Learning Objectives

1. Describe diagnostic criteria and approaches for conditions along the continuum of FASDs, including ARND, ND-PAE, FAS, pFAS, and ARBD.
2. Distinguish major physical and neurobehavioral features for differential diagnosis of FASDs from other genetic and behavioral disorders as well as relevant comorbidities.
3. Explain the importance of screening every patient for a history of prenatal alcohol exposure at birth and during their first clinic.
**FASD Terminology and Acronyms**

- **PAE**: Prenatal Alcohol Exposure
- **FASD**: Fetal Alcohol Spectrum Disorders
  - Umbrella term for a range of effects that can result from prenatal alcohol exposure (not a diagnosis)
  - Encompasses a group of specific disorders (more on these later), including:
- **FAS**: Fetal Alcohol Syndrome
  - The most widely known diagnosis in the spectrum
- **ARND**: Alcohol Related Neurodevelopmental Disorder
  - Used in some dx schemes for individuals without physical characteristics
- **ND-PAE**: Neurobehavioral disorder associated with prenatal alcohol exposure.
  - New category in DSM-5 Section III: Emerging Measures and Models
  - Defines more precisely the developmental and behavioral manifestations associated with PAE

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**The Umbrella of FASD**

- **Fetal Alcohol Syndrome (FAS)**
- **Alcohol Related Birth Defects (ARBD)**
- **Partial Fetal Alcohol Syndrome (pFAS)**
- **Neurobehavioral Disorder-associated with Prenatal Alcohol Exposure (ND-PAE)**
- **Alcohol Related Neurodevelopmental Disorder (ARND)**

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**FASDS – Brief Descriptions**

- **Fetal Alcohol Syndrome (FAS) and Partial FAS (pFAS)**: Facial features and CNS dysfunction or anomalies, with or without growth deficits
- **ARBD** - Congenital anomalies without neurodevelopmental-behavioral effects (rare)
- **ARND** - Neurodevelopmental-behavioral effects without major dysmorphic features (common)
- **ND-PAE** - Neurodevelopmental-behavioral effects regardless of dysmorphic features; for use by behavioral health providers
Most common preventable cause of intellectual disability and behavior problems – likely seen in most practices.

Effects can be lifelong.

Affects development and function more so than other drugs or teratogens.

“Of all the substances of abuse, including cocaine, heroin, and marijuana, alcohol produces by far the most serious neurobehavioral effects in the fetus.”

Can contribute to a range of growth deficits and structural anomalies (FASD)

Areas of the Brain Affected By Prenatal Alcohol Exposure

- Frontal Lobes – impulses and judgment; controls executive function
- Hypothalamus – appetite, emotions, temperature, and pain sensation
- Amygdala – emotions
- Cerebellum – coordination and movement
- Basal Ganglia – spatial memory, switching gears, working toward goals, predicting behavioral outcomes, and the perception of time
- Hippocampus – memory, learning, emotion
- Corpus Callosum – passes information from the left brain (rules, logic) to the right brain (impulses, feelings) and vice versa.

Source: Dr. Sarah Mattson, University of San Diego

General Intellectual Performance

![IQ Scale Chart]

Mattson et al., 1997
FASD: Relevance to Public Health

*High Prevalence*

- **Prevalence in a Midwestern city (May, 2014):**
  - FAS: 6-9/1000 children
  - All FASD: 24-48/1000 children (2.4% to 4.8%)
- **Increased prevalence among children in child welfare (Lange, 2013):**
  - FAS: 60/1000 children (6%)
  - All FASD: 169/1000 children (16.9%)

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FASD: Perspectives on Prevalence

<table>
<thead>
<tr>
<th>Birth defect</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down syndrome</td>
<td>1.2/1000 births</td>
</tr>
<tr>
<td>Cleft lip +/- palate</td>
<td>1.2/1000 births</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>1/1000 births</td>
</tr>
<tr>
<td>Autism</td>
<td>12.5-14/1000*</td>
</tr>
<tr>
<td>Fetal Alcohol Syndrome (FAS)</td>
<td>6-9/1000*</td>
</tr>
<tr>
<td>All FASDs</td>
<td>24-48/1000*</td>
</tr>
</tbody>
</table>

*per 1000 school age children

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Clues that a child may have an FASD

- Developmental, cognitive, or behavioral concerns
- Growth deficits
- History of maternal alcohol or drug use
- A sibling diagnosed with a FASD
- Dysmorphic facial characteristics or other birth defects associated with FAS
### Clues that a child may have an FASD

- **Risk factors:**
  - Other exposures associated with alcohol use (eg, tobacco, marijuana, cocaine, methamphetamine)
  - Adoption, particularly from endemic region (eg, Russia, Eastern Europe)
  - Foster care
  - Parental concern

### Potential Benefits of a Diagnosis

- **Parental relief in the knowledge that the child’s problems have a biological basis**
- **Facilitates access to evidence-based interventions which improve outcomes**
- **Avoids unnecessary additional testing and non-specific referrals or interventions**

### Potential Benefits of a Diagnosis

- **Access to professional expertise, a range of medical, developmental, community and financial resources, and supportive counseling**
- **Discussing the cause with a biological mother may reduce recurrence risk in future offspring**
Risk of Diagnosis: Unwarranted Stigmatization

- Stigma: unfixable
- Bias in management
- Stigma: blame
- Relationship between mother & pediatrician
- Stigma: not in my practice
- Bias against diagnosis
- Stigma: high risk population
- Bias towards populations perceived to be at higher risk

Who Drinks During Pregnancy?

■ Women who drink during pregnancy come from all social, economic and ethnic groups
■ Nationally, 1 in 10 women report alcohol use during pregnancy
■ Many pregnancies are not recognized until the period of risk to alcohol exposure is well established

Who Drinks During Pregnancy?

■ Among pregnant women, the highest prevalence of reported alcohol use was among those who were:
  • Aged 35-44 years (18.6%)
  • College graduates (13.0%)
  • Unmarried (4.6 x married)
  • Tan, Denny, Cheal, Sniezek & Kanny, 2015
Neurobehavioral Effects

**Neurocognitive deficits**
- Low IQ or developmental delay
- Executive functioning deficits
- Impaired learning, memory or specific learning problems (esp. visual-spatial and math)
- Motor functioning delays for younger children

**Self-regulation problems**
- Self-soothing, sleep
- Difficulty managing mood
- Behavior management issues
- Attention problems (esp. shifting attention)
- Poor impulse control
### Neurobehavioral Effects

**Difficulty learning/Delayed adaptive skills**
- Communication deficits, especially social communications such as understanding idioms or jokes
- Problems with social skills
- Problems with self care or daily living skills
- Motor issues in younger children

### Physical Effects
- Weight and/or length growth deficiency (pre or post natal)
- Abnormal brain structures (esp. small cranium, corpus callosum)
- Dysmorphic facial features:
  - Short palpebral fissures
  - Smooth philtrum
  - Thin vermillion border

### Available FASD Diagnostic Guidelines

**Currently available guidelines:**
- Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders (Hoyme et al, Pediatrics, 2016)
- Canadian guidelines for diagnosis (Cook et al, CMAJ, 2015)
- CDC National Task Force on FAS and FAE (2004)
- FASD 4-digit diagnostic code (Astley and Clarren, Alcohol, 2000)

**Historically available guidelines:**
- Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis (Chudley et al, CMAJ) 2005

The Diagnostic and Statistical Manual version 5 published by the American Psychological Association also proposes criteria for neurodevelopmental disorder associated with prenatal alcohol exposure.
2016 Revised IOM Criteria: FAS

I. FAS (requires all of A–D)

A. Minor facial anomalies, including ≥2 of the following:
   1. Short palpebral fissures (<10th percentile)
   2. Thin vermilion border of the upper lip (score 4 or 5 on a racially normed lip/philtrum guide)
   3. Smooth philtrum (score 4 or 5 on a racially normed lip/philtrum guide)

B. Prenatal and/or postnatal growth retardation
   Height or weight <10th percentile, corrected for racial norms, if possible

C. Deficient brain growth, abnormal morphogenesis, or abnormal neurophysiology, including 1 of the following:
   1. Structural brain abnormalities
   2. Head circumference ≤10th percentile
   3. Recurrent nonfebrile seizures

D. Neurobehavioral Impairment
   - < 3 years: Evidence of developmental delay ≥ 1.5 SD below the mean
   - ≥ 3 years: General conceptual ability, verbal or performance IQ ≥ 1.5 SD below the mean, OR
     Cognitive deficit ≥ 1.5 SD below the mean in executive function, learning, memory, or visual-spatial domains, OR
     Behavior deficit ≥ 1.5 SD below the mean in self-regulation (mood, attention, impulse control)
2016 Revised IOM Criteria: Partial FAS

II. Partial FAS

(requires A and B and either C or D)
A. Dysmorphic facial features (as for FAS)
B. Neurobehavioral impairment (as for FAS)
C. Confirmed prenatal alcohol exposure
D. Growth impairment (as for FAS)

2016 Revised IOM Criteria: ARND

III. Alcohol-related Neurodevelopmental Disorder:

A. Documented prenatal alcohol exposure, and
B. Neurobehavioral impairment (as in FAS)

Revised IOM Criteria: ARBD

IV. Alcohol-related birth defects

Documented prenatal alcohol exposure and one or more of the following congenital anomalies:
- **cardiac**: atrial septal defects, aberrant great vessels, ventricular septal defects, conotruncal heart defects;
- **skeletal**: radioulnar synostosis, vertebral segmentation defects, large joint contractures, scoliosis;
- **renal**: aplastic/hypoplastic/dysplastic kidneys, "horseshoe" kidneys/ureteral duplications;
- **eyes**: strabismus, ptosis, retinal vascular anomalies, optic nerve hypoplasia;
- **ears**: conductive or neurosensory hearing loss;
### Spectrum of FASD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAS</td>
<td>Partial or confirmed alcohol-related brain damage</td>
</tr>
<tr>
<td>PFAS</td>
<td>Partial FAS with or without confirmed exposure</td>
</tr>
<tr>
<td>ARBD</td>
<td>Alcohol-related birth defects (ARBD)</td>
</tr>
<tr>
<td>ARND</td>
<td>Alcohol-related neurodevelopmental disorder (ARND)</td>
</tr>
<tr>
<td>ND-PAE</td>
<td>Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE)</td>
</tr>
</tbody>
</table>

Adapted from Neuroscience and Biobehavioral Reviews (2007); 31:230-238

### Steps Toward Diagnosis: Record Review/History

- History of prenatal alcohol exposure
- Birth records (weight, length, head circumference)
- Medical history/records (birth defects?)
- Postnatal growth records
- Developmental/behavioral history
- Psychological testing, including cognitive and behavioral assessments

### The Diagnostic Assessment: Exposure history

- Awareness/acknowledgement of stigma, bias, and potential impact of questions on provider/parent relationship
- Approach with empathy
- Find common ground
- Work toward details (e.g., number of standard drinks, timing during pregnancy, pattern of drinking)
Exposure History in Context

- Screening all children for PAE before suspicion or recognition of problems is ideal
- Introduce review of family, social, and pregnancy histories as part of assessment
- Work up through general exposures, any that caused concern, medications, recreational drugs, then alcohol
- When true, introduce alcohol as commonly consumed before pregnancy is recognized
- Assurance that purpose is not to blame but to help child

AAP Bright Futures

- AAP’s Bright Futures, guidelines for health supervision of infants, children and adolescents, suggest three screening questions for the pediatric situation:
  - How often do you drink beer, wine or liquor in your household?
  - In the 3 months before you knew you were pregnant, how many times did you have 4 or more drinks in a day?
  - During your pregnancy, how many times did you have 4 or more drinks in a day?
- If a positive response is obtained additional questions about amount, frequency and timing may be appropriate for diagnostic purposes.

AAP Bright Futures

- Suggested contact points:
  - All prenatal visits
  - The earliest well child visits
  - All new patient visits
  - Whenever a related concern is observed or raised
Physical Assessment

- Growth measurements
- Palpebral fissure length
- Eye/vision
- Midface recession/hypoplasia
- Philtrum, lip (lip/philtrum guide)
- Palate
- Heart
- Elbows, digits
- Examination for other minor anomalies characteristic of FAS, and those that could lead to the suspicion of another genetic syndrome.

Correct and Objective Measurements are Key: Palpebral Fissure Length PFL

- Measure from inner to outer canthus following the angle of the face
- Plot measurement on graphs available (i.e. in Smith’s Recognizable Pattern of Human Malformation)
- Short PFL defined as ≤10th centile
Lip and Philtrum Assessment

- Ensure the patient has a neutral expression
  - Smiling will falsely increase the score
- Place guide alongside face
- Score lip and philtrum separately
  - 4 or 5 is considered positive

OTHER CHARACTERISTIC FEATURES OF FASD

- Ptosis
- "Railroad track" ear (prominent helical crus)
- Finger contractures
- "Hockey stick" palmar crease
- Limited elbow pronation/supination
- Heart murmur/defect

Neurobehavioral Assessment

- Developmental screening and routine behavioral history may be sufficient if it shows clear cognitive and behavioral or global deficits
- Most will require referral for psychological assessment of neurocognition, self regulation and adaptive function
  - Template referral letters available
  - Request that the psychologist use tests that will examine the affected domains in ND-PAE
- Review data – do deficits fit the diagnosis?
  - Data review checklist available
### Potential Differential & Comorbid Diagnoses

#### Behavioral disorders examples
- ADHD
- Intellectual disability
- Early Trauma
- Conduct disorder/Oppositional defiant disorder
- Parenting issues

#### Genetic and growth disorders examples
- Williams syndrome
- Dubowitz syndrome
- Fetal valproate syndrome
- Maternal PKU fetal effects
- Nutritional insufficiency – growth
- Prenatal smoking - growth

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### PATHWAY TO A DIAGNOSIS

- The AAP FASD Toolkit (www.aap.org/fasd) is a comprehensive resource for identification, diagnosis and medical home management on patients with a FASD
- Toolkit includes information on common diagnostic approaches and tools, a flow diagram for evaluation of FASDs, and guidelines for referral and diagnosis.
Establishing a Diagnosis

Indications for Referral

- For diagnosis: If uncertain whether findings satisfy criteria, depending on available resources:
  - FASD diagnostic clinic
  - Genetics and dysmorphology clinic
  - Neurodevelopmental/behavioral pediatrician (gaining expertise in this area)
  - Neuropsychologist or behavioral psychologists who can work through the ND-PAE route
- For determination of needs for education and behavioral management:
  - Neuropsychologist, clinical psychologist, school psychologist as available

Delivering the Diagnosis

- Approach should be similar to delivering other diagnoses of disorders that have significant impact on a child’s future.
- Be sensitive to the possibility of stigma, particularly when the biological mother is involved.
- Only in the most clear-cut cases of FAS should the diagnosis be made despite the mother’s adamant denial of alcohol use during pregnancy.
- Reference to intent/benefit of diagnosis (to enhance services) is helpful.
Diagnosis Established

What now?

- Counsel re: Natural history (risk of neurodevelopmental manifestations over time)
- AAP toolkit: www.aap.org/fasd

Take Home Messages

- FASD are more common than recognized.
- Obtaining history of prenatal exposure to alcohol is good pediatric practice and should be routine for all patients.
- Children will most likely present with neurodevelopmental/neurobehavioral problems.
- A comprehensive physical and behavior assessment is best to establish the appropriate diagnosis and care plan.

Resources

- Centers for Disease Control and Prevention (CDC): www.cdc.gov/ncbdd/fasd/index.htm
- National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov
- National Organization on Fetal Alcohol Syndrome: www.nofas.org
References

- Hoyme et al., *Pediatrics* 2016;138 (2) e20154256
- May et al., *Pediatrics* 2014;134(5);855-66
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References