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Editor-in-Chief

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IN THIS ISSUE

Common Developmental Disorders in Children and Adolescents

Learning Objectives

After reading these articles, you should be able to:

1. Help patients with trisomy 21 and their families navigate daily life and care.
2. Identify common developmental disorders in children and adolescents, including fetal alcohol spectrum disorders.
3. List the pros and cons of different types of assistance for young adults with developmental disorders.
4. Summarize some of the findings in the literature regarding psychiatric treatment for children and adolescents.

Trisomy 21: An Overview for Child Psychiatrists

Robin Lynn Treptow, PhD. Assistant Professor of Psychology, Divine Mercy University, Sterling, VA.

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Dr. Treptow and Dr. Feder have no financial relationships with companies related to this material.

Ben, a fifth grader with trisomy 21, has trouble concentrating at school. He is sleeping poorly and says that he feels sad. His parents report increased irritability, social withdrawal, and sleep disturbances. On your assessment, he appears to meet criteria for ADHD and major depression.

Trisomy 21 (T21), also known as Down syndrome, is a genetic condition characterized by the presence of an extra copy, or part of a copy, of chromosome 21. The term "trisomy" denotes the presence of three copies of this chromosome, as opposed to the typical pair—one from each parent—that exists for all other chromosomes. T21 occurs in about one in 800 live births across races and

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Diagnosis of fetal alcohol spectrum disorders requires a respectful history and good testing. You won't see physical signs.

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Recognizing implicit bias helps us give our patients the opportunities they deserve.

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Learn to spot kids with dysmorphology so that you can offer them more specific support and treatment.

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Find out whether topiramate might be a tolerable off-label option to prevent weight gain with antipsychotic medications.

Q&A With the Expert

Don't Forget Fetal Alcohol Spectrum Disorders

Ira J. Chasnoff, MD

Professor of Clinical Pediatrics, University of Illinois College of Medicine, Chicago, IL; President, NTI Upstream, Chicago, IL.

Dr. Chasnoff's company, NTI Upstream, receives a licensing fee for the 4Ps Plus© screening instrument. Relevant financial relationships listed for the author have been mitigated.

CCPR: How is fetal alcohol syndrome (FAS) related to fetal alcohol spectrum disorders (FASD)?

Dr. Chasnoff: FASD is an umbrella term for neurodevelopmental conditions that occur with exposure to alcohol in utero. This includes FAS. FAS is the easiest to recognize because of the facial features, impaired growth below the 10th percentile, behavioral and neurocognitive deficits, and, perhaps, intellectual disability.

CCPR: How do rates of FAS compare with other causes of intellectual disability?

Dr. Chasnoff: If you combine children with autism, trisomy 21, trisomy 18, and all other neurodevelopmental disorders apart from FASD, FASD is the most common, though I'm not sure the studies comparing the numbers included lead poisoning. Children with FAS generally get services focused on intellectual disability through the school and do not come to mental health attention, although about 90% have co-occurring mental health conditions.

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CCPR: So if we're not seeing kids with FAS, who are the kids likely to be coming in for psychiatric services?

Dr. Chasnoff: You'll see children with alcohol-related neurodevelopmental disorder (ARND) in pediatric or mental health practices. These children were exposed to any amount of alcohol in the womb and have a behavioral or learning problem. They don't meet criteria for FAS—their growth is normal, their height and weight are above 10th percentile, and physically they look typical. But they have a significant neurobehavioral problem that, if we recognize it, can be amenable to specific supports and interventions. In the DSM-5, neurodevelopmental disorder with prenatal alcohol exposure is a diagnosis similar to ARND and listed in the back for further study. The definition ignores the facial features and growth issues typical of FAS and focuses on behavior and deficits in neurocognition, self-regulation, and adaptive function.

CCPR: How often do ARND and other instances of FASD go unrecognized?

Dr. Chasnoff: In our research, we found that 85.6% of children with FASD were misdiagnosed or missed completely. Many had failed a grade and were having trouble in school, but nobody had considered FASD or even done an evaluation of cognitive functioning (Chasnoff IJ et al, *Pediatrics* 2015;135:264–270).

CCPR: What is the prevalence of FASD?

Dr. Chasnoff: FASD impacts the entire range of ages all the way through adulthood. A study conducted in Midwestern US public schools found that 2%–5% of children meet criteria for FASD (May PA et al, *JAMA* 2018;319(5):474–482). The prevalence of alcohol use during pregnancy hovers around 18%, depending on the population (www.tinyurl.com/54ewnn8c). If that many people are using alcohol during pregnancy, where are the children who are affected? We found that 85.6% of children with FASD are misdiagnosed with conditions such as bipolar disorder, ADD, ADHD, and oppositional defiant disorder. FASD has a high rate of co-occurring mental health disorders, but the alcohol-related diagnoses were completely unrecognized.

CCPR: How should we get that history during an assessment?

Dr. Chasnoff: Most providers ask "You don't use drugs, do you?" That closed-ended question says "Please tell me you *don't* use drugs because I don't want to deal with it." We developed the only validated substance use screening instrument for pregnant people, called the 4Ps Plus©, with a predictive validity of 95%–97% (Chasnoff IJ et al, *J Perinatol* 2007;27:744–748). A key question uses very specific wording: "In the month before you knew you were pregnant, how much beer, wine, or liquor were you drinking?"

CCPR: What is the rationale behind this wording?

Dr. Chasnoff: The goal is to rule in or rule out *any* fetal alcohol exposure. In my experience, most people in the US do not consider beer or wine to be alcohol. So, we spelled it out—beer, wine, or liquor. But if you ask "In the month before you knew you were pregnant, did you drink beer, wine, or liquor?" the question lacks validity. It's another closed-ended question and it's easy to say no. You must ask "*How much* did you drink?" And if you ask "In the month before you were pregnant..." the question again loses validity. But if you ask "In the month before you *knew* you were pregnant..." that's normalizing, making it more likely that you will get an accurate response: "Heck yeah, everybody drinks. But as soon as I knew I was pregnant I stopped drinking."

CCPR: Should mental health providers ask these questions when evaluating a child?

Dr. Chasnoff: Use similar language: "How far along were you in your pregnancy when you found out you were pregnant?" Then ask "In the month before you knew you were pregnant, how much beer, wine, or liquor did you drink?"

CCPR: Should we quantify the amount of alcohol?

Dr. Chasnoff: Although the amount of alcohol the person was drinking before they knew they were pregnant is an important predictor of the child's long-term outcome, your role is to decide whether FASD is in the differential diagnosis. If the person says "Oh, no, we were planning our pregnancy. I stopped using long before we conceived," then you can relax.

CCPR: How does the 4Ps Plus© instrument work among cultural, racial, or socioeconomic groups?

Dr. Chasnoff: It's validated with Black women, White

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non-Hispanic women, and Hispanic women, with some experience in Asian-American populations. The 4Ps Plus© is translated into five languages and used internationally. The rate of positive screens for substance use in general (not specific drugs or alcohol) is similar across socioeconomic, racial, and ethnic groups. One of our studies found higher rates of alcohol use during pregnancy among White non-Hispanic women and in places where there are more wineries (Chasnoff IJ et al. *Perinatal Substance Use Screening in California: Screening and Assessment With the 4Ps Plus Screen for Substance Use in Pregnancy*. Chicago, IL: NTI Upstream; 2008).

CCPR: Do you find bias in identifying FASD?

Dr. Chasnoff: Yes. In 1988, during the "war on drugs," we studied urine samples in a middle-class community in Florida and found that 15% of the women at their first prenatal visit had a positive urine toxicology for any substances. The rate for Black women was 13.5% and the rate for White non-Hispanic women was around 15% (Chasnoff IJ et al, *N Engl J Med* 1990;322(17):1202–1206), so there was no statistically significant difference. But Black women were 10 times more likely to get a urine toxicology done during labor and delivery than White women, and the rate of removal of the babies because of the mother's drug use was 10 times higher in Black women. In addition, more recent research shows that physicians tend to address drug use in pregnant patients but not alcohol use (Chasnoff IJ et al, *Child Welfare* 2018;96:41–58).

CCPR: Moving to clinical signs, what facial features should we look for in FASD?

Dr. Chasnoff: Except for FAS, very few children affected by prenatal alcohol exposure have the facial features because there is only a relatively brief period, from about four to eight weeks gestation, during which facial features are affected. The children who most commonly present to you have behavioral issues without facial features.

CCPR: Can you describe the neurocognitive and behavioral characteristics of FASD?

Dr. Chasnoff: The three domains to look at in FASD are neurocognition, self-regulation, and adaptive functioning. The most common deficits are in neurocognitive functioning, such as executive functioning and memory. Executive function is the ability to plan and complete a task, to sequence, to follow through; to understand cause and effect. A good screen for that is the Behavior Rating Inventory for Executive Functioning (www.tinyurl.com/2spuuw86); there is a fee to use it. It has an age range from 5–18 years old and a self-report version for ages 11–18, with parent and teacher forms too.

"When you evaluate patients for fetal alcohol exposure, ask the parent: 'In the month before you *knew* you were pregnant, how much beer, wine, or liquor did you drink?' This is a normalizing question, making it more likely that you will get an accurate response."

Ira J. Chasnoff, MD

CCPR: What characteristic memory problems do these kids have?

Dr. Chasnoff: Children affected by prenatal alcohol exposure have trouble moving information from short-term into long-term memory. They also have difficulty with working memory—the ability to access information from long-term memory, such as a phone number, and hold it in the brain to use it.

CCPR: What are the problems with self-regulation?

Dr. Chasnoff: Self-regulation is the ability to regulate sensory experience, motor behaviors, and emotions. These children present with mood swings and are often easily overwhelmed by sensory or emotional experiences. This usually requires an occupational therapist to evaluate the child's difficulties. *(Editor's note: For more information, see* CCPR *Oct/Nov/Dec 2022.)*

CCPR: What are the problems with adaptive functioning?

Dr. Chasnoff: Adaptive functioning is the ability to take information you know and apply it to daily living skills, especially communication. This includes reading facial expressions and body language, understanding everything from sarcasm to money, interpreting bus schedules, etc. A person can be bright but have gaps in their executive functional abilities. We produced a documentary film (*Moment to Moment*) that tells the story of a young woman with an IQ of 125 attending college who can't tell time.

CCPR: How do you assess adaptive function?

Dr. Chasnoff: Get psychological testing to measure IQ and adaptive quotient (AQ). For other developmental challenges, such as autism, IQ and AQ usually vary together. But for ARND, IQ can be high while AQ is low. Ask a psychologist who does formal testing to evaluate neurocognition, self-regulation, and adaptive functioning domains.

CCPR: How do you approach treatment with these patients and families?

Dr. Chasnoff: Evidence-based approaches generally include parent education or training, teaching children specific skills that other kids learn through observation or abstraction, and collaboration with school and other treatment providers (Chasnoff IJ et al, *Child Welfare* 2023;101(3):191–208). Four evidence-based treatment approaches for ARND are recognized by the federal government (www.cdc.gov/ncbddd/fasd/treatments.html). Ours is in Chicago, and others are at Emory University, University of Washington in Seattle, and UCLA. The state of California has named additional therapeutic approaches (www.tinyurl.com/yh6ua2vx).

CCPR: What is the role for medication in treatment of ARND?

Dr. Chasnoff: About 74% of children affected by prenatal alcohol exposure meet criteria for ADD/ADHD, but the treatment approach is different (Chasnoff IJ et al, *J Dev Behav Pediatr* 2010;31(3):192–201). In ADD/ADHD, we focus first on the prefrontal cortex, using stimulants that act on the dopamine receptor system. In FASD, the problems commonly impact the limbic system. Mela and colleagues have a treatment algorithm for medications in FASD that lays out typical

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kinds of medications for symptoms with mood, anxiety, mood stability, and ADHD (Mela M et al, *J Popul Ther Clin Pharmacol* 2020;27(3):e1–e13).

CCPR: What do you tell the child and parents about FASD?

Dr. Chasnoff: We created a comic book that parents can use with children starting around 8 years of age: *Everybody's Brain Is Different*. It uses cute, engaging characters to talk about the changes that occur in the brain from prenatal alcohol exposure. It's low-key and has a guide for parents on how to talk to their children. As patients reach adolescence, we want to preserve feelings of self-efficacy and self-esteem, and this approach remains helpful even into adulthood.

(Editor's note: FASD United addresses shame to increase parental engagement in care. They advise that when talking with parents, clinicians should use the term "prenatal alcohol exposure" vs "maternal alcohol exposure." They should also describe "the range of effects that occur when a developing baby is prenatally exposed to alcohol" vs saying "FASD is what happens when a mother drinks alcohol while she's pregnant." For more, see www.FASDUnited.org.)

CCPR: What does prognosis look like?

Dr. Chasnoff: Prognosis varies depending on cognitive functioning as well as other factors. But if you can identify the alcohol-exposed child and start treatment before age 6, you can significantly improve the child's long-term developmental trajectory (www.cdc.gov/ncbddd/fasd/treatments.html). Early recognition and intervention are key. However, it's never too late. The more the family can create a home environment that supports the child neurocognitively and behaviorally, the better the child's going to do long term. It takes a dedicated family and health care system. I have patients who have done extremely well; however, they rarely get away from needing somebody to help them be organized. My latest book discusses the educational and behavioral interventions that can improve the outcome of children and teens with FASD and early trauma (Chasnoff IJ and Powell RJ. *Guided Growth*. Portland, OR: NTI Upstream; 2020).

CCPR: Thank you for your time, Dr. Chasnoff.

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economic levels (Bull MJ, *New Eng J Med* 2020;382(24):2344–2352). Prevalence increases to about one in 100 for mothers at age 40. However, since far more babies are born to younger mothers, 80% of cases occur in mothers under 35 (Song Y et al, *Front Genet* 2022;13:980627). A family history of the condition and medical disorders (eg, diabetes) increases risk.

T21 is the leading genetic cause of developmental delays and is associated with intellectual disabilities, distinct facial features, and various medical conditions, such as congenital heart defects and hearing loss. In addition, a variety of psychiatric comorbidities can impact patients' quality of life and complicate their clinical management. Common comorbidities include:

- Depression and anxiety: Symptoms include social withdrawal, changes in appetite, and sleep disturbances, depression and anxiety can be challenging to diagnose due to overlapping symptoms with T21 and communication barriers.
- Autism: The overlap of autism symptoms with the behavioral phenotype of T21 can make diagnosis difficult. Key indicators include persistent deficits in social communication and interaction, along with restrictive and repetitive behaviors.
- ADHD: Symptoms like inattention, hyperactivity, and impulsivity are common but can be overlooked due to the intellectual disability associated with T21.
- Dementia: Over half of individuals with T21 will develop dementia as they age, particularly Alzheimer's disease. Onset is typically at a younger age compared to the general population, with symptoms often appearing as early as a patient's 40s or 50s.

Treatment of psychiatric comorbidities

Pharmacotherapy

We recommend beginning with relationship-based interventions and addressing sensory, communication, and motor planning before using medications. We also recommend tapering medications if symptoms subside and nonpharmacologic measures can sustain improvement. With that said, the following are pharmacologic treatments for co-occurring conditions often seen with T21.

Depression and anxiety

- Selective serotonin reuptake inhibitors (SSRIs): These are often the first line of treatment for depression and anxiety in patients with T21. Starting doses might be sertraline 12.5–25 mg/day, fluoxetine 5–10 mg/day, and citalopram 5–10 mg/day, with gradual titration based on response and tolerability.
- Serotonin-norepinephrine reuptake inhibitors (SNRIs): While they have more side effects and far less evidence of efficacy in children and teens for depression, consider venlafaxine (Effexor) or duloxetine (Cymbalta) if SSRIs are not effective. Start with lower doses, such as venlafaxine 18.75–37.5 mg/day or duloxetine 20 mg/day.

Autism

- Atypical antipsychotics: Medications like risperidone (Risperdal) or aripiprazole (Abilify) are used for irritability and aggression in autism. Risperidone may be started at 0.25 mg/day, increasing as needed, while aripiprazole can start at 2 mg/day. While these are the only FDA-approved medications for irritability in autism, we prefer less metabolically problematic choices such as lurasidone or ziprasidone, as well as use of metformin or even GLP-1 agonists to prevent weight gain.

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- SSRIs: Start with nonpharmacologic interventions (repetitive behaviors are often part of the patient's stress response or communication). Then, for repetitive behaviors and anxiety symptoms in autism, SSRIs like fluoxetine or sertraline can sometimes be helpful.

ADHD
- Stimulants: Methylphenidate (Ritalin, Concerta) or amphetamines (Adderall, Vyvanse) are commonly used. Due to increased sensitivity, starting doses should be lower than typical (eg, methylphenidate 2.5–5 mg once or twice daily).
- Nonstimulants: In patients who may not tolerate stimulants well, alternatives include atomoxetine (Strattera) starting at 10 mg/day, or guanfacine (Intuniv) starting at 0.5–1 mg/day.

Psychotherapy
Data on psychotherapy interventions and outcomes for youth with T21 are sparse. Therapy should be adapted to the cognitive level of the individual (www.tinyurl.com/yc7uj2xw). One case study used positive activity planning within a multidisciplinary framework and awareness of psychosocial factors to reduce depression in a teen with T21 (Shadan S et al, *Case Rep Psychiatry* 2021;2021:7112034). Increased positive events are an integral part of cognitive therapy, particularly for patients with cognitive challenges (Malik K et al, *BMC Psychol* 2021;9:150). Positive activities are even more effective when combined with:
- Goal setting
- Self-monitoring
- Motivation boosting
- Relapse prevention

Factors that support flourishing include friendships, meaningful service to others, age-normed activities, and optimism about who patients wish to be or what they wish to do in the future (Treptow RL, *International Journal of Health, Wellness and Society* 2017;7(3):33–42). For more parent and provider resources, visit www.thecarlatreport.com/T21resources.

You refer Ben to a psychotherapist for cognitive and supportive therapy for depressive symptoms. You also start him on sertraline 12.5 mg daily. On follow-up, the family reports that his mood has improved. Ben's therapist finds that his mood is worse when he is idle and better when he is among people. The family and therapist help him plan a more robust social schedule. Ben does not appear to have any side effects from the sertraline.

CARLAT VERDICT

Clinicians may be seeing more T21 patients as maternal age increases and the neurodiversity movement embraces the idea of taking T21 pregnancies to term. When you know how to treat patients with T21, you provide a needed service and gain a greater appreciation of the nuances of how different people think and experience their lives.

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Addressing Implicit Bias: Trisomy 21

Robin Lynn Treptow, PhD.

Ben's parents are upset about Ben's perinatal diagnosis of Down syndrome. Their pediatrician tells them they are lucky to have a child who will be happy, be social, and never leave them.

Misconceptions abound about individuals with trisomy 21 (T21) and all patients with developmental and mental health conditions. This article aims to distinguish myths from facts regarding T21 and help you to counteract implicit biases that limit opportunities for our patients.

Myths vs facts about T21

Here are some common erroneous beliefs about T21 as well as some facts:
- Myth: Children with T21 have limited educational attainment and employment opportunities.
- Fact: Although statistics are lacking, some persons with T21 graduate high school and some graduate college (www.tinyurl.com/3we9ye2r). The nonprofit Ruby's Rainbow provides scholarships for students with a T21 diagnosis (www.rubysrainbow.org/about/). Anecdotal data document educational and vocational successes. For example, Sheri Brynard obtained her teaching credential in South Africa without assistance or modification of the testing materials (www.tinyurl.com/y7pd7tck).
- Myth: Children with T21 are happy and good natured.
- Fact: Children with T21 have the same emotions as others. They can become discouraged or disheartened, especially when experiencing exclusion or bias.
- Myth: Children with T21 will always be dependent on their parents.
- Fact: Some people with T21 secure livable incomes and live independently (www.tinyurl.com/urte6998). A 2015 survey shows that many are employed with a variety of jobs in the service industry (eg, restaurant or food service work, office work, cleaning, grocery stores). In addition, some persons with T21 are entrepreneurs, others work in fashion, and still others work in technology, especially as more employers prioritize hiring people with disabilities (Kumin L and Schoenbrodt L, *J Appl Res Intellect Disabil* 2016;29(4):330–345).

The nature of implicit bias

Implicit bias refers to unconscious attitudes and stereotypes, often reflecting societal messaging. For T21, biases:
- Are related to facial traits (Enea-Drapeau C et al, *PloS One* 2017;12(11):e0188513)
- May be phrased kindly, making them harder to detect

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- May be amplified for persons in minority racial/ethnic groups (Chung J et al, *Am J Med Genet A* 2023;191(8):2132–2141; Krell K et al, *Am J Med Genet A* 2023;191(3):742–752)

Health care professionals may hold lower expectations, leading to disparities in care and opportunities (Krell et al, 2023). Parents often hold lower expectations for their child's educational attainment and employment prospects than parents of typically developing children (de Graaf G et al, *Am J Med Genet A* 2019;179(2):161–176).

Ben's infant intervention team members opine that Ben will be a "great guy to have around" but tell his parents not to expect much from him. His parents come to you for a second opinion.

Countering implicit bias in clinical practice

Counteracting implicit bias in clinical practice requires a multifaceted approach that includes reflective practice, objective measurement tools, and structured approaches to intervention.

Reflective practice

Clinicians who take the time to reflect on their own assumptions can address their implicit biases (Diaz BA et al, *Adv Health Sci Educ Theory Pract* 2023;28(4):1191–1204; Sukhera J et al, *Acad Med* 2018;93(1):35–40). The goal is to do what is ethically right for a child with T21.

Set aside facial traits and genetics. What can the child do? What would be one step further? Help the child express what they want in their life. Help them plan how to reach their goals. When you and the parents join your patient in their vision, the likelihood of achievement is far better.

Actively reduce implicit bias using reflective questions, and advise parents and caregivers to think through these same questions (Heffron MC et al, *Infant Young Child* 2005;18(4):323–336):

- What am I assuming about this diagnosis or its impact on this child?
- How might these assumptions impact this child?
- How do my personal history and culture affect how I approach this child?
- What biases do I hold related to my role or toward persons with this diagnosis?
- What shifts in thinking might help this child thrive?

Objective measurement tools

Objective measurement tools can reduce implicit bias and help us make informed decisions about how to help the child and include them in scholastic and community activities (VanPuymbrouck L et al, *Rehabil Psychol* 2020;65(2):101–112).

Obtain reports from multiple sources:

- Patients
- Parents
- Teachers
- Peers

Reports should cover diverse domains:

- Academic
- Eating/nutrition
- Exercise/fitness
- Emotions/mood
- Clinical observation at varied time points (eg, at intake, prior to each visit, during transitions like starting middle school)

Journal entries add rich daily life examples, documenting gains and testifying against views of limited potential.

Structured approaches to intervention

While there is a range of ability for all children, we need to ensure that every child reaches their full potential. Advocate for evidence-based therapies and educational programs, including speech, occupational, and/or physical therapies, plus academic and social supports (Treptow RL, *International Journal of Health, Wellness and Society* 2017;7(3):33–42). Ideally, such experiences occur alongside age-normed peers in settings that are characterized by acceptance and kindness.

Help the child gain competence by providing opportunities at home and school to see others perform a task. Then have the child practice it themselves while adults are present. Show confidence that the child can do the task. These positive experiences strengthen the child's self-esteem, resilience, and willingness to learn additional skills (Treptow RL, *Infant Mental Health J* 2017;38(2):318–320). Create clear goals and orderly interventions that permit children (and families) to navigate their lives. Help parents and teachers believe in the child's potential to make developmental gains.

Start with a routine daily task (eg, clearing their plate from the table or feeding the family dog):

- Model the behavior, talking through each step
- Have the child do the behavior and routinely repeat it

For complex tasks (eg, unloading the dishwasher or taking the dog for a walk), model each step, then give the child chances to practice putting the steps together independently.

Here are additional resources:

- Article: "Psychologists are teaching health care teams to identify and address microaggressions" (www.tinyurl.com/y2hf4rk8)
- Article: "Tactics to disarm and neutralize microaggressions" (www.tinyurl.com/4ftnhhkk)
- Project Implicit, which offers self-education through timed computer-generated tests (www.tinyurl.com/3z7jw49p)

Ben's parents include Ben with typically developing children. Ben is reading and writing by second grade and plays peewee hockey. As a teenager, Ben attends digital art classes, plays basketball with friends, and has an internship at a video game company. His girlfriend is pursuing accounting, and together they enjoy picnics with poetry.

CARLAT VERDICT

Implicit bias is ubiquitous across the range of developmental challenges and mental health conditions. Clinicians need to proactively explore implicit biases to combat the culture of lowered expectations and promote maximum inclusion for patients with T21 and other developmental conditions. *For more on the basics of T21, see feature article in this issue.*

Q&A With the Expert

Dysmorphology for Child Psychiatrists

Marilyn C. Jones, MD

Clinical Service Chief, Genetics, Rady Children's Hospital-San Diego; Distinguished Professor of Clinical Pediatrics, UCSD, San Diego, CA.

Dr. Jones has no financial relationships with companies related to this material.

CCPR: What portion of the population has an identifiable dysmorphological condition?
Dr. Jones: About 3%–4% of the global population has a birth defect or congenital anomaly. That's a lot of kids, and up to 5% of kids have had significant exposure to alcohol prenatally, which is a huge neurodevelopmental risk (May PA et al, *JAMA* 2018;319(5):474–482).
CCPR: What are the most common conditions that you see?
Dr. Jones: The most common genetic disorder of which psychiatrists should be aware is 22q deletion syndrome, formerly known as DiGeorge syndrome or velocardiofacial syndrome. The disorder occurs in one out of 4,000 births. Roughly 20% of affected individuals have major psychiatric problems as they hit adolescence and adulthood, including schizophrenia, depression, and anxiety (Botto LD et al, *Pediatrics* 2003;112(1):101–107; Provenzani U et al, *Int Rev Psychiatry* 2022;34(7–8):676–688).
CCPR: So when we see a teen with schizophrenia, depression, or anxiety, we should have this in the differential diagnosis?
Dr. Jones: Many families already know about it because of associated congenital heart malformations. But not every child with 22q-related heart malformation has somebody to try to investigate the cause of that structural problem.
CCPR: What are we looking for in 22q deletion syndrome?
Dr. Jones: Some of the kids are on the small side relative to their family. Many have learning challenges; a lot of them have hypernasal speech, as if they have a cleft palate, even though the palate may be intact. A congenital heart malformation or cleft palate should make you think about this diagnosis. They have recognizable facial features, which are subtle, but the child doesn't look like their parents. (*Editor's note: Visit www.thecarlatreport.com/dysmorphologyquickref for our "Concise Guide to Dysmorphology" table.)*
CCPR: What other signs or symptoms should we be on the lookout for as tipoffs to a genetic condition?
Dr. Jones: Fragile X is an X-linked deficit of FRMP protein needed for brain development. In fragile X, many affected males have significant cognitive challenges. Females can have a subtle phenotype. But anxiety is a big piece of the neurobehavior of fragile X.
CCPR: Are there other common conditions mental health professionals should know more about?
Dr. Jones: After 22q and alcohol-related neurodevelopmental disorder (ARND), everything else is much less common. ARND tops my list because those kids have tremendous challenges with impulse control and frontal lobe issues that create challenges in school and at home. *(Editor's note: For more on ARND, see our interview with Dr. Ira Chasnoff in this issue.)*
CCPR: Fragile X is further down?
Dr. Jones: Yes. Fragile X usually occurs in a family where there are other individuals at risk. It becomes a reproductive issue, particularly if a couple is interested in having more kids. The next conditions that you might see are sex chromosome aneuploidy conditions. Many of these individuals never have medical problems, but a subpopulation has learning challenges and behavioral issues that may end up with psychiatry. These are kids with XY plus another Y, children with XY plus another X, girls who have three X's, etc. We're picking them up on prenatal genetic screening using cell-free fetal DNA.
CCPR: How does early identification of 22q make a difference in the trajectory of the child's development?
Dr. Jones: You may need to address immunodeficiency, cardiac defects, and learning challenges. A program or group might help with social interactions. Don't let that fester unaddressed.
CCPR: For our readers who are not in the field, how widespread is fetal DNA testing and why is it important?
Dr. Jones: It's the standard in California to offer it to all pregnant people. The state screens for trisomy 21 (T21), trisomy 18, and trisomy 13. You can add sex chromosomal aneuploidy for a fee, and there are companies that will do 22q deletion and some other microdeletion syndromes prenatally as well. Fetal DNA testing could lead you to do a diagnostic test, which would either be a chorionic villus sampling or an amniocentesis, to directly examine the genetic composition of fetal DNA. That might result in better planning for a new child or perhaps in a decision to terminate a pregnancy.
CCPR: Has this affected amniocentesis rates?
Dr. Jones: They've gone way down because there are fewer false positives with this type of screening. But there are ethical issues. For some practices, this just goes with your prenatal labs. Patients have no idea that they've just had genetic screening for T21.

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Expert Interview—Dysmorphology for Child Psychiatrists

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CCPR: I work with people who would not do the testing since they do not plan to terminate a pregnancy based on genetic testing.

Dr. Jones: I think that's the 25% who opt out. They do not want this information since they are not going to act on it, so they don't need it—and that's absolutely a fair approach.

CCPR: Are there guidelines for identifying children we might refer to a dysmorphologist?

Dr. Jones: Think of those kids who have been struggling all along. They have learning challenges, developmental challenges, and now behavioral challenges. Often there's no history of birth injury or meningitis or something that you can relate to the challenges the child is having. Those are the kids who need a closer look.

CCPR: And is that next look a chromosomal microarray?

Dr. Jones: Yes. Microarray and fragile X are reasonable. But genetic testing is not always clear. It's important to explore the cause of a child's difficulties, including genetic reasons; however, that investigation might bring up more questions. You need to warn people ahead of time that there are three results you can get: positive, negative, and a variant of uncertain significance.

CCPR: That's what SPARK is for, right?

Dr. Jones: SPARK is a multisite national effort in the United States where families of autistic kids can provide DNA samples from their child and family members. SPARK is gathering huge numbers of DNA samples hoping that the numbers will help identify new developmental conditions that include autism as part of their picture. However, they are finding many genetic variant that have no known significance.

CCPR: How do parents react to the news that a genetic variant may be related to their child's difficulties?

Dr. Jones: From the perspective of the parent, their child has a behavioral problem, and you try to figure out why the child is having the problem. During your workup, you wonder about genetic components. If there is a genetic finding, how will the parents feel? Will they blame themselves or perhaps each other? Will they feel relieved that there is a cause and that their child is not misbehaving on purpose? There are many possibilities. Ask parents for their thoughts on the results and work with them so that you can support a better relationship between the parents and the child.

"A kid who might need referral to a dysmorphologist is one who has learning challenges, developmental challenges, and now behavioral challenges. Often there's no history of birth injury or meningitis or something that you can relate to the challenges the child is having. Those are the kids who need a closer look."

Marilyn C. Jones, MD

CCPR: How do you talk with kids and parents about these conditions?

Dr. Jones: Usually, I see the child when they're young and I'm talking to the parents, although I do talk to adolescents as well. I take the perspective that all of us have genetic differences and they just have one that we know something about, and it helps us understand why they're struggling and gives us a direction for helping them.

CCPR: Have you encountered issues with implicit bias that might limit the opportunities offered to kids based on low expectations?

Dr. Jones: There's tremendous bias. Forty years ago, people were told to put their kids with T21 in institutions for the intellectually disabled. I remember in medical school taking a field trip out to one of those places and being overwhelmed with cottage after cottage of individuals who were not doing much because there was no expectation. They were sort of warehoused and it was just incredibly sad. I don't see that anymore, but there tends to be a sense that there's nothing we can do because you can't fix the underlying genetic problem. We all need to advocate for these kids to have opportunities to learn and participate in society. It's unfair to take away a family's hope and limit a child's future. Kids haven't read the book about how it's supposed to go, and most of them make liars out of the doctors who talk to their families early on. And then the family never trusts anything they hear from medical professionals. Stigma is a huge problem, especially with some conditions such as those related to alcohol exposure.

CCPR: What we can do about the stigma?

Dr. Jones: Women who drink during pregnancy are stigmatized, and their kids are horribly stigmatized. This makes disclosure of the information to get that history difficult, particularly because few kids have physical findings. Many have neurobehavioral challenges, and the only way you're going to get at that is with a history of exposure, unless the psychologist who is testing them can recognize the pattern of neurobehavioral problems as pointing toward an alcohol-related injury. *(Editor's note: See our other Q&A in this issue for more on how to obtain a history of prenatal alcohol exposure.)*

CCPR: Are there resources for reference or further learning that we could share with clinicians?

Dr. Jones: My book has summaries on hundreds of disorders (Jones KL, Jones MC, and del Campo M. *Smith's Recognizable Patterns of Human Malformation* (8th ed.). Amsterdam: Elsevier; 2021). It can be used at the bedside for a quick once-over on a diagnosis and what you need to know about it. For more in-depth discussion, many genetic disorders have expert GeneReviews online (www.tinyurl.com/4zu4ray5). They're written in an easy-to-use format. Parent support websites often have superb content and a positive take about the kinds of things that help. There is also a facial recognition app called Face2Gene (www.face2gene.com) where you can take a picture of an individual and upload it on their website and they'll give you a differential diagnosis. Many of my colleagues find it helpful.

CCPR: Thank you for your time, Dr. Jones.

Decision Making for Young Adults With Intellectual Disabilities

Joshua D. Feder, MD.

Tony, a 17-year-old who attends a school for students with moderate intellectual disability, takes fluoxetine for depression co-occurring with autism. Prior planned gradual reductions in his medication left Tony unable to attend school or work on coding his video game. However, Tony says he "doesn't feel sick" and plans to stop his medication when he turns 18 in three months. Tony's parents ask you whether he should be allowed to make these decisions.

Many patients with developmental challenges have trouble with specific capacities (ie, making important medical, financial, and relationship decisions). Others have a global lack of competence, which can be memorialized by a court order to ensure the person has the oversight they need in decision making. Clinicians need to understand the assistance options available to patients to guide them and their families.

Levels of assistance

Assistance options range from fully substituted decision making to supported decision making.

Guardianship/conservatorship

Legal guardianships involve minors or disabled persons who require someone to make personal decisions for them but might make financial decisions too. Conservatorships are usually for adults who need a legally responsible party (conservator) to make financial decisions for them but might also make personal decisions. There is a lot of overlap between the two terms, and the precise definitions differ from state to state. For our purposes, we will use the terms interchangeably. In a guardianship, a court assigns another adult or agency to make all decisions for someone who lacks the capacity to make those decisions (www.tinyurl.com/3c6ufxeu). This helps ensure that persons with developmental challenges:

- Take necessary medication
- Avoid agreements that they may not comprehend
- Live safely

Guardianships are criticized for undermining the autonomy and wishes of the person (www.tinyurl.com/2p9ap32u). They may also lead to financial abuse when the guardian has access to the individual's funds and can strain family relationships when the guardian is a family member.

Limited conservatorship

Limited conservatorships preserve some autonomy for the person by listing specific decisions the guardian can make. Depending on the situation, the guardian may be empowered to make decisions for the individual regarding:

- Where to live
- Medical care
- Education
- Finances
- Entering contracts
- Consenting to sexual activity
- Marriage
- Voting
- Owning or carrying firearms

While he has trouble with finances and using public transportation safely, there is no reason to impede Tony from voting or choosing what classes to take at the local community college, so a limited conservatorship might be best if you can't help him understand the benefits and risks of medical treatment.

Healthcare power of attorney (HPOA)

An HPOA (also called "medical power of attorney" or "health care proxy") is typically a notarized document but does not require court approval. It allows a designated individual to make medical decisions for the person if they become incapacitated. HPOA is especially helpful for persons with co-occurring conditions, such as psychotic disorders or degenerative neurological conditions (eg, predictable dementias with trisomy 21).

Supported decision making

New approaches to decision making for disabled adults, such as supported decision making agreements, have come with the rise of self-advocacy among neurodiverse individuals. These are signed, often notarized, agreements to have other adults assist the person in making important decisions. The person retains all their rights; however, this documentation serves to reassure clinicians, bankers, attorneys, and others that the individual can make their own decisions and that their decisions should be respected. They might make some bad decisions, and families need to accept this.

The role of the psychiatrist

Planning for adulthood

Begin talking with patients and families 18–24 months before the patient becomes a legal adult. These are necessary, emotionally challenging, and technically complicated conversations about care options, financial trusts, and planning for when parents will no longer be able to care for the person. Track how your patient is developing their ability to make adult decisions. Courts move slowly, and families often need the help of attorneys.

Informal assessment

- Assess decision making during informed consent (eg, for medication).
- Check the person's ability to understand, explain, and communicate rational decisions.
- Obtain specific examples of how the person functions in daily decision making through cognitive testing and collateral information from family members and other professionals.

Tony does not recall ever feeling depressed. You show Tony his medical record, including times when he became depressed during efforts to gently reduce the fluoxetine; however, Tony only talks about the video game he is creating when it's his turn to talk.

Practical accommodations

Whatever their legal status, help your patients understand decisions and communicate their wishes. Many are not accustomed to being listened to. Here are some techniques to try (Sullivan F and Heng J, *Can Fam Physician* 2018;64(Suppl 2):S32–S36):

- Use simple language: Use words that any 8-year-old might understand to clarify concepts and avoid jargon.
- Review pros and cons: Say "Let's write down the good and bad things that might happen if you do this."
- Slow it down: Wait patiently, even counting to 10 in your head. Patients need time to process and respond.

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Decision Making for Young Adults With Intellectual Disabilities
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- Use statements instead of questions: For example, instead of "Why are you feeling sad today?" try "I don't know why you are sad today. Please tell me." This helps patients feel more relaxed.
- Use AAC/SGD devices: For non-speakers, an augmentative and alternative communication (AAC) device, usually a tablet or laptop, which is sometimes a speech-generating device (SGD), can help a person who would otherwise always say or nod yes to express their thoughts and wishes more fully.
- Hold private conversations: Make time to talk with the patient alone to hear their wishes with less immediate influence.

You draw a simple "program" diagram for Tony showing "happy" when he is on medication, changing to "sad" when he is not, and looping back to happy when he is back on medication. Tony's mother loads this onto Tony's tablet and waits patiently for Tony to read it. Tony states that he does not want to be sad again and decides to stay on his medication when he turns 18.

CARLAT VERDICT

For patients who will have trouble making their own decisions as adults, plan early as they near the age of majority. Advocate for supported decision making whenever possible to preserve your patients' autonomy, and use accommodations with all patients as needed to support rational decision making. For resources on decision making options for developmentally disabled adults, visit www.thecarlatreport.com/decisionmakingresources.

Research Updates IN PSYCHIATRY

MEDICATION

Does Adding Topiramate to Aripiprazole for Mania Improve Metabolic Outcomes?

Dorothy Chyung, MD. Dr. Chyung has no financial relationships related to this material.

REVIEW OF: Arman S and Haghshenas M, *J Res Med Sci* 2022;27:23

STUDY TYPE: Randomized double-blind placebo-controlled trial

There is already a small open-label trial that used topiramate added to olanzapine to prevent weight gain in youth with bipolar disorder (BD) (Wozniak J et al, *J Child Adolesc Psychopharmacol* 2009;19(5):539). But does topiramate also help prevent weight gain with aripiprazole?

In a study from Iran, 40 patients with BD (ages 6–18; mean age 13) were started on aripiprazole 5 mg and were randomly assigned to receive either adjunctive topiramate 12.5 mg or placebo, along with weekly dosage adjustments as needed, with a target dose of 150 mg. The researchers measured weight, height, BMI, waist circumference, abdominal circumference, and blood pressure at one- and three-month follow-up.

At three-month follow-up, patients who received topiramate gained less weight compared to those who received placebo. Patients on topiramate saw their BMIs decrease from 25.41 to 24.09, while those on adjunctive placebo saw their BMIs increase from 23.92 to 24.41. These results translate to approximately eight pounds lost for a 66-inch-tall teen on topiramate vs three pounds gained on placebo. However, there were no clinically significant differences between the groups on other metabolic outcomes at three-month follow-up. Topiramate was also associated with lower Young Mania Rating Scale scores, which was statistically significant but not clinically significant.

The study had limitations, including the lack of an intent-to-treat analysis, small sample size, unblinding due to topiramate side effects, lack of comment on cognitive side effects, the short three-month duration, and the lack of reported confidence intervals.

CARLAT TAKE

Despite the limitations and side effects, these results for BMI are notable. Topiramate may prevent several pounds of weight gain in youths taking atypical antipsychotics for BD, but we suggest you consider metformin first. If you try topiramate, watch for cognitive side effects.

Tolerability of Vortioxetine for Pediatric Anxiety and Depressive Disorders

Kathryn Martin, MD, MPH. Dr. Martin discloses that she owns shares in a variety of pharmaceutical companies. Relevant financial relationships listed for the author have been mitigated.

REVIEW OF: Findling RL et al, *J Child Adolesc Psychopharmacol* 2018;28(1):47–54

STUDY TYPE: Open-label extension study

Both fluoxetine and escitalopram are FDA approved for depression in adolescents. One recent trial of vortioxetine has endorsed its efficacy for depression in adolescents, but what about its tolerability? A recent study provides some data.

This was an industry-funded, open-label extension study that assessed the long-term safety of vortioxetine in children and adolescents. Forty-one participants completed the six-month study. The vortioxetine doses were adjusted at the discretion of the investigators (dose range 5–20 mg/day). Tolerability and suicidal ideation/behavior were assessed every four weeks using the Pediatric Adverse Event Rating Scale and the Columbia Suicide Severity Rating Scale.

Over the course of the study, half of all participants experienced adverse events (AEs) that were considered related to vortioxetine and 49% dropped out. Most treatment-emergent AEs were deemed mild or moderate in

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CME Post-Test

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1. True or false: Children with trisomy 21 (T21) will always depend on their parents (LO #1).
   [ ] a. True
   [ ] b. False

2. According to Dr. Jones, which of the following characteristics are indicative of 22q deletion syndrome (LO #2)?
   [ ] a. Significant psychiatric challenges
   [ ] b. Savant-like cognitive skills
   [ ] c. Deep resonant voice
   [ ] d. Generally taller than other family members

3. What is one recommended technique to try when talking with patients and their families about making decisions and communicating goals (LO #3)?
   [ ] a. Use simple language and avoid jargon
   [ ] b. Try to ask only open-ended questions
   [ ] c. Use accurate and specific medical terminology
   [ ] d. Avoid private conversations with patients

4. According to a 2018 study, what was observed about the tolerability of vortioxetine in children and adolescents (LO #4)?
   [ ] a. 49% of participants experienced mild to moderate adverse events (AEs)
   [ ] b. Stomachaches and constipation were the most commonly reported AEs
   [ ] c. 15% of participants experienced suicidal ideation
   [ ] d. Vortioxetine was well tolerated by most participants when doses were limited to 5–20 mg/day

5. What is the first-line medication treatment for depression and anxiety in patients with T21 (LO #1)?
   [ ] a. Selective serotonin reuptake inhibitors
   [ ] b. Serotonin antagonist and reuptake inhibitors
   [ ] c. Serotonin-norepinephrine reuptake inhibitors
   [ ] d. Cognitive behavioral therapy combined with positive activities

6. According to Dr. Chasnoff, about what percentage of children with fetal alcohol spectrum disorders are misdiagnosed (LO #2)?
   [ ] a. 13%
   [ ] b. 74%
   [ ] c. 86%
   [ ] d. 97%

7. Which of the following care options allows a disabled adult to retain the highest degree of autonomy while reassuring health care, financial, and other professionals that the individual is qualified to make their own decisions (LO #3)?
   [ ] a. Limited conservatorship
   [ ] b. Supported decision making
   [ ] c. Guardianship
   [ ] d. Healthcare power of attorney

8. According to a 2022 study on topiramate for preventing weight gain in children and teens taking aripiprazole, what was observed at three-month follow-up (LO #4)?
   [ ] a. Patients taking topiramate experienced an increase in BMI
   [ ] b. Patients taking topiramate experienced a decrease in BMI
   [ ] c. There were no clinically significant differences between the topiramate and placebo groups
   [ ] d. Patients taking placebo experienced a decrease in BMI

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Reasearch Updates
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intensity, with the most common being headache and nausea. Six adolescents (about 15%) experienced suicidal ideation, one of whom had a nonfatal suicide attempt. None of these cases were considered related to vortioxetine by the investigators.

Notable limitations of the study included small sample sizes, lack of placebo control, no assessment of concomitant psychopathology, and funding by the manufacturer of vortioxetine.

CARLAT TAKE

The rate of reported suicidal ideation associated with vortioxetine in this industry-funded study is notable and much higher than even the relatively high 3.4% we've seen reported for paroxetine (for more, see *CCPR* Oct/Nov/Dec 2020). Moreover, a recent larger study of 616 patients by the same research team found no benefit over placebo (Findling RL et al, *J Am Acad Child Adolesc Psychiatry* 2022;61(9):1106–1118.e2). We cannot recommend vortioxetine without large, non-industry-funded, randomized, placebo-controlled trials to establish its safety, tolerability, and efficacy in youth.

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