at high risk for an alcohol-exposed pregnancy. With respect to surveillance, about 2,000 records have been abstracted so far identifying 144 cases of FAS and 97 probable cases. By the end of 2006, 5 of the 7 states will have implemented their individual level interventions. These are modeled on the Project CHOICES framework. Four of the 7 will have community-level interventions by the end of the year. These are self-guided change interventions based on the work of Linda and Mark Sobell. The interventions also are developing promotional campaigns to advertise a helpline and enroll eligible women. Eligible women are provided self-change materials (educational information and exercises) by mail. Two of the community intervention groups are making materials available online. These are pilot studies that are attempting to reach women at highest risk.

Dr. Floyd then provided an update on Project CHOICES. This was a multi-site randomized control trial of 860 high risk women, over half of whom met the DMS criteria for addiction. They had a 70% follow-up and randomized the women into control and intervention groups. Women in the intervention group had a two-fold increase in the probability of reducing their risk of an alcohol-exposed pregnancy compared to the control group. A publication of these findings will come out in the January 2007 issue of the *American Journal of Preventive Medicine* and will be available online 6 weeks prior to the paper publication at ajpm-online.net. CDC is currently planning how they want to proceed in terms of disseminating this information broadly (e.g., press release).

In collaboration with the American College of Obstetricians and Gynecologists (ACOG), CDC developed the “*Drinking and Reproductive Health: A Fetal Alcohol Spectrum Disorders Prevention Tool Kit*.” The primary component in the tool kit is a CD-ROM that aims to teach women’s health care providers how to screen and advise all of their patients of reproductive age about risky drinking and encourage the use of effective contraception among patients who continue to engage in risky drinking. It also addresses drinking during pregnancy. This tool kit contains: a brief guide, a laminated screening instrument for providers, resource information, and patient handouts that can be downloaded and printed. Continuing medical education credits are also available. An evaluation of this toolkit will be conducted done through a follow-up survey of obstetricians and gynecologists in 2007.

Dr. Floyd reminded that Task Force that Dr. Hani Atrash presented to the Task Force last year on CDC’s efforts on preconception care. The culmination of those efforts can be found in the September 2006 issue of the *Maternal and Child Health Journal* that is now online. Given the complicated web address, CDC indicated that they will send the link in an email to Task Force members. The information is as follows: <http://springerlink.com/content/k33g85g4242v/?p=5e9442a6c00a40888ebe95936ebca50a&pi=4>. The citation is: Preconception Care: Science, Practice, Challenges and Opportunities Guest Editors: Hani K. Atrash, MD, MPH and Louis G. Keith, MD, PhD, Volume 10, Supplement 7, September 2006. The entire issue is about preconception health. There are 3 or 4 articles that deal with alcohol exposures, one of which was included in the Task Force meeting packets. This article examines the prevalence of risk factors for adverse outcomes during pregnancy and preconception, and considers the high risk factors that women have in preconception and carry into pregnancy (e.g., alcohol exposure, tobacco, HIV infection).

Dr. Bertrand updated the group on CDC’s international projects. She reported that CDC funded a project in South Africa that has been underway for a year. It is primarily a prevention project. During the first phase, they conducted an epidemiological survey of women in an urban area of Pretoria (which is completed) and a rural farm community in Cape Town (soon to be completed). The preliminary data reflect high rates of alcohol use; alcohol use during pregnancy; and a lot of comorbid issues such as domestic violence, crime, and poverty. In the last two years of the project, which is now underway, they will implement a fairly comprehensive program with layered levels of intervention. They are developing a media campaign to raise general awareness; conducting provider education seminars and disseminating provider materials; convening local support groups to increase skills among women with messages imbedded about either abstaining from alcohol while pregnant or effective use of contraception; and implementing a one-on-one brief intervention based on the Project CHOICES model. They are in the planning phases for all of these interventions.

CDC has funded a group from the University of Oklahoma Health Sciences Center to translate and adapt the FAS materials from CDC’s FAS Regional Training Centers for use with Russian health providers in St. Petersburg. They are about halfway through a two-year program. In addition to the translation and adaptation of these materials, they will also evaluate how these are disseminated and used. Russia is another high alcohol use country with a high prevalence of FAS.

Moving from primary to secondary prevention, Dr. Bertrand reported on the Danish Cohort Study. This study is going extremely well. This is a follow-up study of 1,800 five year olds who have been followed since 8 weeks of pregnancy through the Danish National Cohort. At this time (five years of age), CDC is doing neuropsychological testing of these children. The great thing about having so many children and having the Danish Cohort is that the sample of 1,800 children are across all exposure levels, so they can really focus in on the low exposure children and the kind of neuropsychological deficits they might have. They also have information on binge drinking and timing of binge drinking. At their recent research meeting, they were able to discuss the types of analyses they might choose to do. For example, five psychologists have participated in doing this testing, so they certainly wanted to do analyses to ensure that they do not have a tester effect. In addition, the study is conducted in three different cities in Denmark, so analyses have been done to ensure that there are no site effects. No tester or site effects have been noted. This is very high quality data collection. In addition to information on alcohol use, they can also get information about smoking and caffeine use. There is also an oversampling of families who participated in a nutrition survey during pregnancy, so they will be able to at least address some of the nutrition questions. Well over 1,000 children have been tested. Data collection is expected to take another year or so.

Discussion:

- Dr. Olson asked what percentage they still had in the Danish Cohort sample. Dr. Bertrand responded that the original sample is over 100,000. Out of that, they selected 3,000 participants to invite into the study. Of those 3,000, they have over 50% participating. They will eventually get their 1,800.
- Dr. Olson wondered whether they were able to keep the 1,800 since 8 weeks of pregnancy. Dr. Bertrand replied that they had kept the entire 100,000 since 8 weeks of pregnancy. It is a cohort because they agreed to participate and be in the cohort. Many things happened to the cohort along the line—that 100,000. This is just a single study out of that cohort of 1,800 alcohol affected and one group of controls.

Public Comment / Adjourn

With no public comments offered, Dr. Wright officially adjourned the meeting for the day.

Wednesday, September 27, 2006

Call to Order

Dr. Wright called the meeting to order. She indicated that the group would first hear the three scheduled presentations, leaving ample time for open deliberations regarding other critically important items of business including motions, sunseting of the Task Force, and future meeting dates and potential agenda items.

SAMHSA FASD Center for Excellence Promising Practices Inventory

Callie B. Gass, FASD Center for Excellence

Ms. Gass indicated that she was asked to share some work that the Center for Excellence has done on promising prevention practices. She explained that one of the Center's mandates was to identify, describe, and assess promising FASD prevention practices in the United States. While the actual charge was "best practices," they recognized that there is a lot of "granny wisdom" in place. The Center's Science and Service Committee spent two years arguing over whether "granny wisdom" could be counted as a "promising practice." Ultimately, as they inventoried and interviewed 267 programs and practices that said they addressed FASD and the Committee determined that they could not, in good conscience, call most of the "granny wisdom" either "best practices" or "promising practices." They might be able to elucidate a few and recommend that someone conduct research on them; however, there really were not any which rose to a level they felt comfortable labeling "promising and best practices" either in

prevention or intervention. She stressed that this was their inventory of programs on the ground five years ago. A second potential problem was that it was not clear whether the intervention programs they were reviewing were, indeed, addressing people with FASD. However, most were never screening or diagnosing their clients.

For this Task Force meeting, Ms. Gass reviewed the prevention piece (e.g., the interventions for women at risk of having an alcohol-affected pregnancy) of this effort. The programs studied were actually delivering services “on the ground” and were not in a test phase. For this investigation, they defined *practice* as “A single technique or method to achieve a specific outcome,” while they defined *intervention* as “A combination of practices implemented to achieve specific outcomes.” In terms of the methods the Center sought input from FASD experts and contact persons, and conducted extensive on-line and literature searches. They also developed a database to document the information obtained. Eligibility criteria for selection from the database were to select practices for assessment against SAMHSA’s National Registry of Evidence-based Programs (NREPP) criteria; describe how practices address NREPP requirements; and rate eligible practices against NREPP criteria. They will report the results to SAMHSA in November. The Science and Service Committee and academic advisors agreed that in order to be included in the database, practices and interventions must address FAS or FASD directly or indirectly (although they had difficulty determining whether intervention programs addressed FASD, given that programs did not define their children that way); the desired outcome had to involve measurable changes in behavior (e.g., woman reduced or stopped drinking, child improved behaviors); include an evaluation component (which eliminated about 250 programs); and be published in a peer-reviewed journal.

According to the NREPP requirements, the evaluation design could be a randomized controlled trial, quasi-experimental, or pre/post. Pertaining to the strength of the evidence, the NREPP research criteria included reliability and validity; intervention fidelity; methods to address missing data and attrition; and appropriate analysis and control for confounding variables. In terms of the results, 275 interventions were recorded in the database, of which 7 were found to be eligible for NREPP rating. Of those, 6 were assessed through randomized controlled trials and 1 was assessed using a quasi-experimental design. The eligible practices and interventions included: Parent-Child Assistance Program (PCAP); Brief Intervention for Alcohol Use in Pregnancy; Brief Intervention With Support Partner; Cognitive Behavioral Intervention (University of Alabama); Project TrEAT (Trial on Early Alcohol Treatment); Project BALANCE (Virginia Commonwealth University); and the AR-CARES Program (University of Arkansas Program). The breakdown of target populations, types of interventions and practices, and outcomes for intervention participants were as follows:

Target Populations:

- Pregnant women with alcohol problems (n=5)
- Pregnant women and their partners (n=1)
- Women of childbearing age (n=2)
- Women receiving or referred for prenatal care (n=5)
- Female college students (n=1)

Interventions and Practices:

- Case management (n=2)
- Motivational interviewing (n=3)
- Use of take-home manual/ workbook (n=3)
- Contraception counseling (n=2)
- Education and self-help (n=1)
- Physician counseling (n=1)

Outcomes for Intervention Participants:

- Greater reductions in drinking rates than controls (n=5)
- Higher quit rates during pregnancy (n=3)
- Larger reduction in risk of alcohol-exposed pregnancies (n=2)
- Better linkage to community services (n=2)

The lessons learned for FASD prevention were that women must be screened for prenatal alcohol use to prevent alcohol-exposed pregnancies; brief interventions for pregnant alcohol users work better when their partners are involved; primary care physicians have great potential to reduce drinking among childbearing women; and comprehensive services can produce long-lasting benefits for low-income, pregnant, and postpartum women and their children. They were surprised by the large number of programs in place that have virtually no science or evidence-based reason to exist. That does not mean they are not doing anything; however, “granny wisdom” may be elevating them. They are somebody’s hunch or idea and, obviously, people are receiving those services. Many of these do not even have customer service satisfaction type evaluation, let alone any kind of outcome measures.

Based on these findings, the recommendations from the Center for Excellence are: to promote more resources to assess FASD practices; to include longer follow-ups to ensure sustainable outcomes (of the 7 which made it into the database, the majority had very short follow-up of typically no more than 30, 60, 90 days); to support more practices for women and their families; and to replicate promising practices at other sites. Ms. Gass noted that the Project CHOICES model was not included in this analysis and that they would like feedback from CDC regarding this project. Aside from the Project CHOICES model, the Center for Excellence believes they have found everything that is currently in place, which shows that there is not a lot. A great deal of work needs to be done to measure what is effective and what is worth putting dollars towards, especially as budgets continue to be reduced.

FASD Prevention Review: Process & Discussion

Scott F. Wetterhall, MD, MPH; RTI International

Dr. Wetterhall reviewed the project that RTI is conducting on behalf of the Task Force. Referring to the minutes from the last NTFFAS meeting, he noted that the Task Force Prevention Working Group produced a draft outline and recommended that a consultant be identified to conduct a review. For this reason, CDC staff engaged CDC’s *Community Guide* team to assist. During the last Task Force meeting, in February 2006, Drs. Elder and Briss gave brief presentations that discussed the *Community Guide* process. Dr. Wetterhall explained that the *Guide to Community Preventive Services* is an evidence-based, rigorous review of the literature that focuses primarily on community interventions in public health as opposed to the *Guide to Clinical Preventive Services*, which focuses on clinical services on an individual basis, particularly in a healthcare provider setting. During the February 2006 meeting, the Task Force approved the motion to engage the *Community Guide* approach to examine FASD prevention strategies. With respect to the challenges, during that meeting, Dr. Briss stated that “the most common problem is sorting through enormous amounts of conflicting information of variable quality.”

Subsequent to the approval of the motion, CDC contracted with RTI International to undertake work related to similar efforts already underway. The contract was awarded in August 2006. There are two parts to this process. The language from the contract is as follows:

- Part I will involve an inventory and synthesis of existing recommendations, evidence-based reviews, evidence-based programs and single intervention studies from the *Community Guide* and other “evidence-based” sources on Fetal Alcohol Spectrum Disorders (FASD) and a summary of these reviews and recommendations which will be communicated in one or more print or web products.

- Part II will involve conduct of one or more new reviews of the effectiveness and cost effectiveness of interventions for Fetal Alcohol Spectrum Disorders (FASD) working with the Task Force on Community Preventive Services and other relevant stakeholders.

Dr. Wetterhall clarified that their first task was basically to systematically look for interventions related to preventing FASD or alcohol consumption among women who are pregnant. That is different from the actual process in undertaking a *Community Guide* review, which is Part II in this effort. Once they have reviewed all of the interventions that fit the inclusion/exclusion criteria, they will then move forward with conducting Part II. The *Community Guide* process is a rigorous one where first an intervention is decided upon, which typically focuses on a key question of interest to the group supporting the effort. Once that intervention is decided upon, an analytical framework or logic model is constructed such that one can weigh the various interventions along a spectrum. A rigorous search, review, and abstraction process is undertaken that includes following the review of the literature in terms of design, strength of effect, various measurements, etc.

Dr. Wetterhall explained that at this point, RTI is being relatively inclusive as far as resources and wisdom will permit them. For Part I, the key question is focusing on community interventions to prevent FASD. Given the acknowledgement that those will be rare, they expanded the key question to include community interventions to prevent alcohol use during pregnancy. He stressed that this was an iterative process and that nothing really was “etched in stone” at this point. He pointed out that it is important to recognize what a community preventive service is and what it is not. For their purposes, it is an intervention (activity) that prevents disease or injury or promotes health in a group of persons. It is not an intervention delivered in an individual, one-on-one clinical setting. The definition is designed to avoid overlap with the *Guide to Clinical Preventive Services*. Dr. Wetterhall said he thought RTI’s efforts would complement those of SAMHSA’s FASD Center for Excellence.

Dr. Wetterhall wanted to obtain feedback from the Task Force based on the work done thus far. Items for consideration by the Task Force included: inclusion/exclusion criteria; search terms; list of variables for the database; and the sample evidence table. RTI will develop an annotated bibliography of interventions related to alcohol use in pregnancy and prevention of FASD (Part 1), which will serve as a foundation for Part II efforts. The annotated bibliography will be put into an Access database and which will be used to create evidence tables—the summary table of what a particular study is comprised of (the final step in the *Community Guide* process).

Thus far, the inclusion criteria are: English language and 1973 to present. Subject-specific inclusion criteria include: community-based interventions; multi-level interventions (e.g., school-based, policy, labeling); intervention effectiveness; childbearing aged women; FASD prevention; and reducing alcohol-exposed pregnancies. Exclusion criteria include: general population-based studies that focus on alcohol consumption and not specific to FASD and clinical-based studies (e.g., conducted primarily in health care settings on a one-on-one basis by a health care provider). They chose an article by Ingersoll that focused on short-term interventions in college-aged women to prevent drinking and to decrease pregnancy exposure in order to develop a series of search terms to begin the search. The search terms currently include the following:

- Pregnancy [MeSH] or Fetus [MeSH] and Alcohol-Related Disorders [MeSH]
AND
- (“prevention and control” [subheading] OR “Primary Prevention” [MeSH]) OR “Counseling” [MeSH] OR “Health Education” [MeSH]
OR
- Fetal Alcohol Syndrome [MeSH]
AND

- (“prevention and control” [subheading] OR “Primary Prevention” [MeSH]) OR “Counseling” [MeSH] OR “Health Education” [MeSH]

Dr. Wetterhall clarified that the “alcohol-related disorders” [MeSH] includes: alcohol-induced disorders; alcohol-induced disorders, nervous system +; cardiomyopathy, alcoholic; fetal alcohol syndrome; liver diseases, alcoholic +; pancreatitis, alcoholic; psychoses, alcoholic; alcoholic intoxication; alcoholism; Wernicke encephalopathy. RTI’s initial search in using the search terms on PubMed resulted in a list of 408 citations. They are currently in the process of reviewing these citations, looking at the titles and abstracts if available, and then pulling those for review.

The suggested list of variables for which RTI will abstract information, from the articles they will review, includes the following: author and year; intervention and comparison elements; study population, description, and size; and results (e.g., effect measures, reported baseline, reported effect, value used in summary, and follow-up time). This information will populate the database that RTI will provide to the Task Force. Dr. Wetterhall reviewed the sample evidence table provided to the Task Force members, noting that a summary table like this would be developed for each study that is abstracted. Given that the *Community Guide* has such a rigorous process, RTI is not undertaking a *Community Guide* abstraction process at this point in the effort. The *Community Guide* uses a 26-page abstraction form for each study that is abstracted and the effort is approximately 4 to 6 hours per study. RTI simply does not have the resources to conduct such an effort. That would be undertaken in Part II if RTI is directed to work forward into that phase.

With respect to next steps, Dr. Wetterhall reiterated that RTI was present to hear feedback from the Task Force. CDC will direct RTI, with the Task Force’s input, on Part I. RTI’s hope is to present the results of Part I activities (e.g., basically the annotated bibliography of community-based interventions) during the next Task Force meeting.

Discussion:

- Dr. O’Connor inquired as to whether RTI was interested in the harm reduction studies, for example, those conducted with college fraternities, sororities, and athletic departments with respect to making changes to accessibility of alcohol on college campuses. Dr. Wetterhall responded that this seemed relevant to RTI’s effort, and he wondered whether the Task Force was interested in RTI pursuing this.
- Dr. Floyd noted that the *Community Guide* has been working on a module pertaining to underage drinking or drinking during adolescence. She wondered whether it would be beneficial to pull in some of these studies in order to widen the net, and whether there might be individual ones people would like to recommend. She stressed that the underage drinking literature is very rich and includes community level interventions that have worked. The component that is not there is a focus on FASD prevention around exposed pregnancies. Nevertheless, if RTI finds that they are not locating sufficient numbers of promising community level studies, identifying other models that might inform future interventions could be beneficial. Dr. Wetterhall responded that there was an effort underway to study some of those issues. They will certainly inform RTI’s process while at the same time help them avoid any unnecessary overlap.
- Dr. Chang inquired as to whether RTI planned to include prevention efforts from Europe and the United Kingdom, particularly given their extensive and perhaps richer experience. She noted that Europe has been further ahead than the U.S. in all of this work and reminded everyone that the brief intervention originated in Finland. Given the structure of the health care system, they may be able to find community prevention efforts. She stressed that they should not be too parochial. Dr. Wetterhall reported that including these did arise in their discussions. Part of not doing so is a resource issue and the other issue is that while studies are being conducted in Europe, the studies are being published in

U.S. literature as well. Nevertheless, that raised an area for which guidance from the Task Force and / or CDC could be helpful in terms of how to approach that.

- The distinction between community and clinical level efforts was somewhat unclear to Dr. Olson. She wondered what that meant they were leaving out, for example interventions that take place on the site of a chemical-dependency treatment center may provide female-oriented services. Dr. Wetterhall responded that many of these decisions predated his engagement in the process, but his understanding was that the distinction between individual clinical services was an attempt to find some sort of demarcation between what the *Guide to Clinical Services* focuses on versus what the *Community Guide* would focus on. He thought they would have to cast a wide net, while being very careful what they include and exclude. He recognized that there is a continuum between individual personal health services and population health services.
- Dr. Damus said that to her, the community includes providers in various localities as well. Given that they are attempting to determine how to prevent FASD, it was not clear to her why they would exclude clinicians. She did not believe they could draw a line between the provider, efforts in a community-based health care facility, and the community. Dr. Floyd responded that the initial discussions pertained to the fact that the community is the area in which less is known about the literature that would inform prevention activities. The interest was in whether there is other literature that could be reviewed to inform other state-of-the-art best practices. She explained that the CDC *Community Guide* made the distinction in the definition and she agreed that this was somewhat arbitrary. Dr. Bertrand added that their thinking was that this is an approach to evaluate the evidence to give them some sense of how to move forward with prevention. She thought in the end they would have to put both of those together. They are currently evaluating the community approach. They had a report published recently pertaining to the clinical approach (i.e., brief intervention). She thought it would be the responsibility of the Task Force to meld those two pieces. While the separation is arbitrary, these are the two mechanisms they currently have for formally evaluating the literature in order to highlight good practices. Dr. O'Connor added that these are distinct in the literature as well.
- Dr. Miller indicated that they intended to include the entire area when the Prevention Work Group initially set out to undertake this task. In order to get this done, they made the arbitrary division. Ideally, they would have found a contractor who could have undertaken both components. She agreed that they had to combine whatever resources they had in order to develop a complete prevention picture.
- Dr. Damus did not agree that they had the answers on the clinical side at all and stressed that this needed to be considered as well. Although there may be some best practices, obviously they are not being carried out well or they would not have this problem. She said that there are some creative efforts in clinical settings, which to her is part of the community, and that the faith-based community also represents a component. She pointed out that if they targeted their search only to alcohol, they would also miss the fact that a lot of this is poly-substance abuse. She stressed that a lot of this information is not in Medline, but could be found instead in the "gray literature." Increasingly, librarians know how to survey the "gray literature," which includes unpublished, unpeer-reviewed literature, presentations at conferences, et cetera. She also indicated that she did not like limiting the search only to women of child bearing age. In the community, much of the substance abuse, regardless of what substance, involves men, significant others, boyfriends, whatever. Limiting to women only may exclude some important information from programs as well. Others agreed that searching the "gray literature" would be important as would searching on other terms such as: substance abuse, poly-substance abuse, alcohol abuse, alcohol misuse, et cetera. This will broaden the findings tremendously. Dr. Wetterhall responded that their searches are not limited to PubMed.

They do have an information specialist at the University of North Carolina who conducts the searches for RTI and for their evidence-based center there.

- Dr. Damus asked whether the Task Force would be able to review the actual resources at some point. Dr. Wetterhall replied that they would.
- Dr. Chang wondered how RTI would handle potential bias. Dr. Wetterhall acknowledged the well-recognized bias. He said he was representing the approach to the *Guide to Community Preventive Services*, which has a particular process in place for assessing the quality of interventions and judging whether the literature supports a particular intervention. Typically, there are some interventions where the recommendation is that the literature strongly supports the intervention. A fair number of interventions, however, have inadequate evidence to judge whether the intervention is effective. He recalled that when the *Guide* was first “getting its feet” in 1996, a great deal of concern was expressed by a number of public health officials that a lot of the community health interventions did not have the evidence base to support a strong recommendation for their existence. There was also concern that there could be backlash against some of the public health efforts because of this. He thought the *Guide* had tried to “walk the appropriate line” in using evidence to support strong interventions and recognize that sometimes there simply is no evidence.
- Dr. Miller pointed out that when people do meta-analyses, they often will go to researchers who may have written something that is very well done, yet it may not have been published because the findings were negative. She wondered if RTI planned to personally contact researchers to look into such interventions. Dr. Wetterhall replied that he would consider that part of the “gray literature,” reiterating that RTI was seeking the Task Force’s input and direction from CDC with respect to the project and that RTI would do as directed. Dr. Miller clarified that she thought the Task Force supported reviewing the “gray literature.” Dr. Floyd added that the *Community Guide* has certain standards that are non-negotiable. However, for Part I, which is the phase in progress, they could do what would be helpful to the Task Force with respect to obtaining information that would inform recommendations. Whatever they work out for Part I will inform Part II. Hopefully this will characterize gaps and help set a research agenda, which is important in terms of thinking about future funding for all of the agencies involved in this effort.
- With respect to searching the underage drinking, treatment of youth engaged in risky drinking, and chemical dependency literature, Dr. Olson suggested that other concepts to consider are family planning and contraception. While reduction in alcohol use is one way to accomplish prevention, the other is reduction of pregnancy. She suggested that this somehow be considered in the search terms. Dr. O’Connor added that Sandra Brown has done a lot of work in what helps people quit drinking spontaneously, particularly young people.
- Dr. Miller inquired as to timeframe limits and whether there will be a narrative. Dr. Wetterhall responded that RTI anticipates that Part I will be completed with the results ready for presentation during the next Task Force meeting. The expectation for Part I is that RTI will have the review and summary tables completed, which will become part of the database. This information can be presented to the Task Force. The annotated bibliography will be summarized into the evidence tables. There is no expectation of a separate narrative report during Part I. Dr. Wright added that once the Task Force is presented with the products of Part I, the next step will be to determine what will be recommended that the contractor do next. She thought they were clear on what Dr. Wetterhall would deliver during the next Task Force meeting. If there was anything additional the Task Force thought would be helpful, Dr. Wright indicated that CDC could negotiate that with Dr. Wetterhall as well.

- Dr. Olson wondered whether the table could be distributed before the next Task Force meeting in order for members to have ample time to review the contents. Dr. Bertrand responded that the Task Force members would see the tables prior to the next meeting.
- Dr. Bertrand requested that the Task Force members comment on whether there were other elements/search terms that should be included in the tables that would help them in reviewing the literature, stressing that they should email CDC any suggestions after the meeting. She noted that there is *Community Guide* work being developed for alcohol in general, some of which could be pulled into the final report. There is also *Community Guide* work being done on adolescent health, so many of the underage drinking issues will be covered there. CDC does not want to spend resources re-reviewing and re-collecting that literature, so they are really looking to locate what goes beyond that for alcohol-exposed pregnancies. They have finite dollars and finite time, which is why they defined the parameters in the way Dr. Wetterhall described.
- Dr. Olson requested that a mass email be sent to Task Force members to remind them of this so that they could respond. Dr. Floyd indicated that CDC would send a reminder email. She also noted that CDC plans to convene weekly conference calls with RTI, so she stressed that Task Force members should submit additional terms, specific studies with enough information that CDC and RTI can access the studies which they believe will be appropriate. Dr. Wetterhall thanked the Task Force for their feedback, reiterating that this is an iterative, collaborative process.

Liaison Updates

American College of Obstetricians and Gynecologists

Robert J. Sokol, MD

First, Dr. Sokol reported on a resource that may be of interest to Task Force members. He thought the grant came from NIAAA to a company called Academic Edge. This grant is to create a DVD targeting parents of children with FASDs. It is currently in a rough draft form. Dr. Sokol looked at the latest version, which he believes is of considerable use. He recommended that Task Force members review it as well.

With respect to ACOG, Dr. Sokol indicated that there has been a long history of work on FAS. The first initiative was in the late 1980s when a group was formed because it was clear that professional education in this area was needed. The educational materials were developed, and the next step was to review the impact of that through a survey sponsored by CDC and others and published in the *Green Journal*. They found that obstetricians who were educated after the initial educational intervention in 1993 knew a great deal more about alcohol and pregnancy than those educated before 1993. This is one of the few studies that demonstrates the effectiveness of an educational intervention. What people did not know was found to be very important, including concepts about how much drinking is too much and what could be done about it. This is the point at which they began the current process, which was to ask, “Is there evidence that would tell us what kinds of information we should be trying to get into the practices of professionals who take care of women?”

With this in mind, two other things occurred: (1) the U.S. Preventive Task Force conducted a meta-analysis that reviewed and documented that the screening and brief intervention strategy is effective in reducing alcohol intake in reproductive age women; and (2) ACOG has a committee process through which they considered the issue of what to do about substance abuse, not just alcohol. The Committee on Ethics came out with a committee opinion, which basically said there are interventions that are as effective as anything being done for diabetes or hypertension. Clearly, outcomes could be improved with these interventions. Therefore, ethically, they *should be* done. They were then faced with the situation that there are interventions that work, experts stressed that these should be implemented, but no one knew precisely what to do. This was the impetus for the current work, which involved the creation of the

toolkit entitled, “Drinking and Reproductive Health.” The toolkit focuses on screening and brief intervention and is clinically useful and practical. The advice is evidence-based and a group of clinicians who reviewed the work for ACOG were very impressed.

The primary component of the toolkit is a CD-ROM, which aims to teach women’s health care providers how to properly screen and advise their patients about risky drinking and encourages the use of contraception if patients continue to engage in risky drinking. It also addresses drinking during pregnancy. The screening tools and interventions have proven efficacy and can be incorporated into routine care. The toolkit also includes downloadable patient and family information handouts and counseling tools. ACOG discovered that about 90% of obstetricians/gynecologists, a group which delivers about 95% of prenatal care services in the U.S., at least ask about alcohol once, but only 25% of the time is formal screening conducted. Formal screening is required to drive intervention. There has been very little done to teach obstetricians/gynecologists minimal intervention.

Dr. Sokol indicated that the toolkit is scheduled to be published in approximately mid-October. It was announced a few weeks prior to this meeting in the publication titled *ACOG Today*. The toolkit will be distributed to obstetricians/gynecologists, family physicians, and anybody else who is appropriate. It explains how to formalize screening through a simple 3-stage process that follows, reasonably closely, the NIAAA publication available online. The process involves asking someone if they have ever had a drink. If the answer is “no,” this is the end of the screening process. If they answer “yes,” there are a series of additional questions. There are then some quantity/frequency questions as well. If either of these is positive (using the published NIAAA standard for what constitutes the upper limit of normal drinking), a brief intervention is recommended. This is a motivational intervention model, for which there is strong evidence in the literature for effectiveness based on randomized clinical trials.

Dr. Sokol also reported on a press release on September 7, 2006 from the Centers for Medicare and Medicaid Services (CMS) announcing a new policy to reimburse physicians for services to identify and treat Medicaid patients’ problems with alcohol and other drugs. Two major blocks to screening are that it takes time and practitioners are not paid for it. Now what people should do is known, they are being provided with a tool to do it, and they can be paid for it. This should help. ACOG has been terrific in response to the contract most recently from CDC and with previous work with NIAAA, and Dr. Sokol believes they will continue to be active. They have also had tremendous support from NOFAS in terms of encouraging ACOG with recognition of their activities in this area. During ACOG’s annual clinical meeting attended by 5,000 to 10,000 people, there will be two charity events with receipts going to NOFAS (e.g., the annual fun run, donation of monies left over from international travel). The most important aspect to Dr. Sokol is highlighting fetal alcohol spectrum disorders for a very critical group of providers where there has not been this level of activity or emphasis previously.

Dr. Sokol made three suggestions regarding useful endeavors from this point forward, given that this effort is not complete. While they have found and documented the need, found interventions for which there is evidence, and have developed a tool, this does not guarantee that it will be used. As a Task Force, Dr. Sokol said he believed they could engage in specific efforts to help the process along. First, as NOFAS did, the Task Force should formally recognize this effort through a thank you letter or statement of some sort. While they were unable to review the toolkit during this Task Force meeting, he did not want another six months to pass before such recognition was made. With that in mind, he suggested circulating whatever they could agree upon for the committee to review and sign, at the time the toolkit comes out. Second, Dr. Sokol stressed that the toolkit must be disseminated widely and there must be some method for getting practitioners to implement it. His recommendation would be perhaps an additional CDC contract for implementation. In addition to the outcome of reducing the amount of damage, they heard two speakers report during the first day of this meeting that ARND cannot be diagnosed without a history of alcohol exposure. If they want to make some progress, exactly as the IOM

stated 10 years ago, this is imperative. If they could get good implementation of screening and brief interventions, this would subsequently get the tool placed in the official ACOG prenatal record, and they could be in a position to have alcohol exposure information for most of the births in the U.S. In that case, if someone saw a child who had an array of abnormalities thought to be associated with ARND, there would be a chance to make a diagnosis. This could improve outcomes and provide the basis for secondary prevention efforts. Third, this could be driven forward by a study funded and participated in by CDC, following the formal survey process ACOG used previously with its fellows, to determine whether practice indeed can be changed.

Discussion:

- Ms. Mitchell indicated that NOFAS had requested that a letter go out from Dr. Williams that would advise practitioners to follow the Surgeon General's Advisory. She reported that in an earlier conversation with Dr. Williams, he seemed to have some apprehension about the moderate drinking issue. Dr. Sokol responded he thought it would be worth trying to coordinate this with the distribution of the ACOG materials. He indicated that he would follow-up with Dr. Williams and suggested that Ms. Mitchell follow-up with a call as well, because he was certain that Dr. Williams would support the effort. He noted that Dr. Williams directs ACOG's Education Division, but that this work came out of Women's Health.
- Regarding the NIAAA guidelines on the limits of normal drinking, Dr. Warren stated that it is actually the threshold for what is considered risk drinking. Dr. Sokol responded that while this is how it is talked about; however, *exceeding* those limits is one of the two triggers for brief intervention for that individual. Not known is exactly what proportion of women would receive the intervention, although they predict that it will be approximately 1 in 5 reproductive age women, though there was very fine crafting to get to the preconception level.

MOTION

Dr. Miller moved that the Task Force immediately draft, review, and send a letter to ACOG thanking and congratulating them on their "Drinking and Reproductive Health" toolkit. The motion carried unanimously.

National Organization on FAS

Kathleen T. Mitchell, MHS, LCADC

Ms. Mitchell updated the Task Force regarding NOFAS's recent activities. She shared samples of NOFAS's posters, developed with HRSA, that are available on the NOFAS website. She indicated that NOFAS is creating curricula, due out in approximately mid-October, outlining the dangers of drinking alcohol during pregnancy for K-12 students. The new curricula will use innovative and proven strategies for educating students in grades K-12 about the effects of alcohol exposure during pregnancy. Education strategies include a storybook, an interactive curriculum using a brain model to demonstrate differences between brains exposed and not exposed to alcohol during pregnancy, and a special episode of NBC's *Law and Order* television program that focuses on legal issues of FAS, which is adapted for a discussion about the social, legal, and ethical implications of alcohol use and pregnancy. The *Law and Order* piece has been edited down to 20 minutes. NOFAS shifted the content areas to focus less on the legal issues and more on what alcoholism is, why some people develop it, and what can happen when a woman drinks during pregnancy. For ages K through 2nd grade, they created a colorful storybook that introduces the term "fetal alcohol spectrum disorders." It includes lesson plans for teachers. The materials for grades 3 through 5 include a series of lesson plans that help youth learn the differences between healthy substances and substances that are harmful. Middle schoolers will work with a model brain that helps children to understand that when drinking occurs during pregnancy, the size of the brain can be altered. The model compares simple parts of the alcohol-exposed brain and the exposure-free brain.

Ms. Mitchell distributed a copy of NOFAS's legislative update that is emailed, a piece on the FASD Caucus, the K through 2nd grade curricula, and their step-by-step guide targeted to those who contact NOFAS to find out how to get involved. NOFAS has held a couple of briefings during 2006 and have gained many new members. NOFAS holds a Hill Day every year, during which they bring in families from all over the U.S., which Ms. Mitchell invited Task Force members to attend and participate in. In addition, the NOFAS 30-second public service announcement cautioning women about the risk of drinking alcohol while pregnant, produced by Women in Film's Los Angeles Chapter for the National Organization on Fetal Alcohol Syndrome (NOFAS), won the 2005 Gold Aurora Award.

With respect to where NOFAS spends their dollars, Ms. Mitchell reported that because they are a non-profit organization, almost the full dollar of every dollar goes back into the community, programs, and materials. They continue to facilitate two medical school classes, one at Northwestern and one at Georgetown. This year, NOFAS plans to get their medical school program into two different universities. They hope with support from CDC, they will be able to move that forward.

Ms. Mitchell explained that the Curriculum for Addiction Professionals (CAP) project would be piloted in October. The plan is to educate addiction professionals who work with the highest risk women to teach them the knowledge of the science, historical perspective and identification of FASD; the behaviors and characteristics through the lifespan; prevention of FASD with high risk women; and counseling techniques for clients (adolescents and adults) with FASD and possible FASD, and their children. NOFAS is also involved in the HRSA Quality Improvement Project, the purpose of which is to test procedures for integrating routine alcohol screening for non- pregnant and pregnant women in primary care. The participants are 4 community health centers in Mississippi, Michigan, and Illinois. Team members consist of physicians, nurses, social workers, and front office staff. With respect to the project, the teams receive: a) a training session on FASD, AUDIT/AUDIT C, brief intervention, and business case; b) on-going technical assistance by expert faculty; and c) patient education materials.

NOFAS also developed a number of patient education materials, adapting the NIAAA materials for a variety of communities. One of their goals again this year is, even though they did not receive the HRSA award, is to work on disseminating many of their materials out to Community Health Centers (CHCs). In addition, they have been working on an on-line course on FASD prevention, which is very comprehensive. It will include video streaming and will teach practitioners how to screen and how to implement brief interventions with follow-up. CHCs are participating in course development. Continuing education credits will be available upon completion. There is audio narration and video role plays. Practice implementation issues will be addressed (e.g., Medicaid billing codes, work flow). The course is expected to be completed by December 2006.

NOFAS also continues to expand their affiliate network. They currently are in 12 states, with two in New York State, one in New York City and one in the Northern part of the state. They also have a NOFAS affiliate in England. New Jersey recently signed on to be one of their newer affiliates. The NOFAS affiliates have been very active and this is a great model that is building momentum across the states. With respect to accomplishments, affiliates participated in NOFAS' outreach to Community Health Centers in their states during National Women's Health Week. They disseminated NOFAS materials (e.g., loop tapes, posters, brochures) screening instruments, and provided workshops. NOFAS Washington State organized the 4th Annual FASD Summer Camp and will be organizing the first Northwest Pacific Regional FASD Conference along with affiliates in Arkansas and Minnesota. NOFAS Connecticut received a March of Dimes grant to conduct statewide public awareness campaigns. Membership on the FASD Caucus has increased due to Hill Day, regular affiliate correspondence, etc. NOFAS New York City convinced television station WPIX to feature FASD in a health segment.

Ms. Mitchell concluded with a legislative progress report, indicating that since June 2006, Senate bill S1722 co-sponsors list has increased to 11 (8 Democrats, 3 Republicans). S1722 (Advancing FASD Research, Prevention, and Services Act) is a Senate bill to amend the Public Health Service Act to reauthorize and extend the Fetal Alcohol Syndrome prevention and services program, and for other purposes. This was introduced and co-sponsored by Senator Lisa Murkowski (R-AK). The House of Representatives bill HR4212 co-sponsors list has increased to 18 (15 Democrats, 3 Republicans). HR4212 is the companion legislation to S1722 in the House of Representatives. The original co-sponsors were Representatives Jim Ramstad (R-MN) and Frank Pallone Jr. (D-NJ). The FASD Caucus membership has increased to 42. The co-chairs are Representatives Jim Ramstad (R-MN) and Frank Pallone Jr. (D-NJ). Congress also observed FASD Awareness Day on September 9th. Senator Murkowski introduced S499, which is a resolution to commemorate this day.

Discussion:

- Dr. Floyd inquired on how NOFAS planned to disseminate the K through 12 curriculum. Ms. Mitchell replied that their affiliate in New York is meeting with the New York City School System to attempt to get it there. NOFAS has applied for funding through a private foundation to get it into the Washington DC public school system. She has also placed calls to Dr. Ann Smith in the Department of Education to meet with her. NOFAS is really just beginning the marketing of this curriculum. Ms. Mitchell noted that she was embarking on a full marketing effort to get it out. She simply has not been able to move forward without having the materials in hand.
- Dr. Brown reported that sometimes the Council for Exceptional Children will distribute publications through an agreement with organizations. They reach people everywhere.

The Arc

Sharon Davis, PhD

Dr. Davis indicated that the Arc has an upcoming national conference October 12-14, 2006. This represents an opportunity for 900 chapters to come together for updates and to conduct annual business. They have a 3-hour workshop scheduled titled *Chapter Leadership in Prevention*. This will begin with a joint presentation by the Arc of New Jersey and the Arc of Warren County, New Jersey reviewing statewide prevention activities with a particular focus on FASD prevention. That will be followed by the Arc of Riverside in California, which has the "Nine/Zero Program, which is nine months with zero alcohol. It is students educating their peers and signing pledges not to consume alcohol during the nine months of pregnancy. That will be followed by the Saint Louis, Missouri Arc reporting on a community-based education/prevention program. That session will conclude with a family panel, which will focus on the challenges families face as well as what the chapters might do to support families. The Health Promotion and Disability Prevention Committee will sponsor an exhibit. The Arc will have their brochures on *Think Before You Drink*, both in English and Spanish, available during the exhibit. They will also make their FAS curriculum available for ordering. The Arc also sponsors a research and prevention luncheon, which will include information regarding chapter funding for prevention activities. While funding amounts are small (\$1,000 to \$3,000), they are enough for chapters to do something. Proposals were solicited early in 2006. The committee has made its recommendations, which go to the Board of Directors, which has not met yet so they cannot be announced at this point. She did report that that five of the projects that will be funded relate to fetal alcohol syndrome spectrum disorders prevention.

Center for Science in the Public Interest

George A. Hacker, JD

Dr. Hacker indicated that the Center for Science in the Public Interest's (CSPIs) activities only relate generally to drinking during pregnancy, FAS, and ARND. They continue to tackle the larger issues regarding alcohol promotion and consumer information. For the last two to three years, they have had a

project titled *Campaign for Alcohol-Free Sports TV*, which focused initially on advertising during college sports telecasts. He reported that they had some success over the summer. The Big Ten Conference, one of the largest college athletic conferences in the U.S., recently signed a 20-year deal with Fox Cable Channel. One of their first requirements to Fox would be that there would be no alcohol advertisements on that network. A [new sports television network](#) operated by the Big Ten Conference and Fox Cable Networks will not have advertisements for beer or other alcoholic beverages. Since then, the University of Minnesota has cancelled its radio contract and has also specified no alcohol. It took a very small financial hit, but that should be reversed over time. They are currently working in the SEC and will be meeting with the representatives of the Presidents' offices and the athletic departments for University of Georgia and Georgia Tech to seek their support.

Recently, when the World Cup was playing in Germany, the CSPI organized a group of 260 groups from 43 countries to protest the alcohol promotion and alcohol advertising during the World Cup. They also convinced the German Drug Czar to issue a statement during the World Cup in Germany opposing the connection of alcohol and sports, which they thought was a plus. However, they have not made too many inroads with FIFA, the organizing body that controls the World Cup.

With respect to underage drinking, for many years the Center for CSPI has been promoting a variety of legislation related to underage drinking, which has culminated in a bill known as the "Sober Truth on Preventing (STOP) Underage Drinking Act." Dr. Hacker reported that in the last month, that bill has taken a decidedly interesting course. They would know by September 29, 2006 whether that bill passed. This bill includes funding for research on underage drinking; better federal coordination related to underage drinking; monitoring of successful, evidence-based programmatic efforts at the state level to implement prevention efforts related to underage drinking; monitoring, though indirect, of media messaging or alcohol advertising on radio and television; community prevention projects and projects at the university level; and a small amount of funding for a parent-focused PSA campaign run by the Ad Council related to preventing underage drinking.

In the last month, this bill has been massaged somewhat by intervention from the Alcoholic Beverage Industry. Every sector of the Alcoholic Beverage Industry has now decided to support this bill and are calling it their own. They watered down many components of the bill in subtle ways, but also included a large section which essentially pays homage to the three-tier system in states (e.g., producer, distributor, and retailer) which is a legacy of post-prohibition regulation of alcoholic beverages. The beer, spirits, and wine wholesalers were concerned about direct sales of wine, and are also concerned about major stores like Costco and Wal-Mart taking over some of the distribution of the system. Therefore, the Alcoholic Beverage Industry inserted language into the bill that basically states that the three-tiered system is a bulwark against underage drinking. This is essentially the argument they have been making in lawsuits and in state legislatures throughout the country. Once they achieved that insertion, they were happier with the bill. In addition, they struck all of the findings which did not sound so good for the Alcoholic Beverage Industry and they struck a voluntary Congressional resolution related to alcohol advertising in the NCAA. The bill is very modest and now includes too much that smacks of industry; however, it is conceivable that it will pass. Unfortunately, without the Alcoholic Beverage Industry's involvement, it would probably never have passed.

Dr. Hacker also reported that since 1972, the CSPI has been trying to get ingredient, calorie, alcohol content, and other kinds of labeling on alcoholic beverage containers. The Tax and Trade Bureau recently put out Interim Rules and Proposed Final Rules on allergen labeling of alcoholic beverages basically because, under FDA law, certain well-known allergens are required to be listed. That was, by report language, extended to alcohol. While the industry wants more time, the Interim Rule is in place. It is voluntary, but it spells out what the essential duties of producers will be after the Final Rule goes into effect. The other areas that the CSPI has petitioned on and that remain pending (there was an Advanced

Notice of a Proposed Ruling in September 2006) relate to ingredients, calories, serving size, number of servings in the container, alcohol content, and serving facts (related to nutritional quality or lack thereof) for alcoholic beverages. The CSPI is waiting to learn whether those proposals are also going to be made. His guess was that if they are made, those regulations would likely be voluntary rather than mandatory mainly due to substantial conflict within the Alcoholic Beverage Industry on those issues.

In conclusion, Dr. Hacker reported that they expect within the next 60 to 90 days a Surgeon General's call to action on underage drinking, which they hope will amplify some of the recommendations that came out of the National Academy of Sciences report in 2003. However, they are now hopeful, given the turnover in the Surgeon General's office, and the fact that this document has been in clearance for many months. This may have some indirect bearing on the issues.

Discussion:

- If this bill did pass, Dr. Floyd wondered whether the enhancement of the ad campaign would be an important step. Dr. Hacker responded that the only benefit of passing that language currently included on the ad campaign would be that it would authorize a program. Currently, the Ad Council public service campaign has been appropriated year after year, with the funding levels bouncing up and down. The current proposal for fiscal year 2007 in the House language is \$200,000 to \$300,000 and in the Senate is \$850,000. It will probably end up somewhere in between. If it is authorized, that will call for potential appropriation of as much as \$1 million. His concern is that the language regarding media campaigns, which was the genesis of the entire effort going back to 1996, will be confused increasingly with the Ad Council's PSA campaign, which was an entirely separate stop-gap measure over the years.
- Dr. Floyd suggested that the Task Force might want to consider contacting SAMHSA about the potential to include some messages about the risks of alcohol exposed pregnancies in underage drinkers along with the campaign. Dr. Hacker responded that the downside is that it is currently limited to a parent-oriented campaign. Thus, the messages have to be directed to parents at this point. Dr. Floyd added that parents need to know also.

March of Dimes

Karla Damus, RN, PhD

Dr. Damus reported on current activities at the March of Dimes (MOD). They continue to work on their National Prematurity Campaign and a major strategy is to attempt to prevent preterm births. There is a clear link with substances (e.g., alcohol, smoking, prescription drugs, over-the-counter-drugs, etc). Hence, this is very relevant to the MOD. They are also doing a lot of research and funding around issues related to genomic, proteomic, metabolomic predispositions for preterm births. Clearly, this field, like every other field in the area of alcohol needs more and more research in that area. Therefore, the MOD strongly supports that the federal agencies continue to do that. The MOD has an Office of Governmental Affairs that can and does lobby the Hill every day on issues related to maternal and child health.

To summarize what the MOD has been doing, Dr. Damus characterized it as a lot of progress and yet a lot of frustrations. The campaign continues and will go through 2010. A major issue is that people are not aware that there is a problem or do not believe there is a problem and, therefore, will not pay attention to the messaging no matter how good it is. However, the MOD is determined to get the rates to go down even though they keep going up. They have seen preliminary data for 2005 and the rates have jumped again for the nation. This translates to more than a 30% increase in the last two decades, which means more than a half a million babies are being born at less than 37 weeks. With that in mind, the campaign goals are to: (1) increase public awareness of the problems of prematurity to at least 60% for women of childbearing age and 50% for the general public by 2010; and (2) reduce the rate of preterm birth from 12.3% in 2003 to the HP2010 objective of 7.6%.

With respect to where this is most common in the United States, there are numerous risk factors (e.g., race ethnicity, poverty, age of mother, recurrence, etc.) but also important is geographic location. Dr. Damus reported that since she last presented, it is now known that most of spontaneous preterm births are really classified as a common complex disorder like heart disease or cancer. Hence, addressing the risk factors associated with those serious chronic conditions can also prevent a lot of spontaneous preterm births. Given that communities understand such risk factors, this is an opportunity that the MOD is attempting to take advantage of in their campaign.

MOD has also been involved in several initiatives. The Preconception Summit was over a year ago. The MOD was very involved in that and the recommendations that came out in April 2006. To ensure that the recommendations go somewhere, they have established working groups. Dr. Damus is on the National Clinical Care Working Group, while the MOD's Senior Vice President for Education and Health Promotion is on the Consumer Working Group, so the MOD has a major role in the pre- and interconception activities going on nationally. The Georgia chapter of the MOD is doing a lot to have a web-based portal regarding all substances and alcohol and at what point a lot can be done to prevent alcohol exposure when and if the woman gets pregnant.

They also have been focusing on the late preterm, which is the reason why the rates are going up nationally. The 34 to 36 week deliveries used to be called "near-term." However, they are not term. They are still preterm if they are less than 37 completed weeks. There was a major Late Preterm Conference at NICHD in July 2005. As a result of that conference, there are two volumes of *Seminars in Perinatology Supplement* (Volumes 1 and 2, 2006) that offers information for health care providers regarding risks of delivering babies early. If it is obstetrically or medically indicated, of course the baby should be delivered early. However, increasingly more women are having babies in the late preterm area that may not be obstetrically/medically indicated.

The Institute of Medicine (IOM) recently published a report titled: *Preterm Birth Causes, Consequences, and Prevention 2006*. The MOD played a major role in that as well. IOM also had a report in 2001 titled *Environmental Toxicants and Preterm Births*. Both of these contained references to the importance of substance abuse, including alcohol, and what can be done about it. The MOD is also engaged in a great deal of research work. The entire month of November is Prematurity Awareness Month. Prematurity Awareness Day (PAD) brings focus to the nation on what can be done, including preventing preventable preterm births. They also have a lot of continuing education and reinforce the messages that no amount of alcohol has been shown to be safe in pregnancy. There is a preventable intervention and some strategies on how to deal with that and substance abuse. The MOD is also working with Family Medicine on what they call the Continuous Quality Improvement Initiative. More than 18 sites are involved, with whom they will meet during late October, mainly in the northeast (e.g., Pennsylvania, Massachusetts, New York). This stresses modifiable issues, including substance abuse as well as the importance of family planning. A major cause of unintended pregnancy in the U.S. is alcohol use. They are also doing a lot internationally, which they have to do for the genomic, proteomic, and metabolomic research. They are also addressing the issue of stress and how people attempt to relieve their pain by self-medicating. To address this issue, the MOD will provide services in the Katrina-ravaged sections of the U.S. with mobile units (MomVans) that provide education and care, which are going to be launched this year. Dr. Damus is the program director for an initiative in Kentucky that will be launched in January 2007 to reduce the rates of singleton preterm births in parts of the state by 15%.

Dr. Damus stressed that there were many opportunities to deal much more efficiently, based on the life course perspective, with inappropriate risk in terms of exposure of the fetus to substances, including ethanol. At the preconception summit, many papers were presented. There is an entire volume in the *Maternal and Child Health Journal* that recently came out, which is devoted to preconception care. It is

very important for providers to have this and all of this is available through the MOD website. The MOD is trying to get messages out. Dr. Damus and Dr. Sokol discussed their hopes that there could be a press release from the MOD with ACOG on the important toolkit that Dr. Sokol shared earlier. She reiterated that the reason the rates are going up is mainly due to late preterms driving the system up. The conference attempted to consider all of these issues in the two volumes mentioned earlier. These PDFs are also available on the MOD website as are the ones related to the *MCH Journal* on preconception health.

The MOD showed that interestingly, in the U.S. the most common week of delivery shifted one week to the left from 40 to 39 in the past decade, which is pretty dramatic. So, things are changing. A little bit of good news for African-American moms and babies in this nation for singleton births (which represent about 96.7% of all live births) is that very preterm births actually decreased, as did 32 and 33 week deliveries and there was no increase in late preterm. For every other group (about 80% of total births in this nation) the reason the rates go up is late preterm births, which are related to so many of the issues related to alcohol. Therefore, the issues pertain to getting women to think about going to term (e.g., what questions they should ask their providers; stopping smoking, alcohol and other drugs, and medications, and how to integrate a lot of this, including whether preterm births may be genetic) are very important. Birth weight and gestational age are predictive for many chronic diseases. The importance of folic acid is well-known, but alcohol will eliminate folic acid, so there is a major link here. The MOD will be focusing on these clinically and, of course, they integrate poly-substance abuse and smoking cessation. They also have a nursing module that gives 5.5 contact hours to nurses on perinatal substance abuse, so they are trying to provide continuing education and tools to nurses. For physicians they have grand rounds.

Dr. Damus reported that there will be an increasing focus on progesterone. She indicated that she is co-author on a paper that considers the behavior of providers which indicates that, based on maternal/fetal medicine physicians' responses to a survey, the rate of use of progesterone (which can help to prevent recurrent preterm births) increased from approximately 36% to almost 70% in about 18 months. In that paper, there are numerous reasons physicians are using progesterone. The MOD testified for FDA in August 2006, encouraging that progesterone (which will be called Gestiva based on focus-group input) be readily available. This is important because women need to begin receiving progesterone early in the next pregnancy in order for it to be effective. Substance abusers often have delayed care, if any, so it is important to get the message out to women who may benefit from this in their next pregnancy. Because of FASD, it is known that alcohol use is going to contribute to a greater likelihood of being in the group which experiences recurrence. There is a lot of education around this and it will become readily available, even for Medicaid families.

A paper titled *Research agenda for preterm birth: Recommendations from the March of Dimes*, which came out a year ago in the *American Journal of Obstetrics and Gynecology*, puts forth a national research agenda targeting primarily very preterm births and represents the first time that preterm birth is discussed as being like heart disease and cancer. The issues addressed that need to be considered in terms of moving forward on the research include: disparities, inflammation/infection, genetic, gene-environmental interactions, stress, high risk interventions (multifetal, artificial reproductive technology), and promising clinical interventions. Also addressed in the paper, and of great importance, are pathways. While the pathways are not all defined, the importance is the way these pathways interact with the external environment (e.g., secondhand smoke, issues around nutrition and how that is impacted, and behaviors such as alcohol use) as well as the genetics, genomics, immune status, medical management and interventions, and other conditions. Dr. Damus stressed that this is the best type of model for other adverse outcomes—not only preterm births, but also recurrent pregnancy loss and many of the components of the FASD reproductive spectrum affecting a woman and her pregnancy outcome. The MOD is attempting to understand the mechanisms and how they work in the entire cascade, particularly

with respect to the spontaneous early preterm birth. Things begin to get even more genomic and mechanistic when you look at maternal and genetic contributions of the infant and the inflammatory response. It is well-known that any substance abuse causes a relative immuno-suppression. The mother is already relatively immuno-suppressed while she is pregnant, so all of these will confound the pathways.

Dr. Damus reported that two of the MOD's funded grantees have recently had publications describing their identification of a variant in the SERPINH1 gene, which helps to control production of collagen, which is particularly important for fetal membrane. More specifically, SERPINH1 controls the production of the protein collagen, a key component of many body tissues, including cartilage, ligaments, tendons, bone and teeth. Variations of the gene were identified that result in reduced amounts of collagen, which could lead to weakened fetal membranes, increasing the chance of rupture triggering preterm birth. This genetic variant is much more common in African Americans. Another MOD-funded grantee found that PRCP E112D could be a highly sensitive and specific early predictor of preeclampsia among women with chronic hypertension long before pregnancy. Chronic hypertension in both African-American and non-African American women has a significant association with preeclampsia. Thus, they are beginning to understand the importance of genetic predispositions in preterm birth. Given that, the MOD is reassessing the way they have looked at traditional predictive risk factors of preterm birth.

In conclusion, with respect to preterm legislation introduced, Dr. Damus reported that the "PREEMIE Act" and the "Prevent Prematurity and Improve Child Health Act of 2005" passed the Senate and are awaiting passage in the House. The "PREEMIE Act" authorizes expansion of research into the causes and prevention of prematurity and increases federal support of public and health professional education as well as support services related to prematurity. The "Prevent Prematurity and Improve Child Health Act of 2005" calls for improved access to health coverage for pregnant women, infants and children. It would provide states increased flexibility and federal resources to expand access to maternity care for income-eligible pregnant women and increased access to health coverage for infants and children with special health care needs.

Other Business

Update on Early Childhood Longitudinal Studies Birth Cohort Database

Carole W. Brown, EdD

Dr. Brown reported on the Early Childhood Longitudinal Studies—Birth Cohort (ECLS-BC), which is part of two studies that were conducted by the National Center for Educational Sciences (NCES). The Early Longitudinal Studies Kindergarten Cohort was begun in the late 1990s with children in kindergarten, who are currently in 8th grade. As soon as the NCES began the work on the Early Longitudinal Studies Kindergarten Cohort, they realized that they started much too late, and they began planning the ECLS-BC in 2001. The ECLS-BC is drawn from a sample of nearly 4 million children born in 2001 who will be followed until they are in kindergarten, meaning that this year, some of the children are starting kindergarten and next year most of the children will begin kindergarten. The ECLS-B sample consists of 10,688 children who were selected and 10,221 of these who were directly assessed at 9 months. The sample is representative of "all" children born in 2001. This is a large, comprehensive study in which even all fathers were interviewed. The study was funded by a number of federal agencies, including NIAAA.

The basic conceptual framework for the study is the relationship between parent status/demographic and family level factors and child developmental outcomes. The study is designed to follow children longitudinally through kindergarten and is directed at being able to predict the relationship and interactions of family, child, and community (e.g., child care and preschool factors to kindergarten readiness). Data collection to respond to these topics comes from extensive parent interviews of fathers and caretaking parents, self-administered questionnaires, direct observation and assessment of the infant, video analysis of observations of infant/parent interaction at 9 months, 24 months, 4 years, 5 years, and 6

years of age. With respect to relevance to alcohol consumption and child development, questions on alcohol consumption levels are included for the 3 months before pregnancy; last 3 months of pregnancy; and at 9 months of child's age. These questions are asked of the parents when the child is 9 months of age. The 9 month and 2-year old data are currently available.

Dr. Brown will be studying not only the issues relevant to FAS, but also the characteristics that are associated with irregularities in development in that area. This will include diagnosis of FAS on the birth certificate; physical health symptoms; and growth (e.g., birthweight, weight and height, head circumference available for infants who were born prematurely). At the 9 month data point, consideration is given to social interaction (NCATS); the Infant Symptom Scale (DiGangi, et.al); and mental and motor scores (Bayley Short Form Infant Development). At 24 months, consideration is given to separation/attachment (Two Bags Test); mental/motor skills; physical health and services received; child care received; and early intervention. On-going data collection occurs at 48 months and kindergarten.

With respect to the statistics, alcohol consumption levels reported pre-pregnancy are quite a bit lower than the rates being reported nationally. The study is considered to be nationally representative. It has been weighted in order to meet the standards. For example, during pre-pregnancy approximately 35% are reporting some type of drinking; whereas, in the study that is reported in the paper it is approximately 54%. During pregnancy, approximately 3% are reporting drinking during the last three months of pregnancy. However, there are still adequate numbers for analysis with 186 (1.7%) women reporting drinking less than 1 drink per week, 95 (.9%) women reporting 1 to 3 drinks per week, 9 (.1%) women reporting 4 to 6 drinks per week, and 6 (.1%) women reporting 7 to 13 drinks per week. The data at 9 months is more similar to the preconception stage.

Dr. Brown invited questions and comments from Task Force members via email regarding any information they could offer with respect to assisting her in thinking more clearly in the future about the issues related to this analysis.

Proposed Motions and Discussion

The following is the final open discussion among Task Force members regarding several recommendations as well as the sunseting of the Task Force. To set the stage for these deliberations, Dr. Wright reminded those present that at least three ideas had emerged from the Task Force membership during this meeting: (1) convening a conference; (2) the Task Force holding a joint session with the Interagency Committee; and (3) a potential motion regarding the Task Force playing a role in encouraging research, perhaps through a letter. To open the discussion, Dr. Heather Olson offered the following proposed motion for Task Force Consideration:

PROPOSED MOTION

This motion was composed with the assumption that Task Force efforts to advance FASD prevention are underway, and so these are not addressed here. This proposed motion is an initial effort; member input and discussion are encouraged, but ongoing discussion will need to occur following this meeting.

Motion: Send a strongly worded letter to advise the Secretary of Health and Human Services (and/or other appropriate recipients) on funding of a research agenda. This letter could be composed by an ad hoc working group of volunteer members of the Task Force, who meet by teleconference and send edits to the letter by email. This process was successfully used in composing the letter regarding the IDEA reauthorization. The letter would then be taken by CDC staff through the clearance and approval process.

Basic Structure of the Letter: Begin with a brief restatement of the mission of the Task Force and its accomplishments. Then present a strong rationale for the importance of societal and research attention to FASD, and an overview of the productive and meaningful accomplishments of researchers and funding agencies (including NIAAA, CDC, and SAMHSA) since the Task Force was initiated in 2001. Finally, point out what remains to be done.

Basic Concepts for the Letter: The Task Force strongly supports funding of a research agenda directed towards:

- Clarifying diagnostic criteria for the full spectrum of deficits arising from fetal alcohol exposure, including those present in the absence of facial dysmorphology. Productive research directions include study of brain-behavior relationships and neurobehavioral profiles, methods of early detection and high-risk population screening, and validity and reliability of a range of diagnostic techniques and approaches.
- Appropriately controlled research investigations and systematic field-initiated studies to respond to the pressing need for family support and efficacious interventions (from early intervention and across the lifespan) for individuals affected by prenatal alcohol exposure and their caregivers. These can include interventions at the individual, family, community, and system levels. These interventions can be behavioral, educational, nutritional, pharmacologic, or environmental in focus.

Discussion:

- Dr. Olson pointed out that the proposed motion seemed to be a reasonable, practical, doable motion that could be accomplished by this Task Force. Given that the clearance process is time-consuming, she requested that the Task Force work to develop the formal motion and hopefully form the ad hoc committee during this meeting in order to move the letter writing process forward. Dr. Olson noted that she specifically used the phrase “efficacious interventions,” which did not mean that it had to be already evidence-based intervention, but that they could even add the word “promising” to modify the word “efficacious.”

- Dr. Bertrand indicated that in speaking with CDC's policy expert, she indicated that they needed to be careful with respect to research funds and issues pertaining to funding, given that it could be construed as lobbying and/or could take funds away from other efforts in progress. Dr. Olson responded that they could remove the word "funding."
- Dr. Wright reminded the group that earlier, there had been requests for further clarification with respect to the purview of the Task Force. One of her reactions was that if they took this to committee off-line, they could obtain further information pertaining to the most effective way to proceed as well as any constraints. Dr. Bertrand responded that Jackie Vowell would develop a list of the products that would be permissible for the Task Force to produce, as well as a list of what specifically is not permissible.
- Dr. Damus pointed out that the efforts of the Task Force should be beneficial; therefore, they should not create a motion that would close their options. She acknowledged that the proposed motion represented a tremendous amount of effort which reflected how the Task Force appeared to feel about the issue. While she agreed that the efforts described in the motion needed to be made, the group needed CDC guidance on what would serve the agency and could be carried out quickly.
- Dr. Wright noted that while the proposed motion focused on a research agenda, another issue of importance raised that she would like to see the Task Force address /recommend /encourage regarding the continuation of the good work of the FASD Center for Excellence. If they were going to propose a joint session, perhaps that could be raised there as well.
- Mr. Hacker expressed his hope that in terms of what the appropriate form of a communication might be, the Task Force would explore the extent to which this could go directly or indirectly to the members of Congress who are most responsible for making decisions related to funding on these issues and who could ask the right questions of agency heads during hearings and authorization proceedings. He thought it was perfectly legitimate for the Task Force to educate policymakers regarding the issues and what needs to be addressed. He did not think that was necessarily lobbying and requested that they explore the options. Dr. Bertrand responded that there are rules which must be followed carefully, but that they could explore the possibilities. Dr. Floyd added that after something is put forward, it does not belong to the Task Force. It becomes public domain and anyone could use the information to state that the National Task Force endorsed certain ideas, efforts, etc. For example, NOFAS could pick up the advocacy aspect and carry it forth.
- Dr. Ohlemiller said it was muddy for her to think about all of the concepts combined in the one proposed motion, given that they each had a different emphasis. The proposed motion and other suggestions had profound emphases, particularly with respect to finishing the work that the Task Force was commissioned to do and driving forward the issues on ARND clarification. She thought it was worthy of a committee massaging it and that the proposed motion was an excellent one that would give them a great start. She stressed that should parcel out the SAMHSA FASD Center for Excellence issue, given that is an emergency and would likely occur before they could even set a telephone conference date. Her understanding from the SAMHSA update was that the FASD Center for Excellence was due to end in December. Dr. Bertrand responded that for this issue, they could perhaps do the same thing they did about the letter to ACOG.
- Dr. Morris agreed that research should continue in ARND; however, she also thought that there had been enough experience in the last few years (along with some of the research coming out of the Consortium) that it would be appropriate to schedule a meeting similar to one held a few years ago around diagnosis and criteria for FAS. Whereas this could not have been done a few years ago, it now can be done for ARND. She said she would like the Task Force to endorse the idea of having

CDC convene a meeting to include clinicians and researchers to develop guidelines for ARND. She thought this should be scheduled even while continuing research was on-going which may refine the guidelines.

- Ms. Mitchell concurred, stressing that NOFAS would like to push that agenda forward. Being in touch with many folks working on this issue, she appreciated the idea that they needed to continue to conduct research for further understanding. However, hearing the presentations from the previous day, they are not there yet. Hence, NOFAS's hope would be that the Task Force would want to move this forward, bringing a collective effort together in the form of a committee to "iron this out." She hears often from those who are diagnosing that they "know it when they see it."
- Mr. Hacker reiterated that perhaps they should include language regarding the Task Force advising Congress, noting that the charter states that the Task Force is advisory to the Secretary of Health and Human Services. While concern was raised by some participants with regard to whether this would be appropriate, Dr. Warren pointed out that the Task Force is mandated by Congress. With that in mind, Dr. Olson indicated that she would include "and/or other appropriate recipients" in her motion language.

MOTION

Dr. Olson moved that the Task Force immediately create an ad hoc committee to discuss how to advise the Secretary of Health and Human Services and/or other appropriate recipients on promotion of a productive research agenda on Fetal Alcohol Spectrum Disorders (FASDs). Dr. Damus seconded the motion. The motion carried unanimously.

The following Task Force members volunteered to serve on the proposed ad hoc committee: Dr. Carole Brown, Dr. Mary O'Connor, Dr. Karla Damus, Dr. Melinda Ohlemiller, and Dr. Heather Olson.

The following CDC representatives will serve on the proposed ad hoc committee: Dr. Jacqueline Bertrand, Dr. Louise Floyd, Ms. Mary Kate Weber, and support staff.

Discussion:

- Dr. Floyd commented that Dr. Olson prefaced her introduction to the original proposed motion by mentioning the assumption that everything with regard to primary prevention is underway. She encouraged the Task Force to give thought to including a third bullet that indeed addresses that. While a great deal is known about what works, the problem is getting that information to the women who are at risk for an alcohol-exposed pregnancy. She also thought the important efforts that must be made in getting information disseminated to providers, and evaluating that information and improving it, represents work that is not fully funded which needs to be carried out as well.
- Dr. Wright then returned the group's attention to the proposed conference.
- Ms. Mitchell suggested that they first view a potential conference as a mechanism for collecting information on what is being done by various clinicians. An inquiry was posed regarding whether the NOFAS survey of clinicians could form a basis for doing that. Ms. Mitchell responded that they started that process but lost funding to convene the meeting. However, they do have data that they collected during the survey and have sketched out an outline of how this might be presented, although their thinking was not about trying to obtain a consensus at this point. NOFAS has a list of practitioners who potentially could be invited to a meeting and they would be happy to share that.
- Dr. Warren indicated that the Collaborative Interactive Fetal Alcohol Syndrome Spectrum Disorders (CIFASD) project is coming up for competitive renewal this year and NIAAA will soon issue the

RFA for that. NIAAA has strongly emphasized to the investigators that they need to disseminate data. Since the neurobehavioral issue, and the neurobehavioral phenotype, is one of the major issues that they are involved with as well as diagnosis, he anticipated that in less than a year, data should be out which would have a direct bearing on this. NIAAA is exerting a great deal of pressure on investigators so that information will be published and available in other forums. In his view, this is a critical component and not having the update on the data is “putting the cart before the horse.” He thought going to the clinicians first would be operating backwards. It was his belief that they must have the data first. Dr. Miller responded that this was why she suggested bringing the clinicians and researchers together.

- Dr. Wright wondered whether this idea was ready for discussion by the Task Force group or if it needed ad hoc committee deliberations as well. Dr. Sokol responded that this sounded reasonable, but stressed that there are many stakeholders and many people who need information. He thought there would be strength as well as problems in convening such a meeting, but pointed out that they should take into consideration where definitions had come from. The original definitions came from investigators and were formalized by the Fetal Alcohol Study Group of RSA twice. Those definitions were used widely in driving the field forward in publications. Then the Institute of Medicine (IOM) became involved and also introduced some terms, which unofficially carried great weight given that these came from NIAAA. The term “ARBD” originated from one scientist at IOM who suggested that this was a better way given the problems with the term “FAE,” which continues to be a problem because it is still used though nobody knows what it means. The same problems are occurring currently because terminology has been proposed that does not have consensus across all of the stakeholders. Moreover, FASD is not being used consistently which is muddying the literature, making it extremely difficult to figure out whether investigators have comparable findings. With respect to ARND, he did not think this could be done merely from the phenotype, nor did he think most pediatricians thought so either. Dr. Sokol stressed that a definition should not be developed without involving the American Academy of Pediatrics, psychiatrists, and others who use diagnostic categories. This is extremely important because this is the key to what is paid for, which is certainly of concern when trying to get information widely dispersed. While not speaking for or against, Dr. Sokol indicated that he was suggesting that great care be taken in coming to a decision to make a move before involving more stakeholders.
- Dr. Olson summarized that there seemed to be four issues on the floor: (1) the creation of an ad hoc committee, which they passed; (2) the possibility of a conference; (3) a statement and/or recommendation from the Task Force about continuing the SAMHSA FASD Center of Excellence; and (4) the education conference in the summer of 2007.
- Dr. Brown inquired as to whether the Task Force could investigate the possibility of a Task Force meeting being convened near the time of the Department of Education’s conference in Washington, DC in the summer of 2007. Dr. Wright responded that this related to the timing of the Task Force meeting, for which they did not need a motion given that this could be decided internally. Dr. Warren pointed out that Sally Anderson could work on this.

MOTION

Dr. Miller moved that the Task Force direct CDC to convene a meeting of appropriate stakeholders and clinicians involved in the diagnosis and treatment of children with FASDs to begin the process of formulating diagnostic criteria or guidelines for ARND (there is a definition).

Dr. Bertrand proposed a friendly amendment: Replace “direct CDC to convene” with “direct CDC to investigate the feasibility of convening a meeting,” given that budget issues must be taken into consideration.

Dr. Sokol proposed a friendly amendment: With respect to feasibility, consider timing so that this could form the basis for Task Force logistics discussions with the ICCFAS.

Dr. Olson proposed a friendly amendment: Replace “children” with “individuals affected” so that the lifespan perspective is addressed.

Dr. Damus seconded the motion. The motion carried unanimously.

Discussion:

- Dr. Floyd pointed out that they should also plan ample time to obtain data from NIAAA.
- Dr. Ohlemiller commented that not everybody uses or agrees on the term “ARND.” Therefore, she suggested that they consider using the terminology “nondysmorphic-alcohol exposure” so that when this is publicized they do not convene a group strictly about ARND, given that it could turn people off. Dr. Olson suggested “full spectrum of deficits arising from fetal alcohol exposure, including those present in the absence of facial dysmorphism.”
- Returning to the issue of the SAMHSA FASD Center for Excellence, Dr. Ohlemiller stressed the importance of having the minutes reflect that, with the possibility of the FASD Center for Excellence soon ending, this would leave a great deal at risk. She proposed that the Task Force endorse the continuation of the work of the Center for Excellence, acknowledging that while the Task Force could not dictate contracts, the work that has been begun should be completed and continued into the future. Dr. Brown cautioned that perhaps they should say “the work of a center to promote” rather than just “the work” because it could be decentralized in a way that would lose the essence of the coordination. Dr. Miller added that they should also express appreciation for the work that has been accomplished by the FASD Center for Excellence. Dr. Floyd responded that this was moving into an area where they likely needed some consultation. She did not believe that normally the Task Force would recommend that the FASD Center for Excellence be funded. This is similar to dealing with the research agenda and how to propose it within the purview of the Task Force. In addition, this would need to go through CDC clearance. If time is a problem, this mechanism may not be the most suitable. An alternative would be for another organization to write a letter and have each Task Force representative organization sign it. However, this would be an individual effort rather than a function of the Task Force.
- Dr. Ohlemiller pointed out that she deliberately did not use the word “funding” and wondered why they simply could not recommend a continuation of the work itself. Dr. Sokol inquired as to whether the committee could request, as an agenda item, a report from SAMHSA regarding the plans for continuing the funding for the work of the FASD Center of Excellence. Callie Gass noted that while she did not want to overstep her boundaries given that she is a contractor, the last Congressional mandate for the FASD Center for Excellence was for the body (e.g., SAMHSA) to be responsive to

directions from the Task Force. Her scope of work is to complete the four mandates and the work in them, and to respond to direction within budget and SOW from the Task Force. The contractor anticipates a cost extension beyond November 30, 2006.

MOTION

Dr. Wright moved that the Task Force explore the correct method to commend SAMHSA for the FASD Center for Excellence work and express their concern regarding closure to the work and where that responsibility may lie.

Dr. Sokol seconded the motion. The motion carried unanimously.

Discussion:

- Dr. Ohlemiller inquired as to whether someone could speak to the potential sunset of the Task Force. Dr. Wright responded that the Task Force was due to sunset in 2007. She noted that during the Task Force's last meeting, she had the sense that Dr. Gerberding was reorganizing advisory committees at CDC and that this committee may be bundled into another group. Dr. Bertrand responded that Mary Kate Weber, who was unable to attend, had information on this, but that it was her understanding that the Task Force would not be bundled given that it was a federally mandated committee. Dr. Bertrand indicated that Maggie Kelly has been working with the CDC policy office in Washington, DC as well as NOFAS regarding putting forward legislation that would reauthorize the Task Force along with other components. They are currently looking at pulling out just the sunset, just the Task Force information, and attaching that to some other bill in order to get it done in time within the current or next session. Dr. Floyd added that CDC had been providing information at the request of the CDC Washington, DC office and to NOFAS about the many accomplishments of this Task Force, which have been truly extraordinary.
- Dr. Damus requested an update on the work with the nursing school on the curriculum, given that it is key to get nurses on board. She wondered whether someone could report on the timeframe. Elizabeth Dang responded that the New Jersey Regional Training Center has been working with the Jefferson School of Nursing and they have conducted some training already. She reported that they were happy to connect with Dr. Damus and that with respect to the timeframe, she could have Susan Aduabato contact Dr. Damus.

Next Meeting/Meeting Dates

Dr. Bertrand indicated that there probably would be a February meeting to work on the Task Force's prevention report. If they could convene jointly with the ICCFAS, that may mean that the Task Force would meet in February and July 2007.

Public Comment/Adjourn

With no public comments offered or further business raised, Dr. Wright officially adjourned the meeting.

Minutes approved on 12/20/2006
by Jean A. Wright, MD, MPH
Chair, National Task for on FAS/FAE