Father Factors
The clinical ways paternity matters

Clinical Feature
How to identify and treat bullying
Quiz: What makes a bully?

Pharmacologist’s Notebook
Urine drug screens: Interpreting results

NEW
Recognize & Refer
What one pediatric endocrinologist wants you to know

Practice Improvement
Improve compliance to save your medical home
How does managing food allergies affect the lives of patients and their families?

Some patients and their families face daily challenges that can negatively affect their quality of life as they work to avoid food allergens.¹ They may also struggle to understand the symptoms, severity, and management of food-induced allergic reactions.²

“I’m always nervous, always vigilant. I can’t let him be by himself.”

—Caregiver

*Data from a study of 38,408 children.*

REFERENCES

Young children whose parents are screened via telephone about their offspring’s development are far more likely to be referred for evaluation and to receive services than children who receive usual care from their primary care provider (PCP), a randomized trial involving 152 youngsters found.

Included in the study were children aged from 12 to 42 months who received well-child care at a community health center that primarily serves Hispanic families. Half the group received usual care while the parents of the other half (intervention group) were connected with a trained care coordinator who conducted developmental screening over the phone, using the Parental Evaluation of Development Status Online system. The coordinators were part of a Los Angeles County program (211LA) to detect and address early childhood developmental and behavioral concerns among families who call 2-1-1, a national telephone access number for connecting people to local health and human services.

Based on their assessment of developmental risk during the phone call, the care coordinators made referrals to intervention services and followed up with the families, usually about 15, 30, and 60 days after initial contact, to assist with connecting to evaluations and services. Coordinators also connected families with other services, such as transportation, food, and utility assistance to address any barriers to getting help.

After 6 months, significantly more children in the intervention group than those receiving usual care were referred (32% vs 9%) and were receiving more services (16% vs 1%). These differences between the 2 groups remained even after adjustment for age, sex, and primary language.

To get a better handle on relevant “usual care” at the health center, investigators reviewed the medical records of 142 other children aged from 12 to 42 months who had well-child care during the 6 months before the study started. The review showed that although almost all children had documented developmental surveillance, only 4% had been screened using a structured, validated screening tool (Nelson BB, et al. Pediatrics. 2019;143(4):e20181064).

I confess to a bit of regret that this process, bypassing the child’s doctor, is more effective in screening and completing referral for development concerns. However, the results, at least in this setting, are impressive and show a real benefit to these children. If this project is taken to scale, I hope that the child’s physician is kept in the loop when the screen is abnormal and after referral and evaluation are complete. These patients and their families will need an ally in dealing with the developmental conditions that are identified.

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Contemporary PEDIATRICS®

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Office- and hospital-based pediatricians and nurse practitioners use Contemporary Pediatrics’ timely, trusted, and practical information to enhance their day-to-day care of children. We advance pediatric providers’ professional development through in-depth, peer-reviewed clinical and practice management articles, case studies, and news and trends coverage.

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A novel, once-daily treatment option for patients with ADHD 6 years and older

**The first and only ADHD stimulant dosed in the evening**

When dosed in the evening, the delayed-release and extended-release technology of JORNAY PM enables the drug to be delivered in the early morning—and it lasts throughout the day.

**Mornings matter. Learn more at JORNAYpm.com and prescribe today.**

**Indication and Important Safety Information**

**INDICATION**
JORNAY PM is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older.

**IMPORTANT SAFETY INFORMATION**

**WARNING: ABUSE AND DEPENDENCE**
CNS stimulants, including JORNAY PM, other methylphenidate-containing products, and amphetamines, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.

**CONTRAINdications**
- Known hypersensitivity to methylphenidate or other components of JORNAY PM. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with methylphenidate products.
- Concurrent treatment with a monoamine oxidase inhibitor (MAOI), or use of an MAOI within the preceding 14 days because of the risk of hypertensive crisis.

**WARNINGS AND PRECAUTIONS**
- **Serious Cardiovascular Reactions:** Sudden death, stroke, and myocardial infarction have been reported in adults treated with CNS stimulants at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmias, coronary artery disease, and other serious cardiac problems.
- **Blood Pressure and Heart Rate Increases:** CNS stimulants may cause an increase in blood pressure and heart rate. Monitor all patients for hypertension and tachycardia.
- **Psychiatric Adverse Reactions:** CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychiatric disorder and may induce a manic or mixed episode in patients with bipolar disorder. In patients with no prior history of psychotic illness or mania, CNS stimulants, at recommended doses, may cause psychotic or manic symptoms.

**ADVERSE REACTIONS**
- **Priapism:** Prolonged and painful erections, sometimes requiring intervention, have been reported with methylphenidate products in both pediatric and adult patients. Priapism has also appeared during a period of drug withdrawal. Immediate medical attention should be sought if signs or symptoms of prolonged penile erections or priapism are observed.
- **Peripheral Vasculopathy, including Raynaud’s Phenomenon:** CNS stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud’s phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants.
- **Long-Term Suppression of Growth:** CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Monitor height and weight at appropriate intervals in pediatric patients.

**PREGNANCY AND LACTATION**
- CNS stimulant medications, such as JORNAY PM, can cause vasoconstriction and thereby decrease placental perfusion.
- The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for JORNAY PM and any potential adverse effects on the breastfeeding infant from JORNAY PM or from the underlying maternal condition. Monitor breastfeeding infants for adverse reactions, such as agitation, insomnia, anorexia, and reduced weight gain.

Please see additional safety information in the Brief Summary of Prescribing Information for JORNAY PM on adjacent pages.

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INDICATIONS AND USAGE
JORNAY PM is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients 6 years and older.

DOSAGE AND ADMINISTRATION
JORNAY PM should be taken only in the evening. Adjust the timing of administration between 6:30 pm and 9:30 pm to optimize the tolerability and efficacy the next morning and throughout the day.

The recommended starting dose for patients 6 years and above is 20 mg daily in the evening. Dosage may be increased weekly in increments of 20 mg per day up to a maximum daily dose of 100 mg. Capsules may be swallowed whole or opened and the entire contents sprinkled onto applesauce.

Do not substitute for other methylphenidate products on a milligram-per-milligram basis.

CONTRAINDICATIONS
Hypersensitivity to methylphenidate or other components of JORNAY PM. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with methylphenidate products.

Concomitant treatment with monoamine oxidase (MAO) inhibitors, or within 14 days following discontinuation of a monoamine oxidase inhibitor, because of the risk of hypertensive crisis.

WARNING AND PRECAUTIONS
Potential for Abuse and Dependence CNS stimulants, including JORNAY PM, other methylphenidate-containing products, and amphetamines, have a high potential for abuse and dependence. Assess the risk for abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.

Serious Cardiovascular Reactions Sudden death, stroke, and myocardial infarction have been reported in adults treated with CNS stimulants at recommended doses. Sudden death has been reported in pediatric patients with structural cardiac abnormalities and other serious cardiac problems taking CNS stimulants at recommended doses for ADHD. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, coronary artery disease, and other serious cardiac problems. Further evaluate patients who develop exhalation chest pain, unexplained syncope, or arrhythmias during treatment with JORNAY PM.

Blood Pressure and Heart Rate Increases CNS stimulants may cause an increase in blood pressure (mean increase 2 to 4 mmHg) and heart rate (mean increase 3 to 6 bpm). Individuals may have larger increases. Monitor for hypertension and tachycardia.

Psychiatric Adverse Reactions Exacerbation of Pre-existing Psychosis CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a preexisting psychotic disorder. Induction of a Manic Episode in Patients with Bipolar Disorder CNS stimulants may induce a manic or mixed episode in patients. Prior to initiating treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, or depression). New Psychotic or Manic Symptoms CNS stimulants, at recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) without a prior history. If such occur, consider discontinuing JORNAY PM. In a pooled analysis of studies of CNS stimulants, psychotic or manic symptoms occurred in approximately 0.1% of CNS stimulant-treated patients, compared with 0 in placebo-treated patients.

Prionism Prolonged, painful erections, sometimes requiring surgery, have been reported with methylphenidate in both pediatric patients and adults. Prionism was not reported with drug initiation but developed after time on the drug, often after an increase in dose. Prionism has also appeared during a period of drug withdrawal (drug holidays or during discontinuation). Patients who develop abnormally sustained or frequent, painful erections should seek immediate medical attention.

Peripheral Vascularopathy, including Raynaud’s Phenomenon CNS stimulants, including JORNAY PM, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud’s phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud’s phenomenon, were observed in post-marketing reports at different times and at therapeutic doses in all age groups throughout the course of treatment. Signs and symptoms generally improve after reduction in dose or discontinuation of drug. Careful observation for digital changes is necessary during treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

Long-term Suppression of Growth CNS stimulants have been associated with weight loss and slowing of growth in pediatric patients. Careful follow-up of weight and height in children 7 to 10 years of age randomized to either methylphenidate-treated and placebo over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and placebo-treated patients over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth (on average, 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period. Closely monitor growth (weight and height) in children treated with CNS stimulants, including JORNAY PM. Patients not growing or gaining weight or height as expected may need their treatment interrupted.

ADVERSE REACTIONS
Clinical Trial Experience Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. Clinical Trials Experience with Other Methylphenidate Products in Children, Adolescents, and Adults with ADHD Commonly reported (≥2% of the methylphenidate group and at least twice the rate of the placebo group) adverse reactions from placebo-controlled trials of methylphenidate products include: appetite decreased, weight decreased, nausea, abdominal pain, dyspepsia, dry mouth, vomiting, insomnia, anxiety, nervousness, restlessness, affect lability, agitation, irritability, dizziness, vertigo, tremor, blurred vision, blood pressure increased, heart rate increased, tachycardia, palpitations, hyperhidrosis, and pyrexia. Clinical Trials Experience with JORNAY PM in Pediatric Patients 6 to 12 years with ADHD The safety of JORNAY PM was evaluated in 280 patients 6 to 12 years of age who participated in two controlled clinical studies of patients with ADHD. Study 1, conducted in pediatric patients 6 to 12 years of age, was comprised of a 6-week open-label dose-optimization phase in which all patients received JORNAY PM (n=126; mean dose 50 mg). Following a 1-week, double-blind controlled withdrawal phase in which patients were randomized to continue JORNAY PM (n=65) or switch to placebo (n=54). During the open-label JORNAY PM treatment phase, adverse reactions reported in >5% of patients included: any insomnia (41%), decreased appetite (27%), affect lability (24%), headache (19%), upper respiratory tract infection (17%), upper abdominal pain (9%), nausea or vomiting (9%), increased diastolic blood pressure (8%), tachycardia (7%), and irritability (6%). Three patients discontinued treatment because of affect lability, panic attacks, and agitation and aggression. Because of the trial design (6-week open-label active treatment phase followed by a 1-week, randomized, double-blind, placebo-controlled withdrawal), the adverse reaction rates described in the double-blind phase are lower than expected in clinical practice. No difference occurred in the incidence of adverse reactions between JORNAY PM and placebo during the 1-week, double-blind, placebo-controlled phase. Study 2 was a 3-week, placebo-controlled study of JORNAY PM (n=81; mean dose 50mg) in pediatric patients 6 to 12 years. Most Common Adverse Reactions (incidence of ≥5% and at a rate at least twice placebo): any insomnia, decreased appetite, headache, vomiting, nausea, psychomotor hyperactivity, and affect lability or mood swings. One patient in the JORNAY PM group discontinued from the study due to mood swings. Table 1 provides the incidence of adverse reactions reported in Study 2 (incidence of 2% or more and at least twice placebo) among pediatric patients 6 to 12 years in a 3-week clinical trial.

Table 1: Adverse Reactions Occurring in ≥2% of JORNAY PM-treated Pediatric Patients and Greater than Placebo in a 3-Week ADHD Study (Study 2)

<table>
<thead>
<tr>
<th>Body Organ System</th>
<th>Adverse Reaction</th>
<th>JORNAY PM (N=81)</th>
<th>Placebo (N=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td>Any insomnia</td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>Initial insomnia</td>
<td>14%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Middle insomnia</td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>Terminal insomnia</td>
<td>11%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Insomnia, not specified</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Affect lability/Mood swings</td>
<td>6%</td>
<td>1%</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Decreased appetite</td>
<td>19%</td>
<td>4%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Psychomotor hyperactivity</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Blood pressure diastolic increased</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Vomiting</td>
<td>9%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>Infectious and infestations</td>
<td>Nasopharyngitis</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>Pharyngitis streptococcal</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>Contusion</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Musculoskeletal and procedural complications</td>
<td>Back pain</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rash</td>
<td>2%</td>
<td>0%</td>
</tr>
</tbody>
</table>
**Postmarketing Experience** The following adverse reactions have been identified during postmarketing use of methylphenidate products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

**Blood and Lymphatic System Disorders:** Pancytopenia, Thrombocytopenia, Thrombotic thrombocytopenic purpura

**Cardiac Disorders:** Angina pectoris, Bradycardia, Extrastyle, Supraventricular tachycardia, Ventricular extrastyle

**Eye Disorders:** Diplopia, Mydriasis, Visual impairment

**General Disorders and Administration Site Reactions:** Abdominal pain, Chest discomfort, Hyperepyrexia

**Immunologic System Disorders:** Hypersensitivity reactions such as Angioedema, Anaphylactic reactions, Auricular swelling, Bulbous conditions, Exfoliative conditions, Urticaria, Pruritus, Rash, Eruptions, and Exanthemas

**Investigations:** Alkaline phosphatase increased, Bilirubin increased, Hepatic enzyme increased, Platelet count decreased, White blood cell count abnormal, Severe hepatic injury

**Musculoskeletal Disorders:** Connective Tissue and Bone Disorders: Arthritis, Myalgia, Muscle twitching, Rhabdomyolysis

**Nervous System Disorders:** Convulsion, Grand mal convulsion, Dyskinesia, Serotonin syndrome in combination with serotonergic drugs

**Psychiatric Disorders:** Disorientation, Hallucination, Hallucination auditory, Hallucination visual, Libido changes, Mania

**Urogenital System Disorders:** Priapism

**Skin and Subcutaneous Tissue Disorders:** Nopecia, Erythema

**Vascular Disorders:** Raynaud’s phenomenon

**DRUG INTERACTIONS**

**MAO Inhibitors** Do not administer JORNAY PM concomitantly with MAOIs or within 14 days after discontinuing MAOI treatment. Concomitant use of MAO inhibitors and CNS stimulants can result in an acute toxic crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy** Risk Summary Published studies and postmarketing reports on methylphenidate use in pregnancy are insufficient to inform a drug-associated risk of adverse pregnancy-related outcomes. No teratogenic effects were observed in embryo-fetal development studies with oral administration of methylphenidate to pregnant rats and rabbits during organogenesis at doses up to 2 to 9 times the maximum recommended human dose (MRHD) of 100 mg/day given to adolescents on a mg/m² basis, respectively. However, spina bifida was observed in rabbits at a dose 31 times the MRHD given to adolescents. A decrease in pup body weight was observed in a pre- and post-natal development study with oral administration of methylphenidate to rats throughout pregnancy and lactation at doses 3.5 times the MRHD given to adolescents. The background risk of major birth defects and miscarriage for the indicated population is unknown. However, in animal reproduction studies, maternal toxicity in rat and rabbit studies occurred at doses 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies. Clinical Considerations: Fetal/Neonatal Adverse Reactions CNS stimulant medications, such as JORNAY PM, can cause vasoconstriction and thereby decrease placental perfusion. No fetal and/or neonatal adverse reactions have been reported with the use of therapeutic doses of methylphenidate during pregnancy; however, premature delivery and low birth weight infants have been reported in amphetamine-dependent mothers. Data: Human Data A limited number of pregnancies have been reported in published observational studies and postmarketing reports describing methylphenidate use during pregnancy. Due to the small number of pregnant women and fetal outcomes reported with methylphenidate exposure in pregnancy with known outcomes, these data cannot definitely establish or exclude any drug-associated risk during pregnancy. Animal Data In studies conducted in rats and rabbits, methylphenidate was administered orally at doses of up to 222 and 100 mg/kg/day, respectively, during the period of organogenesis. Teratogenic effects (increased incidence of fetal spina bifida) were observed in rabbits at the highest dose (5 times the MRHD of 100 mg/day given to children on a mg/m² basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (approximately ≥ 2.5 times the MRHD of 100 mg/day given to children on a mg/m² basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

**Geriatric Use** JORNAY PM has not been studied in patients older than 65 years of age.

**DRUG ABUSE AND DEPENDENCE**

**Controlled Substance** JORNAY PM contains methylphenidate, a Schedule II controlled substance.

**Abuse** CNS stimulants, including JORNAY PM, other methylphenidate-containing products, and amphetamines, have a high potential for abuse. Abuse is characterized by impaired control over drug use, compulsive use, continued use despite harm, and craving. Signs and symptoms of CNS stimulant abuse include increased heart rate, respiratory rate, blood pressure, and/or sweating, dilated pupils, hyperactivity, restlessness, insomnia, decreased appetite, loss of coordination, tremors, flushed skin, vomiting, and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed. Abusers of CNS stimulants may chew, snort, inject, or use other unapproved routes of administration, which can result in overdose and death. To reduce the abuse of CNS stimulants including JORNAY PM, assess the risk of abuse prior to prescribing. After prescribing, keep careful prescription records, educate patients and their families about abuse and on proper storage and disposal of CNS stimulants, monitor for signs of abuse while on therapy, and re-evaluate the need for JORNAY PM use.

**Dependence** Tolerance (a state of adaptation in which exposure to a drug results in the reduction of the drug’s desired and/or undesired effects over time) can occur during chronic therapy with CNS stimulants including JORNAY PM. Dependence Physical dependence (a state of adaptation manifested by a withdrawal syndrome produced by abrupt cessation, rapid dose reduction, or other actions) may occur in patients treated with CNS stimulants, including JORNAY PM. Withdrawal symptoms after abrupt cessation following prolonged high-dosage administration of CNS stimulants include: dysphonic mood, depression, fatigue, vivid, unpleasant dreams; insomnia or hypomnia; increased appetite; and psychomotor retardation or agitation.

**OVERDOSAGE**

**Signs and Symptoms** Signs and symptoms of acute methylphenidate overdose, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: nausea, vomiting, diarrhea, restlessness, anxiety, agitation, restlessness, hyperactivity, increased blood pressure, tachycardia, headache, insomnia, akathisia, hypertension, tachycardia, palpitations, cardiac arrhythmias, hyperpyrexia, hypotension, tachycardia, mydriasis, dryness of mucous membranes, and rhabdomyolysis

**Management of Overdose** Consult with a Certified Poison Control Center (1-800-222-1222) for up-to-date guidance and advice on the management of overdose with methylphenidate. Provide supportive care, including close medical supervision and monitoring. Treatment should consist of those general measures employed in the management of overdosage with any drug. Consider the possibility of multiple drug overdosages. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. Use supportive and symptomatic measures.
Living in a dwelling that is close to greenspace reduces youngsters’ risk for behaviors associated with neurobehavioral problems. This relationship varies with the type of behavior, the child’s age, and the proximity of the greenspace, according to a study conducted in an ongoing prospective birth cohort.

Investigators estimated greenspace exposure using satellite-derived images of children’s homes that were translated into a vegetation index. Using a validated instrument for assessing a child’s adaptive behaviors in the community and home setting (the Behavioral Assessment System for Children, BASC-2), investigators assessed the risk for problematic behaviors at ages 7 and 12 years in 562 and 313 children, respectively. Analyses accounted for varying degrees of proximity to greenspace and adjusted for neighborhood deprivation, maternal education, race, and sex.

Living in a home with more nearby residential greenspace was associated with lower risk of conduct problems at age 7 years and, at age 12 years, of anxiety problems, along with a lower risk for depression and somatization problems. These effects varied somewhat with the distance from the child’s home to the greenspace (Madzia J, et al. J Pediatr. 2019;207:233-240).

As a parent who spent lots of hours reading an old-fashioned, well-worn copy of Goodnight Moon, I would be interested in knowing which medium gave the parent more joy. There aren’t many things in life as sweet as reading a book to your own child. If you work in a setting with the Reach Out and Read program, this study is an endorsement for your participation. If not, consider prescribing application for a library card as part of your anticipatory guidance for toddlers.
Urine drug screens: Caveats for interpreting results

Rapid drug screening immunoassays quickly assess pediatric patients for drug exposure. However, certain limitations of these immunoassays call for caution when interpreting presumptive positive results.

Urine drug screens (UDS) have an integral role in the clinical management of pediatric patients. Pediatric Trauma Society guidelines recommend universal screening for all pediatric trauma patients aged older than 12 years, and substance abuse in the pediatric population is associated with increased injury severity, length of hospital stay, and mortality.

Rapid screening methods, such as immunoassays, are commonly used in the emergency setting to screen patients for the presence of illicit drugs. These methods are advantageous because they can be readily automated and integrated into the workflow of high-throughput laboratories, providing a rapid turnaround time to enable timely patient management decisions. However, inherent limitations of UDS immunoassays necessitate caution when interpreting results.

Urine is the specimen of choice for UDS due to the increased window of drug detection compared with blood specimens and the relatively noninvasive nature of urine collection.

The detection window represents the amount of time after drug administration a person continues to excrete the drug and/or metabolite at a concentration exceeding a cutoff level. The detection window (typically 1 to 3 days) can be influenced by several factors, including dose, route of administration, metabolism, urine concentration, pH, and lipophilicity.

Limitations of UDS immunoassays

Despite the many advantages of immunoassay-based UDS, considerable limitations should be noted. First, because the results are qualitative (positive or negative), the interpretation of...
UDS immunoassay results is based on cutoff values for each drug. Although the cutoff value is established by the manufacturer of each testing device and represents the quantitative number above which there is a high probability of detecting a drug if it is present, each laboratory may use different cutoff values.

All UDS immunoassays entail the binding of antibodies to drug molecules. However, the type of antibody employed can result in considerable differences in assay performance. Polyclonal antibodies generally detect a wide range of drugs within a particular class, but these antibodies also allow for more cross-reactivity with drugs outside this class, increasing the risk of false-positive results. In comparison, immunoassays using monoclonal antibodies detect fewer members of a drug class, thus reducing the likelihood of cross-reactivity with similar drugs outside the drug class. Additionally, positive results from class-specific immunoassays cannot be attributed to an individual drug, complicating interpretation.

The US Department of Health and Human Services (HHS) Substance Abuse and Mental Health Services Administration (SAMHSA) guidelines recommend that initial drug screens test for the following commonly abused drugs or their metabolites: amphetamines, cocaine, marijuana (tetrahydrocannabinol/THC), opiates, and phencyclidine (PCP). Several studies have shown that UDS immunoassays for these drugs are subject to false-positive results (Table).

### TABLE

<table>
<thead>
<tr>
<th>TEST</th>
<th>REPORTED INTERFERING MEDICATIONS/ SUBSTANCES</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amphetamines</strong>&lt;sup&gt;9-11&lt;/sup&gt;</td>
<td>Bupropion, Chloroquine, Labetalol</td>
<td></td>
</tr>
<tr>
<td><strong>Cannabinoid</strong>&lt;sup&gt;15-20&lt;/sup&gt;</td>
<td>Efavirenz, Lumacaftor, Pantoprazole, NSAIDs</td>
<td></td>
</tr>
<tr>
<td><strong>Cocaine</strong>&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Coca tea (mate de coca)</td>
<td>True positive test result due to presence of coca metabolite, benzoylecgonine</td>
</tr>
<tr>
<td><strong>Opiates</strong>&lt;sup&gt;21-23&lt;/sup&gt;</td>
<td>Dextromethorphan, Naloxone, Poppy seeds</td>
<td>Poppy seeds yield a true positive test result due to presence of codeine and morphine in the seed</td>
</tr>
<tr>
<td><strong>Buprenorphine</strong>&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Morphine (high doses)</td>
<td></td>
</tr>
<tr>
<td><strong>PCP</strong>&lt;sup&gt;25-28&lt;/sup&gt;</td>
<td>Desvenlafaxine, Dextromethorphan, Diphenhydramine, Doxylamine, Labetalol, Imipramine, Ketamine, Lamotrigine, Meperidine, Tramadol</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; PCP, phencyclidine.


Immunoassay tests and their reported false positives vary by vendor. Consult with testing laboratory and consider confirmation testing if a false-positive immunoassay result is suspected.

Reported causes of false-positive results

The major metabolite of labetalol can cause false-positive amphetamines UDS results.<sup>9</sup> False-positive amphetamines UDS results in pregnant women given high-dose labetalol for the treatment of hypertensive disease have been reported.<sup>9</sup> Chloroquine<sup>10</sup> and bupropion<sup>11</sup> also have been shown to cause false-positive amphetamines immunoassay results.

False-positive results from a cocaine UDS immunoassay have been reported. However, a definitive cause for the interference was not identified.<sup>12,13</sup> Although it is not considered a cause of false-positive cocaine UDS results, coca tea (mate de coca) ingestion can cause positive cocaine results due to the presence of the coca metabolite benzoylecgonine, which is also a metabolite of cocaine.<sup>14</sup>

Pantoprazole, a commonly prescribed proton pump inhibitor (PPI) for the management of gastrointestinal (GI) symptoms, can cause false-positive test results with some cannabinoid immunoassay UDS.<sup>15-17</sup>
addition to pantoprazole, nonsteroidal anti-inflammatory drugs and the antiretroviral drug efavirenz have been implicated in false-positive cannabinoid UDS immunoassays.\textsuperscript{18,19} Recently, the combination therapy lumacaftor/ivacaftor, which is used in a subset of cystic fibrosis patients, was identified as a cause of false-positive cannabinoid screens.\textsuperscript{20}

Naloxone, which is recommended by the American Academy of Pediatrics (AAP) for the treatment of pediatric opioid overdose, cross-reacts with one type of opiate UDS immunoassay.\textsuperscript{21} Dextromethorphan exhibits a growing trend of abuse potential in adolescents and it cross-reacts with an assay for opiates, causing false-positive results.\textsuperscript{22} Another opiate-testing caveat is that poppy seed ingestion can cause a positive result on opiate UDS immunoassays, due to the presence of morphine and codeine in the seeds.\textsuperscript{23} Conversely, high-dose morphine can cause a false positive in the UDS immunoassay for buprenorphine, an opiate-addiction medication.\textsuperscript{24}

Although PCP abuse has declined recently, PCP remains a common component of UDS testing.\textsuperscript{8} False-positive PCP UDS immunoassay results can be caused by several drugs, including dextromethorphan, ibuprofen, imipramine, meperidine, ketamine, lamotrigine, and tramadol.\textsuperscript{25-28}

False-negative UDS immunoassay results
Another limitation of UDS immunoassays is the possibility of unexpected and false-negative results. A strict interpretation of a negative UDS result is that at the time of specimen collection, the concentrations of those drugs for which a test was performed were less than the threshold limits required to call the test positive. For drug-class UDS assays, antibody cross-reactivity can vary considerably within the drug class, leading to unexpected negative results. For example, many opiate UDS immunoassays have little-to-no cross-reactivity with fentanyl.

Caveats when interpreting positive results
Because of the limitations of UDS immunoassays described above, positive UDS results should be interpreted as “presumptive positive” results, and, if definitive results are required, confirmatory testing by mass spectrometry should be conducted. The protocol for screening and confirmation differs between laboratories depending on clinical needs, test menu, methodology employed, and the testing capability of the laboratory. Interpretive result comments and consultation with a laboratory director are valuable approaches to aid the accurate interpretation of UDS immunoassay results and other toxicology testing.

Positive UDS immunoassay results do not provide sufficient information to determine the exposure time, dose, or the frequency or pattern of drug use.\textsuperscript{29} Among the many variables to be considered when interpreting UDS immunoassay results are drug-drug interactions, assay cross-reactivity, drug formulation impurities, urine adulteration, genetic variation in drug-metabolizing enzymes, dose management, and drug half-life. Misleading but true-positive results can be obtained. Knowledge of the potential causes of false-positive and false-negative UDS immunoassay results is critical when determining the appropriate course of action in the context of patient care.

NOTE FROM DR LEE
No medical test is perfect. The awareness of false-positive tests for drugs of abuse is extremely important when managing the care of challenging social situations that may result in legal consequences.

— CARLTON LEE, PHARMD, MPH, FASHP, FPPAG

Because of the limitations of UDS immunoassays, positive UDS results should be interpreted as “presumptive positive” results, and, if definitive results are required, confirmatory testing by mass spectrometry should be conducted.

For references, go to ContemporaryPediatrics.com/urine-drug-screens
Fever and neck swelling in a teenaged girl
LYNDSY VAN DER LAAN, MD, MPH; YARON IVAN, MD

A previously healthy 15-year-old female presents to the emergency department (ED) with complaints of right-sided neck swelling, pain, decreased range of motion, and fever for 3 days. She also reports a sore throat and mouth pain with decreased oral intake. She denies any rhinorrhea, shortness of breath, difficulty swallowing, vomiting, or dental pain.

The patient was previously evaluated by her primary care doctor earlier this same week with similar symptoms. She tested negative for mononucleosis and *Streptococcus pharyngitis* and was prescribed amoxicillin-clavulanate for suspected bacterial lymphadenitis. The parent and the girl report that the symptoms persisted and worsened despite the oral antibiotics. There is no other significant past medical history, family history, or surgical history.

Blood was obtained for analysis while the patient was in the ED and included a complete blood count, basic electrolytes, and inflammatory markers. Significant laboratory results included a total white blood cell count of 15,040 per mm$^3$ with a differential count including 72% neutrophils. The C-reactive protein was elevated to 39.9 mg/L and erythrocyte sedimentation rate was 24 mm/h. The remaining laboratory values were normal.

**Differential diagnosis**
Differentials include Ludwig angina, Lemierre syndrome, cervical adenitis, brachial cleft cyst, sialadenitis, and sialolithiasis (Table 1). Ludwig angina is a form of cellulitis of the submental, sublingual, and submandibular spaces. Patients may present with swelling of the lower jaw and neck, mouth pain, and/or inability to open the mouth. This condition often spreads rapidly and can be life threatening due to the potential of upper airway obstruction.$^1$ Ludwig angina is a rare diagnosis in the pediatric population, and because of the unfamiliarity of pediatric providers with the condition, children...
can potentially experience delay in diagnosis and treatment. This serious condition should be treated with intravenous antibiotic and possibly judicious surgical intervention.¹

Lemierre syndrome is a rare type of oropharyngeal infection that is characterized by thrombosis of the internal jugular vein and multiple septic metastases/emboli.² Patients with Lemierre syndrome often present with manifestations related to the primary infection such as fever, abdominal pain, nausea, vomiting, or cervical lymphadenopathy. The primary infection progresses to affect the parapharyngeal space invading the posterior compartment along the path of the carotid artery and ultimately leads to a thrombophlebitis of the internal jugular vein.²

Children with cervical adenitis may present with an acutely tender and inflamed cervical lymph node that will appear as neck swelling, similar to this case presentation. It is usually related to a recent upper respiratory infection and mainly affects the submandibular or anterior cervical lymph nodes.² Pus is usually not visible in the roof of the mouth, unlike with sialadenitis.

**Sialadenitis in the pediatric population accounts only for 10% of all salivary gland disease.**⁵

Brachial cleft cysts may present as a painless, unilateral neck mass, unless they have become secondarily infected. Although present at birth, many cases of brachial cleft cysts do not become evident until later in childhood or adolescence.⁶

Finally, sialolithiasis are salivary stones that can occlude the salivary ducts and lead to inflammation and infection, or sialadenitis. These patients present with neck swelling, pain, fevers, and occasionally drainage from the salivary ducts. Sialolithiasis causing sialadenitis was diagnosed in this patient due to classic presentation and supporting lab work and imaging.

**Diagnosis: sialadenitis and sialolithiasis**

Sialadenitis is defined as inflammation of the salivary glands and can be caused by infection, obstruction, or less commonly autoimmune or allergic processes. Sialadenitis in the pediatric population accounts only for up to 10% of all salivary gland disease.⁴ A multitude of factors contribute to inflammation of the salivary glands including viral or bacterial infections, genetics, immunologic diseases, congenital abnormalities, dehydration, and allergies.⁶ Additional predisposing factors include sialolithiasis (or salivary stones), mucus plugs, stenosis, or foreign bodies.⁶ Sialolithiasis is a common etiology in the adult population. However, the prevalence of sialolithiasis in the pediatric population is thought to be as low as 3% of all cases.⁷

**PATHOPHYSIOLOGY**

Sialadenitis is a multifactorial process with multiple etiologies. Francis and Larsen composed a list of sialadenitis etiologies (Table 2) and included major causes such as viral, bacterial, immune, or traumatic.⁶ Prior to the measles/mumps/rubella (MMR) vaccine, visceral sialadenitis was most commonly caused by mumps and affected the parotid gland. This has become less common with immunization efforts. Less common viral etiologies include Epstein-Barr virus (EBV), parainfluenza, and human immunodeficiency virus (HIV). Bacterial sialadenitis is most commonly caused by *Staphylococcus aureus* and *Streptococcus* species and presents with acute swelling, presence of pus, fever, and leukocytosis.⁸ Ductal stenosis can lead to obstructive sialadenitis and is more common in the parotid ductal system.⁹ Juvenile recurrent parotitis (JRP) is an important immunologic cause of sialadenitis and is thought to be the third-most common salivary disease in children, after mumps and viral infection.

While discussing sialolithiasis, it is important to understand the mechanism that leads to sialadenitis. Obstruction via a salivary stone causes inflammation, salivary stasis, postobstructive dilation, tissue damage, and remodeling that causes further inflammatory changes. Several theories have been proposed on how the salivary stone forms. One theory, proposed by Bodner and colleagues, states salivary mucin, bacteria, and desquamated epithelial cells form an initial organic nidus in which material deposits, forming a salivary stone.¹⁰,¹¹ Another theory states the initiating factor is an infection, which changes salivary composition and leads to stone formation.¹²

<table>
<thead>
<tr>
<th>TABLE 1 DIFFERENTIAL DIAGNOSIS FOR FEVER AND SWELLING IN THE NECK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ludwig angina</strong></td>
</tr>
<tr>
<td><strong>Lemierre syndrome</strong></td>
</tr>
</tbody>
</table>

Author created.
Contemporary Pediatrics

The most common location for stone formation in the pediatric population is the submandibular gland. A study by Chung and colleagues of 29 pediatric patients demonstrated that the submandibular gland was affected in more than 90% of cases. This finding is similar to studies in adults. Another study by Lustmann and colleagues revealed the submandibular gland was affected in 94% of patients of all ages. Possible reasons why the submandibular gland is most often affected may be due to slower flow of secretions as well as higher calcium content. The submandibular gland is the second-most common location and rarely the sublingual and minor salivary glands are involved. Sialolithiasis in children are usually smaller, occur distally within the duct, and present with shorter symptoms duration.

**Clinical Presentation**
The clinical presentation of sialadenitis is consistent with the inflammatory state. The most common presenting symptom is swelling, followed by pain. Other symptoms include erythema, swelling associated with eating, and tenderness to palpation. Many times, purulence and/or mucus may be expressed by gentle manipulation of the gland and duct. In severe cases, systemic complications can extend into adjacent tissues or spread to distal sites.

**Diagnosis**
Diagnosis of sialolithiasis/sialadenitis can be made by serology or gram stain when viral or bacterial etiologies are suspected. Imaging modalities may be necessary to rule out other life-threatening conditions such as Ludwig angina. These imaging modalities include plain radiographs, ultrasound, computed tomography (CT) with intravenous (IV) contrast, and sialography. In a retrospective case control study by Nahlieli and colleagues, 10 of the 15 cases (67%) of pediatric sialolithiasis were visible as radiopaque objects on radiographic film. However, up to 20% of submandibular salivary stones may be radiolucent on plain radiographs.

Ultrasound can confirm the presence of an inflamed gland/duct, identify abscesses, and guide in aspiration, if clinically required. Computed tomography is the image modality of choice when abscess formation or systemic complications are suspected. However, information may be limited if the stones are smaller than 2 mm in size, and CT is often discouraged if the stone is palpable on exam. However, CT may be used for surgical planning for cases of salivary stones to detect the inflamed gland and identify the size, number of calculi, and location of the stones.

Sialography is the gold standard for evaluation of sialolithiasis. It is performed by injecting radiopaque dye into the intraductal system, followed by a plain radiograph. Sialograms are reported to be up to 100% effective in detecting ductal and intraglandular calculi. However, they are contraindicated in the acute phase as a sialogram is thought to aggravate the inflammatory state.

**Management**
Treatment of sialadenitis is often conservative and targeted toward the suspected etiology. Sialolithiasis causing acute symptoms is initially managed conservatively with broad spectrum antibiotics, analgesics, hydration, warm massage, and sialogogues. Most common bacterial etiologies include gram-positive organisms whereas gram-negatives are less frequently seen. Therefore, penicillin derivatives and cephalospo-
rins will provide appropriate coverage as first-line antibiotics. A list of likely organisms is shown in Table 2.

Spontaneous passage is more probable if the salivary stone is small and located in the distal section of the duct. In one study, the success rate with conservative management for a period of 3 months was only 10%.

Surgical removal of salivary stones should be considered if conservative management fails. In a retrospective clinical review by Woo and associates, intraoral submandibular salivary stone removal led to complete recovery in 82.4% of pediatric patients. Salivary endoscopy has been validated in pediatrics as a safe and efficacious tool for the diagnosis and treatment of salivary gland disorders.

**Patient outcome**

Because of the concern for Ludwig angina in this patient, which may also present with a painful neck swelling, a CT neck with contrast was ordered and was significant for obstructing sialolithiasis with a 4-mm stone and resulting sialadenitis involving the right submandibular gland and Wharton’s duct (Figures 1 and 2). Several small reactive lymph nodes were noted as well. Treatment with intravenous ampicillin-sulbactam was initiated and the patient was admitted to the pediatric ward for further therapy.

During her only day of hospitalization, therapy with intravenous antibiotics was continued as well as sialogogue agents such as sour candy that led to spontaneous expression of pus and drainage. Infectious Disease and Otolaryngology were consulted and recommended transitioning to oral therapy with oral clindamycin and referral for outpatient management. The patient was discharged with 600 mg of clindamycin every 8 hours and a follow-up appointment with Otolaryngology in 1 week.

At her follow-up appointment, the patient demonstrated persistent enlargement and pain. She was continued on clindamycin and scheduled for submandibular duct dilation and stone removal. About 2 weeks after initial admission, she underwent surgery with removal of a 0.2-cm x 0.2-cm x 0.2-cm stone. At her 1-week follow-up, there was no residual pain and the patient had made a full recovery.

**Lessons for the clinician**

Sialolithiasis and sialadenitis are rare conditions in the pediatric population. Although uncommon, these conditions represent unusual emergencies and should be diagnosed and treated in a timely fashion.

The treatment of sialolithiasis and sialadenitis is often conservative with antibiotics, analgesics, hydration, and sialogogue agents. However, failure of conservative therapy is an indication for surgical removal. Pediatric emergency physicians should suspect these diagnoses when the child presents with swelling, pain, erythema, and tenderness to palpation over the jaw or mouth. A Pediatric Otolaryngologist should be consulted early in the course of treatment.

**ACKNOWLEDGMENT:** The authors wish to thank Stacy McConkey, MD, FAAP, Medical Director of Pediatrics Program, Advent Health for Children, Orlando, Florida, for her contributions to this article.

**Dr van der Laan** is a Pediatrics resident at Advent Health for Children, Orlando, Florida.

**Dr Ivan** is a pediatric Emergency Medicine physician, Department of Emergency Medicine, Advent Health for Children, and assistant clinical professor, University of Central Florida School of Medicine, Orlando. The authors have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

For references, go to ContemporaryPediatrics.com/puzzler-0619
Fathers’ influence on development and well-being of children

Despite the growing involvement of fathers in their children’s lives, there persists a lack of focus on fathers in pediatric care. Updated guidelines can help pediatricians to better engage fathers in the care of their children.

MARY BETH NIERENGARTEN, MA

Growing evidence shows the positive influence that fathers have on the development and well-being of their children. Longitudinal data published over the past decade or so support that paternal involvement from the prenatal stage through a child’s lifetime benefits the psychosocial and behavioral development of their children, often in ways different from and complementary to maternal involvement. Other data exploring the biological and epigenetic influences of fathers on their children are revealing the complexity of this paternal influence on their children. Among the most studied areas of research is paternal depression and the associated adverse effects on children.

In 2016, the American Academy of Pediatrics (AAP) updated its guidance for pediatricians on the role of fathers in the care and development of their children based on the increasing number of “high-quality” studies that now quantify and qualify this role. According to the guideline, among the drivers underlying this increased interest in fathers are socioeconomic forces in which the traditional roles of men and women are changing. More mothers are working outside

“Fathers don’t mother.”

—Kyle D. Pruett, MD, clinical professor of Child Psychiatry, Yale School of Medicine, researcher and host of the TV series “Your Child Six to Twelve With Dr. Kyle Pruett.”

Ms Nierengarten, a medical writer in Minneapolis, Minnesota, has more than 25 years of medical writing experience, authoring articles for a number of online and print publications. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

20 Father’s epigenome affects reproductive health
24 Paternal involvement boosts infants’ neurodevelopment
25 Early paternal bonds impact offspring’s cardiovascular health
27 Older fathers linked to problems with pregnancies, births
the home and more stay-at-home fathers are taking on caregiving activities. Fathers also are increasingly taking on the primary caregiving role as single parents. Also highlighted are changing social mores encouraging more involvement by fathers beyond their historic protector and provider role. Data show this, with involvement by fathers in childcare nearly doubling between 1965 and 2011.14

Despite this growing involvement of fathers in their children’s lives, pediatric visits largely still focus on the mother-child relationship.15,16 A recent systematic review of father-inclusive perinatal parent education in the United States found only a small number of early parent education programs for fathers.18 In addition, recent survey results of 100 pediatric primary care providers found that less than 50% of the respondents regularly implemented recommendations for engaging fathers as listed in the recent guidelines by the AAP.16 The survey also found that supporting parenting skills and perinatal depression screening for fathers were the least implemented recommended practices.

Craig F. Garfield, MD, professor of Pediatrics and Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois, attending physician at the Ann and Robert H. Lurie Children’s Hospital of Chicago, and one of the authors of the AAP guidelines on fathers, emphasizes the persisting lack of focus on fathers when it comes to pediatric care.

"Pediatrics has been slow in embracing the roles of fathers," he says, citing, for example, a recently published AAP guideline on postnatal depression that largely focused only on maternal depression.17

This article reviews some of the data on ways fathers contribute positively to the development and well-being of their sons and daughters, and suggests opportunities for pediatricians to better engage fathers in the care of their children.

Defining the role of father

When talking about the role of fathers in their children’s development and well-being, it is important to define what is meant by “father” as the term carries several assumptions that may not be completely accurate given the changing family structure. In the AAP guideline on fathers, father is defined broadly as “the male or males identified as most involved in caregiving and committed to the well-being of the child, regardless of living situation, marital status, or biological relation.” Along with the biological father, this definition includes foster fathers, stepfathers, and grandfathers.1

Underlying this discussion of who is a father is the recognition of the evolving and changing nature of family structures, societal norms, and understanding of masculinity and femininity that is creating additional complexity to understanding the multiple influences on childhood development. Research shows that the influence of fathers on the psy-

### TABLE 1

**FATHER INVOLVEMENT BY STAGE OF CHILDHOOD DEVELOPMENT**

<table>
<thead>
<tr>
<th>Perinatal involvement</th>
<th>Early childhood</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers are 1.5 times more likely to receive first-trimester prenatal care, with reductions in prematurity and infant mortality.</td>
<td>Expand size and variety of vocabulary and language; fathers more likely to introduce new words while mothers choose words the child already knows.</td>
<td>Decrease in adolescent risk behaviors, especially in boys.</td>
</tr>
<tr>
<td>Smoking reduction in mothers who smoke.</td>
<td>Less child maladaptive behavior; decreased mental health symptomatology; enhanced social competence linked to play.</td>
<td>Enhanced cognitive development and reduced behavioral problems in boys.</td>
</tr>
<tr>
<td>Skin-to-skin contact with infant linked to infant crying less, becoming drowsier sooner, and less wakefulness.</td>
<td>Negative influence of maternal depression mitigated by father’s involvement and thereby reduced the risk of problem behaviors and development in the child.</td>
<td>Decreased psychosocial problems in girls.</td>
</tr>
<tr>
<td>“Rough and tumble” play encourages exploration and independence in children.</td>
<td></td>
<td>Decreased risk of early puberty, early sexual experiences, and teenaged pregnancy in girls.</td>
</tr>
<tr>
<td>Yogman M, et al.1</td>
<td></td>
<td>Improved cognitive development, social responsiveness, independence, gender role development, particularly in girls.</td>
</tr>
</tbody>
</table>

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1Yogman M, et al.1
chosocial and behavioral development of children is distinct from that of mothers. However, it is difficult to tease out of this current research how these different influences are related to the biological distinctiveness of masculinity or femininity. Emerging research on the neurobiology of parenting provides some preliminary signs by showing just how complex the interplay between hormonal and neural circuitry is in men and women and how these biological processes manifest differently in parenting behavior.

Benefits of fathers’ early involvement

Data show that getting fathers involved early in their children’s lives predicts later involvement. Prenatal involvement by fathers, along with living with the mother, is the strongest predictor of their involvement by the time a child is aged 5 years. Paternal involvement just after a child is born is also critical. “Good research shows that the more men take time to spend at home with a child after birth, 2 weeks or more, they are almost 2 times as likely to be involved in diapering, feeding, cleaning, and caring for their baby at 9 months,” says Garfield. Helping fathers to be more confident in taking care of their children helps their children during all stages of their development (Table 1). Garfield highlights 3 main areas in which involvement by fathers is distinct from, and often complementary to, involvement by mothers.

The bottom line for this entire discussion of fathers is to underscore what best benefits the child. “A child thrives when parents thrive.”

Interplay of biology with caregiving

An emerging area of research on the biologic and epigenetic influences of fathers and mothers on children is offering further insight into the complexity of parental biology on childhood development and caregiving. For example, recent studies explore the interplay of biologic and environmental influences of fathers on childhood atopic dermatitis, the efficacy of treatment for attention-deficit/hyperactivity disorder (ADHD) in children, paternal diet and breast cancer risk in daughters, and increased incidence of childhood autism and cancers associated older paternal age.

Further research is looking closer at how caregiving behavior is linked to the biological distinctiveness of masculinity or femininity. Emerging research on the neurobiology of parenting provides some preliminary signs by showing just how complex the interplay between hormonal and neural circuitry is in men and women and how these biological processes manifest differently in parenting behavior.

The bottom line for this entire discussion of fathers is to underscore what best benefits the child. “A child thrives when parents thrive.”

---

Number of US fathers of children aged 17 years or younger living apart from at least 1 of their children.

1 in 4

~1 in 4

Number of US fathers of children aged 17 years or younger living apart from at least 1 of their children.

—CDC National Survey of Family Growth; 2017.
to neural and hormonal mechanisms of mothers and fathers as recently reported in a study examining the role of hormones (oxytocin, testosterone, prolactin, and arginine vasopressin) and their interplay on parenting behavior, and brain changes and parenting behavior.7

Fathers and postnatal depression
An important area of research is on the influence of fathers’ mental and physical health on their children. Among the most studied areas is that of paternal postnatal depression and the adverse effects on children. An updated meta-analysis found paternal depression in 8% of men during the first trimester and 1-year postpartum period.12 Data also show that by the time their children are aged 12 years, more than 20% of fathers will experience depression.10 In addition, during the first 5 years of fatherhood, those fathers who reside with their children have reported a 68% increase in their symptoms of depression.9

Despite this prevalence, the recently published AAP guidance on postnatal depression focused almost exclusively on mothers, as mentioned previously.17 “With the exception of a short paragraph talking about the problem of paternal postnatal depression, dads were missing from the report,” says Garfield.

The need to better recognize, identify, and address postnatal depression in fathers is highlighted by data showing the associated adverse effects on children—notably, poorer behavioral and emotional outcomes.15

Additional data show that when mothers are depressed, fathers play an indirect but key role in helping their children by supporting mothers, which mitigates the impact of maternal depression.20

Including fathers in pediatric practice
For Garfield, the bottom line for this entire discussion of fathers is to underscore what best benefits the child. “A child thrives when parents thrive,” he says.

Garfield emphasizes this includes both mother and father. “There are many opportunities that open up when we think more broadly

---

**TABLE 2**

**RECOMMENDATIONS FOR INVOLVING FATHERS IN ONGOING CARE OF THEIR CHILDREN**

- Welcome fathers and express appreciation for attending a clinic visit; actively engage fathers beginning with a prenatal visit.
- Introduce yourself to both parents during a clinical visit and politely explore the father’s relationship to the mother to assess type of relationship (married, living together, etc) and the personal beliefs of the father as to his role in caring for the child.
- Recognize possible differences in parenting style between the mother and father and serve as mediator, without siding with either parent, to discuss these differences.
- Emphasize to fathers that they are role models for their children and therefore encourage them to model positive behavior, such as using seat belts in cars and helmets with bikes, and limiting behavior such as alcohol, tobacco, and other substance use.
- Screen fathers for perinatal depression.
- Review vaccines for both parents to keep them up-to-date on vaccines, such as flu and pertussis.
- Discuss family composition, cultural beliefs about fathering and the role of men in families, the division of childcare tasks within the family, and the physical health of each parent.
- Encourage the early participation of fathers in the care of children, particularly alone time with children to build the father’s confidence and develop his own style of interaction. Talk to fathers about skills they may find lacking.
- Inform and discuss with parents the normal responses that fathers will have in becoming a father, including elation, fatigue, and challenges including those to intimacy and the sexual relationship.
- Educate fathers about how to support mothers who are breastfeeding.
- Discuss how the parents are adapting to parenthood after each child; encourage them to continue to engage in activities without the children.
- Identify current and necessary future public policies that support fathers’ involvement with their children, such as promoting the Family Medical Leave Act and flexible work schedule.
- Ascertain when it might be important to include both parents when needing permission for performing a medical procedure on a child. Try to include fathers in written communications about the child, such as test results.

Adapted from Yogman M, et al.1
beyond just mothers and think more broadly about the family and what the real opportunities are for the child in terms of parenting and our support as pediatricians and health-care providers,” he says.

With the rising interest in fathers becoming more involved in their children’s lives, and the changing family structure that is creating more opportunities for fathers to be primary caregivers, more attention to fathers is needed to ensure they thrive as fathers.

The recommendations offered in the 2016 AAP guidelines on fathers is a good place to start (Table 2). As stated in the guidelines, adopting just 1 or 2 of the recommendations during the next office visit with a father and child is a step in the right direction.1

**Summary**

Creating opportunities for fathers to be more involved in the caretaking needs of their children is critical at a time when the changing mores and expectations of society are seeing more fathers involved in caregiving activities with their children. Growing evidence shows that fathers contribute to the development and well-being of their children in unique and often complementary ways to mothers. As stewards of children’s health, pediatricians play a vital part in ensuring that children receive the best care possible—and that means a greater inclusion of fathers. Recent AAP recommendations for pediatricians provide useful tips on how to engage fathers and can be used as a good starting point in expanding the focus of pediatric care to include fathers. ■

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**Fathers’ epigenome affects reproductive health**

New research suggests fathers need to live healthy lives well before conceiving children.

LISETTE HILTON

When it comes to the health of their unborn children, fathers’ environmental and lifestyle-related exposures matter.¹

Potential epigenetic links between fathers and their offspring can be far reaching. One study, published in July 2016 in *Breast Cancer Research*, suggests paternal nutrition could affect a father’s future daughter’s risk of developing breast cancer. The researchers in this case used an animal-based, high-fat diet in rodents, which showed increased breast cancer risk in daughters after administration of the carcinogen 7,12-dimethylbenz[a]anthracene (DMBA).²

This study on a father’s influence on his daughter’s breast cancer risk contributes to a new area of research on environmentally induced risk for chronic diseases in offspring through the father, researchers write in another paper published in October 2016 in *Breast Cancer Research*.¹

“[F]ew epidemiological designs explore potential influences from the paternal environment of offspring health. This is surprising given that it’s surprising that whereas women are encouraged to improve their lifestyle habits, no specific recommendations are applied for male partners.”

—ADELHEID SOUBRY, MSC, PHD
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numerous animal models have provided evidence that the paternal environment plays a role in the non-genetic inheritance of preconceptional exposures through the male germ line,” according to Adelheid Soubry, MSC, PHD, an epigenetic epidemiologist and associate professor at KU Leuven University, Belgium. Soubry authored the paper “POHaD: Why we should study future fathers,” published in April 2018 in *Environmental Epigenetics.*³

**Why study fathers?**

Recent finding in humans suggest that the epigenome of sperm cells can indeed be affected by paternal exposures, says Soubry, who has been busy at epigenetic meetings advocating for the Paternal Origins of Health and Disease (POHaD) paradigm, to complement the more maternally focused Developmental Origins of Health and Disease (DOHaD) research field.

“For obvious reasons, future mothers have been targeted in terms of their lifestyle during pregnancy. A future mother needs to take care of her health, which will benefit her child. This is indeed important, and prevention and policies in this regard are necessary,” Soubry says.

During the last decade, researchers have been studying and have published on the potential effects on sperm epigenome and offspring of paternal obesity, lifestyle, nutrition, and more. For example, Soubry and colleagues have studied and shown epigenetic effects in offspring from paternal obesity⁴ and exposure to organophosphates in humans.⁵

“In a cross-sectional study in healthy volunteers living in North Carolina, we found an association between aberrant traces of environmental pollution (organophosphates, from exposures to flame-retardants) in the same individuals, suggesting transmission of harmful effects from a father’s environment to his child,” she says.

**Prepregnancy health includes both parents**

In essence, both parents’ lifestyles, environments, and health are important even before pregnancy for the health of the future child.

“The ‘preconceptional window’ and lifestyle during this period can change the epigenome in male and female germ cells, which can serve as a messenger from the environment toward the child,” Soubry says. “This can have both positive and negative consequences. Hence, ‘adaptation’ and ‘risk for diseases’ are 2 concepts that have come [to light].”

The terms “preconceptional window” and “exposure” need to be interpreted broadly, according to Soubry.

“Because of differences in the biology in male versus female germ cell development, we believe that windows of susceptibility are different by sex. An epigenetic change facilitated by the environment may differ if it was the developing oocyte or the sperm cell that was exposed earlier in life,” Soubry says.

It’s surprising, according to Soubry, that whereas women are encouraged to improve their lifestyle habits, no specific recommendations are applied for male partners. Animal and human studies suggest providers and others should encourage men to live healthy lives before having children, she says.

“More research, and more papers on this topic, will help us understand the mechanisms behind this, and help clinicians and the general public to implement these findings, so men and their partners are aware of the potential consequences of unhealthy lifestyle choices,” Soubry says.
Should antibiotics be prescribed for pink eye?

Viral conjunctivitis is the most common cause of infectious conjunctivitis, also known as pink eye.¹ With significant overlap between viral and bacterial infections in clinical signs and symptoms, a misdiagnosis of type could lead to serious complications, spread of infection, unnecessary antibiotic prescriptions, ocular allergies and toxicities associated with antibiotic use and antibiotic resistance.

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Fathers’ involvement in caretaking and emotionally supporting their spouses has a positive impact on their infants’ neurodevelopment, including motor, communication, and problem-solving skills, South Korean researchers report in a study published in December 2016 in *BMC Pediatrics*.1 Whereas this study on fathers’ involvement and its impact on neurodevelopment in their offspring focused on 3- and 4-month-old babies, researchers had previously reported that paternal engagement positively impacted older children.

"Father engagement seems to have differential effects on desirable outcomes by reducing the frequency of behavioral problems in boys and psychological problems in young women, and enhancing cognitive development, while decreasing delinquency and economic disadvantage in low [socioeconomic status] families," according to a review published in February 2008 in *Acta Paediatrica*.2 Paternal disengagement with infants as early as the third month of life is associated with behavioral problems in children at age 1 year, researchers reported in the *Journal of Child Psychology and Psychiatry and Allied Disciplines*,2 in January 2013.

**Study data supports fathers’ influence**

Because fathers’ roles are especially important during their offspring’s infancy,1 the South Korean researchers studied 255 married mothers of healthy infant boys and girls by surveying them about their husbands’ involvement, babies’ development, and maternal stress. Experts also visited participants’ homes to observe and report on infant neurodevelopment. The study’s aim was to look at the direct relationship between paternal involvement and infants’ neurodevelopment, as well as how maternal parenting stress might mediate that relationship.1

The researchers found:

- Paternal involvement had a positive relationship on infants’ neurodevelopment according to scoring on the developmental questionnaire completed by the experts making home visits.
- Fathers directly affected offspring’s neurodevelopment through such caretaking activities as diaper changes, dressing, and feeding their babies. Fathers also directly impacted their babies’ neurodevelopment by emotionally supporting their spouses.
- Mothers’ responses to such items as “My husband helps me by soothing the baby if he or she cries at night,” “My husband and I share the same values about child rearing,” and “It is very helpful to talk to my husband about our child” measured fathers’ caretaking activities and support from the mothers’ points of view.
- Parental distress, as indicated by mothers’ responses to items such as feeling trapped by parenting or that their babies rarely make them feel good, in part diminished the benefits of paternal involvement.

Further analysis showed that fathers’ involvement reduced mothers’ parenting stress, leading to positive infant outcomes, the authors write. Reducing maternal parenting stress is important because it directly influences infant development, negatively impacts parenting behavior, and delays stable attachment between parent and child, according to the researchers.

“The present study reveals that infant neurodevelopment benefits from paternal involvement even at 3 to 4 months. Although additional studies are necessary to confirm whether this benefit continues into later childhood,” say the investigators.

"Fathers also directly impacted their babies’ neurodevelopment by emotionally supporting their spouses."

For references, go to ContemporaryPediatrics.com/fathers-and-neurodevelopment

**Paternal involvement boosts infants’ neurodevelopment**

**Fathers taking an active role in childcare and supporting their spouse effect positive behavioral and emotional outcomes in their offspring.**

LISETTE HILTON

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Early paternal bonds impact offspring’s cardiovascular health

Parental roles are important to establishing healthy behaviors, but a new report delves into the cardiovascular effects of these relationships and the differences between maternal and paternal bonds.

RACHAEL ZIMLICH, RN, BSN

The relationship a child has with his or her parent early in life can set up the child’s own cardiovascular health for the teenaged years, and mothers and fathers have different influences on these trends.

Published in Preventive Medicine in March 2018, the study examines the effects that parent/child relationships in childhood could have on the development of cardiovascular risks by adolescence.

Researchers used 917 parent-child pairs from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Study of Early Child Care and Youth Development, investigating physical health and features as well as social elements of child/parent relationships and how they impacted cardiovascular health markers later in life.\(^1\)

The team found that overall, parent relationships had significant effect on cardiovascular health markers, but whether these effects were good or bad relied on the type of relationship and the parent involved.

Relationships with fathers were associated with increased growth rates of triceps skinfold thickness in teenaged girls, but not teenaged boys, according to the report. Additionally, conflict scores that were higher in maternal/daughter dyads led to increased growth rate in body mass index (BMI) percentiles among teenaged girls, whereas there were lower rates of BMI growth in paternal/son dyads with high conflict levels. Hostile paternal/daughter relationships were associated with increased triceps skinfold thickness in girls.

Although these measurements may seem insignificant in the teenaged years, they are indicators of lifelong health status. “A number of psychosocial stressors influence the development of cardiovascular health measures in youth,” the report notes.

Effects of maternal/paternal discord

However, there are some differences not only in how positive the parent relationship is in terms of how it impacts the child, but also which parent the relationship is with. Researchers found that hostile mother/son relationships were associated with increased BMI.

“The results indicate that boys’ adiposity development may be highly sensitive to the quality of paternal relationships,” the report notes. “This finding is consistent with previous findings that boys show more aggressive behaviors toward their parents and were more frequently exposed to parental conflict and hostility, and that boys might be more susceptible to adverse effects of family discord.”

In girls, too, high levels of conflict and hostility in paternal relationships increased adiposity measures in the teenaged years. “Our results indicate this dynamic may have a powerful impact on the development of maternal/son discord.”

Parental involvement and support early in life have long been shown to have significant impact on lifelong growth and development, but this study highlights that both positive and negative relationships impact health development, and that parental gender plays a role as well.

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of certain health measures during adolescence,” the report notes.

In fact, hostile paternal relationships between fathers and daughters had an impact on triceps skinfold thickness development that was 3-fold greater than the effect from maternal relationships.

“This finding might be explained by the fathering vulnerability hypothesis, which suggests that the father-child relationship appears more susceptible to the influence of parental hostility than mother-child relationship,” the study suggests.

“Thus, the results emphasized a more influential effect of the father in girls’ general adiposity development, rather than what is traditionally emphasized on mother’s influence.”

**Parent relationships and cardiovascular health**

Zhongzheng Niu, a PhD student in epidemiology at the University of Buffalo, New York, and the first author of the study, says the research was funded by the American Heart Association and highlights the importance of the parent relationship on future cardiovascular health, noting that these effects are modified by both the parents and the children.

“Our study found differences in the impacts on children’s cardiovascular health between maternal and paternal relationships with their children,” Niu says. “We first examined parent/child relationships in 2 separate domains—closeness and conflict. We found maternal conflict was associated with accelerated adiposity growth in girls and with accelerated heart rate growth in boys. Meanwhile, maternal closeness may have a protective effect as associated with decelerated heart rate growth in boys. However, none of these effects were observed in the father/child relationship.”

Several parent/child combinations were tested, Niu says, assessing different types of relationships and cardiovascular effects.

“Interestingly, we found a mother/child hostile relationship was associated with children’s blood pressure and heart rate, whereas father/child dramatic relationships were associated with children’s adiposity,” Niu says. “There is no direct answer to these observed differences. We deemed one possible reason is the different family functions of the father and the mother in the study cohort as a mother may spend more time and effects in taking care of the child than a father does, while a father may spend more time at work or so. Children also may have different perception of their parents and thus may have quite different reactions to their father and mother even if the underlying psychological stress is the same.”

**Effects of gender and sex**

Bin Xie, PhD, professor of Community and Global Health at Claremont Graduate University, Claremont, California, and the principal investigator of the study, says previous studies have focused on parents as a whole or maternal impacts on teenagers.

“We found the impact of the parent/child relationship on adolescent cardiovascular health not only depends on the gender of the parents but also on the sex of the child. In particular, the mother/child relationship seems to affect only boys’ blood pressure and heart rate but not on girls,” Xie says. “Interestingly, a dramatic paternal relationship may accelerate adiposity growth in boys but may decelerate that in girls. This may be due to different weight perception between boys and girls, and their different perceptions of the father’s role. There were also other studies that found boys showed more aggressive behavior toward their parents than girls, and that boys might be more susceptible to adverse effects of family discord than girls are.”

More research is needed to determine more specifically the influences fathers have separate from mothers, but Xie says there are some early ideas that help explain the difference in paternal

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In 2016, fathers reported spending on average 8 hours a week on childcare—about triple the time spent in 1965.

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In 2017, 68% of fathers who see gender differences in parenting styles say these differences are mostly based on biology.
effects on children.

“Research on parental attachment has suggested some qualitative differences between fathers and mothers in terms of their responses to child distress,” Xie says. “Fathers provide emotional support to their children through encouraging independence and exploration, whereas mothers provide emotional support by responding sensitively to child distress.”

It’s important to understand the factors that lead to accelerated adiposity growth in childhood, Niu says, because it’s such an important risk factor of obesity later in life. It can also lead to increased blood pressure and heart rates, which are 2 independent risk factors of future heart disease.

“Our study results indicate that warmth in parental relationship with children may impact their future cardiovascular health,” Niu says. “Pediatricians may provide guidance on fostering a warmer and less hostile relationship between parents and children. In addition, one cannot ignore the father’s important role in protecting children from initiating undesirable development of cardiovascular health later in life.”

Xie adds that there is much more researchers need to know, but it’s clear that parent relationships play a big role in cardiovascular health development.

“As adolescents may undergo a phase with sensitive feelings and vulnerability to family relationships, more patience and warmth are needed to protect them from obesity and undesirable trajectories of future health,” Xie says. “Further research is also needed to understand the mechanisms underlying the associations observed in this study.”

REFERENCE


Older fathers linked to problems with pregnancies, births

Motors usually take the title of geriatric pregnancy at an advanced age, but research suggests older fathers may have to take on that title as well.

RACHAEL ZIMLICH, RN, BSN

While maternal age remains one of the biggest influencers on infant morbidity, fathers play an important role, too.

Michael Eisenberg, MD, associate professor of Urology and Obstetrics and Gynecology at Stanford University, Stanford, California, and co-author of a new study on paternal age, says the report highlights the fact that the mother’s age isn’t the only one impacting birth outcomes.

“The etiology remains uncertain. Investigators have postulated genetic or epigenetic effects that may occur as the father ages, which may lead to the offspring and maternal outcomes that were observed,” Eisenberg says.

The purpose of the study, published in the *BMJ*, was conducted to evaluate the effect of paternal age on maternal and perinatal outcomes. Traditionally, maternal age is the primary concern in many cases when assessing the risk status of a pregnancy. However this study shows that higher paternal age was associated with an increased risk of premature birth, low birth weight, and low Apgar scores. More specifically, the research team found that infants born to fathers aged older than 45 years had 14% higher odds of premature birth and 18% higher odds of seizures compared with infants born to fathers aged 25 to 34 years. The odds of a mother developing gestational diabetes were also 34% higher in mothers with the oldest partners, and 13.2% of premature births and 18.2% of gestational diabetes in births were attributed to advanced paternal age.

Paternal age is trending up

Whereas there is a relatively low prevalence of high paternal age in the United States, it is trending up. According to the report, paternal age has doubled in the United States over the past generation, making it increasingly important to understand the impact that paternal age has on outcomes rather than focusing on maternal age.

The number of births to women aged older than 35 years has increased
by about 2% each year since the 1970s, according to the report, and births to fathers aged 40 years and older have doubled to 9% over the same period. The effects of maternal age on perinatal outcomes have been studied extensively, but there has been limited information on the effect of paternal age outside congenital diseases. Previously, advanced paternal age and the number of male germ cell divisions in those fathers have been linked to increased prevalence of autism, genetic abnormalities, psychiatric morbidity, and neoplasia in children. However, more recent studies have turned to investigating the paternal effect on perinatal morbidity overall.

Research suggests that epigenetic changes occur within spermatocytes in the same regions that are responsible for several diseases in children of fathers of advanced age. Alterations to developing germ cells could be a precursor to embryonic and placental development, the report notes, with some studies suggesting that paternal imprinting of aging could affect both fetal growth and maternal health during pregnancy.

Given the fact that older fathers are still not all that common in the United States, it has been difficult to provide conclusive data given small samples sizes, the report notes. However, using data from the National Vital Statistics System, researchers investigated more than 40 million live births between 2007 and 2016. After adjusting for multiple other factors that could contribute to infant morbidity, the team found that the oldest fathers were associated with the worst outcomes. Gestational ages were lower in infants whose fathers were aged older than 45 years, and those infants had 45% higher odds of preterm birth. There were no differences when in-vitro fertilization results were excluded.

**Fathers’ age impacts mothers, too**

The study also investigated the impact of the pregnancy on mothers whose partners were of advanced age. Having a partner aged older than 45 years increased the rate of gestational diabetes in mothers by 28%.

The research team notes that because the study was carried out using data from multiple decades with similar results across the study period, it indicates that the trends seen in this study were not influenced by more recent changes to medical practice.

Overall, the research team attributed 13.2% of premature birth, 14.5% of low-birth-weight births, 15.1% of neonatal intensive care unit admissions, and 18.2% of gestational diabetes cases to fathers who were aged older than 45 years.

Eisenberg says that although this study did not directly compare outcomes between maternal and paternal ages, it is fair to assume that maternal age remains more impactful to infant morbidity. The information in this study, however, highlights that there is a paternal effect present, and the information from this study may help guide future research and decision-making.

"I think the study provides further information to couples about reproduction. Whereas many factors go into deciding when to start a family, the study provides data on how to incorporate the father’s age," Eisenberg says. "I think the message is to understand that fertility is a team sport and both members are important."

**REFERENCE**


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Number of US men with at least 1 child who either agree or strongly agree that “the rewards of being a parent are worth it, despite the cost and the work it takes.”

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How to identify and treat bullying

Bullying is a preventable health problem that has lasting impacts. Pediatricians need to screen patients for risk factors, empower families with coping skills, and advocate for antibullying resources in their communities.

Although bullying was once thought of as a rite of passage into adulthood, it is now more appropriately considered a preventable health problem that not only has lasting impacts, but that the pediatrician can address in his or her office. This article will describe what bullying is, its impacts on the child, risk factors for bullying, and finally how the pediatrician can address bullying in the office.

**Definition of bullying**

The Centers for Disease Control and Prevention (CDC) defines bullying as “any unwanted aggressive behavior(s) by another youth or group of youths that are not siblings or current dating partners that involves an observed or perceived power imbalance and is repeated multiple times or is highly likely to be repeated. Bullying may inflict harm or distress on the targeted youth including physical, psychological, social, or educational harm.”

Cyberbullying uses social media and other electronic means in order to hurt others. It is different from traditional bullying in that it can be done at any time, often anonymously, and spread to a greater audience quickly. Not surprisingly, young persons involved as both bullies and victims are frequent users of electronic media, and there is significant overlap in the characteristics of both traditional and cyberbullying.

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Magnitude and consequences

Estimates of traditional bullying at school and cyberbullying range from 18% to 31% and 7% to 15%, respectively. The 2013 National Youth Risk Behavior Surveillance System (YRBSS) estimated that approximately 20% of high school students were bullied and 15% were cyberbullied.4

Victims of bullying are at increased risk for a number of adverse consequences such as:
- Depression⁵
- Anxiety⁴
- Relationship problems⁶
- Poor health¹
- Poor academic performance³
- Suicidal ideation and attempts⁵

Likewise, children who only bully are more likely to develop antisocial personality disorder and participate in criminality. Recent research has additionally identified another high-risk group—the “bully/victim.” These children not only bully other children but are also the victims of bullying. Observational research indicates that these children experience overall worse outcomes through adulthood.

The bully/victim:
- Engages in more acts of bullying compared with a pure bully.⁷
- Experiences more thoughts of self-harm and suicidality.⁴
- Is more likely to have mental health issues in childhood and more intense anxiety and depression.⁶,⁹
- Is more likely to smoke and participate in other substance abuse.⁶,¹⁰
- Is less likely to graduate high school.⁶
- Experiences more intense anxiety and depression.¹⁰
- Is more likely to be socially isolated and may not have any friends at all.⁷

Risk factors

Whereas there are a number of methodological issues with attempting to identify independent risk factors associated with bullying, the literature is able to identify many children impacted by bullying.⁴

INDIVIDUAL RISK FACTORS

Boys are at greater risk of being physically bullied and girls are at greater risk of being emotionally or cyberbullied.⁴

Lesbian, gay, bisexual, transgender, and questioning/queer (LGBTQ) adolescents report being victims of bullying more than twice as often as their heterosexual peers. These LGBTQ youth also are less likely to report it.¹,¹² This may be a factor in increased risk of suicide among this group. More supportive environments (schools with gay-straight alliances and antibullying policies specifically protecting LGBTQ adolescents) were associated with fewer suicide attempts.¹³,¹⁴

HEALTH CONDITIONS

Overweight children are more than twice as likely to be bullied than their normal-weight peers.¹⁵,¹⁶ Children with autism spectrum disorder, attention-deficit/hyperactivity disorder (ADHD), and learning disabilities also report increased risk of being bullied.¹⁷ Finally, children with chronic conditions such as epilepsy or food allergy also report increased rates of being bullied.¹⁸

ENVIRONMENTAL RISK FACTORS

A child’s relationship with peers impacts his/her risk of being bullied. Middle school children who make friends more easily are less likely to be bullied than those reporting more difficulty.¹¹

A number of parenting behaviors have relationships to bullying, although the effect size was small for youth involved as victims and moderate for those involved as bully/victims.¹⁹ Negative parenting behaviors increase risk of being involved as a victim and bully/victim whereas overprotection was only associated with being a victim.¹⁹ Low socioeconomic status is also associated with increased risk of being bullied.²⁰

Protective factors

A number of factors have been found to be protective of both becoming
a bullying victim as well as on adverse effects of bullying. Parent connectedness or some form of caring adult is protective for young persons involved as bullies and victims whereas having caring friends further protected youth who are involved as victims.21 Positive parenting also has been noted to have small to moderate effects on bullying.19

Although school climate is challenging to study due to a number of methodological issues, it can impact bullying. The Olweus Bullying Prevention Program significantly decreased bullying in Norwegian schools but has been difficult to replicate in US schools.22,23 Positive school climate has been found to have a small to moderate effect on decreasing bullying.24 Providing teachers engage, telling teachers is one coping strategy; others include ignoring the situation and taking steps to avoid a bullying situation altogether. Finally, empowering children with better skills to cope with their own feelings related to bullying behavior can be protective.

What the pediatrician can do
The pediatrician can incorporate a process both to screen for bullying as well as to provide support and resources for parents and caregivers.

As with many other issues impacting pediatrics, the pediatrician:
1. Identifies the problem.
2. Gathers more information.
3. Intervenes and provides support.

IDENTIFY BULLYING
Systematically screening is one way to identify bullying across an entire practice. Bright Futures questionnaires include age-appropriate questions about bullying.25 The HEEADSSS inventory (Home, Education/Employment, Eating, Activities, Drugs, Sexuality, Suicide/Depression, and Safety)26 is a framework to take comprehensive social history from an adolescent that can identify bullying. (For other published questionnaires that are available for pediatricians, see “Additional clinician resources,” left.)

The review of systems may reveal somatic complaints such as abdominal pain or headaches that may be associated with bullying. Additional warning signs that would prompt the pediatrician to examine bullying more closely include social withdrawal, school absenteeism, declining grades, behavioral problems, and suicidal ideation.

GATHER MORE INFORMATION
After identifying bullying, the next step is to understand the circumstances surrounding bullying. It is important for the pediatrician to identify when, where and how often bullying is occurring. Providers should determine context (e.g., is the bullying direct [being hit, slapped, or pushed] or indirect [rumors or cyberbullying]). It also may be important to get information from teachers. If indicated, consider validated screens for anxieties and depression.

Additionally, the pediatrician needs to be aware that the behaviors may represent another type of hurtful behavior altogether such as peer conflict, dating violence, harassment, or hazing. Finally, the pediatrician needs to incorporate the previously mentioned risk factors and protective factors into...
Lesbian, gay, bisexual, transgender, and questioning/queer (LGBTQ) adolescents report being victims of bullying more than twice as often as their heterosexual peers. These LGBTQ youth also are less likely to report it.1,12

their assessment and plans for the bullied child.

INITIATE INTERVENTION

Interventions can range from individual to programmatic. The following suggestions focus on what the pediatrician can do in his/her office.

1 ENSURE SAFETY. Although most cases can be handled in the office setting, it is important for the pediatrician to identify if a child is in imminent danger or has been the victim of physical or sexual abuse. When necessary, the pediatrician must contact the appropriate law enforcement authorities and school. Likewise, if the pediatrician is concerned about suicidality, he/she must contact an appropriate mental health professional or transport the patient to the emergency department.

2 BUILD SKILLS. Through role playing in the office and encouraging caregivers to model at home, children can learn how to respond to bullying.

One possible method of interaction with a bully that can be modeled is as follows:

- Look directly at the bully and confidently speak to him/her in a firm, loud voice. Examples might include:
  - “You don’t scare me!”
  - “Be really cool and stop this!”
  - “Why are you talking to me?”
- Immediately walk away with confidence (do not run) and with your head held high.
- Tell a parent or teacher.

Children may need to be told to tell a different adult if they have previously reported bullying and nothing was done. As many children do not report bullying, it is also important to explain to them that discussing with an adult will not only provide support but will also help develop a plan to stop bullying.

If the child is a victim of cyberbullying, the pediatrician can recommend:

- Don’t forward, respond, or “like” online content that is harmful to others.
- Keep evidence of cyberbullying such as dates, times, descriptions, screen shots, e-mails, and texts.
- Block the cyberbully.
- Talk to a trusted adult.
- Report bullying to school and law enforcement as appropriate.

At a more general level, the pediatrician should incorporate being a good digital citizen into age-appropriate education. Parents should be encouraged to be aware of what their kids are doing online and to talk with their children about how text and other online content can be perceived and the very real-world consequences of it. Parents need to remind children that digital content can spread quickly online and discuss what to do if they or someone else is being victimized by a cyberbully.

3 RECOMMENDATIONS AND FOLLOW-UP. Invariably, the school should be involved. The pediatrician should advise parents and caregivers to meet with teachers or counselors to discuss concerns and work up the school administrative ladder if needed. Additionally, the pediatrician can consider calling or writing to a teacher/counselor to discuss concerns.

Provide parents and youth with recognized resources, such as stopbullying.gov.

Just as with any other medical problem, the pediatrician should offer a follow-up visit. If initial interventions are not successful or have worsened, consider referral to a mental health professional.

4 OUTSIDE INDIVIDUAL CARE. Outside the care of individual patients, the pediatrician can advocate locally, regionally, and nationally to prevent and provide programs surrounding bullying. Most states have laws to prevent bullying in schools, but there is significant variation in the strengths of these laws.

Consider working with schools and local policymakers to strengthen antibullying laws, provide education, and improve services.

Empower adults and kids to stop bullying

When parents or teachers see bullying in progress, they should step in and stop it. However, because most bullying takes place outside the presence of adults, can interventions empower students to stop bullying? Hawkins demonstrated that when student bystanders intervened, 57% of episodes ceased within 10 seconds.27 The problem is that children intervene only 15% to 20% of the time.28
A school-based antibullying program in Finland—KiVa—takes a multipronged approach to try to decrease bullying and its impacts. Its goals are to:
- Increase awareness that groups play in maintaining bullying.
- Promote empathy toward victims.
- Promote children’s skills in supporting the victim and increase their self-efficacy to do so.
- Increase coping skills for the victimized.

In intervention schools, peers both defended victims more commonly and had greater antibullying attitudes as well as empathy toward victims of bullying. Self-reported victimization and bullying decreased in intervention sites by 30% and 17%, respectively.

Condemn the behavior, not the bully
Garandeau looked at the intentions of youth who bully to change behavior as part of a school-based intervention wherein schools were randomized to a confrontational versus nonconfrontational method of dealing with a bullying incident. Those who bullied were anonymously surveyed following the incident.

Condemning the behavior and making those who bullied feel empathy for the victim were significantly associated with more intentions to stop bullying compared with those treated with the confrontational approach.

Screen bullies for psychiatric or behavioral problems
Sourander found that large numbers of youth involved as pure bullies and bully/victims demonstrated symptoms that may indicate a psychiatric problem. Advocating for more mental health services to get children the help they need rather than asking school systems to handle these problems is another area of potential advocacy.

In conclusion
Bullying is a significant problem impacting young persons today. Pediatricians need to be aware of risk factors and impacts, and develop office-based systems to screen for and address this problem. Further, the pediatrician needs to be aware of and advocate for more antibullying resources in his/her community.

The authors have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

For references, go to ContemporaryPediatrics.com/identify-bullying
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Unfortunately, patients are often non-compliant with recommendations by pediatricians. Many parents fail to fill prescribed medications, and those that do often do not complete a full course of therapy. Patients frequently do not see consultants once referrals are made or make dental appointments for their children. Let’s take a look at the many reasons for noncompliance among patients and parents, and detail solutions that will improve compliance rates for a wide variety of issues.

**Routine care outside the medical home**

One of the most egregious compliance failures is when patients don’t see their primary care physician for routine illnesses or well-child checks and choose instead to utilize urgent care clinics (UCCs).

There are many reasons for this. First and foremost, office visits can be expensive, and most parents have high-deductible insurance plans as a consequence of the Affordable Care Act. Parents save substantially by using the UCC down the street rather than making an appointment to be seen in your office. Many pediatric practices do not provide the extended evening and weekend hours that UCCs provide, and many practices do not facilitate access to care (see "Improve your practice: Facilitate patient access, Contemporary Pediatrics, January 2017)."

In many pediatric practices, parents may be subjected to long waits on hold in order to speak with a secretary; convenient appointments often are not available; and patients are sometimes compelled to speak with a triage nurse even before an appointment is permitted to be scheduled. Additionally, if a family is enrolled in a large practice, they may not be able to see their own primary care provider due to availability of appointments.

As a consequence, the patient’s “medical home” is broken, care is fragmented, and unless practices take appropriate actions to remedy this situation, parents will continue to utilize UCCs. (See “Renovating your medical home,” Contemporary Pediatrics, July 2014). The solution is simple. You need to modify your practice to compete with UCCs. This means modifying your practice style to improve availability; lower patient costs (see “How to help parents cut healthcare costs,” Contemporary Pediatrics, February 2018); and modify your schedule to accommodate walk-in patients.

If patients had a choice, most would prefer to see their own physician who is familiar with the patient and family. Primary care pediatricians can promote patient allegiance, and dissuade patients from using UCCs, by adopting the policy of shared decision-making; ie, giving patients options for diagnosis strategies and management. By partnering with patients, rather than providing inflexible recommendations, compliance is likely to improve significantly.
WHAT ABOUT OUR OWN COMPLIANCE?

I WOULD BE REMISS, in an article about patient/parent compliance, if I did not take the opportunity to remind pediatricians that there are many pediatric practices that are not compliant with the Bright Futures guidelines for preventive care services. Many practices do not screen patients at risk for lead poisoning, perhaps assuming it will be done by Women, Infant, and Children (WIC) programs. Many do not perform hearing and vision screening on young children because the equipment is expensive. In addition, many pediatricians do not perform blood pressure measurements on young children; have integrated developmental screening into their practices; or perform lipid screening at recommended ages.

In addition, we are not very compliant with quality measures developed by the National Committee for Quality Assurance (NCQA) to benchmark the medical care provided to children (see Table). We cannot expect patients to be compliant with our recommendations if we are not compliant with our own! —ANDREW J SCHUMAN, MD, FAAP

### Compliance varies with diagnosis

Parents’ compliance with recommendations depends on the parental perception of the diagnosis as well as the consequences of noncompliance. For example, consider a child with new-onset seizure disorder. Seizures are a dramatic and frightening event for children and families. Parents will tend to be compliant with administering anticonvulsant medication in order to prevent further seizures and will almost always attend follow-up visits for repeat electroencephalograms (EEGs), imaging studies, and neurologists’ consultations. Similarly, one would expect excellent compliance on the part of parents whose children are diagnosed with cancers, hematologic disorders, and diabetes, to name a few. For these conditions, the lack of compliance may have devastating consequences.

In my experience, responsible parents of children with attention-deficit/hyperactivity disorder (ADHD) who are well controlled with medication are likely to make and keep regular follow-up appointments for medication renewals. In contrast, when patients are given a less “profound” diagnosis, for which the consequences of noncompliance are likely not severe, then parents are likely to let follow-up appointments slip, and only seek new guidance when there are exacerbations of a chronic medical condition.

<table>
<thead>
<tr>
<th>MEASURE</th>
<th>COMMERCIAL INSURANCE %</th>
<th>MEDICAID %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documentation of BMI percentile</td>
<td>70.3</td>
<td>72.5</td>
</tr>
<tr>
<td>Pediatric patients receiving nutrition counseling</td>
<td>64.3</td>
<td>67.1</td>
</tr>
<tr>
<td>Pediatric patients receiving physical activity counseling</td>
<td>59.5</td>
<td>60.6</td>
</tr>
<tr>
<td>Children up-to-date with immunizations by age 2 y</td>
<td>53.4</td>
<td>35.4</td>
</tr>
<tr>
<td>Chlamydia screening of sexually active women aged ≥16 y</td>
<td>43.7</td>
<td>54.2</td>
</tr>
<tr>
<td>Appropriate use of strep tests before prescribing antibiotic</td>
<td>86.8</td>
<td>78.3</td>
</tr>
<tr>
<td>Appropriate follow-up care for children prescribed medication for ADHD</td>
<td>41.6</td>
<td>44.6</td>
</tr>
<tr>
<td>Children diagnosed with URI and not given antibiotic</td>
<td>88.8</td>
<td>89.1</td>
</tr>
</tbody>
</table>

amples of these situations are many and include compliance for regimens given for constipation, allergies, asthma, and many others.

Make compliance easy
It is easier to comply with a provider’s recommendations when your practice makes efforts to facilitate compliance. Parents are much more likely to agree to have a lead screening and hemoglobin test done if you perform these tests in your office using point-of-care devices. Consider offering the fluoride varnish application to young patients so parents will not need to visit their dentist to have this done. If a child fails an otoacoustic emission (OAE) hearing screen, it would be advantageous to be able to perform a pure tone audiogram in your office rather than refer a patient to an audiologist.

Consider performing point-of-care polymerase chain reaction (PCR)-based strep tests so patients won’t need to wait for lab confirmation days later when a throat culture returns. In addition, many pediatricians have integrated mental health providers including psychiatrists or psychologists into their practice to facilitate access to mental health services. There are many ways practices can be creative in order to improve compliance.

Use education and care coordinators
Another way to improve compliance is to educate parents about the consequences of noncompliance. These may include recurrence of an ear infection if the antibiotic is not administered correctly or for the duration recommended; wheezing in the asthmatic child who fails to take controller medications regularly; or out-of-control blood sugars for the diabetic child who does not monitor sugars as advised. Reminders sent by e-mail can be helpful.

Helpful, too, is the incorporation of a care coordinator, usually a nurse with special training, into your practice. Following a visit, have selected patients visit your care coordinator prior to checkout. The coordinator can book referrals and schedule imaging studies, which will dramatically increase the likelihood of compliance. Thus, the patient leaves with a scheduled appointment for services in hand, rather than “getting around” to making the appointment themselves. The coordinator also can be used to reinforce instructions you provide patients, or, if necessary, take a few minutes to educate patients.

Care coordinators also can be utilized to contact patients several days following a visit to check in. These calls are much appreciated by patients and build confidence in you and your practice, increasing the likelihood of future compliance.

Telehealth improves compliance
I’ve been a fan of Telehealth for years. Now that my state has mandated coverage for Telehealth visits, I have assimilated this service into my own clinic and use it routinely.

Although I typically use Telehealth visits for patients being treated for ADHD, depression, and anxiety, such visits can be used for patients with acne, asthma, conjunctivitis, rashes, and other conditions not requiring auscultation or an otoscopic examination. A telehealth visit also can be used by nursing staff to triage patients and provide advice.

Because FaceTime video communications are now universally accepted by patients, pediatric practices would be well advised to have nursing and office staff communicate with patients routinely via HIPAA-compliant video calls. (The Health Insurance Portability and Accountability Act [HIPAA] of 1996 provides data privacy and security for patients’ medical information.) One can communicate more effectively by interacting with parents and patients face-to-face as you do in the office, because this method lets you determine the parent’s level of concern and visually determine where and when an ill child needs to be seen.

In conclusion
This article has described measures that will improve patient access and compliance with your recommendations. If you transform your practice, you will be able to preserve the patient’s medical home and encourage parents to bypass the UCCs that are now on every street corner.

Dr. Schuman, section editor for Practice Improvement and Editorial Advisory Board member of Contemporary Pediatrics, is clinical assistant professor of Pediatrics, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire. He is CEO of Medgizmos.com, a medical technology review site for primary care physicians.
patients will lack systemic symptoms such as flushing, gastrointestinal (GI) symptoms, bone pain, syncope, or bronchospasm. If the exam is equivocal, biopsy can be done and will show increased mast cell numbers or activating KIT mutations.¹

**Differential diagnosis**

It is essential to distinguish these lesions from cafe-au-lait macules (CALM), which can be associated with a diagnosis of neurofibromatosis type 1 (NF1). The borders of UP lesions are ill defined compared with the well-demarcated borders of CALM. Also, CALM will not urticate. Severe cases of UP can blister and can be mistaken for bullous dermatoses such as epidermolysis bullosa and linear immunoglobulin (Ig) A bullous dermatosis. Lastly, these lesions can be confused with arthropod bites or juvenile xanthogranulomas.⁴

**Management**

Because these lesions will likely resolve without sequelae, patients can be monitored annually at their well-child visits, and no treatment is required. Symptomatic therapy with topical corticosteroids and oral antihistamines can be offered to combat pruritus.⁵ Although systemic involvement is rare in children, it can be evaluated and ruled out with a complete blood count with differential, liver function tests, and a serum total tryptase.⁶ Patients with systemic symptoms can be managed with oral antihistamines, antileukotriene drugs, and omalizumab.⁷

**Patient outcome**

Clinicians reassured the patient and her mother that the spots were benign mastocytomas rather than cafe-au-lait macules and that they did not have to worry about neurofibromatosis. The mother was counseled about the benign nature of the spots and told that there was no treatment or further evaluation needed for her daughter unless anything changed. □

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**The characteristic lesions in UP are scattered small (1-cm to 2-cm), red-brown or yellow-tan thin papules or plaques that develop a wheal and erythema upon physical manipulation (Darier sign).**

---

**Ms Marchalik** is a fourth-year medical student, Georgetown University School of Medicine, Washington, DC.

**Ms Shrock** is a fourth-year medical student, Johns Hopkins University School of Medicine, Baltimore, Maryland.

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we make the diagnosis as early as possible, and therefore pediatricians are really the first to think about possible diagnosis and to make the appropriate referrals or do the appropriate initial testing.

So, when should pediatricians think about Turner syndrome? First and foremost, if one deals with a girl or adolescent who has unexplained short stature, one has to rule out Turner syndrome. If one deals with an adolescent girl who has delayed onset of puberty, who has primary amenorrhea, one needs to rule out Turner syndrome. In any newborn with the diagnosis of lymphedema or a significant left-sided heart defect like a bicuspid aortic valve, one has to think of Turner syndrome. Also, in any girl who has the typical phenotypic facial features of Turner syndrome, one also should consider that an absolute indication for genetic testing to rule out Turner syndrome. Some of the typical phenotypic facial features of a girl with Turner syndrome will include bilateral ptosis of the eyelids, somewhat low-set but prominent external ears, maybe a small mandible that’s retrognathic, a high-arched palate, and a short and sometimes wide neck or a girl who presents with swelling of the hands and feet in the first years of life. These are absolute indications for testing for Turner syndrome and that testing is done by doing a karyotype, a cytogenetic analysis of the patient’s chromosome.

Q. Once pediatricians do decide they meet the kind of characteristics for a patient and they’ve thought about referring to a specialist, what are the best treatment options available, in your opinion? How do we treat patients with Turner syndrome?

A. That’s a good question. The primary subspecialist who manages Turner syndrome is a pediatric endocrinologist and that has to do with the many comorbidities related to the hormonal system—short stature and delayed puberty and, of course, infertility. When a pediatrician thinks that the child he or she examines could have Turner syndrome, he or she should always call the endocrinologist to discuss this, but one should feel free to do the karyotyping.

Once the diagnosis is confirmed, a number of screening tests need to be done because they’re so important for long-term morbidity and mortality. The screening tests include a referral to Cardiology to rule out underlying heart disease, which is most often left-sided congenital heart disease. A referral also needs to be done to Radiology for renal ultrasound because about a third of girls with Turner syndrome have kidney abnormalities. A referral also should be made to Pediatric Endocrinology. Usually the pediatric endocrinologist coordinates these other referrals that I just mentioned but the specific reasons to refer to Pediatric Endocrinology are to treat the short stature and to treat the delayed puberty.

The short stature can be treated adequately with growth hormone therapy, and the earlier the diagnosis is made, the earlier treatment can be started and the more likely it is that there will be a much-improved adult height outcome. The treatment of puberty consists of, first, an assessment of the patient’s potential to have some typical changes on her own. If that is not the case, puberty is induced by estrogen replacement therapy and progestin replacement therapy in a manner to duplicate what usually happens naturally.

Discussions need to be done regarding the potential for infertility, and oocyte retrieval is a possibility in some girls to preserve long-term fertility. Some girls with Turner syndrome do have spontaneous onset of puberty and may go through puberty on their own, although most of these girls will do so incompletely and may still need estrogen treatment. Very few girls have menstruation on their own and a very, very small amount of Turner syndrome women are able to cycle.
recognize & refer

“The crucial thing, and I cannot underscore this enough, is that people need to think about Turner syndrome as an explanation for a girl who doesn’t grow normally, who falls off the growth curves.” —PHILIPPE F. BACKELJAUW, MD

These comorbidities have variable prevalences but some of the most common ones are hypothyroidism and cardiovascular morbidity.

Q. Thank you so much. You gave us a lot of great information. Is there anything else you’d like to add just for community practitioners?

A. Yes. The crucial thing again, and I cannot underscore this enough, is the earlier diagnosis and that people need to think about the possibility of having Turner syndrome as an explanation for a girl who doesn’t grow normally, who falls off the growth curves. One doesn’t necessarily have to wait until the girl is below the third percentile. If there is a growth deceleration at any point in her childhood or adolescence that cannot be explained by another reason, one has to think of Turner syndrome. If a girl is late with puberty, one has to think of Turner syndrome. If a girl has had the beginning of puberty but does not have onset of menstruation and has primary amenorrhea or secondary amenorrhea, the provider needs to think of the possibility of Turner syndrome. The neonatologist needs to think of Turner syndrome with any neonate who has some of the typical features or some of the congenital heart disease.

It happens too often that people just don’t think about Turner syndrome and that’s the main message. Think about it and talk with colleagues, look up the typical features. The findings may be subtle, but people need to first think about Turner syndrome in order for them to be able to make the decision to order the test. That’s of crucial importance.

Dr Johanek is a staff pharmacist at Southwest General Health Center, Middleburg Heights, Ohio. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.
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Fuzzy brown spots on a healthy 3-year-old

RACHEL MARCHALIK, BA, MS4; CHRISTINE SHROCK, AB, MS4; BERNARD COHEN, MD

A healthy 3-year-old girl presents for evaluation of light brown spots on her trunk and extremities that have appeared over the last 2 years. The spots are not symptomatic but the girl’s parents are worried that she could have neurofibromatosis.

FIGURE Note the light brown, slightly elevated papules and plaques on the patient’s back. These areas urticated when rubbed.

URTICARIA PIGMENTOSA

Discussion

First described in 1869 by Nettleship and Tay, mastocytosis is a pathogenic expansion of mast cells. It is considered a clonal disease attributed to activation mutations found in the C-Kit gene, which leads to increased survival and proliferation of mast cells. Disease can be limited to the skin, or it can involve other organs such as the bone marrow, gastrointestinal tract, liver, or spleen. In children, 9 of 10 cases are cutaneous, the majority of which are urticaria pigmentosa (UP), also called maculopapular mastocytosis.

In a systematic review of 1747 cases by Méni and colleagues, 90% of cases presented by the age of 2 years, and almost 70% of cases at least partially regressed. Urticaria pigmentosa is more common in boys, although the sex-ratio data inverts in adulthood.

In the Figure, note the lesion on the top-right side of the patient’s back. It urticated when rubbed while the area to the left with normal skin did not.

Clinical findings

The characteristic lesions in UP are scattered small (1-cm to 2-cm), red-brown or yellow-tan thin papules or plaques that develop a wheal and erythema upon physical manipulation (Darier sign). These lesions also can have increased skin markings. Most
Dr. Backeljauw, can you tell us a little bit about Turner syndrome and why you think that’s something of particular concern for pediatricians?

Turner syndrome is a disorder that solely affects females, so girls and women can be diagnosed as having Turner syndrome. It is the most common sex chromosome disorder for females and it is caused by a complete or partial loss of 1 of the 2 sex chromosomes. In other words, Turner syndrome females will have 1 X-chromosome that’s normal and then they may miss the second X-chromosome, or they may miss part of the X-chromosome, or they may have an abnormal sex chromosome that could be an abnormal Y-chromosome. Because they lose a second sex chromosome, they can present with a number of clinical features, some of them known as sort of classic Turner syndrome features. Nowadays, we like to view Turner syndrome from a broader perspective, and the few clinical features with which it may present may simply be short stature or delayed puberty or absence of menstrual periods—amenorrhea—and they may have little-to-no other phenotypic features. Patients may not have a lot of facial characteristics of Turner’s, and they may not have some of the classic comorbidities. That’s sort of what Turner syndrome is about.

Now, why it is important for primary care doctors to know about Turner syndrome is that they are most often the first-line physicians and providers to diagnose girls with Turner syndrome, and they should be aware of what the clinical presentation can be and what the absolute indications are to diagnose a girl with Turner syndrome. In the United States, if a girl with Turner syndrome is not diagnosed prenatally or is not diagnosed during infancy by the neonatal period or the first year of life, very often the diagnosis is not made until age 8 or 9 years. Girls with Turner syndrome sometimes get diagnosed as late as age 12 to 15 years, and many women end up being diagnosed during adulthood. In order to provide the best care, make the best recommendations for clinical management of all the potential comorbidities, it is essential that
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