Assessment of Dyslipidemia in Children and Adolescents

By Amy L. Peterson, MD

Educational Objectives
After reading this article and answering the review questions, the reader will be able to:

1. Describe the importance of lipid screening for cardiovascular health in pediatric patients
2. Order appropriate lipid screening tests and accurately interpret results
3. Design a treatment plan for common patterns of pediatric dyslipidemia

Case
Michael, a 12-year-old male, is seen in your clinic; his mother wants her son “checked out” because heart disease runs in the family. Michael’s father recently underwent coronary artery bypass grafting at 33 years of age after developing severe chest pain. The father’s total cholesterol (TC) was greater than 500 mg/dL. Michael’s paternal grandmother died of a heart attack at the age of 52. Further review shows that Michael’s BMI has been tracking along the 95th percentile but has recently started to increase. His mother reports that she has been scared to let him exercise because he might have a heart attack. Michael reports his favorite foods are pizza, ice cream, and macaroni and cheese. He drinks 2% milk and refuses to eat vegetables, as he considers them to be “rabbit food.”

Michael’s fasting lipid profile shows a TC of 320 mg/dL, low-density lipoprotein (LDL) of 254 mg/dL, high-density lipoprotein (HDL) of 45 mg/dL, and triglycerides (TG) of 80 mg/dL.

Case Discussion
Familial Hypercholesterolemia

Disclosure:
The FDA has approved atorvastatin, rosuvastatin, simvastatin, fluvastatin, lovastatin, ezetimibe, and colesevelam for the treatment of pediatric heterozygous and homozygous Familial Hypercholesterolemia in children 10 years of age and older. Pravastatin is FDA-approved for the same indications in children as young as 8 years old. Any other descriptions of medication use in this article are off-label uses.

– continued on page 2
This patient meets clinical diagnostic criteria for Familial Hypercholesterolemia (FH). FH is an autosomal dominant inherited disorder affecting 1 in 300 to 500 people, and is considered to be the most common life-threatening inherited condition. It is characterized by a markedly elevated LDL that is present from birth. Generally, HDL cholesterol and triglycerides are normal. FH should be suspected in a patient 20 years of age or younger if the untreated fasting LDL is ≥ 160 mg/dL or the total non-HDL cholesterol is ≥ 190 mg/dL, values that are substantially above the 95th percentile.

The diagnosis is confirmed if the patient has a first-degree relative with premature atherosclerosis and an LDL > 200 mg/dL. Even in a screening population, if the LDL > 190, there is an 80% chance the child has FH.

The most common form of FH is caused by a loss-of-function mutation in the LDL receptor on hepatocytes, which is responsible for binding LDL and facilitating its metabolism in the liver. The relative loss of receptor functionality is variable, hence, LDL levels and age of cardiovascular disease onset in patients with FH is also variable. Despite the variability, if untreated, approximately half of males and 25% of females will have a cardiovascular event before 50 years of age.

In FH, lifestyle changes are critical to management but are almost never adequate to drop LDL levels back to normal. First-line therapy is a combination of lifestyle management with pharmacotherapy, usually a statin. Statins are FDA-approved for use in pediatric patients with FH as young as eight years of age. The goal of treatment is reduction of LDL below 130 mg/dL or a 50% reduction from baseline LDL (whichever is less aggressive), along with normalization of the rest of the lipid profile. Rarely, pediatric patients will require additional cholesterol-lowering medications to reach goal levels.

In adults, the use of statin medications is remarkably effective at reducing cardiovascular mortality. The Simon Broome Familial Hyperlipidaemia Register Group showed impressive reductions in cardiovascular mortality (48% with primary prevention and 25% with secondary prevention), as well as a 33% reduction in all-cause mortality with statin use in their FH population. In children with FH, use of statins leads to significant reductions in carotid intimal medial thickness, a well-validated surrogate marker for atherosclerotic burden in adults. Even more importantly, a cohort of children with FH started on a statin between 8 to 18 years of age already have, only 10 years later, a lower cardiovascular event rate than their affected parents did at the same age.

Despite the well understood, long-standing association with FH and ischemic heart disease, FH is woefully underdiagnosed. In the US, less than 10% of patients with FH are appropriately diagnosed, and a smaller number still are appropriately treated.

To complete this article, read more about the screening recommendations and management of dyslipidemia in children, and receive CME credit, please go to uwhealth.org/pediatricpathways

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To schedule an appointment with Dr. Peterson at the Pediatric Preventive Cardiology Clinic (PPCC), please call (608) 263-6420 or visit our website at uwhealthkids.org/cholesterol
As more children with complex medical needs are living longer and more productive lives, caring for these patients deserves increasingly greater attention from leading children’s hospitals. To address this need, UW Health’s American Family Children’s Hospital in Madison has just launched its own Pediatric Complex Care Program.

“Children with medical complexity are relatively small in number, but they are frequent consumers of the healthcare system,” says Mary Ehlenbach, MD, medical director of the Pediatric Complex Care Program at the American Family Children’s Hospital. “Our goal is to provide patients and families with highly-coordinated care with a global perspective in mind, and to help patients and families navigate the healthcare system, which can be very confusing when kids are seen by multiple specialists.”

This approach, says Dr. Ehlenbach, can be especially helpful not only for families, but also for primary care or referring physicians who seek a contact person at the Children’s Hospital who can help with coordinating all of a medically complex child’s care. Enhanced coordination, says Dr. Ehlenbach, should also help decrease the child’s frequency and length of hospitalizations and/or Emergency Department visits.

Patients who qualify for the new program will:

- Have three or more affected organ systems,
- See four or more pediatric specialists, and
- Have been recently hospitalized or seen in the Emergency Department.

Patients whose care is coordinated through existing disease-specific programs will not be enrolled. “This program will focus on children with medical complexity who are followed by many specialists at the children’s hospital, but do not have a specific group in charge of their care overall,” says Dr. Ehlenbach.

“Typically,” says Dr. Ehlenbach, “children managed by complex care programs around the country may have been born prematurely, have genetic abnormalities or have survived a long stay in the Pediatric Intensive Care Unit.”

For the family’s convenience, clinic appointments often will be scheduled in conjunction with the child’s other pediatric specialty clinic visits.

In addition to Dr. Ehlenbach, the Pediatric Complex Care Team consists of Ryan Coller, MD, Kristan Sodergren, NP and Teresa Wagner, RN. Dr. Coller, who came to Madison in 2013, previously served as medical director of the Pediatric Medical Home Program at Mattel Children’s Hospital UCLA.

More information about the Pediatric Complex Care Program is available by contacting Dr. Ehlenbach at mehlenbach@pediatrics.wisc.edu. To refer a patient to the Pediatric Complex Care Program, please visit uwhealth.org/referapatient
An 18-month-old Girl Who is Not Talking

By Tina Iyama, MD

Educational Objectives
After reading this article and answering the review questions, the reader will be able to:

1. Recognize early signs of autism spectrum disorders (ASDs)
2. Describe the process of diagnosis for ASD
3. Explain how to find resources that will help an autistic child and his/her family

Case
Madelyn is an 18-month-old girl who presents to your office with her mother who is concerned that “she is not talking.” Her mother reports that Madelyn lacks speech and rarely responds to verbal commands. She does not consistently turn when parents call her name. Madeline has a history of recurrent otitis media and was seen in ENT clinic at 15 months of age, where behavioral audiometry raised concern for profound hearing loss. A sedated auditory brainstem response (ABR) was scheduled and the hearing pathways were intact. Tympanostomy tubes were then placed, but this did not lead to increased verbalizations.

Madelyn was a very quiet baby, who has always been “very independent.” She rarely cried, and always seemed content. She has never had much interest in toys, but prefers anything that opens and closes or has spinning parts. She likes to turn pages in books, but does not want her mother to read to her. She walked at 14 months. She sometimes babbles to herself, but not to others. She does not wave “bye” and does not point to indicate wants or interests. Her eye contact is poor.

Pregnancy, birth and neonatal history are unremarkable. Madelyn has been in good health except for the ear infections. There is a family history of “learning disabilities” in the maternal uncle. He is 28 and lives at home with Madelyn’s maternal grandparents. He seems smart, but is not very social and cannot live on his own.

Physical exam shows normal growth, mild macrocephaly (just above the 98th percentile), mildly low muscle tone and hyperextensible joints. There are no clearly dysmorphic physical characteristics. Distal tendon reflexes are normal. She is very self-contained, does not smile at you, and does not make eye contact. She flaps her hands when distressed. You suspect that she has an autism spectrum disorder (ASD).

Discussion

Early Signs of ASDs
Babies who will go on to have autism may seem perfectly fine to parents, although they may have temperamental extremes, either very passive like Madelyn, or very irritable and hard to console. Motor milestones may be normal or mildly delayed. Language milestones may be very impaired, especially receptive language – not turning to name (typically achieved by 6-8 months), not following simple requests (12-15 months) and not pointing to body parts on request (18 months). Expressive language is also typically delayed and may include a history of loss of babbling or loss of a few words. Absolute indicators for an autism evaluation are listed in Box 1.

Diagnosis of ASDs
The clinical diagnosis of ASD is made based on meeting diagnostic criteria by history and on observations of a child’s social interactions in a clinical setting. We are in a transition phase between DSM-IV and DSM-V diagnostic manuals (See Box 2). Our clinic is continuing to use DSM-IV until the State, which approves some of the funding for autism interventions, decides to change. It is not clear whether the new criteria will change the number of diagnoses that are made. Our staff do not anticipate a significant shift.

Box 1. Absolute Indicators for an Autism Evaluation
- No single, meaningful words by 16 months
- No communicative gestures by 12 months
- No flexible 2 word phrases by 2 years
- ANY loss of ANY social or language skill at any age
All children with language delays should have an audiologic evaluation. Children with ASDs are especially hard to test and need an audiologist with pediatric skills. All children who are diagnosed with ASD should also have two basic medical diagnostic tests performed: 1) Array comparative genomic hybridization (aCGH), a detailed look at chromosomes which can detect small but clinically significant microduplications and microdeletions, and 2) Molecular fragile X testing. Specific gene mutations are not identified by aCGH, so fragile X cannot be diagnosed by aCGH, and is not easily diagnosed on physical exam, especially in young children. Furthermore, because the recurrence risk in families is high and fragile X syndrome is a relatively common cause of ASD, it is important to test for fragile X in all children with an ASD diagnosis. Madelyn has a maternal uncle who may be affected, and this pattern strongly suggests that fragile X should be ruled out. In children with ASD who have average developmental abilities (eg, average IQ) and no dysmorphic features, we are unlikely to find a specific medical cause of ASD. Children who have ASD plus other findings (eg, episodes that suggest epilepsy, severe hypotonia that suggests metabolic disease) should also have appropriate medical diagnostics performed.

ASD Prevalence

What we call “autism” has changed radically over the last 35 years. The spectrum has expanded to include many more mildly affected children, with an expected rise in numbers. Current estimates are that 1-2% of children have an ASD.

ASD Treatment and Resources

The only evidence-based treatment for autism is early, intensive behavioral intervention (EIBI). Working with children in a 1:1 setting for 20 to 35 hours per week for 2 to 4 years has resulted in substantial and unexpected progress for about 50 percent of those treated. There is evidence for both a strictly behaviorally based program as well as a play-based program, with similar results for both groups.

There is also evidence for use of medications to improve some challenging symptoms in autism. Risperidone is FDA approved for children with autism to reduce irritability and hyperactivity.

Good behavioral problem-solving should be undertaken before any medication is prescribed. We often create challenging behaviors in children when adults expect children to do things that are beyond their capacity; creating appropriate expectations for parents may help mitigate this situation.

There are other plausible interventions for which we lack evidence, including: speech and language therapy, occupational therapy, social skills training and special educational support. There are many, many implausible interventions, which also do not have evidence-based support (special diets, vitamin supplements, hyperbaric oxygen). There is, of course, substantial evidence that immunizations do not cause autism. We should do our best to direct our families to the therapies that are most likely to provide the most benefit.

Payment for intensive services varies widely within communities and across states. Wisconsin-based insurance companies are required to pay for autism interventions under the “autism insurance mandate.” Those without this insurance option can apply for state funds, and, if they meet the state’s criteria for need, can be put on a waiting list for the “autism waiver program.” The wait for these state funds can be years long. Some children only qualify for what the school system can provide. The system is far from fair. It is appropriate to suggest to families that they call their Regional Center (brochures can be obtained by writing or calling Wisconsin First Step: 800-642-7837), which is staffed by resource specialists, who are very up-to-date with the latest rulings and information for families.
The patient discharge process has long been in need of improvement with about half of UW Health inpatients and their families expressing dissatisfaction with their experience, according to Press Ganey survey results.

“It was never the same experience twice. Sometimes it felt rushed; other times it felt delayed,” says Irene Ekleberry, UW Health Patient and Family Advisor and a member of the Discharge Collaborative, an interdisciplinary group working to improve the process.

Following eight months of planning, the first standardized process for patient discharge at UW Health will soon be implemented across all general care units. Designed to improve the patient and family experience, the new process will include entering and tracking an anticipated discharge date, as well as a confirmed date and time.

Scheduling a discharge time has been shown to be successful at other health systems, including Mayo Clinic and Cadence Health, and has been piloted on one unit at UW Hospitals and Clinics. It offers key advantages, from enabling patients and family members to make timely transportation arrangements, to allowing more time for patient education, to reducing admission delays for incoming patients.

“The UW Health Pediatric Transplant Program is the only center in the region offering this protocol, making it unique compared to what is being done in most of the transplant community.”

Dr. Bartosh presented the University of Wisconsin experience with this unique protocol last summer at the meeting of the International Pediatric Transplant Association in Poland.

To learn more, please visit uwhealth.org/transplant

The protocol consists of two doses of a unique immunosuppressive agent alemtuzumab during the transplant hospitalization, followed by mycophenolate mofetil and tacrolimus administered as outpatient medications. Candidates for this regimen are generally low-risk children who are receiving their first transplant, either from a living or deceased donor, and who are at low risk for disease recurrence.

Enhancing the Discharge Process – Step by Step

Children who have received a kidney transplant such as Devin, now 13, have done well while on a steroid-free regimen.

Exciting News For Pediatric Kidney Recipients

Approximately 60 percent of newly transplanted pediatric kidney transplant patients in the U.S. are maintained on a prednisone-based immunosuppression regimen. However, in addition to its many other potential adverse effects, chronic prednisone exposure may slow growth and development in children, which is especially concerning in children whose kidney failure may have already adversely affected their growth and development.

Dr. Sharon Bartosh, director of the UW Health pediatric renal transplant program, has been offering a non-prednisone regimen since 2004. Originally a research protocol approved by the Institutional Review Board and FDA-supervised, her team has completed more than 30 successful cases since that time, and Bartosh is very pleased with the results.

“Unlike many children treated with prednisone that have characteristic body habitus and facial features, our children look completely normal, are growing beautifully and are doing well with their transplant,” said Bartosh.

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UW Health Sciences Learning Center
Madison, Wisconsin
Watch via live stream at http://live.videos.med.wisc.edu

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Under the Radar – Identifying & Responding to Chronic Neglect
Friday, April 25, 2014
7:30 AM – 12:30 PM
American Family Insurance Conference Center
6000 American Parkway, Madison

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Wednesday, June 11, 2014
Monona Terrace Community and Convention Center, Madison

Interdisciplinary Perspectives on Spinal Muscular Atrophy: Defining Your Role

June 13, 2014
Gaylord Nelson Resort and Conference Center
National Harbor, MD

Seminars in Pediatrics 2014

September 18-19, 2014
Monona Terrace Community and Convention Center, Madison
http://seminars.pediatrics.wisc.edu

Seminars in Pediatrics 2015

October 1-2, 2015
Monona Terrace Community and Convention Center, Madison

CME Information

Release date: April 15, 2014
Expiration date: April 15, 2015

Method of Participation

The articles in this document are an introduction to a CME opportunity that is available online. To obtain CME credit, go to uwhealth.org/pediatricpathways, read both complete articles and submit your answers to the review questions. A score of 80% correct or better will allow you to claim your credit. Credit letters will be automatically generated if you receive a passing score. Estimated time to complete the activity: 1.0 hour.

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Questions?

Please contact Barb Anderson, at cme@pediatrics.wisc.edu or (608) 263-8542.

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Dr. Amy Peterson does not have any financial relationships with commercial interest to disclose, she may reference unlabeled or unapproved uses of drugs or devices.

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uwhealth.org/pediatricpathways
The American Family Children's Hospital's Access Center is open 24 hours a day, seven days a week to handle all issues surrounding patient admissions and referrals. Referring physicians can use the Access Center to:

- Obtain rapid consultations with specialty staff or
- Refer patients on an inpatient basis or
- Request Med Flight or ground transport (CHETA)

Please note: Access Center is for the exclusive use of physicians and other health care providers caring for patients. Patients wishing to schedule appointments may call 1-800-323-8942 (Outside Madison) or (608) 263-6420.

Referral information
To facilitate smooth and timely transfers, we kindly ask physicians to provide the following information:
- Patient’s name
- Birth date
- Patient address and telephone number
- UW Hospital patient registration number (if known)
- Insurance information, including the name of insurance plan or HMO, pre-admission requirements and second surgical opinion guidelines, if appropriate.

Prior authorization
To assure compliance with payor-based prior authorization requirements, insurance information is necessary at the time of referral. Please call (608) 263-8773 (or send a fax to 608-263-9422) to contact trained admission and insurance staff. If your patient has no health insurance, an advisor may be contacted at (608) 263-8770 to review possible sources of assistance.

For listings of physicians by specialty, please visit uwhealthkids.org