PROGRAM

Recognizing Alcohol-Related Neurodevelopmental Disorder (ARND) in Primary Health Care of Children

October 31–November 2, 2011 ▪ Rockville, MD 20852

Case Study: ARND

David is a Caucasian male followed by the teratology clinic on four occasions, at ages 6 months, 20 months, 3 ½ years and 5 ½ years. He was removed from the custody of his birth mother when he was 3 weeks old and placed with his maternal aunt, Marcia Long, who has adopted him and two of his siblings. The family lives in an upscale suburban community in a large metropolitan area.

David's birth mother, 22 years old when he was born, has a long history of alcohol and drug use and is reported to have used during this pregnancy. Exposures during this pregnancy included alcohol, crystal methamphetamine, Xanax and Lortab.

David was born at term with no neonatal problems. Growth was not affected either at birth or at any subsequent visit. Dysmorphology examination at 6 and 20 months noted some physical features associated with prenatal alcohol exposure but not the sentinel features required for a FAS diagnosis. At 3 ½ years, these features were not found and, at 5 ½ years, this examination was not repeated.

Developmental assessment at 6 months found him to be functioning within the average range in most areas. However, his fine motor skills were noted to be a relative deficit in relation to other skills. Assessment at 20 months found him to be functioning the average to low average range on Cognition (SS=95, 37th percentile) and Language (SS=91, 27th percentile), but to show a significant deficit in motor skills (SS=76, 5th percentile). At these ages, Adaptive skills were consistent with his cognitive development.

At 3 ½ years, David's Ability was found to be in the Average range, with an overall cognitive standard score of 96 (39th percentile) but a spatial standard score of 87 (19th percentile) with a weakness in hand/eye coordination and graphomotor skills. Consistent with these findings, his score on the Developmental Test of Visual-Motor Integration, which is often associated with later learning disabilities, was 62 (<1st percentile). Preacademic screening measure indicated that he was performing at a level commensurate with his cognitive ability. In contrast, Adaptive Behavior was consistently in the Low Average range (SS=79, 8th percentile).

At 5 ½ years, David's ability could not be assessed due to his behavior during testing. He was extremely oppositional and tearful. On the single Verbal score obtained, he was found to be functioning at the 86th percentile. A subsequent test of nonverbal ability found him to have a standard score of 107 (68th percentile). The School readiness screener was at the 37th percentile and in the Average range. At this assessment, David was noted to be in a general classroom setting with special education resources provided.

No health problems were reported during his first several years, but chronic diarrhea and GI referral were noted at the 3 ½ year assessment. He was not toilet trained until he was 4 years old. He is reported to have a small appetite and to be a "picky" eater and to prefer foods based on their appearance. David is reported to have had problems with sleep that were first noted at 6 months, were persistent at 20 months and included frequent night wakenings. These problems were resolved by 3 ½ years but at this time he was noted to have significant problems with behavioral regulation, including tantruming, hyperactivity, and noncompliance. At this time, he was noted to have Clinically Significant elevations on Externalizing Behavior both at home and in the school setting. Attention Problems were noted by his caregiver. At 5 ½ years of age, David was having frequent tantrums or "melt downs" and exhibiting aggressive behavior. These behaviors were associated with "transitioning" from one activity to another and with not getting his own way. Clinically Significant elevations were noted by parents in Attention, Aggressive Behavior, and Internalizing and Externalizing Behaviors. His special education preschool teacher did not note any behavior problems.

Diagnoses have included: Developmental coordination disorder (315.4), Cognitive Disorder, NOS, (294.9); Behavior Disorder, unspecified (312.9); Atypical Autism (299.80); Oppositional/Defiant Disorder (313.81), and Prenatal Exposure to Alcohol (760.71).

Recognizing Alcohol-Related Neurodevelopmental Disorder (ARND) in Primary Health Care of Children

Initiative of the

Diagnostic Issues Work Group
Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders

Sponsored by the

Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders
National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health
Centers for Disease Control and Prevention
American Academy of Pediatrics

October 31–November 1, 2011

National Institute of Alcohol Abuse and Alcoholism
5635 Fishers Lane
NIH Fishers Lane Conference Center
Terrace Level, T508
Bethesda, MD 20892-9304

November 2, 2011

Legacy Hotel & Meeting Centre
Rose Hill Ballroom, Salons I and II
1775 Rockville Pike
Rockville, MD 20852

Welcome Message from the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD)

On behalf of ICCFASD, welcome to a conference on Recognizing Alcohol-Related Neurodevelopmental Disorder (ARND) in Primary Health Care of Children. This conference is an effort to move research to practice to promote the well-being of children affected by prenatal alcohol exposure.

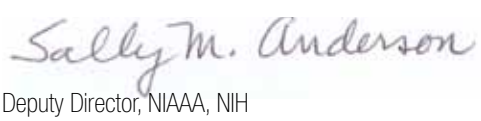
ICCFASD (formerly called the Interagency Coordinating Committee on Fetal Alcohol Syndrome) was created in October 1996, following a recommendation in the Institute of Medicine report Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment that the National Institute on Alcohol Abuse and Alcoholism chair a broad Federal effort to coordinate activities associated with fetal alcohol syndrome and related health conditions. The mission of ICCFASD is to enhance and increase communication, cooperation, collaboration, and partnerships among disciplines and Federal agencies to address health, education, developmental disabilities, alcohol research, and social services and justice issues that are relevant to disorders related to prenatal alcohol exposure. (More information about ICCFASD, its mission, vision, membership, work groups, and past activities is available at http://www.niaaa.nih.gov/AboutNIAAA/Interagency/Pages/default.aspx.)

Credit for conceptualizing and initiating this conference goes to the ICCFASD Diagnostic Issues Work Group, one of four work groups established by ICCFASD to address special issues and to plan and implement directed activities. Since late 2008, the ICCFASD Diagnostic Issues Work Group has been working to determine if sufficient evidence exists to encourage screening and diagnosis (or referral for diagnosis) of ARND in pediatric care. Past activities are a scientific workshop to review how ARND is being diagnosed in specialty clinics and how FASD researchers are defining ARND in their studies and two conference planning meetings that included the American Academy of Pediatrics.

ICCFASD now is hosting this consensus development-style conference to obtain additional input from others outside of the FASD community. We have assembled a broad-based panel of knowledgeable and unbiased critical thinkers to hear and evaluate evidence presented by experts in the field. Our goal for the meeting is to arrive at recommendations and future directions on whether to encourage screening and diagnosis (or referral for diagnosis) of ARND in primary health care of children.

Thank you for joining us in this important venture.

Kenneth R. Warren, Ph.D.
Acting Director, NIAAA, NIH
Coordinator and Executive Secretary



Sally M. Anderson, Ph.D.
Deputy Director, NIAAA, NIH
ICCFASD
Chair, ICCFASD
NIAAA, NIH

About FASD and ARND

The nondiagnostic umbrella term "fetal alcohol spectrum disorders (FASD)" is now used to characterize the full range of damage from prenatal alcohol exposure, varying from mild to severe and encompassing a broad array of physical defects and cognitive, behavioral, emotional, and adaptive functioning deficits. FASD includes diagnoses such as fetal alcohol syndrome (FAS), partial FAS (pFAS), alcohol-related neurodevelopmental disorder (ARND), and alcohol-related birth defects (ARBD), which are congenital anomalies including malformations and dysplasias of the cardiac, skeletal, renal, ocular, auditory, and other systems.

The negative effects of prenatal alcohol exposure on the developing brain and the resulting neurological and/or cognitive, behavioral, emotional, and adaptive functioning deficits are seen in individuals with FAS, pFAS, and ARND. Significant alcohol exposure early in prenatal development often results in growth retardation and facial anomalies. These physical characteristics have been useful tools for diagnosing FAS and pFAS. Identifying persons who do not have the physical characteristics of FAS but do have neurodevelopmental disorders induced by prenatal alcohol exposure has proven to be much more challenging, with broad implications. Current prevalence estimates for FAS range from 0.5 to 7 cases per 1,000 live births in the United States, and the prevalence of FAS and ARND combined is thought to be three times that of FAS alone.

In 2004, the National Center on Birth Defects and Developmental Disabilities of the Centers for Disease Control and Prevention and the National Task Force on FAS and Fetal Alcohol Effect issued *Guidelines for Referral and Diagnosis of FAS*. Evidence for recommending screening and referral for diagnosis of ARND was considered insufficient at that time. In the past 7 years, a large body of research evidence has been published on further characterization and differentiation of the cognitive, behavioral, emotional, and adaptive functioning deficits associated with prenatal alcohol exposure. The time has come to reassess whether there is now sufficient evidence to recommend screening and/or referral for diagnosis of ARND in primary health care of children.

Vignettes

Persons with neurological and/or cognitive, behavioral, emotional, and adaptive functioning deficits due to prenatal alcohol exposure have significant difficulty navigating most stages of life and, even as adults, have difficulty in maintaining a job and living alone. The vignettes included in the final section of the program and the inside front and back covers illustrate some of the lifelong ramifications of FASD. Fortunately, early identification and intervention have been shown to improve outcomes for individuals and lessen the burden on their families and society. Pediatric health care and early school years provide prime windows of opportunities to recognize and respond early to ARND and other FASD.

Consensus Development-Style Conference Format

A consensus development-style conference, simply put, is a "jury trial" on health or scientific issues. The panel (jury) is a broad-based, nongovernmental, nonadvocacy, unbiased group with appropriate expertise. The panel listens to the scientific evidence presented by invited experts and to comments from other conference attendees. The panel then meets in closed sessions to synthesize this information, along with sometimes conflicting interpretations of the evidence, into clear consensus statements that respond to a set of predetermined questions. Those statements, or recommendations, are presented to attendees by the panel chair at the end of the conference.

The statement rendered by the panel is not a legal document, practice guideline, or primary source of detailed technical information. Rather, it reflects the views of a panel of thoughtful people who understand the issue before them and can evaluate the evidence. The panel statement provides a context for the issues and may pose next steps in their resolution. It may reflect uncertainties, options, or minority viewpoints.

The objective of a consensus development-style conference is to arrive at a statement that advances an understanding of the issue and that will be useful to health professionals. To that end, the recommendations of the panel will be refined and widely disseminated. A report of this conference will be prepared and posted on the ICCFASD Web page. *The recommendation statement and the conference report, however, should not be considered as a policy statement of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders, the National Institute of Alcohol Abuse and Alcoholism, the National Institutes of Health, the Centers for Disease Control and Prevention, the Federal Government, or the American Academy of Pediatrics.*

The predetermined questions posed to the panel and on which this conference is based are:

Question 1: What is ARND and how is it diagnosed (classical, current diagnostic schemes, in practice today)?

Question 2: Can ARND be differentiated from other disorders?

Question 3: What prenatal alcohol exposure evidence is necessary for an ARND diagnosis?

Question 4: What signs and symptoms will be useful as screening criteria?

Question 5: What are the treatment needs for those those diagnosed with ARND?

Expert Chair

Claire D. Coles, Ph.D., Professor, Departments of Psychiatry and Behavioral Sciences and Pediatrics, Emory University School of Medicine and Director of the Fetal Alcohol and Drug Exposure Center at the Marcus Institute in Atlanta, GA, will lead the assembled experts in presenting the available scientific and clinical evidence on ARND to the panel during public sessions.

Panel Chair

Joseph F. Hagan Jr., M.D., Hagan Rinehart Connolly Pediatricians, Burlington, VT, and Clinical Professor in Pediatrics at the University of Vermont College of Medicine and the Vermont Children's Hospital; Co-Editor of *Bright Futures Guidelines for Health Supervision of Infants, Children, and Adolescents*, Third Edition, published by the American Academy of Pediatrics, will lead a distinguished panel of specialists knowledgeable about developmental disorders to craft a consensus statement with practical recommendations based on these questions.

Conference Leadership Team

Kenneth Warren, Ph.D.
Acting Director, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health; Chair, Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders

Sally M. Anderson, Ph.D.
Coordinator and Executive Secretary, Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders; National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health

R. Louise Floyd, RN, D.S.N.
Team Leader and Behavioral Scientist, Fetal Alcohol Syndrome Prevention Team, National Center for Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention

Holly Noteboom Griffin
Manager, Screening and Public Health Preventions Programs, Division of Children with Special Needs, American Academy of Pediatrics

Joseph F. Hagan, Jr., M.D.
ARND Conference Panel Chair; Hagan, Rinehart and Connolly Pediatricians; Chair, American Academy of Pediatrics Committee on Psychosocial Aspects of Child and Family Health; Co-Editor, *Bright Futures*, American Academy of Pediatrics

ICCFASD Diagnostic Issues Work Group

Sally M. Anderson, Ph.D.
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Jacquelyn Bertrand, Ph.D.
Senior Scientist, Fetal Alcohol Syndrome Prevention Team, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention

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Ira Chasnoff, M.D.
President, Children's Research Triangle; Professor, Clinical Pediatrics, University of Illinois College of Medicine, Chicago

Claire D. Coles, Ph.D.
Professor, Departments of Psychiatry and Behavioral Science and Pediatrics, Emory University School of Medicine; Director, Fetal Alcohol Program, Marcus Autism Center

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John H. McGovern, M.G.A.
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Mary Jo Spencer, RN, CPNP, M.P.H.
Clinical Consultant, Minnesota Organization on Fetal Alcohol Syndrome; Pediatric Nurse Practitioner, University of Minnesota Physicians, Department of Pediatrics

Scientific Planning Committee

The Scientific Planning Committee developed the conference questions, drafted a general agenda, titled the conference, proposed dates, and nominated potential panel members and expert speakers. All final decisions were made by the Conference Leadership Team.

Claire D. Coles, Ph.D.
Professor, Department of Psychiatry and Behavioral Science and Pediatrics, Emory University School of Medicine; Director, Fetal Alcohol Program, Marcus Autism Center

Sarah N. Mattson, Ph.D.
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Blair Paley, Ph.D.
Associate Clinical Professor, Principal Investigator, SEEDS Program at UCLA for Infants and Toddlers with Prenatal Alcohol Exposure, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA

Yasmin Suzanne Nable Senturias, M.D.
Assistant Professor, Department of Pediatrics, University of Louisville; Clinical Director, FASD Clinic; Developmental-Behavioral Pediatrician, Weisskopf Child Evaluation Center

Elizabeth R. Sowell, Ph.D.
Director, UCLA Developmental Cognitive Neuroimaging Laboratory; Professor of Pediatrics, Division of Children, Youth and Families, Department of Pediatrics, Keck School of Medicine, University of Southern California

Mary Jo Spencer, R.N. CPNP, M.P.H.
Clinical Consultant, Minnesota Organization on Fetal Alcohol Syndrome; Pediatric Nurse Practitioner, University of Minnesota Physicians, Department of Pediatrics

Joanne Weinberg, Ph.D.
Professor and Distinguished University Scholar, Department of Cellular and Physiological Sciences, University of British Columbia

Technical Assistance Committee

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Tamica Wilkerson
Staff Assistant, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health

Agenda

MONDAY, OCTOBER 31, 2011 – Day 1

NIAAA, 5635 Fishers Lane, Rockville, MD – Terrace-Level Conference Center – T500

8:30 AM – 9:00 AM

WELCOME: Opening Remarks and Welcome, Kenneth R. Warren, Ph.D.

Charge to Panel, Tom Donaldson, Conference Moderator

Conference Overview and Panel Activities, Joseph F. Hagan, Jr., M.D., FAAP, Panel Chair

9:00 AM –10:15 AM

OVERVIEW OF TOPIC:

Alcohol-Related Neurodevelopmental Disorder (ARND): Clinical and Empirical Evidence for an Independent Effect on Behavior, Claire D. Coles, Ph.D., Expert Chair

QUESTIONS AND DISCUSSION and Break

10:15 AM –12:00 PM

QUESTION 1: What is ARND and how is it diagnosed (classical, current schemes, in practice today)?

Part A: Evidence of Central Nervous System Neurodevelopmental Abnormalities

- **The Neurologic Examination Is a Component in the Evaluation of the Brain for Diffuse Structural Alterations Associated With Fetal Alcohol Spectrum Disorder**, Sterling K. Clarren, M.D., FAAP
- **Biobehavioral Markers of ARND**, Sandra W. Jacobson, Ph.D.
- **The Brain in Children With FASD**, Elizabeth R. Sowell, Ph.D.
- **Animal Models of FASD: Defining the Pathologies That Inform Behavior**, Susan Smith, Ph.D.

QUESTIONS AND DISCUSSION

12:00 PM – 1:00 PM

Lunch on your own

1:00 PM – 3:00 PM

QUESTION 1 (continued): What is ARND and how is it diagnosed (classical, current schemes, in practice today)?

Part B: Evidence of a Complex Pattern of Behavior and Cognitive Abnormalities

- **Neurocognitive Profile of Children With ARND**, P.W. Kodituwakku, Ph.D.
- **Socioemotional and Mental Health Issues in Individuals Prenatally Exposed to Alcohol**, Mary J. O'Connor, Ph.D., ABPP

- **ARND Symptoms of Dysregulation and Poor Adaptive Functioning**, Julie A. Kable, Ph.D.
- **Animal Models of FASD: Focus on Behavior**, Joanne Weinberg, Ph.D.

QUESTIONS AND DISCUSSION and Break

3:00 PM – 5:00 PM **QUESTION 2: Can ARND be differentiated from other disorders?**

- **The Role of Genetic Investigations in the Assessment of Children at Risk for FASD**, Albert E. Chudley, M.D.
- **Differential Diagnosis of ARND: Other Toxic Exposures**, Joseph L. Jacobson, Ph.D.
- **Ecological Factors: Influence of Diagnostic Criteria for Alcohol-Related Neurodevelopmental Disorders (ARND)**, Ira J. Chasnoff, M.D.
- **Specificity of the Neurobehavioral Profile of ARND: Comparisons With ADHD**, Sarah Mattson, Ph.D. and Jeffrey R. Wozniak, Ph.D.
- **ARND: Mechanisms of Phenotype Expression and Comorbidity**, Larry Burd, Ph.D.

QUESTIONS AND DISCUSSION

5:00 PM **Adjournment for the Day**

TUESDAY, NOVEMBER 1, 2011 – Day 2

NIAAA, 5635 Fishers Lane, Rockville, MD – Terrace-Level Conference Center – T500

8:30 AM – 8:45 AM **Review of Day 1 and Overview of Day 2**, Tom Donaldson, *Conference Moderator*

8:45 AM – 10:45 AM **QUESTION 3: What prenatal alcohol exposure evidence is necessary for an ARND diagnosis?**

- **Animal Models of FASD/ARND: What Moderate Ethanol Exposure Paradigms Suggest About Fetal Alcohol Effects and Fetal Alcohol Exposure**, Daniel D. Savage, Ph.D.
- **What Evidence Is Necessary for an ARND Diagnosis?** Nancy L. Day, Ph.D., M.P.H.
- **What Prenatal Alcohol Exposure Is Necessary for an ARND Diagnosis?: Experience From the Washington State Fetal Alcohol Syndrome Diagnostic and Prevention Network Clinic**, Susan J. Astley, Ph.D.
- **Population Diversity and Moderators of Risk**, Philip A. May, Ph.D.

QUESTIONS AND DISCUSSION and Break

Agenda

10:45 AM – 12:00 PM **QUESTION 4: What signs and symptoms will be useful as screening criteria?**

- **Screening for ARND in the Context of Developmental Delay and Other Red Flags: Perspectives from Primary Care and Subspecialty Practice**, Christine Loock, M.D., FRCPC, DABP
- **Collaboration With Schools To Screen for ARND**, Molly N. Millians, D.Ed
- **The Minnesota Experience: Establishing Systems of Care for Fetal Alcohol Spectrum Disorders (FASD)—Screening, Referrals, Diagnosis, and Interventions**, Mary Jo Spencer, RN, C.P.N.P., M.P.H.

QUESTIONS AND DISCUSSION

12:00 PM – 1:00 PM Lunch on your own

1:00 PM – 3:00 PM **QUESTION 5: What are the treatment needs for those diagnosed with ARND?**

- **What Are the Treatment Needs of Individuals With ARND and Their Families? General Overview**, Heather Carmichael Olson, Ph.D.
- **Early Intervention for Fetal Alcohol Spectrum Disorders**, Blair Paley, Ph.D.
- **Empirically Validated Treatment Approaches for School-Age Children With FASD**, Joanne F. Rovet, Ph.D.
- **Treatment Needs and Interventions for Adolescents With FASD**, Jacqueline Pei, Ph.D., R.Psych.

QUESTIONS AND DISCUSSION

3:00 PM **Adjournment of Public Session**

WEDNESDAY, NOVEMBER 2, 2011 – Day 3

Legacy Hotel & Meeting Centre, 1775 Rockville Pike, Rockville, MD – Rose Hill Ballroom, Salons I & II

9:00 AM – 11:00 AM **Presentation of Draft Consensus Statement**

Public Discussion

11:00 AM **Adjournment of Public Session**

Panel Members

Joseph F. Hagan, Jr., M.D., FAAP

Panel Chair

As panel chair, Dr. Hagen has taken part in all major conference planning activities and is responsible for chairing the plenary sessions and the panel's deliberations.

Pediatrics Clinical Professor, University of Vermont College of Medicine and the Vermont Children's Hospital, Burlington, VT

Dr. Hagan is co-editor of *The Bright Futures Guidelines for Health Supervision of Infants, Children, and Adolescents, Third Edition*, published by the American Academy of Pediatrics (AAP) and designated in the recent health reform legislation as the standard for preventive care for youth up to age 21. He is the past chairperson of the AAP Committee on Psychosocial Aspects of Child and Family Health, and he chaired AAP's Task Force on Terrorism. He has served as an advisory board member of the Maternal and Child Health Benefits Study of the National Business Group on Health. Dr. Hagan chairs the Vermont Citizen's Advisory Board for the Vermont Agency of Human Services Department for Children and Families. He practices primary care pediatrics in Burlington, VT.

Steven W. Evans, Ph.D.

Professor and Co-Director, Center for Intervention Research in Schools, Ohio University, Athens

Dr. Evans conducts school-based treatment development and evaluation research for adolescents with attention deficit hyperactivity disorder (ADHD) and related problems. He developed the Challenging Horizons Program for middle school students with ADHD and a modified version of the program for high school students. His research is currently funded by grants from the National Institute of Mental Health and the Institute for Education Sciences (IES). His publications have appeared in journals related to psychology, medicine, and education. Dr. Evans is the editor-in-chief of the journal *School Mental Health*, and he chaired the panel for the IES practice guide on managing behavior problems in secondary schools.

Eva J. Klain, J.D.

Director, Child and Adolescent Health, Center on Children and the Law, American Bar Association, Washington, DC

As director of Child and Adolescent Health, Ms. Klain researches and analyzes health law policy, including legal responses to the health and developmental needs of court-involved infants and toddlers, children, and adolescents. She examines and works to promote interdisciplinary collaboration on issues such as healthy attachment and the developmental needs of very young children and on policies addressing substance abuse, teen pregnancy, statutory rape, domestic child trafficking for sexual exploitation, bullying (including cyberbullying), medical-legal partnerships, and medical homes for children in foster care. Ms. Klain also has conducted national, State, and local training for attorneys, judges, child welfare professionals, and other stakeholders on these issues. Among her publications are *Healthy Beginnings, Healthy Futures: A Judge's Guide and Healing the Youngest Children: Model Court-Community Partnerships*.

Barry Kosofsky, M.D., Ph.D.

Goldsmith Foundation Professor of Pediatrics and Chief, Division of Pediatric Neurology, New York-Presbyterian Hospital/ Weill Cornell Medical Center, New York, NY

Dr. Kosofsky has been chief of the Division of Child Neurology for the past 7 years, during which his clinical and research staff have created an

academic clinical service to improve the diagnosis and treatment of infants and children with developmental brain disorders. His National Institutes of Health (NIH)-funded clinical research includes the application of advanced morphometric magnetic resonance (MR)-based brain imaging methods. In particular, his focus has been on developing and implementing computer-based methods for analysis of structural MR data from children exposed to drugs of abuse *in utero*, including cocaine, methamphetamine, alcohol, and nicotine. He directs other ongoing translational research studies in the fields of autism, traumatic brain injury, and gene therapy for neurogenetic disorders. His NIH-funded preclinical research uses a mouse model of prenatal cocaine exposure to identify epigenetic mechanisms resulting in alterations in gene expression that underlie persistent changes in brain structure and function.

Elizabeth B. Kozleski, Ed.D.

Professor, School of Social Transformation, Arizona State University, Tempe

Dr. Kozleski's research includes examining and theorizing approaches to system changes in urban and large school systems; exploring how identity, culture, ability, and practice are negotiated in classrooms and schools; and understanding how schools become conscious and purposeful sites for professional learning. Dr. Kozleski co-edits with Alfredo Artiles a book series for Teachers College Press on disability, culture, and equity. She received the Pearson-Merrill Award for Excellence in Teacher Education in 2011 and published *Inclusive Education on Five Continents: Unraveling Equity Issues* the same year. Her research on families and children with special education needs has been published internationally. She served as a United Nations Educational, Scientific and Cultural Organization (UNESCO) chair of International Inclusive Education research. She was a special education teacher for several years.

Paul Lipkin, M.D.

Director, Center for Development and Learning, Kennedy Krieger Institute, Baltimore, MD; Associate Professor, The Johns Hopkins University School of Medicine, Baltimore, MD

Dr. Lipkin served as a 2010–2011 Robert Wood Johnson Foundation Health Policy Fellow in the Office of the U.S. Secretary of Health and Human Services. At the Kennedy Krieger Institute, Dr. Lipkin oversees the clinical outpatient program for the diagnosis and treatment of children with neurodevelopmental disabilities, including autism spectrum, attention, learning, and language disorders. He serves on the faculty of the Institute's Leadership Education in Neurodevelopmental Disabilities (LEND) training program, as well as the medical school's Genes to Society curriculum and pediatrics programs. Dr. Lipkin is past chairman of the Council on Children with Disabilities and chaired the Policy Revision Committee for the 2006 American Academy of Pediatrics (AAP) Policy Statement on Developmental Surveillance and Screening. He was also principal investigator for the AAP Developmental Surveillance and Screening Policy Implementation Project (D-PIP), translating policy into practice for the early identification of children with developmental problems. He is board certified in pediatrics, neurodevelopmental disabilities, and developmental and behavioral pediatrics. The AAP is awarding Dr. Lipkin with the Arnold J. Capute Award in 2011 in recognition of his work on behalf of children with disabilities.

Joyce Maring, Ed.D., PT

Associate Professor, Director of Physical Therapy (DPT) Program and Interim Chair, Physical Therapy and Health Care Sciences, The George Washington University (GWU) School of Medicine and Health Sciences, Washington, DC

Dr. Maring is a physical therapist with more than 30 years of clinical and 20 years of faculty experience. She currently serves as director of the DPT program at GWU. She also is responsible for the development and

implementation of content related to pediatrics in the DPT curriculum. Her current clinical practice primarily focuses on the assessment and intervention of children and adults with developmental disabilities, including those with impairments and disabilities associated with prenatal alcohol exposure. She is active in the Pediatric, Neurology, Education, and Research sections of the American Physical Therapy Association and has served on several national committees and task forces. Dr. Maring has conducted research in the areas of early intervention outcomes, education outcomes, and motor control and movement disorders.

Rita H. Pickler, Ph.D., RN, PNP-BC, FAAN

Nurse Scientist, Center for Professional Excellence and Perinatal Institute, and Cincinnati Children's Hospital Medical Center, Ohio; Professor Emerita, Virginia Commonwealth University, Richmond, VA; Adjunct Faculty, University of Cincinnati, Ohio; Research Professor, Ohio State University, Cincinnati

Dr. Pickler has more than 30 years of clinical, teaching, and research experience and more than 20 years of funding to study the care of the preterm infant. Her current National Institutes of Health (NIH)-funded study will test the effect of patterned caregiving on neurobehavioral development in preterm infants. She is a fellow in the American Academy of Nursing and is co-chair of the Child/Adolescent/Family Expert Panel. She is a member of the National Association of Pediatric Nurse Practitioners, for whom she is the Research Committee chair. Dr. Pickler has provided service to NIH for more than 10 years as a reviewer for numerous scientific review panels. She is currently chair of the Nursing Research Review Committee.

Lisa Albers Prock, M.D., M.P.H., FAAP

Assistant Professor, Harvard Medical School, Boston, MA; Director, Developmental Medicine Center, Children's Hospital Boston, MA

Dr. Prock is a developmental behavioral pediatrician with clinical and research interests in children with a history of deprivation, particularly those with a history of adoption and foster care. Her clinical work has included hospital- and community-based assessment and treatment for children with a range of developmental and behavioral challenges. She currently directs the Developmental and Behavioral Pediatrics Fellowship Training Program at Children's Hospital Boston and teaches medical students and pediatric residents at Harvard Medical School. Dr. Prock is the immediate past-chair of the American Academy of Pediatrics Section on Adoption and Foster Care and a member of the Massachusetts statewide Task Force on Fetal Alcohol Exposure.

Edward P. Riley, Ph.D.

Distinguished Professor and Director of the Center for Behavioral Teratology, San Diego State University, CA

Dr. Riley has authored more than 250 papers, primarily on the effects of prenatal alcohol exposure. His work focuses on the impact of alcohol exposure on the developing brain and the behavioral consequences. He oversees the Collaborative Initiative on Fetal Alcohol Spectrum Disorders, an international consortium project sponsored by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and is a member of the NIAAA Council. He has served on multiple national task forces and expert panels focusing on the topic of prenatal alcohol exposure, including chairing the U.S. National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect. He is a past president of the Research Society on Alcoholism (RSA) and the Fetal Alcohol Study Group of the RSA. He is the recipient of the RSA Distinguished Researcher Award, the National Organization on Fetal Alcohol Syndrome (NOFAS) Research Recognition Award and, most recently, the Frank Seixas Award from the RSA. His work has been continuously funded by NIAAA since 1978.

John T. Walkup, M.D.

Director, Division of Child and Adolescent Psychiatry, Weill Cornell Medical College, New York, NY; Adjunct Professor, The Johns Hopkins Center for American Indian Health, Baltimore, MD

Dr. Walkup has been involved in a number of the large definitive clinical treatment trials for childhood psychiatric disorders, including the Treatment for Adolescents with Depression Study (TADS), the Child/Adolescent Anxiety Multimodal Study (CAMS), the Comprehensive Behavioral Intervention for Tics Study (CBITS), the Treatment of Early Age Mania study (TEAM), and

the Treatment of Adolescent Suicide Attempters (TASA).

He also has been funded for large projects working with American Indian tribes in the southwest United States. "Cradling our Future" is a National Institute on Drug Abuse-funded clinical trial of an in-home intervention delivered by American Indian paraprofessionals to pregnant teens; "Celebrating Life and Empowering our Spirits" is a suicide prevention study funded by the Substance Abuse and Mental Health Services Administration under the Garrett Lee Smith Memorial Act. Dr. Walkup has won a number of awards and honors, including the Charlotte and Norbert Reiger Award for Scientific Achievement from the American Academy of Child and Adolescent Psychiatry in 2009.

Dr. Walkup is the current chair of the Medical Advisory Board of the U.S. Tourette Syndrome Association and serves on the scientific advisory boards of the Trichotillomania Learning Center and the Anxiety Disorder Association of America. He is the author of several articles and book chapters on mood and anxiety disorders, Tourette syndrome, psychopharmacology, and community-based participatory research with American Indian communities.

Carol Weitzman, M.D.

Associate Professor, Pediatrics and Child Study Center; Director, Developmental and Behavioral Pediatrics; and Program Director, Fellowship in Developmental and Behavioral Pediatrics, Yale University School of Medicine, New Haven, CT

For the past 12 years, Dr. Weitzman has directed the Yale Adoption Clinic and overseen all of the clinical services of Yale's Developmental and Behavioral Pediatrics. Nationally, she is on the executive board of the Society for Developmental and Behavioral Pediatrics and the executive committee of the American Academy of Pediatrics Section on Developmental and Behavioral Pediatrics. She is a member of the Fetal Alcohol Spectrum Disorder (FASD) Leadership Team in New Haven, CT. Her research has focused on assessing and treating mental health disorders in children and parents within primary care settings. She recently developed a national, peer-reviewed autism curriculum for pediatric trainees in collaboration with the Centers for Disease Control and Prevention and the Maternal and Child Health Bureau. She has written about and lectured widely on a number of developmental and behavioral pediatrics topics, including attachment disorders, FASD, autism, attention deficit hyperactivity disorder, maternal depression, and addressing mental health issues within primary care settings.

Kimberly Yolton, Ph.D.

Associate Professor, Division of General & Community Pediatrics, Cincinnati Children's Hospital Medical Center, Ohio

Dr. Yolton is a developmental psychologist with more than 20 years of experience in implementing instruments to study the impact of prenatal and early life factors on neurobehavior in infancy and childhood. She has extensive experience with infants and children who were prenatally exposed to substances of abuse, were born prematurely or at low birth weight, or who come from disadvantaged home environments. She was involved in the initial development of the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS), a neurobehavioral assessment tool used with healthy and high-risk newborns. She has implemented the tool for clinical, research, and teaching purposes locally, nationally, and internationally. She is using the NNNS to study subtle differences in the neurobehavior of infants who have been prenatally exposed to environmental toxicants. Dr. Yolton's current research focuses on exposures to environmental toxicants (e.g., tobacco, plastics, insecticides, flame retardants, lead, methylmercury) and neurobehavioral outcomes from infancy through childhood. Her research has been funded by the National Institutes of Health and the Flight Attendant Medical Research Institute. She collaborates with investigators from multiple institutions, both domestically and internationally.

Speakers & Abstracts

Tom Donaldson, Conference Moderator

The conference moderator is responsible for the smooth conduct of the meeting. He will ensure that speakers adhere to time limits; allow ample opportunity for scheduled discussion; and invite questions and comments from panellists and other conference attendees, taking questions from members of the panel first.

Chief Executive Officer (CEO) and President, National Organization on Fetal Alcohol Syndrome (NOFAS), Washington, DC

Mr. Donaldson has served as CEO of NOFAS since 1998, and he became its President in 2002. He is responsible for formulating and carrying out the NOFAS strategic and business plans and all programmatic, development, and policy initiatives. He has extensive experience in nonprofit governance, public policy, government affairs, media relations, social marketing, grassroots organizing, coalition building, and public health. Under his leadership, NOFAS has established a network of 31 affiliated organizations, expanded services to all 50 States, and helped ensure a four-fold increase in Federal and State investment in fetal alcohol spectrum disorder (FASD)-related research and public health and services, among numerous other achievements.

NOFAS is the leading voice and resource of the FASD community. Founded in 1990, NOFAS is the only international nonprofit organization committed solely to FASD primary prevention, advocacy, and support. NOFAS seeks to create a global community free of alcohol-exposed pregnancies and a society supportive of individuals already living with FASD. NOFAS effectively increases public awareness and mobilizes grassroots action in diverse communities and represents the interests of persons with FASD and their caregivers as the liaison to researchers and policymakers. By ensuring that FASD is broadly recognized as a developmental disability, NOFAS strives to reduce the stigma and improve the quality of life for affected individuals and families.

Claire D. Coles, Ph.D., Expert Chair

As expert chair, Dr. Coles will lead expert speakers on presenting available scientific evidence on ARND to the panel during public sessions.

Professor, Departments of Psychiatry and Behavioral Sciences and Pediatrics, Emory University School of Medicine, Atlanta, GA; Director, Fetal Alcohol Syndrome and Drug Exposure Center, Marcus Autism Center, Atlanta, GA

Dr. Coles' Maternal Substance Abuse and Child Development project has carried out longitudinal research since 1980, focusing on the neurodevelopmental and behavioral effects of prenatal exposure to drugs and alcohol and on the interaction of these effects with the postnatal environment. In 1995, Dr. Coles established the Fetal Alcohol Center within the Marcus Autism Center. This Center provides diagnostic, clinical, and educational services to alcohol- and drug-affected children and their families and carries out clinical research to develop and evaluate intervention methods to improve outcomes for affected children. Dr. Coles has served on a number of advisory boards that address the problems of individuals and families affected by fetal alcohol spectrum disorders (FASD). These have included the Institute of Medicine's Committee on Fetal Alcohol Syndrome (FAS); the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effect; and the FAS Work Group, Office of Special Education Programs, U.S. Department of Education.

Abstract

Alcohol-Related Neurodevelopmental Disorders (ARND): Clinical and Empirical Evidence for an Independent Effect on Behavior

Prenatal alcohol exposure has a teratogenic effect on the central nervous system that leads to cognitive deficits and behavioral disorders. It is frequently stated that these effects on the brain are the most devastating sequelae of maternal alcohol abuse and yet, of the four criteria used in the diagnosis of FASD, that of "neurodevelopmental" effects is perhaps the most difficult to characterize. Even more difficult is the identification of ARND in the absence of the growth retardation and physical dysmorphology associated with FAS. There are many reasons for these difficulties, including genetic and environmental factors that influence development as well as those that are associated with parental alcohol abuse. Nevertheless, an accumulated body of scientific evidence argues that a neurobehavioral syndrome associated with prenatal alcohol exposure can be identified and used to support screening and diagnostic services that will provide for better outcomes for affected individuals. The diagnostic category of ARND was proposed more than a decade ago and, at that time, it was felt that evidence for the specific criteria that would define the diagnosis was not yet available (1). Indeed, the Institute of Medicine, in including ARND in their suggested diagnostic categories, did not differentiate ARND from the description of the neurodevelopmental characteristics that made up the fourth central nervous system criteria for FAS. Since that time, scientific information bearing on ARND has been obtained using many approaches. Malformations can be seen on autopsy and in animal models and affected individuals demonstrate a number of conditions with a known basis in brain injury, like seizure disorders or motor deficits. Electrophysiology and neuroimaging data allow the study of alcohol effects in human samples. Neurobehavioral studies using both clinical and exposure samples provide evidence of both general and specific deficits associated with prenatal alcohol exposure. A major concern is the extent to which any phenotypic signature, seen as a result of prenatal alcohol exposure, is "unique" to this condition or is similar to other conditions that result from early developmental insults. The more characteristic the pattern of effects, the more useful it is in diagnosis. The challenge has been to "sort out" the behavioral signature of prenatal alcohol exposure from a very busy background that includes genetic differences in families in which alcohol abuse is common, and the sociodemographic vagaries associated with the abuse of alcohol.

1. Stratton K, Howe C, Battaglia F, eds. Fetal Alcohol Syndrome: Diagnosis, Epidemiology, Prevention, and Treatment. The Institute of Medicine Report. Washington, DC, National Academy Press, 1996.

Question 1: What is ARND and how is it diagnosed (classical, current diagnostic schemes, in practice today)?

Part A: Evidence of CNS Neurodevelopmental Abnormalities

Sterling K. Clarren, M.D.

CEO and Scientific Director, Canada Northwest FASD Research Network; Clinical Professor of Pediatrics, University of British Columbia; Clinical Professor of Pediatrics, University of Washington, Seattle

Dr. Clarren has applied his training in dysmorphology, neuropathology, neuroembryology, and developmental pediatrics to the problems of fetal alcohol spectrum disorders (FASD) since 1975 in clinical diagnosis, clinical evaluation and intervention, and clinical and basic research. Dr. Clarren wrote the first major summary article of the clinical pattern of malformation associated with alcohol teratogenesis in the New England Journal of Medicine in 1978. In that article, he coined the term "fetal alcohol effects." He has participated since that time in all major works on the definition of FAS and related conditions for the Research Society on Alcoholism and the Institute of Medicine. In 1978, Dr. Clarren developed one of the first pediatric clinics focused on the difficult diagnosis of FAS and related conditions. As the founding director of the Washington State FAS Diagnostic and Prevention Network, he led the team that developed the 4-Digit Diagnostic Code for FAS and has refined the clinical approach over many years.

Abstract

The Neurologic Examination Is a Component in the Evaluation of the Brain for Diffuse Structural Alterations Associated With Fetal Alcohol Spectrum Disorders

The behavioral difficulty that links together the majority of those with FASD is persistent maladaptation, in spite of detection and intervention with specific functional problems like attention deficit hyperactivity disorder or learning disability. Maladaptive behaviors may have their source in multiple etiologies that include environmental influences (e.g., chronic health problems, aberrant or inadequate nurture, poor nutrition), mental health disorders, or structural brain changes that result in cognitive and performance deficits. Not only are the causes of maladaptation varied, the treatments and expectations for improvement and resolution also depend on the cause. Those with diffuse organic brain damage are the most likely to have maladaptation represent a true lifetime disability.

Animal studies have clearly demonstrated that ethyl alcohol can alter the structure of most parts of the brain in myriad ways and from a microscopic to macroscopic level.

Patient reviews over decades now suggest that those exposed to alcohol *in utero* and who are maladaptative over time are likely to have multiple causes for their difficulties. Sorting out these components is important diagnostically and prognostically. Finding those with significant cognitive and processing difficulties identifies those most likely to be disabled. Therefore, a central focus of a clinical diagnostic process for FASD is to determine the likelihood of some level of brain damage. This can be done through three processes: identifying brain alteration through imaging of many forms, identifying neurological problems like seizures or cerebral palsy that are fixed or ongoing, or using a broad battery of neurocognitive tests. Because of the wide variation in presentation of those who might have FASD and structural brain changes as a cause for maladaptation, all of these approaches need to be included in the tool kit of a diagnostic and intervention program. This approach is reflected in the 4 Digit Diagnostic Code and in the Canadian Guidelines, which are used in virtually all FASD diagnostic clinics in Canada.

What is ARND and how is it diagnosed (classical, current diagnostic schemes, in practice today)?

Sandra W. Jacobson, Ph.D.

Professor, Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI; Honorary Professor, Departments of Human Biology and Psychiatry, University of Cape Town Faculty of Health Sciences, South Africa

Dr. Jacobson was trained as a developmental and clinical psychologist. Her research, in collaboration with Joseph Jacobson, Ph.D., has focused on the effects of prenatal exposure to neurotoxic agents on cognitive and behavioral development in infants and children. The Jacobsons' research on fetal alcohol spectrum disorders (FASD) includes a 19-year longitudinal study of inner-city Detroit children prenatally exposed to alcohol at moderate-to-heavy levels. In 1996, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) invited her to participate in a site visit to South Africa to investigate reports of a very high incidence of fetal alcohol syndrome (FAS). This visit led to a currently ongoing 9-year prospective longitudinal study on FAS in Cape Town. Her research has identified eyeblink conditioning as a particularly sensitive and reliable behavioral indicator of FASD. In 2005, under a grant from Fogarty International Center at the National Institutes of Health, the Jacobsons and their colleagues launched the first neuroimaging studies of children in Cape Town. She served as president of the FASD Study Group and on the NIAAA and National Institute on Drug Abuse expert panels.

Abstract

Biobehavioral Markers of ARND

Diagnosis of ARND is problematic since the observed deficits are phenotypically similar to those seen in other disorders, such as attention deficit hyperactivity disorder (ADHD), despite very different etiologies. Moreover, most neuropsychological tests are complex, providing little information about which specific aspects of cognitive function are adversely affected. To address this problem, Castellanos and Tannock (1) advocate going beyond descriptive symptom-based approaches to diagnosis to identify specific biomarkers derived from cognitive neuroscience that are "closer to the site of the primary causal agent" than to the manifest behavioral phenotype. The most useful biobehavioral markers are narrow-band endpoints for which information is available regarding the neural pathways and processes that mediate observed effects. Identification of biobehavioral markers has the potential to improve FASD diagnosis by grounding it in specific aspects of central nervous system function that can be linked biologically to fetal alcohol exposure.

Eyeblink conditioning (EBC) is a classical Pavlovian nonverbal learning paradigm in which a conditioned stimulus, typically a tone, is paired with a brief air puff to the eye that elicits a reflexive blink. After repeated pairings, the tone comes to elicit a conditioned eyeblink response. The neural circuitry that mediates this form of learning is well-documented in the animal model (2-5). EBC is an impressively consistent biobehavioral marker of fetal alcohol exposure. In our 5-year follow-up study in Cape Town, not a single child with fetal alcohol syndrome met criterion for conditioning, as contrasted with 75 percent of the controls (6). With respect to ARND, more than 60 percent of heavily exposed nonsyndromal children failed to meet criterion for conditioning. We have since reported similar EBC impairment in school-age children with heavy alcohol exposure, and findings at both ages were unrelated to IQ or ADHD (7). These findings corroborate the EBC deficit reported in a sample of U.S. school-age, alcohol-exposed children, in which the rate of successful conditioning for children with ADHD was similar to controls (8). In a diffusion tensor imaging, or DTI, study, we found that poorer white matter integrity in a portion of the EBC cerebellar circuit plays a significant role in mediating the effect of alcohol exposure on EBC performance (9).

Saccadic eye movement, another behavior with well-documented neural circuitry, can be used to assess executive function. Antisaccades, voluntarily looking away from a stimulus, rely on suppression of the more automatic prosaccade response. Reynolds and associates (10) have found the children with FASD (including those with ARND) perform more slowly and make more errors on antisaccade trials than controls, indicating a functional deficit in the frontal cortex and basal ganglia neural circuitry known to mediate this response (11-12). Arithmetic is the academic domain most strongly

affected by prenatal exposure (13-19). Brain lesion and neuroimaging studies have identified two distinct functional neural networks relating to arithmetic: (a) magnitude comparison, which entails a fundamental understanding of relative quantity, and (b) calculation, which involves manipulation of verbally encoded numbers and knowledge. Prenatal alcohol exposure is associated specifically with poorer magnitude comparison, a deficit that mediates the poorer arithmetic performance in children with ARND (10). These findings indicate that EBC, saccadic eye movements, and magnitude comparison can be used as objective measures of specific brain injury in ARND, revealing behavioral deficits that are distinct from those found for children with ADHD and other disorders.

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What is ARND and how is it diagnosed (classical, current diagnostic schemes, in practice today)?

Elizabeth R. Sowell, Ph.D.

Professor, Department of Pediatrics, University of Southern California/Children's Hospital Los Angeles, California; Director, Developmental Cognitive Neuroimaging Laboratory, University of California, Los Angeles (UCLA)

Dr. Sowell completed a National Institute of Mental Health postdoctoral fellowship at the UCLA Laboratory of Neuroimaging, where she specialized in advanced image analysis technology in developmental populations. Her research has focused on multimodal magnetic resonance imaging and neurocognitive correlates of normative brain development and brain morphologic abnormalities in children with various neurodevelopmental disorders, such as fetal alcohol syndrome and attention deficit hyperactivity disorder. More than 50 publications in her field have been cited nearly 5,000 times in the scientific literature. She has been the recipient of numerous National Institutes of Health (NIH) awards, including awards from the National Institute on Drug Abuse to conduct longitudinal studies of children with prenatal methamphetamine exposure using functional and structural neuroimaging, from the National Institute of Child Health and Human Development (NICHD) to conduct multimodal image analyses in typically developing children, and from NICHD to evaluate the impact of perinatally acquired HIV and prenatal exposure to antiretroviral medications on adolescent brain development. Dr. Sowell has been the principal investigator of the brain imaging project for the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) for the last 7 years, and she has more than 25 publications on brain imaging and neurobehavioral correlates in FASD. Dr. Sowell was a pioneer in the field of neuroimaging in adolescent brain development, and her 1999 paper—published in *Nature Neuroscience*—localized postadolescent development of the frontal lobes for the first time. She has been a consultant to various NIH Institutes focusing on new directions in brain imaging of neurodevelopmental disorders and typical brain development, and she is currently a consultant to the National Institute on Alcohol Abuse and Alcoholism on the issue of diagnosis of alcohol-related neurodevelopmental disorder.

Abstract

The Brain in Children With FASD

Heavy prenatal alcohol exposure can cause devastating, lifelong neurological deficits and is the leading preventable cause of neurodevelopmental disability. While fetal alcohol spectrum disorders (FASD) are 100 percent preventable, heavy alcohol use among pregnant women continues to occur worldwide. In order for a diagnosis of full fetal alcohol syndrome (FAS), an individual must have facial dysmorphology, growth restriction, central nervous system involvement (e.g., microcephaly, cognitive impairment, neurological problems), in addition to alcohol exposure *in utero*. Not all children who were exposed to alcohol *in utero* have the facial dysmorphology or growth restriction for the FAS diagnosis, though they still have difficulties with behavior and cognition that impair their functioning in society. The neuroimaging literature over the past decade has continuously shown that brain morphology and function are abnormal in children without "the face," and yet, without a "formal" diagnosis, it is difficult for families to obtain interventions that could improve overall functioning of individuals with FASD throughout life.

In this talk, I will discuss recent brain imaging research from multiple institutions and investigators that highlight brain structural abnormalities among children across the FASD spectrum that are predictive of cognitive performance. I will discuss relationships between the brain in children with FASD, and continuous measures of facial dysmorphology, which suggest that regardless of where a child falls along the FASD continuum, greater facial dysmorphology (i.e., palpebral fissure length, upper lip morphology) is associated with greater brain dysmorphology. Further, I will discuss some emerging findings from longitudinal data that suggest altered maturation in the brains of children with FASD relative to unexposed controls, years after the perinatal insults to the developing brain. Finally, I will describe new efforts to quantify subtler aspects of facial morphology using three-dimensional facial images integrated with brain imaging data in the same individuals.

Susan Smith, Ph.D.

Professor, Department of Nutritional Sciences, University of Wisconsin, Madison

Dr. Smith is the immediate past president of the Fetal Alcohol Spectrum Disorders (FASD) Study Group. She was chair of the Neurotoxicology and Alcohol (NAL) study section for the National Institutes of Health (NIH) and serves on numerous NIH study sections in the areas of alcohol, nutrition, toxicology, and development. She received the Future Leader in Nutrition award from the International Life Sciences Institute and was a fellow of the Muscular Dystrophy Association. She serves on the editorial boards of the journals Birth Defects Research (Part A) and Developmental Dynamics. Dr. Smith's laboratory investigates the mechanisms of dietary and molecular teratogens, including alcohol, isotretinoin, trichloroethylene, and selective serotonin re-uptake inhibitors. Her research into the molecular mechanisms that mediate alcohol's neurotoxicity in FASD is supported by a 10-year Method to Extend Time in Research (MERIT) award from the National Institute on Alcohol Abuse and Alcoholism. Her current studies investigate genetic and nutritional modifiers of FASD outcome and employ a range of models, including rodent, chick, zebrafish, and human.

Abstract

Animal Models of FASD: Defining the Pathologies That Inform Behavior

Animal models have substantially informed our understanding of the structural and functional deficits that are characteristic of FASD. Although alcohol does not interact in a classic ligand/receptor paradigm, its specific interactions with neurologically important proteins have been mapped at the amino acid level. A range of vertebrate models including mammalian, avian, and piscine species define a reproducible set of neurobehavioral and anatomical anomalies that result from developmental alcohol exposure. These models have been critical in isolating the effects of alcohol from the effects of other confounder such as genetics, environment, and polydrug use. These models have permitted the exploration of alcohol's effects in ways not possible in human studies.

Key findings from animal models of FASD include that the effects of alcohol are consistent and reproducible across a range of vertebrate species. The findings are concordant with the neuroanatomical and behavioral characteristics of those with FASD. These studies reveal that the apparent "heterogeneity" of FASD outcomes is a reflection of exposure dosage, duration, and time of initial exposure. Ongoing research examines additional factors that modify the impact of alcohol exposure including maternal nutrition, genetic background, and environmental stressors.

Animal models replicate the neuroanatomical features of FASD. Advances in imaging permit precise characterization of these changes. The most prominent features are consistent volume reductions in the hippocampus, frontal cortex, cerebellum, and corpus callosum, deficits commonly observed in MRI of those with FASD. The magnitude of change is influenced by the alcohol exposure dose and timing. Animal studies demonstrate that these structural reductions are accompanied by reduced numbers in selected neuronal populations. These neuronal losses are caused by ethanol-induced neurodegeneration, changes in proliferative rates, and precocious differentiation of neural stem cell progenitors.

Animal models also document that alcohol dysregulates the orderly progression of neuronal development. Neuronal migration through the cortical layers is altered, producing derangements that may contribute to the abnormal connectivity observed in FASD. The abnormal migration also produces occasional heterotopias, and these may be linked to increased seizure risk in FASD. Axonal formation is delayed and myelination is blunted, accounting for the white matter deficits and anomalies seen in neuroimaging.

These structural changes are accompanied by altered neuronal activity and responsivity. Neurotransmission is slowed and larger stimulus currents are necessary to produce normal responses. There are lasting alterations in multiple neurotransmitter systems including the dopaminergic, serotonergic, and glutaminergic systems. These mediate

the neurobehavioral domains affected in FASD, including learning and memory, executive function, state regulation, stressor hyperresponsiveness, and motor function.

Animal studies affirm that, in the absence of the growth deficits and facial changes that partly typifies FAS, prenatal alcohol exposure causes reproducible anatomical and physiological alternations that underlie the behavioral phenotype of FASD.

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Part B: Evidence of a Complex Pattern of Behavior and Cognitive Abnormalities

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Dr. Weinberg has served as president of the International Society for Developmental Psychobiology and the Fetal Alcohol Spectrum Disorders (FASD) Study Group, on the Board of Directors and the Program and Education Committees of the Research Society on Alcoholism, and on the editorial advisory boards of Alcohol, Alcoholism: Clinical & Experimental Research, Neurotoxicology and Teratology, and Physiology and

Behavior. She is currently a member of the advisory panel of the Intervention Network Action Team, Canada Northwest FASD Research Network, and is co-leader of the FASD Project of NeuroDevNet, Networks of Centers of Excellence. The research in Dr. Weinberg's laboratory uses a rat model to examine the long-term effects of prenatal alcohol exposure on neuroendocrine and immune function. Studies aim to elucidate mechanisms underlying the increased incidence of secondary disabilities and health problems in children with FASD.

Abstract

Animal Models of FASD: Focus on Behavior

Studies on children exposed to alcohol prenatally have been critical in identifying the spectrum of problems/ deficits/disorders that result from this prenatal insult, and in providing evidence that alcohol exposure results in brain injury. However, the ability to probe the brain and to investigate mechanisms underlying alcohol's adverse effects is limited in human research. Well-defined animal models are valid and effective tools for examining outcomes and investigating mechanisms of alcohol's actions on the developing fetus, while controlling environmental, genetic, and maternal variables that are impossible to control in human populations. Such models have been particularly important in gaining insight into the neurobehavioral and neurobiological alterations that occur in alcohol-related neurodevelopmental disorders (ARND), where functional deficits are observed in the absence of overt physical and morphological abnormalities. Importantly, outcomes in humans direct animal research and conversely, animal data from animal research inform deficits in humans.

The neurobehavioral domains affected by *in utero* alcohol exposure in animal models are remarkably consistent with those found in human studies. In broad terms, these domains include: (a) neonatal behavior (suckling, ultrasonic vocalizations, orientation, and state control) (1-3); (b) neurocognitive deficits (learning, memory and executive function, attention and distractibility, spatial learning and memory (4-7); (c) motor function (reflex development, coordination, gait, balance) (8,9); (c) adaptive functioning, self-regulation, arousal, and social behavior (reduced habituation to novel or challenging stimuli/environments, sensory processing, deficits in social interaction, hormonal and behavioral responses to stress) (10-12); (e) activity/ hyperactivity (13); and (f) psychopathology, including changes in depressive- and anxiety-like behaviors (14).

The power of animal models in linking behavioral alterations with changes in key brain regions will be illustrated (e.g.,14,15). In addition, examples of how animal models have been used in the development of intervention strategies will be presented (8,9).

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As a clinician, Dr. Kodituwakku has extensive experience in the assessment of children with fetal alcohol spectrum disorders (FASD) and those with neurogenetic syndromes. He and his colleagues successfully established a multidisciplinary fetal alcohol diagnostic clinic at the UNM Center for Development and Disability, which provides services for alcohol-affected children throughout New Mexico. Dr. Kodituwakku's research has focused on the delineation of a neurocognitive profile of children with FASD. Using a process-oriented approach to neurocognitive assessments, he has shown that children with FASD have difficulty with complex tasks that involve integration of multiple elements or relations. As an investigator on a P-20 grant funded by the National Institute on Alcohol Abuse and Alcoholism, he is researching training-induced plasticity of motor and attention systems in children with FASD, using both behavioral and imaging methods. Dr. Kodituwakku also is involved with international neurobehavioral studies. Having joined the Fulbright Senior Specialist Roster, he currently is involved in the development and validation of neuropsychological tests in Sri Lanka.

Abstract

Neurocognitive Profile of Children With ARND

There is a large body of literature on neurocognitive functioning of children with FASD. Within this literature, the main findings can be summarized under two broad headings: general functions and specific functions.

General functions

Intellectual ability: While intellectual abilities of children with heavy prenatal alcohol exposure (PAE) vary widely, their average IQ scores fall within the borderline range (1,2). Intellectual disabilities of this group have been reported to be pervasive (2) and persistent (1).

Information processing: Consistent with diminished intellectual abilities, children with PAE exhibit slow information processing (3). Information processing difficulties of alcohol-affected children become more pronounced when task complexity increases (4). Infants with PAE also display evidence of slow processing (5,6).

Attention and executive functions: While some studies report alcohol-related deficits on tasks assessing sustained and focus components of attention, one study found greater deficits in the components that involve executive attention (e.g., shifting) (7). Children with PAE display poorer performances on tests assessing different aspects of executive control, including planning, extra- and intradimensional set shifting, verbal and nonverbal fluency, concept formation, working memory, and response inhibition (8).

Specific functions

Language: Evidence from prospective studies indicates that children exposed to light to moderate amounts of alcohol do not exhibit significant deficits in language (9). However, children from clinic-referred samples show significant deficits in both receptive and expressive language (10). As children with PAE grow older, they show difficulties in complex language tasks such as social communication (11).

Visual perception: One study found that children with PAE are unimpaired at facial recognition, but are impaired at visual motor integration and visual construction (12).

Memory and learning: Children with PAE show deficits in both verbal and visual memory, particularly with encoding information (8). One study found that these difficulties persist beyond childhood (13). Children with PAE also are impaired at place learning (14). There is evidence that children with PAE are impaired at free recall but unimpaired at recognition memory (15). Also, there is evidence that they are impaired at declarative memory but unimpaired at procedural memory (16).

Social cognition: Children with PAE exhibit deficient performances on tests assessing social cognition such as affect recognition (17) and theory of mind (18). However, social deficits in FASD are distinctly different from those seen in autism (19). Social difficulties in FASD are associated with deficits in higher order skills such as executive functions (18, 20).

Number processing: Children with PAE tend to perform poorer in math than in other academic subjects. One study of number processing of children with PAE found intact performance on simple numerical tasks (e.g., number reading), but impaired performance on demanding ones (e.g., cognitive estimation) (21).

Motor functions: Children with PAE exhibit motor deficits, as indexed by poorer performances on tests assessing manual dexterity, strength of grip, balance, and motor coordination (8). These deficits, particularly in motor coordination, persist beyond childhood (22).

Our interpretation: The foregoing findings indicate that children with PAE exhibit slow information processing and poorer test performance with increased task complexity. We have interpreted this pattern of results as indicating a deficit in the processing and integration of information (8,23).

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Dr. O'Connor holds a specialty board certification in clinical child and adolescent psychology and has taught medical students, psychiatry residents, child psychiatry fellows, and child clinical psychology interns for more than 25 years. Over the past 25 years, Dr. O'Connor has conducted research on the prevention of alcohol consumption by pregnant women; intervention with children and adolescents with prenatal alcohol exposure; and medical and allied health education on prevention, diagnosis, and treatment. All of her recent work has been on collaborative national initiatives with the long-term goal of developing best-practice models to be disseminated on the local, State, and national levels. She has served on multiple national task forces and expert panels focusing on the topic of prenatal alcohol exposure.

Abstract

Socioemotional and Mental Health Issues in Individuals Prenatally Exposed to Alcohol

Reviews of studies examining the relationship between prenatal alcohol exposure (PAE) and various indices of children's emotional adjustment have noted that some of these linkages may be attributable to PAE and yet these linkages remain relatively unexplored in the literature. Furthermore, despite the evidence of a significant association between alcohol exposure *in utero* and psychiatric risk, experience suggests that exposure, and even fetal alcohol syndrome (FAS), is infrequently identified by mental health practitioners (1). Failure to recognize the broad and unique needs of individuals with fetal alcohol spectrum disorders (FASD) and their families can lead to multiple treatment failures, consequent worsening of symptoms, and high personal and societal costs. Following is a review of developmental findings.

Infancy and early childhood. At birth, there are signs of central nervous system dysfunction in infants born to mothers who report consuming alcohol during pregnancy. These include jitteriness, irritability, autonomic instability, hypotonia, slow habituation, low levels of arousal, increased levels of activity, and disturbances in sleep (2). The significance of these early neurobehavioral effects is

apparent in the impact they have on early mother-child transactions. Some studies have incorporated a transactional model to explain the relation between PAE and socioemotional functioning in infancy and early childhood and have found links between early irritability, mother's sensitivity and responsiveness, attachment relations, and childhood depression (3-6). Expanding this line of inquiry to children with high levels of cumulative risk associated with living in poverty reveals even higher levels of attachment insecurity and depression (7.8).

Middle childhood. A few studies are notable for examining psychopathology in children with FASD in middle childhood with rates as high as 97 percent of children meeting criteria for an Axis I diagnosis on the DSM-IV (9,10). One study comparing a nonclinic group of children with and without PAE, revealed statistically significant effects of PAE in predicting internalizing disorders of depression, separation anxiety disorder and generalized anxiety disorder, and externalizing disorders of mania, attention deficit hyperactivity disorder, oppositional disorder, and conduct disorder (11). Furthermore, child characteristics and environmental factors appeared to add to the prediction of psychopathology. Specifically, having a lower IQ, poorer social skills, and living with a single/divorced or a non-biological caregiver was associated with greater risk.

Adolescence and young adulthood. Mental health problems are hallmark secondary disabilities in adolescents and young adults with PAE. In their seminal cross-sectional study of the developmental outcomes of adolescents and adults with PAE, Streissguth and associates found that 94 percent reported mental health problems (12). Other investigators have found that PAE was associated with higher levels of conduct disorder symptoms, even after controlling for the effects of parental externalizing disorders (illicit substance use disorders, alcohol dependence, and antisocial/ behavioral disorders), prenatal nicotine exposure, monozygosity, gestational age, and birth weight (13). Longitudinal research suggests that individuals with PAE also exhibit problems with the misuse of alcohol and other drugs as they mature (14-17).

Research on the psychiatric disabilities suffered by individuals with PAE throughout the lifespan highlights the need for training of mental health professionals in the identification of people with FASD and the provision of specific treatments to address the unique features of this developmental disability since early identification and treatment have been demonstrated to be protective against more serious psychiatric outcomes (12,18).

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Dr. Kable is a licensed pediatric psychologist who has more than 17 years of experience working with children with neurodevelopmental disabilities, with a particular focus on children with a history of prenatal alcohol exposure. She is the vice president of the Fetal Alcohol Spectrum Disorders (FASD) Study Group, a professional organization dedicated to scientific inquiry into the etiology of fetal alcohol syndrome (FAS), the characteristics of FASD, and methods to improve the lives of individuals with FASD. Her work has involved both research and the clinical care of children with FASD. She has been instrumental in the development of innovative interventions for children with FASD that focus on improving self-regulation, early math skills, and adaptive living skills. In addition to her intervention research, Dr. Kable has participated in several prospective longitudinal studies on the impact of various teratogens (e.g., alcohol, tobacco, cocaine) on development throughout the lifespan, including studies using neuroimaging procedures with adults who were prenatally exposed to alcohol. Dr. Kable has also served on expert panels related to the identification and care of individuals with FASD.

Abstract

ARND Symptoms of Dysregulation and Poor Adaptive Functioning

Prenatal alcohol exposure has been associated with a range of deficits that impact self-regulation and adaptive functioning. These deficits impact the way individuals with alcohol-related neurodevelopmental disorders (ARND) learn from their experiences, interact with others, and care for themselves. Self-regulation involves regulating one's arousal and behavior to meet environmental demands. In early infancy, it involves regulating sleep habits and the earliest forms of attention and learning. Later effortful control of behavior is established allowing for more complex learning and environmental interactions. Children with ARND have been found to have deficits in these early forms of self-regulation and continue to have deficits in self-regulation or behavioral control throughout their lifespan. The brain structures involved in self-regulation include ventral and dorsal pathways of the reward/control systems and portions of the prefrontal cortex, striatum (especially the caudate), thalamus, and amygdala. Each of these areas has been found to be adversely impacted by prenatal alcohol exposure, suggesting there is a clear neural basis for the self-regulation deficits seen in children with a history of PAE. Self-regulation difficulties disturb learning by disrupting attentional responses, affective shifting, coping with negative feedback, handling high levels of stimulation or arousal, and working memory and planning skills. Given the disruption to these basic learning mechanisms, it is not surprising that children with ARND also have deficits in their adaptive behavioral skills. Children with ARND have deficits in functional communication, independent living skills, and motor skills. These children may have initial delays in language skills but later have deficits in the integrative use of language, which involves organizing the components of language (semantic, symbolic, and grammatical) into meaningful communication. Deficits in independent living skills include delays in acquiring basic life skills, such as dressing, toileting, making change, learning the rules of personal safety, organizing schedules, and understanding time concepts. Deficits in motor functioning begin in the neonatal stages and persist throughout the lifespan, but later deficits may be less obvious and often involve disruption to coordination and balance. Among individuals with ARND, adaptive skills have been found to show a relative decline across age, suggesting a cumulative learning deficit. Interventions that target self-regulation skills have been found to improve problem-solving strategies and to facilitate learning.

Question 2: Can ARND be differentiated from other disorders?

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Dr. Chudley is a medical geneticist and pediatrician with experience in the etiology and gene discovery of disorders that cause birth defects and/or intellectual disabilities. He has a particular interest in the recognition, diagnosis, prevention, and intervention strategies related to fetal alcohol spectrum disorders (FASD). He is the lead author of the Canadian guidelines for the diagnosis of FASD. Dr. Chudley served on Health Canada's National Advisory Committee on FASD and is currently a member of the National FASD Screening Tool Steering Committee of the Canadian Association of Paediatric Health Centres and Public Health Agency Canada. He is one of the team leaders in the FASD stream of NeuroDevNet, established by the National Centres of Excellence. He previously served as a board member on the Canada Northwest FASD Research Network and remains a member of the clinical network. He is a former president of the Canadian College of Medical Geneticists. Dr. Chudley has been a consultant to provincial, national, and international organizations and governments on issues related to FASD. He is co-chair of the Second International French FASD meeting, to be held on December 15–16, 2011, in Strasbourg, France.

Abstract

The Role of Genetic Investigations in the Assessment of Children at Risk for FASD

FASD is a complex set of disorders primarily caused by the effects of prenatal alcohol exposure on the embryo and fetus. The resulting clinical phenotype can be highly variable, even in the face of equal amounts of frequency and timing of alcohol exposure. A multitude of maternal and fetal risk and/or protective factors that modify teratogenesis is likely influenced by genetic, epigenetic, and environmental factors, which explains this variability in expression. Several lines of evidence suggest that genetic factors influence the effects of alcohol on fetal development and phenotype (1-3). Neurobehavioral and neurobiological dysfunctions induced by gestational alcohol exposure are correlated to the genetic background of the affected child and/or epigenetic modifications in gene expression (4,1).

Although most experienced clinicians can recognize a child with fetal alcohol syndrome (FAS) by the characteristic clinical features, many other disorders also mimic this phenotype. In addition, many children who have been exposed to prenatal alcohol have few or absent dysmorphic features but express cognitive, behavioral, and neurological findings similar to children with FAS, which is referred to as ARND. It is this group that presents the greatest challenge for diagnosis.

An approach to the genetic assessment of the child with possible FAS and ARND will be discussed and some illustrative cases to highlight this challenge will be presented. The differential diagnosis of FASD and a strategy for genetic testing depending upon the clinical scenario will be proposed. Since the introduction of comparative genomic hybridization arrays, the identification of micro deletions and micro duplications has doubled the diagnostic yield of abnormalities in children who present with developmental or intellectual disabilities when compared to results from chromosome analysis (5-7). There is scant published evidence of the utility or yield of micro array analysis in children with FASD, and clinical practice and testing is likely highly variable amongst centers.

As molecular technology such as next generation sequencing, exome sequencing, and epigenetic signature patterning studies emerge into clinical practice over the next decade, these powerful tools may help better identify genetic disorders that may mimic FASD (8). Conversely, this technology may also identify a molecular biomarker that may augment or confirm an FASD-related diagnosis. Evaluating possible epigenetic mechanisms as mediators of alcohol's adverse effects on the fetus may be important to understand

the phenotypes associated with FASD (9). Studies are currently underway to answer some important questions about the use of molecular investigations in FASD assessment (10).

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Dr. Jacobson is a developmental psychologist whose research, in collaboration with Sandra Jacobson, Ph.D., has focused on the effects on development of prenatal exposure to neurotoxic agents. The Jacobsons' research on environmental contaminants includes an 11-year prospective, longitudinal study on prenatal exposure to polychlorinated biphenyls (PCB) in western Michigan and an 11-year prospective study on the effects of environmental contaminants on Inuit children in Arctic Quebec. Their Michigan study was the first to report adverse effects of prenatal PCB exposure on infant recognition memory and IQ in childhood, and their recent study in the Arctic is the first to directly link prenatal methylmercury exposure to reduced IQ scores in school-age children. The Jacobsons' research on fetal alcohol spectrum disorders includes a 19-year Detroit longitudinal study on the effects of moderate-to-heavy prenatal alcohol exposure and a 9-year longitudinal study on fetal alcohol syndrome in Cape Town, South Africa. Dr. Jacobson has used behavioral and neuroimaging assessments to study the effects of alcohol exposure on number processing in both of these cohorts. He has served on expert panels for the Institute of Medicine, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute of Environmental Health Sciences.

Abstract

Differential Diagnosis of ARND: Other Toxic Exposures

This talk will compare the neurobehavioral deficits seen in alcohol -related neurodevelopmental disorders (ARND) with those reported in other toxic exposures. The most extensively studied exposure to an environmental toxin is postnatal lead exposure, which results when toddlers and young children ingest lead-contaminated paint chips and dust. The most consistent neurobehavioral sequelae observed in postnatal lead exposure are reduced

IQ scores (1,11,19), an increased incidence of ADHD (2), and conduct problems, including court-adjudicated delinquency (23) and criminal arrests (35). By contrast to the FASD literature, few studies have tried to delineate specific aspects of neurocognitive function that are affected by lead exposure, and those few studies that have addressed this issue have found that effects on IQ are generally stronger than on more narrowly defined endpoints (5) and are seen at remarkably low levels of exposure (6). IQ is also a highly sensitive endpoint for prenatal exposure to methylmercury (10,20) and polychlorinated biphenyls (15,27).

One striking contrast between these toxic exposures and ARND is that, although reductions in IQ are also seen in ARND, particularly in retrospective cohorts composed primarily of more heavily exposed, clinic-referred cases, effects on IQ are not seen reliably in moderately exposed, prospectively recruited longitudinal samples. In our Detroit study, for example, prenatal alcohol was not related to reduced IQ in the sample as a whole but only in more vulnerable subgroups, including children born to older mothers and to mothers with a history of alcohol abuse and/or dependence (17). Reduced IQ scores were also evident only in subgroups within the moderately exposed Pittsburgh (33) and Seattle 50029 cohorts. By contrast, certain specific domains of cognitive function were much more sensitive than IQ to prenatal alcohol exposure, including verbal learning and memory (22,32,34,9,24), verbal fluency (26,3,4,18,31,25), working memory (28,21,4,13), and arithmetic (29,30,7,12,14,16)—endpoints that have been consistently linked to FASD in the other studies cited here as well.

By contrast to the other toxic exposures, extensive information is available about specific domains of function that are affected in ARND. However, what makes diagnosis difficult is that so many different domains are affected in ARND and so many of these domains are also impaired in other disorders. That is why we believe that advances in our understanding of which specific components of these domains are affected is important for improving both differential diagnosis and treatment and that an understanding of the brain regions and neural processes that mediate these effects will lead to more firmly grounded diagnosis and development of more effective interventions. For example, arithmetic is affected in both ARND and ADHD. However, we have found that, whereas magnitude comparison is more directly affected in ARND than calculation, calculation is more affected in ADHD (16). Moreover, the effect of ADHD on calculation is mediated by IQ and executive function, whereas the effect of ARND on calculation is mediated primarily by magnitude representation, indicating injury to different brain regions. These data suggest that children with ADHD can benefit from interventions focused on enhancing executive function skills in the context of number processing, but that in ARND it will be necessary to focus more on fundamental concepts relating to relative magnitude, an approach that is emphasized in Coles et al.'s (8) MILE intervention program.

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Dr. Chasnoff's most recent work focuses on community approaches to the integration of behavioral health services into primary health care for women and children. He has authored numerous research articles and seven books, the most recent of which, The Mystery of Risk, explores the biological and environmental factors that affect the ultimate development of alcohol- and drug-exposed children and presents practical strategies for helping children reach their full potential at home and in the classroom.

Abstract

Ecological Factors: Influence on Diagnostic Criteria for Alcohol-Related Neurodevelopmental Disorder (ARND)

Although there is general consensus as to the criteria for the diagnosis of fetal alcohol syndrome (FAS) (1,2), the diagnosis of ARND remains an issue of contention, as it has been recognized that many of the neurodevelopmental deficits characteristic of alcohol-exposed children can be produced by environmental factors, especially early neglect and trauma, physical or sexual abuse, and placement in the child welfare system.

Streissguth and her colleagues (3) originally distinguished between the primary and secondary disabilities of FAS and fetal alcohol effects (FAE), defining primary disabilities as those directly related to intrauterine alcohol toxicity. The notion of secondary disabilities was used to "encompass the measurable difficulties that people with FAS/FAE face as they mature…" Following Streissguth's early work, later studies have continued to substantiate the high prevalence of mental health difficulties among individuals with prenatal alcohol exposure (4,5).

However, a wide range of neurodevelopmental deficits—including memory, executive functioning, and behavior, as well as global cognitive functioning and long-term mental health problems—can be the result of early neglect and trauma in the life of a child (6-9). This is especially pertinent in that a high percentage of children affected by prenatal alcohol exposure are in out-of-home placement through the child welfare system. These issues are evident as one examines the literature regarding the etiology of behavioral and mental health disorders in children with prenatal alcohol exposure.

O'Connor et al. (4,10) suggested that the high proportion of children with mood disorders was due to the damage sustained by the basal ganglion and cerebellum. Fryer et al. (5) postulated that the higher rates of psychopathological conditions among the alcohol-exposed children were associated with placement in a non-relative foster or adoptive home.

Studies that examined negative affect in infants, which included infant behaviors such as whining, fussing, crying, screaming, and frowning, and gestures in older children such as angrily throwing toys and depression (11,12) suggest that a combination of prenatal and postnatal factors contribute to the high rates of mental health disorders in alcohol-exposed populations. O'Connor posits that in addition to a genetic predisposition for depression and difficult temperaments that are a result of their prenatal exposure to alcohol, the children's mothers' alcohol problems and mood disorders impede the development of optimal relationships between mother and child.

The role of environmental factors, particularly those related to out-of-home placement, is an especially important question in considering a child's diagnosis of ARND, since most research has documented an increased prevalence of psychopathology among children in the foster care system (13-15). A recent paper by Wells et al. (16) examines the prevalence of neuordevelopmental dysfunction and mental health disorders among alcohol-exposed children in out-of-home placement as compared to a similar group of children in out-of-home placement who had no prenatal exposure to alcohol. In this study, there was no difference between the two groups in the rate of co-occurring mental health disorders; 63.5 percent of the children with FAS/ARND met criteria for two or more disorders, similar to

the 69.6 percent rate of co-occurring mental health disorders found in the comparison non-exposed group. Examination of the behavioral health diagnoses demonstrated a significantly higher rate of deficits in attention and focus and diagnosis of ADHD in the alcohol-exposed group, a significantly higher rate of mood disorder in the non-exposed group, and similar rates of anxiety disorders in the two groups. Through predictive discriminant analysis (PDA), it was found that prenatal alcohol exposure and number of prior placements in the child welfare system were the two primary factors responsible for the significantly higher rate of attention deficit hyperactivity disorder among the children with prenatal alcohol exposure. The most significant predictive factors for anxiety disorder were a history of physical or sexual abuse and less time at current placement, and mood disorder was predicted by length of placements rather than prenatal alcohol exposure.

The issue of the relative contribution of biological (prenatal alcohol exposure) factors and environmental (the dynamics of out-of-home placement) factors to the high rate of mental health disorders in children with FAS or ARND is a difficult research question to answer. In an optimal analysis, one would include a wide array of additional environmental variables, such as parenting practices, negative peer influences, and community factors. From a policy perspective, current findings stress the importance of utilizing stringent markers for the documentation of prenatal alcohol exposure and consideration of ecological contributors to neurodevelopmental dysfunction before making a diagnosis of ARND.

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Dr. Mattson is a neuropsychologist with expertise in fetal alcohol spectrum disorders (FASD). Her recent research has focused on the determination of the neurobehavioral profile of FASD and whether this profile is specific to the effects of prenatal alcohol exposure. Her research involves both the neuropsychological and neuroimaging assessment of children affected by heavy prenatal alcohol exposure. She served as president of the FASD Study Group and currently serves on the Interagency Coordinating Committee on FASD Diagnostic Issues Work Group and its Diagnostic and Statistical Manual of Mental Disorders (DSM) Revision Subcommittee. Dr. Mattson has authored more than 90 articles and book chapters.

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Dr. Wozniak is a pediatric neuropsychologist who divides his time among clinical work, research, and training activities. He currently serves as the assistant director of the University of Minnesota's clinical psychology internship program. Dr. Wozniak's research is focused on understanding the neurodevelopmental aspects of fetal alcohol spectrum disorders (FASD). He conducts neuroimaging studies in FASD in conjunction with the university's Laboratory for Neuropsychiatric Imaging, where he directs the neurocognitive section. For the last 2 years, Dr. Wozniak has been conducting the first randomized controlled trial of choline supplementation in children with FASD. His ultimate goal is to combine his interests in the form of new studies that will use modern neuroimaging methods to evaluate the outcomes of treatments specifically designed for FASD.

Abstract

Specificity of the Neurobehavioral Profile of ARND: Comparisons With ADHD

Fetal alcohol syndrome (FAS) is characterized by a broad array of neurobehavioral deficits including those in general intelligence, learning, attention, and visuospatial and executive functioning. These deficits also occur in individuals exposed prenatally to alcohol but who do not meet the criteria for fetal alcohol syndrome (FAS). Nearly 40 years of research has documented consistent deficits in multiple cognitive domains that occur across the spectrum of alcohol's effects. Thus, the fact that prenatal exposure to alcohol causes cognitive and behavioral deficits is well documented. Recent research has tried to better define the profile of effects that occurs in fetal alcohol spectrum disorders (FASD). While larger samples and targeted assessments have lead to better understanding of this profile, further research is needed. One question that remains is whether this emerging profile is specific to FASD. One line of research focused on the comparison between FASD and attention deficit hyperactivity disorder (ADHD). ADHD is common among children with FASD and thus is a logical comparison group. Studies comparing these two clinical groups have documented both similarities and differences. The groups are similar when comparing parental reports of attention, communication and socialization aspects of adaptive function, and performance on a measure of executive function (Wisconsin Card Sorting Test). Group differences are apparent on laboratory measures of attention, other measures of executive function, verbal learning, mathematics and numerical processing, motor competence and balance control, eyeblink conditioning, and daily living skills. Greater understanding of the specificity of the behavioral profile will ultimately improve our ability to both identify and intervene with children affected by prenatal alcohol exposure.

Can ARND be differentiated from other disorders?

Larry Burd, Ph.D.

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Dr. Burd has been with the Pediatric Therapy Program at the University of North Dakota for 31 years, during which he has evaluated more than 15,000 children with birth defects, developmental disorders, and mental illness. He has ongoing longitudinal studies of linked cohorts of subjects with Tourette syndrome, autism, FAS, and infant mortality risk that are in their 26th year of data collection. He has published more than 130 professional papers on topics dealing with development and behavior in children and adolescents. Dr. Burd is a co-principal investigator for the Prenatal Alcohol in Sudden Infant Death Syndrome (SIDS) and Stillbirth (PASS) Network study, which is examining outcomes from 12,000 pregnancies with an emphasis on prenatal exposures to alcohol, smoking, and other environmental factors.

Abstract

ARND: Mechanisms of Phenotype Expression and Comorbidity

Fetal alcohol spectrum disorders have four categorical entities, one of which is ARND. This category may be the most prevalent expression of adverse outcomes from prenatal alcohol exposure. Previous reviews have demonstrated that the phenotype for ARND likely will be composed of neuropsychological impairments, developmental delays, and mental disorders (1-6). For adults the phenotype may also need to include impairments in independent living. This presentation will offer a screening strategy for ARND, with a phenotype composed of: (a) increased susceptibility to expression of genetic and environmental adversity; (b) increased severity for expression of these disorders; (c) increased rates of comorbidity; and (d) exposure without identifiable effect. The model for ARND diagnosis used by the North Dakota FAS Center will be reviewed (7). Diagnosis of ARND is complicated by lack of thresholds for exposure resulting in adverse effects, and postnatal influences on phenotype expression that may accumulate into adult life.

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Question 3: What prenatal alcohol exposure evidence is necessary for an ARND diagnosis?

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Dr. Savage directs the Developmental Alcohol Research Center, which focuses on fetal alcohol spectrum disorders (FASD) and is funded by the National Institute on Alcohol Abuse and Alcoholism. He currently serves on the Science Advisory Board for the Collaborative Initiative on FASD, the Research Society on Alcoholism Board of Directors, and the editorial boards of Alcoholism: Clinical & Experimental Research and Neurotoxicology & Teratology. He is the 2011 recipient of the Henry Rosett Award for excellence in FASD research. Dr. Savage's primary research interests center on how moderate drinking during pregnancy causes long-term impairments of the neurobiologic mechanisms that subserve synaptic plasticity and learning. His current translational research projects include the preclinical screening of putative therapeutic agents for treating fetal alcohol-induced learning deficits and the development of novel biomarkers for earlier detection of fetal alcohol-induced functional brain damage.

Abstract

Animal Models of FASD/ ARND: What Moderate Ethanol Exposure Paradigms Suggest About Fetal Alcohol Effects and Fetal Alcohol Exposure

Much of the preclinical research on the effects of prenatal ethanol exposure has used moderate- to high-dose ethanol exposure paradigms, administered either in binge-like patterns or by more prolonged exposure through *ad libitum* access to ethanol liquid diets. These exposure paradigms often cause neuroanatomical alterations in offspring ranging from cell loss in select neuronal populations to reductions in brain regions or whole brain size in affected offspring. Many behavioral abnormalities have been associated with fetal ethanol-induced alterations in brain structure.

Less research activity has focused on the effects of relatively low to moderate levels of fetal ethanol exposure. Typically, the effects of moderate exposure do not produce neuroanatomical damage discernible at least to the light microscopic level. The behavioral deficits associated with moderate ethanol exposure become more apparent as the behavioral task becomes more challenging. Some behavioral and neurophysiologic deficits have been observed at a maternal peak blood ethanol concentrations as low as 30 mg/dL.

Generally speaking, low to moderate prenatal ethanol exposure produces few changes in neurotransmitter levels or neurotransmitter receptor numbers. However, emerging evidence has revealed fetal ethanol-induced alterations in receptor subunit composition along with alterations in the extracellular milieu and intracellular signaling systems that modulate neurotransmission. Further, fetal ethanol-exposed offspring respond to some neuroactive medications differently than nonexposed offspring. Nevertheless, recent studies indicate that fetal ethanol-induced behavioral and neurophysiologic deficits can be ameliorated with therapeutic agents with some reasoned prospect of approval for clinical use. Aditionally, animal models of moderate prenatal ethanol exposure hold promise for facilitating advances in the identification of novel biomarkers for fetal alcohol exposure and fetal alcohol effects.

What prenatal alcohol exposure evidence is necessary for an ARND diagnosis?

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Dr. Day directs or co-directs three training grants in epidemiology focusing on reproductive epidemiology, alcohol research, and psychiatric epidemiology. She has mentored both pre- and post-doctoral students and was awarded the Provost's Award for Excellence in Mentoring. She served as a member and chair of the Psychosocial Research Initial Review Group, National Institute on Alcohol Abuse and Alcoholism (NIAAA) Prevention and Epidemiology Subcommittee; president of the Fetal Alcohol Spectrum Disorders Study Group; and member of the NIAAA Council. Dr. Day has been active in the Research Society on Alcoholism (RSA), serving as an advocate in Washington, DC, and was awarded the Frank Seixas Award for Distinguished Service to the RSA. Her research has followed a cohort of women and their offspring from their fourth month of pregnancy until the offspring were 22 years of age. This research has focused on the social, environmental, psychological, and physical consequences of alcohol and other drug exposures during gestation.

Abstract

What Evidence Is Necessary for an ARND Diagnosis?

This question is really two separate questions. The first is: What is known about the association between the level of exposure and the diagnosis of alcohol-related neurodevelopmental disorder (ARND)? To address this question, the literature on levels of exposure will be reviewed. There is considerable agreement on the effects of heavy drinking and/or alcoholism on ARND. There is far less agreement on the effects of moderate and light drinking on the development of ARND. This presentation will present literature that specifically addresses the issue of the effects of moderate and light exposure. The literature on this question is limited and the results are disparate. Although a number of reports document an effect of lower levels of drinking on ARND, there are an equal number of reports that do not find an association. The reasons for these differences will be discussed. Differing sample characteristics, drinking patterns, and characteristics of the mothers are among the variables that affect the determination of the effects of drinking during pregnancy. Further, methodological differences in study design and measurement may lead to conflicting answers.

A determination of what evidence, what level of drinking, is necessary for an ARND diagnosis is a related, but separate, question. Considered from the view of the subject/patient, what level of alcohol exposure would allow the clinician or researcher to assume that prenatal alcohol exposure is part of the diagnosis? This is a much more difficult question to answer. Although the best answer to this question requires case/control and retrospective studies, some extrapolation can be made from the current research to provide some guidance about what measures and what data would aid the clinician in judging whether a specific diagnosis is associated with prenatal alcohol exposure.

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Dr. Astley has conducted laboratory, clinical, and public health research in the field of fetal alcohol spectrum disorders (FASD) since 1981. Her recent work has been in the development of FASD diagnostic, screening, surveillance, intervention, and prevention tools/programs (e.g., FASD 4-Digit Diagnostic Code, FAS Facial Photographic Analysis Software, FASD Online Course, and the Foster Care FAS Screening Program). As director of the FAS DPN, she has diagnosed more than 2,500 patients

with FASD. She and her colleagues have recently published a study of the diagnostic utility of magnetic resonance imaging (MRI), MR spectroscopy (MRS), and functional MRI (fMRI) for FASD. A focal publication documents Washington State's success in preventing FASD through reduction of maternal alcohol use during pregnancy.

Abstract

What Prenatal Alcohol Exposure Is Necessary for an ARND Diagnosis? Experience From the Washington State Fetal Alcohol Syndrome Diagnostic and Prevention Network Clinic

What prenatal alcohol exposure is necessary for an alcohol-related neurodevelopmental disorder (ARND) diagnosis? ARND requires confirmed exposure during pregnancy at any reported level. A threshold level of exposure cannot be required because quantity/frequency/duration details are often not available and their accuracy can never be confirmed. Exposure must be confirmed because ARND does not have a physical or functional feature that is specific to (caused only by) prenatal alcohol exposure.

Who were the sources of confirmation: Among 1,400 patients with confirmed prenatal alcohol exposure who were diagnosed in the Washington State FAS DPN clinics, the sources of exposure history were birth mothers (43 percent), a person who directly observed birth mother drinking (34 percent), and medical/legal/social reports (22 percent).

What constitutes confirmation? One can confirm exposure but not know the details of quantity, frequency, and duration. The highest level of confirmation is through a birth mother report, but recall and willingness to report can affect accuracy. We often have multiple sources of corroborating evidence (e.g., self-report, witnesses, medical records). The following are risk factors for exposure but do not confirm exposure: birth mother is an alcoholic, used illicit drugs during pregnancy, drank during other pregnancies, and gave birth to other children with FASD.

How can alcohol exposure be documented in clinic: The New Patient Information Form has been used by the Washington State FAS DPN to collect alcohol exposure information on more than 8,000 patients since 1997 (1). It documents alcohol use before and during pregnancy (quantity/frequency/trimester/type of alcohol/alcohol treatment).

Should thresholds/patterns of use be required? The answer is no for the following reasons. The accuracy of reported exposure in a clinical setting can never be confirmed. Among 1,400 Washington State FAS DPN patients with confirmed exposure, less than 50 percent were able to report details such as quantity, frequency, and duration. A threshold sends the wrong public health message: "Exposure below the threshold is SAFE." And risk to individuals is highly variable. Children with full FAS have "reported" levels of prenatal alcohol exposure of as low as one drink weekly in the first trimester. Is this inaccurate, or were these children especially vulnerable? In the human population, alcohol is never the only risk factor contributing to a child's impairment. But, in a primate alcohol study where all other risk factors were eliminated, there is clear evidence of cognitive impairment among primates exposed to binge drinking once/week for just the first 3 weeks of pregnancy, or one to two drinks once per week throughout pregnancy. The primary motivation to set a threshold exposure for ARND is because the term implies a causal association between exposure and outcome in an individual. As published by Aase, Jones, and Clarren, "A diagnosis that implies causation should not be applied unless the relationship can be proven. If exposure has taken place, exposure should be indicated and abnormalities reported (2)." This is the approach taken by the FASD 4-Digit Code since 1997. The term ARND was replaced by neurodevelopmental disorder/alcohol exposed. To date the Washington State FAS DPN has diagnosed 1,762 patients with the equivalent of ARND since 1997, requiring confirmed exposure but no threshold level. Twenty-five percent of our referrals are from medical doctors.

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What prenatal alcohol exposure evidence is necessary for an ARND diagnosis?

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Dr. May's research is primarily on the prevalence and epidemiological characteristics of fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (PFAS), and alcohol-related neurodevelopmental disorder (ARND). Dr. May is a principle investigator of studies to research the characteristics of FASD among select groups of Native Americans, South Africans, Italians, and the general population of the United States. He and his colleagues are focused directly on refining the most salient criteria for diagnosing the entire spectrum of FASD, the specific characteristics of individual FASD diagnoses in children of primary school age and infancy, maternal risk and protective factors for FASD, and a neurobehavioral phenotype for children with FASD. Efficacy studies of how to best prevent FASD in select populations are also ongoing in South Africa.

Abstract

Population Diversity and Moderators of Risk

In this presentation, we will review the utilization of sequencing, types of questions asked, and time periods covered in questionnaires employed in population-based epidemiological studies to collect data on alcohol exposure among women who have given birth to children of various diagnoses (i.e., normal morphology/ normally performing children and children with ARND, partial fetal alcohol syndrome (PFAS), and FAS). Evidence of mean alcohol intake and lower and upper thresholds does not always follow a linear pattern across the spectrum. Data indicate significant variance in the levels of alcohol consumed across various substrata of mothers of children within each diagnostic category. Significant variance in child outcomes is found, based not only on alcohol consumption, but also on several childbearing and maternal demographic categories. Multiple variables that are associated with child dysmorphology and child cognition and behavior will be presented as they influence the impact of alcohol on the fetus. Finally, the criteria used by our clinical research team to diagnose ARND in population-based epidemiological studies will be explained.

Question 4: What signs and symptoms will be useful as screening criteria?

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Early in her training in the United States, Dr. Loock developed an interest in "social pediatrics." She is a distinguished teacher clinician who is exploring innovative approaches for health service delivery to socially vulnerable children and families in Canada. Her clinical and research work has been focused on fetal alcohol spectrum disorders (FASD). She was a member of the Canadian National Advisory Committee on Fetal Alcohol Syndrome and co-author of the Canadian guidelines for diagnosis of FASD. She currently is on the Canadian Association for Paediatric Health Centres' Advisory Committee for developing a national screening toolkit for FASD.

Abstract

Screening for ARND in the Context of Developmental Delay and Other Red Flags: Perspectives from Primary Care and Subspecialty Practice

FASD is common, expensive, and preventable. Making an earlier diagnosis is possible, meaningful, and necessary to begin early interventions for the child and his or her mother and family, as well as to address issues that are both predisposing and perpetuating for alcohol-related disorders (1,2). As with any disability—physical, neurodevelopmental, or combined—the diagnosis of an FASD requires interdisciplinary collaboration and intersectoral communication for the coordination of appropriate services (2,3). The ultimate goal should be meaningful inclusion of the individual in both activities of daily living and participation in society (4).

The key to screening is to do no harm, to have a plan for those who "screen in" as well as for those whom we "screen out," and to have adequate resources for ongoing support (5). The prevalence of developmental disabilities (DD) in the general population is approximately 1 in 7 (6). We should use reliable and valid screening tools, which facilitate access to diagnosis, without sociodemographic barriers. Patients can't sort themselves into queues to facilitate referral, and informal clinical screening is unreliable. Parent report tools, however, are both valid and universally available (3, 7). Population-based surveillance tools for preschoolers, and now for older children, are currently being introduced in Canada (8,9).

Screening for an FASD, and in particular for alcohol-related neurodevelopmental disorder (ARND), can be problematic. Who should be screened, and by whom? Screenings can be targeted, based on known significant prenatal alcohol exposure or adverse postnatal events (e.g., multiple foster placements (10) or adoption), or screening can be integrated into more universal developmental screening strategies (3) (i.e., based on functional differences in development, learning, behavior, and mental health). In British Columbia, we have developed tiers of service delivery for the screening and referral of children with DDs, including autism, FASD, and genetic and other low-incidence disorders, and a standardized tracking assessment report (STAR) is being piloted (11). Across Canada, an FASD screening toolkit has been developed for use in a variety of settings (e.g., women's health centers, community schools, corrections programs, and in both primary care and referral-based practices) (12).

ARND concerns are multiple, significant, and concurrent with interacting environmental and epigenetic mechanisms. Although no "phenotype" for the "FASD brain" has been agreed upon or validated (13), there is converging evidence that functional differences are related to exposure. But, without a "reportable" name for the spectrum of significant "nondysmorphic" neurodevelopmental effects from prenatal alcohol exposure (e.g.,

ARND), it remains difficult to navigate systems of care. Having an International Classification of Diseases (ICD)- or Diagnostic and Statistical Manual of Mental Disorders (DSM)-reportable condition (and, in the United States, linked to billing codes) would bring not only acknowledgment, but also better treatment and resources to affected individuals, families, and communities.

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Dr. Millians received a doctorate in special needs and inclusive instruction from the University of South Africa. She is a special education teacher certified to teach children from prekindergarten through high school. For the past 8 years, she has been a member of the Marcus Autism Center's fetal alcohol spectrum disorder (FASD) interdisciplinary diagnostic team, conducting educational assessments and evaluations and working with schools and teachers in Georgia to support children with FASD in their educational settings.

Abstract

Collaboration With Schools To Screen for ARND

Children affected by prenatal alcohol exposure without alcohol-related dysmprophia are at risk for academic, social, and behavior problems at school. However, these children often are overlooked for evaluation and treatment (1). To ensure that children at risk for alcohol-related neurodevelopmental disorder (ARND) are identified, collaboration between clinicians and educators would be beneficial. The objective of this collaboration would be to develop screening programs to identify children in need of a comprehensive evaluation to rule out possible ARND (2). Programs would need to train teachers, school psychologists, social workers, and staff to be aware of cognitive and developmental delays

associated with prenatal alcohol exposure that hinder children's school functioning and require a referral for a comprehensive evaluation completed by an interdisciplinary team (2).

Though a neurobehavioral profile for children affected by prenatal alcohol exposure has not been defined, deficits in sustained visual attention, encoding verbal and visual information, processing speed, and executive function are associated with these effects (4-6). School-aged children with difficulties in these areas may display incomplete understanding of material, have poor recall of information, and demonstrate inconsistent academic performance (7). Children with deficits in executive functioning may exhibit difficulties formulating and generalizing conceptual information, use inefficient problem-solving strategies, and demonstrate a rote understanding of material (8,9). Academically, children affected by prenatal alcohol exposure may exhibit problems processing numerical information and often receive low scores on mathematics achievement tests (10-13). Deficits in visuospatial abilities may contribute to problems in mathematics (14). Also, children who have visuospatial weaknesses may have difficulties with spatial orientation or judging distance and may have problems navigating the classroom or school layout (4,15). Deficits in visuospatial abilities, executive functioning, speed of processing, and encoding may influence children's skills to interpret and respond appropriately to social situations at school (16,17)

Difficulties with self-regulation may result in behavioral problems in a classroom setting. However, behavior difficulties may not be a direct result of prenatal alcohol exposure but a combination of factors including chaotic home environments, multiple foster placements, and caregiver substance abuse (18,19).

Given the range of impairments associated with the effects from prenatal alcohol exposure, the impact of environmental factors as well as possible co-morbid disorders indicates the need for collaboration among the medical community with teachers, school psychologists, social workers, and administrators to identify children at risk for problems secondary to ARND and to refer for a comprehensive evaluation to guide interventions.

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Ms. Spencer, a pediatric nurse practitioner since 1983, specializes in health care for foster and adopted children and those in out-of-home placements, including residential and day treatment, juvenile detention, and homeless shelters. As a consultant to MOFAS, she facilitates adding FASD diagnosis to Minnesota primary care pediatric and family practice clinics. Her clinical practice with the University of Minnesota/St. Joseph's Home for Children Clinic Collaboration includes FASD diagnosis, FASD care coordination, and medical resident instruction. Her clinic received one of the original grants from the Substance Abuse and Mental Health Services Administration to participate in a regional FASD diagnosis project in 2000–2003. She participated in medical evaluation and sample selection for the hallmark Bucharest Early Intervention Project, a MacArthur Foundation-funded 10-year ongoing longitudinal intervention study comparing the neurodevelopment of Romanian children from orphanages, foster care, and the community, notable for the project's exclusion of children with characteristics of fetal alcohol syndrome (FAS). Ms. Spencer presents and participates on panels on FASD. She presented last month in Russia on "Parenting Foster and Adopted Children with FASD" and "Medical and Developmental Needs of Foster and Adopted Children" at multisector conferences to transform child welfare in St. Petersburg, Moscow, and Nizhny-Novgorod, Russia.

The Minnesota Experience: Establishing Systems of Care for Fetal Alcohol Spectrum Disorders:

Screening, Referral, Diagnosis, and Interventions

MOFAS works to prevent prenatal alcohol exposure and to identify and ensure care to those affected by FASD. To that end, MOFAS has supported the development of Minnesota FASD diagnosis clinics and community expertise to provide screening, referral, and local support and intervention services.

MOFAS supports screening for prenatal alcohol exposure (PAE), FASD, and referral for diagnosis or to early intervention. In 2006, MOFAS piloted their PAE screening tool. Currently, nine clinics have each received 18-month grants of $20,000 to incorporate PAE screening and brief intervention into their standard of care for all prenatal visits. The clinics range from rural public health clinics to urban family practice clinics. The PAE screening project is selected for the Substance Abuse and Mental Health Services Administration's Service-to-Science Program.

During 2010–2011, an FASD screening tool for primary care clinics was developed by an expert advisory panel, including the presidents of the Minnesota chapters of the American Academy of Pediatrics (AAP) and the National Association of Pediatric Nurses and Practitioners, MOFAS staff, an FASD diagnosis consultant, University of Minnesota FASD faculty, and governmental departments. This FASD screening tool is now being piloted in four primary care clinics via 3-year grants of $210,000. The clinics are paired for 1 year with mentor FASD diagnosis clinics to provide clinical expertise and to develop an FASD referral and care coordination system network.

MOFAS supported preschool screening for PAE in the Minneapolis schools in 2009. In the 2010-11 school year, 3,981 preschoolers were screened and 66 referred for FASD diagnosis evaluations due to positive PAE and social and emotional concerns. One major value of this program is to have another source-written documentation about PAE. Three other school districts in Minnesota now are replicating this program at their own expense.

MOFAS strongly supports establishing FASD diagnosis practices in Minnesota clinics. FASD diagnosis clinics are housed in existing clinical practices, including primary care clinics for children, child and adolescent behavioral and mental health clinics, and a residential treatment center. The practices have broad geographic and cultural range.

The FASD diagnosis evaluation is adapted to fit the clinic's existing practice model. This flexibility is one of the critical deciding factors for clinics considering adding FASD diagnosis to their practices. Many FASD diagnosis practices successfully collaborate with health care professionals outside of their clinic system, as is done for other chronic conditions such as autism, post-concussion syndrome, and diabetes. There are 500 FASD diagnosis evaluation appointments available per year in Minnesota. Billing for diagnosis services is fee-for-service, with the potential for health care home care coordination funding, and managed within each clinic system.

There are currently six 12-month community FASD intervention grants for $10,000 that are supported by MOFAS. These grants are diverse in scope, and support intervention services for children, youth, and adults with FASD, including an online education program in school; a transition-to-adulthood program; an independent living skills program; a family support and education program; a teen peer-mentoring program; a social development program for children using equine experiences, which includes parents in the therapeutic model; and a home visiting program for severely stressed children and families. Evaluation will occur for a 6-month post-intervention period.

MOFAS demonstrates model public-private partnership to address FASD in Minnesota. The current strategy of MOFAS encompasses providing community-saturated support for preventing PAE and improving FASD identification and care.

Question 5: What are the treatment needs for those diagnosed with ARND?

Heather Carmichael Olson, Ph.D.

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Dr. Carmichael Olson's general research interests center on the impact of parental substance abuse on children's development. She has focused on the underserved group of children with fetal alcohol spectrum disorders (FASD), who typically have challenging neurodevelopmental disabilities and behavior problems. Carmichael Olson's research is aimed at developing practical FASD assessment and intervention methods, including behavioral consultation intervention for families raising school-aged children with FASD and behavior problems. Carmichael Olson and colleagues currently are involved in multiple research projects: descriptive study of clinical data on children with FASD, birth to 8 years; descriptive neuroimaging, neuropsychological, and spectroscopy study of several groups of children aged 8 to 16 years with FASD and matched controls; and a pilot study of what appears to be a high prevalence of sleep disorders among children and adolescents with FASD. Carmichael Olson also provides clinical services to families raising children with FASD. These clinical experiences, which allow her to learn from families, inform her research efforts.

Abstract

What are the Treatment Needs of Individuals With ARND and Their Families? General Overview

Abstract not available at time of printing.

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Dr. Paley is the principal investigator and director of the NIAAA-funded Strategies for Enhancing Early Developmental Success (SEEDS) Program for Young Children with Prenatal Alcohol Exposure at UCLA. She has previously served as an investigator and co-investigator on several federally funded grants aimed at developing and evaluating evidence-based interventions for children with fetal alcohol spectrum disorders (FASD), and designing FASD-related curricula for medical school students and faculty. Dr. Paley is a member of the Diagnostic and Statistical Manual on Mental Disorders (DSM) Revision Subcommittee of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders Diagnostic Issues Work Group. Dr. Paley regularly provides training to community medical and mental health providers, social services agencies, and court personnel on the assessment and treatment of individuals with FASD.

Abstract

Early Intervention for Fetal Alcohol Spectrum Disorders

Infants, toddlers, and preschool-aged children with a history of prenatal alcohol exposure (PAE) exhibit early signs of developmental delay (1-6) and dysregulation (7-10). These impairments do not appear to be transient, but are manifested in a host of neurocognitive, behavioral, and social problems throughout the life span (11-14).

In order to circumvent what is often a downward spiral for many children

affected by PAE, it is critically important to provide early intervention that addresses multiple levels of need (15,16). However, multiple challenges exist in ensuring the young children with PAE receive appropriate early intervention services. Such challenges include a failure to identify children impacted by PAE early in their development and a lack of awareness by medical and mental health providers regarding the full range of effects of PAE. Olson, Jirikowic, Kartin, and Astley (17) reported on data from the Washington State FAS Diagnostic and Prevention Network (FAS DPN), which indicated that the average age of referral for diagnosis was 9.5 years. Additional challenges are experienced by children with FASD who come under the auspices of the child welfare system, including the limited information regarding their prenatal history that is often provided to adoptive and foster parents, and the exacerbation of pre-existing dysregulation in the alcohol-exposed child as a result of multiple placements and disrupted attachment relationships (18).

Such challenges highlight the importance of providing both direct child services and family-level interventions for young children with FASD and their caregivers. Direct child services include occupational therapy, physical therapy, speech and language therapy, and child development/early education services. Such early intervention services can be enhanced for children with FASD with some modest modifications. Interventions targeting parents and caregivers include parenting skills, parent education and advocacy training, parent-child relationship interventions, parent support and advocacy groups, and alcohol/substance abuse treatment. An example of an early intervention approach for this population is the SEEDS (Strategies for Enhancing Early Developmental Success) Program at UCLA, which is a multicomponent program focusing on promoting self-regulation in infants and toddlers with PAE by improving parental knowledge and skills and enhancing the parent-child relationship.

Recommendations to enhance treatment and services for young children affected by PAE include improvements in screening of young children for FASD, improved training for medical and mental health providers in the evaluation and treatment of FASD, consideration of conditions on the FASD continuum as qualifying diagnoses for early intervention services, and support for clinical research programs focused on implementing and evaluating interventions for young children with FASD and their families.

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Dr. Rovet is a research neuropsychologist whose laboratory focuses on the impact of various exposures or lack thereof (insufficient thyroid hormone) on the developing brain. Her approach involves clinical, experimental, and neuroimaging studies of children and adolescents. As a cofounder of the SickKids' Motherisk Follow-up Clinic for the diagnosis of fetal alcohol spectrum disorders (FASD), Dr. Rovet has been involved in characterizing the behavioral phenotype of FASD and developing screening tools to aid in FASD diagnosis. Recent studies include detailed investigations of memory, executive functions, and social cognition with a view to identifying the underlying neuroanatomy of deficits in these areas. Currently, she is examining brain and behavioral changes in children with FASD following self-regulation training. Her research is funded through grants from the Canadian Institute of Health Research and the Canadian Foundation for Fetal Alcohol Research.

Abstract

Empirically Validated Treatment Approaches for School-Age Children With FASD

Despite recognition that early intervention is critical to prevent the later adverse effects of FASD, few empirically validated published interventions exist. While numerous strategies have been offered for dealing with this difficult population, these are not specific to FASD, and so may not work. According to Kodituwakku (1), interventional approaches should foster neuroplastic change in regions associated with their specific cognitive and behavioral difficulties by addressing their distinct deficit profile. In my presentation, I will review the extant literature on efficacious treatments for the specific cognitive disabilities this population manifests and describe findings from 10 studies only. These will include a language training study, a memory training study, two attention training studies, and two executive function studies as well as a math-training program

and two pharmacological intervention studies. Despite some promising findings, the evidence is relatively scant, with some domains never having been tackled therapeutically (e.g., visuospatial abilities and psychiatric problems). To date, the only study involving a neuroplastic approaches is one from our lab revealing functional changes in expected regions following self-regulation training. Finally, I will conclude with a pragmatic approach for improve cognitive functioning in these children within classroom and clinical settings.

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Dr. Pei began her career as a criminologist and forensic counselor working with incarcerated youth. Motivated by this early work, she returned to academia to study youth at risk, child development, and neuropsychology, leading to her current focus on interventions for individuals with fetal alcohol spectrum disorders (FASD). Building on her work with various community and government agencies, including serving on the FASD Clinical Diagnostic Team at the Glenrose Rehabilitation Hospital, Dr. Pei currently leads the Intervention Network Action Team (iNAT) for the Canada Northwest FASD Research Network. She also has been a practicing registered psychologist for the past 10 years.

Abstract

Treatment Needs and Interventions for Adolescents With FASD

FASD present unique challenges in the provision of intervention services. Researchers have underscored the importance of early identification and intervention to optimally meet the needs of this group and prevent the development of secondary disabilities (1,2). However, some children do not receive these early services, and even those who do will continue to require supports throughout their lifetimes. Investigation into effective interventions for individuals with FASD is progressing, but is in its early stages. This is particularly true for interventions for adolescents with FASD, an area with little research. Yet this group faces significant challenges as environmental and developmental expectations grow; because of their prenatal alcohol exposure they experience increasing difficulties performing to these expectations (3). This increasing gap between adolescents with FASD and their peers may reflect the executive function (EF) deficits reported for this population (e.g., 4-7), which may not be evident in their cognitive function as measured by intelligence testing (8). This in turn contributes to the high rate of secondary disabilities reported for this population (1), which can include trouble with the law (9), mental health issues (e.g., 10-12), increased drug and alcohol abuse (e.g., 13,14), and increased risk of suicide (e.g., 15.16). Also contributing to these secondary disabilities are the frequent environmental contributors, such as victimization and unstable family environments (2).

Consequently, adolescence is a period of convergence of high-risk factors, including increased expectations for independence, increased demand on executive function systems, and heightened likelihood of environmental stressors, all of which come together

What are the treatment needs for those diagnosed with ARND?

to produce high-risk behavior that has a large impact on society (18). Given these treatment needs, the importance of effective interventions for this group is clear, yet the evidence lags. Current areas of interventions being explored include coordinated efforts to increase the capacity of both the youth and the support system. Preliminary findings are positive, and key themes identified include the need for reasonable expectations, involvement of both the youth and caregivers/service providers, supports to facilitate communication between service providers, increased coordination between organizations involved, stability in the home environment, and targeting high-risk behaviors (19,20). Early evidence indicates that intervention supports with adolescents with FASD can have a positive impact, but increased investigation into the best approaches is necessary.

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Vignettes

Always Ask All Women…..

I first saw Ian in the ENT chair, with his mom. He was a scrawny 6-week-old with bilateral cleft lip and palate. He was failing to thrive. One look at him, and I knew I needed to ask. Important—not urgent.

I remind myself of the basic steps of communicating in emotionally challenging settings. Sit down, slow down, and listen first. Ask what they know and what worries them, especially when the baby has had them up in the middle of the night.

Lilly knew. She had told the Genetics doctors in her prenatal visit after the ultrasound had shown a large oral facial cleft.

Lilly told me Ian was her special gift from God. She was older and had never been pregnant. She hadn't planned to get pregnant. The father had left, thank goodness, as the violence had escalated. She knew where to get help. She had been abused before.

She had an amniocentesis for advanced maternal age, intrauterine growth retardation and the craniofacial anomaly. All was normal. She ate well and went to live with her mom. Delivery was at term. Ian was tiny, all his paramenters less than the 3rd percentile. She was immediately connected with our Cleft Palate Craniofacial Team at the Children's Hospital.

This was her first visit to our team. Ian had "referred" on (not passed) his newborn hearing screen. And feeding wasn't going well at all. This was not a typical isolated (nonsyndromic) cleft lip and palate. He took way too long to feed, even with the specialized cleft nursing bottle. The feeding expert, our nurse practitioner, was concerned. She asked the orthodontist to back off on the oral cleft appliance, molded to facilitate the lip repair in 6 weeks time. This kid had to eat first. She asked me to step in to see if there was something else.

Ian was swaddled in his mom's arms. She was singing to him. What a cute, but gaunt little baby. His eyes were the first clue; his size next; heightened by his mom's anxiety and guilt. "This is all my fault."

Ian actually sailed through the next 2 years, with his surgeries for lip repair followed by palate repair and tubes in his ears. Our plastic surgeons are incredible. They do over 50 repairs a year, not including their international work.

Development was slower, but he was responding. Services were in place. So we had time to develop the trust. By then, I had also received, with Lilly's consent, the prenatal genetics report. My original working diagnosis was confirmed. I had also excluded all of the other things that might have been in the differential diagnosis for his presentation, including "FISH" for 22 q11. (I knew it would be negative, although I have had one other cleft palate only patient who had a concurrent (22q11) diagnosis.)

We discussed together that Ian had a "fetal stress disorder" (FSD) that contributed to his condition. Although no more pregnancies were planned, we talked about folic acid, and cutting down on her alcohol and cigarettes. Lilley shared that she had gone cold turkey as soon as she found out she was pregnant with Ian. She had also cut back on her smoking and now only smoked outside.

It soon became time to plan for kindergarten at age 4. Speech therapy was progressing. He would need another procedure for fistula repair in his palate. That would help some of his speech sound development and hypernasality. Language was also progressing, but at a slower rate. He still used some signs. He was inattentive, but not "driven by a motor." Sleep wasn't great. His hearing was ok. No more tubes have been required since his second set at age 3.

We started talking about Lilly getting help. Her anxiety was increasing. As was her agoraphobia. She couldn't get back to work. She needed subsidies for extra speech therapy. She was having trouble making ends meet. Our team social worker became her anchor. Her GP retired. I became the "family doctor" in the interim.

Then her mom died. Ian was age 5.

Lilly has placed Ian into care recently, just before kindergarten started. She has requested treatment for herself. She has a supportive GP. Ian has begun to be assessed by our child development (CDBC) team. I continue to see him in both settings.

Ian actually has full FAS. I should code him as ARND, because how can I truly judge a repaired bilateral cleft lip? (e.g., 4 digit code 4244; but our surgeons are really good at rebuilding lips and philtrums if there is something there to build on the prolabium. Ian doesn't have one despite their skill.) His brain scores, based on recent psychology and OT, are in the "borderline" range (neurobehavioral disorder, brain ranking 2). One could argue 4224 for now. These are all technicalities.

Ian is younger than 6, so he still qualifies for an FASD diagnosis under our stringent Canadian Guidelines. There are areas that need more assessment after he is 6, in particular his language; and then his executive function, which is more reliable to test as he gets closer to middle school. His maternal reports on his adaptive behavior need corroboration. (Also borderline, … but she was so anxious and over protective.)

Ian is in a good foster home. I saw him yesterday at CDBC. He is anxious, sad, and confused. He misses his mom. I will continue to see him in my role as the Cleft Team Developmental Pediatrician and reassess him after

he has a language and additional psychology assessments, when things settle down.

His mom is struggling. But she is alive. And before her mother died, she told her daughter "to hang in there." Ian saved her life. It was now time to take care of Lilly.

Suspected ARND In a 5-Year Old Girl

Maya is a 5 year old African-American girl who appears older than her stated age, as she is very tall and slender. She was adopted 2 years before her diagnostic assessment by Anna White, a single woman in her late 40s who works in the post office. Before coming to live in her present home, Maya suffered from sexual and physical abuse and exposure to domestic violence. Her adopted mother has worked hard to ameliorate effects of previous abuse. Currently, her outside activities are limited due to caring for Maya's behavioral problem (i.e., she cannot attend church).When seen for diagnosis by the interdisciplinary team, Maya presented as well groomed and appropriately dressed, without any difficulty in separating from her mother. Initially, she was appropriate socially and interested in the assessment process but had a difficult time in maintaining her focus. She gave her best performance during the early part of the session, but eventually required considerable structuring to complete her work. She was very active during the session, but her behavior appeared to be provocative rather than the result of an inability to maintain focus. She repeatedly "tested" the examiner's resolve by asking to go to the rest room, making unreasonable requests, and refusing to hold the pencil correctly, which interfered with her performance. She also alternated between whispering and shouting her answers to test items, with the clear intention of provoking the examiner. When these attempts were ignored, she abandoned them and returned to appropriate behavior. Throughout, she was social and friendly in her manner and did not appear to be resentful that she was not able to dominate the situation. In fact, following the examination, she was engaging and affectionate toward the examiner.

As the result of an interdisciplinary team evaluation, the following observations were made. Prenatal alcohol exposure was confirmed through medical record. In addition, there is a history of substance abuse and a biological sibling has been given a diagnosis of FAS. Examination using a Dysmorphology Checklist yielded a score of 10, which is just at the threshold of effects on this measure, but all three of the sentinel facial features were not present. Growth retardation was not noted at birth, and she is currently well above average in height and weight. Regarding evidence for an impact on the CNS, Maya is of average ability and achievement on standardized tests. Her global IQ score is 91 (27th percentile) with a Verbal Standard Score of 93 (32nd percentile) and a Nonverbal Standard Score of 90 (32nd percentile). Preacademic scores were in the high average range. She does have a history of seizures and mild hemiplegia suggestive of CNS involvement. However, we cannot rule out other factors (e.g., lead poisoning) as contributors. On measures of behavior, both parent and teacher indicated that she shows an elevated level of Externalizing Behavior and endorsed items that indicated problems with Attention. No other problems were endorsed. During the Assessment process, Maya was noted to have a high energy level, to be impulsive and nonreflective in her interactions with the examiner. She also exhibited a number of noncompliant and oppositional behaviors. However, she did respond appropriately to structuring and to behavioral management and she did seem to be concerned about social reinforcement.

In terms of recommendations for care, Maya did not need support in cognitive or academic development. However, she appeared to have difficulty with impulsive behavior and attentional focus. She was also somewhat oppositional in her interactions with adults. Family therapy to support the implementation of behavioral management techniques to reduce her oppositional behavior and support a less impulsive style was recommended. Also of concern was her history of severe sexual and physical abuse, which should be the focus of weekly counseling with a play therapist. Finally, the interdisciplinary team recommended that her development be monitored to anticipate any future medical or educational problems.

Case Study: Sasha the Internationally Adopted Child

Sasha is a 6-year-old White female adopted from an Eastern European orphanage at 15 months. The older adoptive parents are well educated, upper middle class professionals who have no other children. Records from the country of origin note that her birth mother, age 37, was a "registered alcoholic" and used "drugs." (In the birth country, this description generally refers to injected heroin.) The child was born at 32 weeks gestational age (8 weeks preterm) and was noted to have a number of medical problems at birth, including positive tests for Hepatitis C, Cytomegalovirus, and Toxoplasmosis. Tests for Hepatitis B, HIV, and Syphilis were negative. Child was abandoned in the hospital following birth and, when stable, was transferred to a "baby home" where she remained until adopted. It appeared that the orphanage did not provide adequate stimulation and that there was no opportunity to form an attachment with a caregiver while in this facility. By report, she was severely delayed at 15 months; she couldn't sit up and she had very low muscle tone when her parents first brought her home. There is a history of bilateral strabismus, and she is followed by pediatric ophthalmology. Previous chromosome studies, microarray analysis, and Fragile X (Autism Panel) are normal. Parents have private health care insurance.

In the United States, Sasha received services from her county's early Intervention programs until age 3 years and was then entered into special needs preschool with a diagnosis of autism. After sometime at this preschool, she was referred for further evaluation to rule out fetal alcohol syndrome (FAS).

Medical examination for physical signs associated with prenatal exposure revealed the following signs: weight less than the 5th percentile, hirsutism of the skin, posterior rotation of the ears, short palpebral fissures, epicanthal folds, bilateral strabismus, upturned nares, small philtrum, and thin vermillion border of upper lip. Toxoplamosis and Herpes Simplex were no longer noted and Hepatitis C was not active. Developmental evaluation performed by psychologist resulted in an overall IQ score of 50, with all other measures of language and adaptive functioning being consistent with intellectual disabilities in the Mild to Moderate range. Language and Communication abilities (Scores in the 60s) were higher than Nonverbal and Motor Skills, consistent with patterns often observed in fetal alcohol spectrum disorders (FASD). The child was noted to have problems with motor tone and graphomotor planning and hand grasp. No behavioral characteristics consistent with a diagnosis of autism spectrum disorders were noted. Psychologist noted that behaviors associated with institutionalization are often mistaken for autism. FAS (760.71), Mild Intellectual Disabilities (317) and Motor Coordination Disorder (315.4) were diagnosed in addition to the medical problems noted above.

Recommendations for future care were made in several domains: 1) *Medical*—Follow-up care with developmental pediatrics, with attention to effects of prenatal infections; ophthalmology, with regard to persistent strabismus. 2) *Physical and Occupational Therapy*—to address delays in motor and graphomotor skills. 3) *Educational*—Special Educational Services. Based on her level of intellectual functioning she will require special educational services for the foreseeable future and is eligible for these based on Federal law and State regulation. 4) *Social and Family Support*—There are a number of support groups and agencies that provide information and support for families with FAS, intellectual disabilities and families who have adopted internationally. 5) *Monitor Development and provided anticipatory guidance*—The child will require specialized care over her life time. She should be closely followed by her pediatrician, and developmental assessments should be carried out by appropriate professionals during childhood and adolescence to monitor development and behavior. Parents may need support in adjusting to her diagnosis and in providing care.

9-Year-Old Boy

Riley is a 9 year-old Caucasian male with a history of attention deficit hyperactivity disorder and significant behavioral and learning problems. His prenatal history is significant for exposure to alcohol throughout gestation. Riley was the product of a twin birth, and both he and his fraternal twin were adopted at 1 month of age by his current adoptive parents. The twins were born at 36 weeks gestation. The patient has had no major illnesses, medical hospitalizations, surgeries or head traumas. He has no known allergies, and immunizations are current. There are no hearing problems; however, Riley has mild strabismus and is nearsighted, for which he requires glasses.

Riley currently attends the Kable Elementary School in a third grade, special day class. He receives occupational therapy due to difficulty in fine motor skills and coordination. He also is reported to have problems in language and math. At school, Riley has had problems with hyperactivity, distractibility, inattention, and impulsivity, for which he has received accommodations. Riley is reported to have poor social skills, repetitive behavior, poor body boundaries, sensory sensitivities, and concrete thinking. Cognitive testing conducted by Paley Anderson, Ph.D., in April 2008 revealed a Full Scale IQ on the WISC-IV of 81. There was considerable variability across various domains of functioning, with a Verbal Comprehension Index of 75, Perceptual Reasoning Index of 96, Working Memory Index of 80, and Processing Speed Index of 86. Riley's current adaptive functioning is significantly below his chronological age and cognitive performance with an Adaptive Behavior Composite score of 63 on the Vineland Adaptive Behavior Scales. Subtest standard scores are: Communication 72; Daily Living 58; and Socialization 64. Various neurocognitive tests reveal problems in executive memory and language functioning. Riley is currently diagnosed with mood disorder NOS and oppositional deviant disorder. He has problems with dysregulation and explosive behavior characterized by discrete episodes of failure to resist aggressive impulses resulting in purposeful destruction of property at home and at school and assaultive acts toward parents. These aggressive outbursts were noted at the age of 6, when patient would throw toys and other objects at his mother or smash toys on the floor. Parents note that he is noncompliant with non-preferred activities. When asked to do something at home that he does not want to do, he will yell, swear, slam a door, punch furniture, or hit and kick his parents. Mother notes that

Riley frequently lies and has taken money from her purse to give to other children. Mood symptoms include rapid changes in affect, trouble sleeping, poor appetite, and irritability alternating with pressured speech and grandiosity. The patient has had multiple medication trials with little positive effect: Ritalin, Focalin XR, Intuniv, and Risperdal.

FASD Examination

The adverse effects of alcohol on the developing human represent a spectrum of structural and neurocognitive disabilities most accurately termed fetal alcohol spectrum disorders (FASD). This patient was examined according to the criteria set forth in the 1996 Institute of Medicine Report refined by Hoyme, May, Kalberg, et al., 2005. This system examines the magnitude of expression of four key diagnostic features of FASD: (a) growth deficiency; (b) facial phenotype, including short palpebral fissures, flat philtrum, and thin upper lip; (c) central nervous system dysfunction (CNS); and (d) gestational alcohol exposure. Using this system, the patient can be described as belonging to one of four diagnostic categories which include fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorder (ARND), or alcohol-related birth defects (ARBD). FAS requires the fulfillment of all four diagnostic criteria. Partial FAS (pFAS) diagnostic criteria are similar, though the diagnosis requires that either the growth deficiency or CNS impairment criterion be met, and not both. ARND applies to those individuals with prenatal alcohol exposure and problems associated with CNS impairment but who do not demonstrate physical features or growth deficits. ARBD applies to those individuals who have a pattern of congenital structural malformations in different organ systems but do not manifest features of the other diagnostic categories described above.

Growth: Height = 129.5 cm 25th percentile

Weight = 21 kg 10th percentile

Face (Eyes, Mouth, Ears): There is midface hypoplasia with a flat nasal bridge. *Palpebral fissure length is 25 mm (> 10th percentile) left eye and 26 mm (> 10th percentile) right eye, flat philtrum (4) with typically developed upper lip (3). Myopia, small jaw, high arched palate, poorly formed pinna. Other dysmorphologies: Clinodactyly 5th digit bilaterally, asymmetrical pelvic bone, hockey stick crease on left hand

CNS: OFC = 52 cm > 10th percentile

Evidence of a complex pattern of behavior, learning, and adaptive abnormalities that are inconsistent with age, cognitive, or developmental level.

Prenatal Alcohol Exposure: Known

Diagnosis: Alcohol-Related Neurodevelopmental Disorder, Prenatal Alcohol Exposure Known

Recommendations

1. It is recommended that Riley follow up with an outpatient psychologist for individual supportive psychotherapy. Riley would benefit from individual therapy focusing on social skill-building and reducing maladaptive, unsafe behaviors. This treatment should include role modeling and practice of appropriate behaviors both in the office and in real-life situations.

2. Riley's developmental history is significant for challenges in the social communication domain. In order to promote social development, Riley will likely benefit from social skills training to help him develop age-appropriate interaction skills. During these social skills lessons, planned interactions with typical peers (intensive individual or group instruction) will focus on teaching Riley to recognize social cues and engage in age-appropriate social interactions.

3. Riley's parents, at their discretion, should receive parent training from a qualified mental health professional who is trained in applying behavioral techniques and has experience working with individuals with prenatal alcohol exposure to aid them in working effectively with Riley. Parent training should stress consistency and giving clear instructions, as well as teaching basic principles of reinforcement and contingency management.

4. It is recommended that Riley receive ongoing supports within a small school setting to facilitate his academic progress, ensure his ability to access the curriculum, and direct and monitor appropriate participation in goal-directed activities. He will continue to require instructional accommodations, such as, but not limited to, supports for written expression; allowances for oral information to be repeated and broken down into smaller sections; and extended time to complete certain tasks as well as to respond to information. In addition, it is recommended that Riley have opportunities for individualized contact with a designated teaching staff (e.g., teacher, counselor) on a daily basis. He will likely require, and clearly benefits from, monitoring during his school day in order for him to maintain adaptive participation in goal-directed activities. It is recommended that Riley receive a new IEP that focuses on his individual strengths and weaknesses.

5. Given that Riley still exhibits impulsivity, maladaptive behaviors, concentration and attention regulation problems, and social communication problems; it is recommended that he see a child psychiatrist for psychotropic medication management.

*Values rounded to the nearest mm.

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Joan, Age 26

My parents died from drinking, and I lost a sister to FAS. I was diagnosed with ARND while I was in treatment for the sixth time. I tell people I have FAS because it's easier to explain. As a child I was hyper and had a hard time learning. I was always late for school and could never find all my stuff. We had a hard time at home and my dad was mean when he was drinking. During school I thought I was dumb but, as I got older, I was able to do some things. I had a time getting my homework done and getting all my stuff together every day. I am really disorganized and have a hard time telling time. I miss a lot of meetings and am late for some things; once I went to a meeting 2 days early. When I was little I had problems, and I still have most of them with new ones. Drinking has been a problem since I was 9 years old. I had the same problems in treatment I had in school. They always go too fast, and when I get overloaded I can't remember. I have always had a hard time in group because of this. I could work if I wasn't drinking and it was really structured. I have tried several times to live by myself but it never works out. So I have someone to help with my money and to help me plan my week. This works better, but it's still hard. I have two children and am in the middle of a divorce. I had to go back to treatment when this started. I have attention and memory problem, and the medicine helps. I get anxious and am on medication for depression. This seems to help but I still have a hard time. My life would be better if I didn't have so many meetings with all the people helping me. I need services, and they are always trying to take them away when I get to doing well. One of my big problems is that I can't figure out how to make things better. I have not been in jail for several months so that's good. I keep coming up with new problems and I have to have so many people help me. They often get upset that I can't get things done and that makes me upset. I have had this since I was little and in foster care. Right now my big problem is staying sober. I'm coming up on a year (again) and this is a hard time for me.

"The Courage to Come Back"

Sasha is a 38-year-old mother of six who had her first contact with our inner-city outreach team shortly after the birth of her youngest child. Sasha and all her children have PAE (prenatal alcohol exposure), but not all have an FASD diagnosis (fetal alcohol spectrum disorder). Sasha now feels that her community and family (specifically her dad) and the professionals who helped her access community programs have helped her "with the courage to come back."

Sasha describes herself as the youngest of 8 girls, and the 16th of 17 children for her mother. She was her dad's first, and she has a full sibling, a brother, 3 years younger. Her mother struggled with addiction and mental health concerns and, during Sasha's pregnancy, this included alcohol and solvents. There were no open doors for Sasha's mother, who died from cirrhosis and alcohol poisoning when Sasha was 16.

Sasha's early life was complicated by frequent infections and frequent moves. Sasha recalls attending several schools. She has a scar on the left side of her chest and was told she had heart surgery as a baby. Sasha and her brother were in and out of different foster homes while living with their mother, sometimes together, but often apart due to their behavior. Most of these foster placements were "closer to home," thanks to her dad and

his coworkers, who lobbied to keep the kids connected to him. With community support, Sasha's dad went for treatment and anger management to gain custody of his two children when Sasha was 10.

Her dad understood her, but that didn't fix the school problems or her problems with making choices [judgment and executive function], for her choice in boyfriends. After repeating grade 7 in behavioral modification class, she was in and out of youth court services, and attended three different high schools. She got pregnant at 16 in grade 10 and delivered her first daughter shortly before her mom died. She then binged heavily on alcohol. She had a very violent relationship with the baby's dad. They both went to jail.

Her second daughter was born soon after Sasha was paroled at 19. The two girls went into the care of their grandfather's coworkers. At 21, Sasha had a son, who also went into foster care. Her dad kept her in contact with the three kids. He started to work at the local community centre and had frequent contact with his grandkids.

Sasha started to engage with her older kids more regularly and was settling down. It was 5 years before Sasha had a fourth child. Suddenly, Sasha's father died of a heart attack, at 63. He had been sober for the last 18 years. She was lost without her father in her life. At 26, her binge alcohol pattern returned. Add cocaine and a fifth pregnancy. Her dad wasn't there to keep them connected. These last kids were removed and placed in care out of the community. She had no access.

Four years later, Sasha got pregnant again. She found out early this time. And there was an open door, close to home, that she could walk through without being judged. They all seemed to understand her, and accommodated for her forgetfulness and weak executive function and adaptive skills. It was her time to make a change. She began to see the intergenerational impact of alcohol on her family. This pregnancy was her healthiest, and by choice, her last. After delivery, Sasha asked us to assess her son and then herself for FASD diagnosis. That was the first step—to acknowledge and receive support to allow her to be a "special needs parent."

Sasha had partial FAS. Her baby showed no effects. Just like the movie, "I am Sam," her story touched all of us who worked with her. And she was determined to regain access to the two girls she "lost to the system." Her community helped back her, and the girls were eventually returned to her custody this past year.

Sasha now lives with her three youngest kids in the same housing co-op where she grew up. She has remained connected to her three young adult children ages. Her 19-year-old daughter, diagnosed with partial FAS at age 12, graduated as a member of the inner-city championship basketball team and now works at the community Starbucks. Sadly, her 17-year-old son, also abused in foster care, is now in jail and has never been formally assessed. The girls, 10 and 12, were diagnosed with "FSD" (family and fetal stress disorders) including ARND and full FAS, respectively. Her oldest child, age 21, like her 8 year old, does not have evidence for ARND.

The younger kids all attend Sasha's old elementary school. Last week, the principal gave our team the "thumbs up", and exclaimed, "I will always have time for Sasha and her kids. Her story runs deep. No problems here!"

An active volunteer in community programs and mentor in a young moms' support group, Sasha has returned to get training to work in the local daycares and received the city's prestigious "Courage to Come Back" award from the YWCA. Sasha explained to us after her award, "I always knew I had something that made it [school] harder, but my courage came from my dad, who never gave up on us. He didn't know either, but he still tried. He got us back. And he stayed sober."

When I asked what else made a difference in her life, Sasha recalled the support of one particular community foster mom who still works at the community center, followed by her doctors and nurses and counselors, and one social worker in particular. "He helped me get a diagnosis [of FASD]". When asked what has worked best for her, Sasha said, "Stay in the moment; keep to my routines and structure; attend my programs and educate myself, because it keeps me from being judged by judgmental workers; work with my kids' support systems, like the school and your doctors and nurses [nurse practitioners] in the community; and support other mothers."

Sasha's name is a pseudonym, phonetically similar to a name her mom used, as a term of endearment when she was small. Sasha agreed to have her story told to help others who need support to find "the courage to come back." Her message is "never give up."

Sarah

Sarah was 7.7 years old when she was diagnosed with Static Encephalopathy/Alcohol Exposed (4-Digit Code 1134), or severe "ARND." Sarah does not present with growth deficiency (Growth Rank 1) or any of the FAS facial features (Face Rank 1). She presents with significant brain dysfunction (CNS Rank 3) and a confirmed exposure to high levels of alcohol exposure (Alcohol Rank 4). Sarah's case is unique in that she was not only raised by her two birth parents (both of whom have some college education), but she has no other prenatal or postnatal adverse exposures or experiences (the 4-Digit Code Prenatal and Postnatal Ranks were both 1). An absence of other risk factors is very rare in our FASD clinic population. We have observed this in only 4 of 1,400 (0.2 percent) patients evaluated in our FASD clinic. Most children we see in clinic have a multitude of other risk factors, including prenatal exposure to illicit drugs, poor prenatal care, multiple home placements, and/or physical/sexual abuse. Eighty percent of our cases are in foster/adoptive care at the time of their FASD diagnostic evaluation.

In a parent interview during the FASD diagnostic evaluation, Sarah's mother described feeling that something was "different" with Sarah right from birth. She had some unusual difficulties sleeping as an infant and had problems with vomiting her feedings. At 7.7 years old, Sarah is described as a child who needs extra support with daily activities. One of her parents' biggest concerns is her lack of judgment and impulsivity; she will still run into the street without looking at times. She has some unusual behaviors—hand- wringing and head tipping—particularly if she is stressed or excited. Sarah can definitely learn and has some real strengths, such as puzzles, but often is extremely fearful of new situations. Despite her ability to learn new things, she does have problems recognizing consequences of actions and learning from experience. She just "doesn't get it" at times. Sarah is also described as having poor social skills and is starting to feel socially isolated at school. Sarah is extremely active and prone to intense tantrums. She has poor balance, some delayed motor skills—most notably she has difficulty using silverware to eat. Sarah is also a very sensitive child, with sensitivities to touch and sound.

Sarah has been receiving special education services (including reading, math, written language) in school since preschool. She is now in the second grade. She was diagnosed with ADHD at 4 years of age. A short course of Ritalin was initiated, but deemed ineffective and discontinued. Sarah has also been diagnosed with a sensory integration disorder, an auditory processing disorder, and a social communication/pragmatic language disorder. Sarah has received a number of assessments over the years. At 7.7 years of age, Sarah received a Full Scale IQ of 102 on the Test of Nonverbal Intelligence. At 4.4 years of age, Sarah received a school-based evaluation. Sarah scored significantly below average (< 4th percentile) in all areas of the Mullen Scales of Early Learning. A Vineland Adaptive Behavior Scales completed by the mother resulted in an Adaptive Behavior Composite at the 3rd percentile. Results of the Preschool Language Scale-3 indicated significant impairments in both receptive and expressive language skills (3rd percentile) with the Total Language Score in the severe range of impairment (2nd percentile). Sarah's head circumference has always been in the normal range (50th percentile). She has never had her brain imaged and has no history of seizures or other neurologic problems.

Sarah's mother was 33 years old at the time of her birth. Sarah has two siblings, 3 and 5 years older than her. Both are normally developed. Sarah's mother has 2 years of college education. She described herself as a closet alcoholic and did not receive treatment until 5 years after Sarah's birth. She reports drinking all three trimesters, two to five glasses of wine, three days per week. Sarah's birth father was 35 years old at the time of her birth, has three years of college education, and a history of alcohol abuse.

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