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Educational Gap

New recommendations for blood pressure and lipid screening were issued by the American Academy of Pediatrics in November, 2011, and are addressed in this article.

Objectives

After completing this article, readers should be able to:

1. Understand the Life Course Health Development framework for examining the impact that childhood factors have on adult health.
2. Understand cardiovascular disease and the risk factors for its development, including pediatric criteria for the metabolic syndrome.
3. Understand the consequences of poor nutritional habits and obesity in childhood and adolescence.
4. Know the risk factors for hypertension and hypercholesterolemia, as well as how to evaluate and treat both conditions.
5. Screen for, diagnose, and treat type 2 diabetes mellitus.

Introduction

Many of the most common and costly chronic adult health conditions have their origins in childhood and adolescence. This recognition is leading to both a profound shift in our understanding about the developmental origins of diseases, such as hypertension, dyslipidemia, and type 2 diabetes mellitus (DM), and a greater focus on how different risk and protective factors influence the developmental pathways that determine optimal health across the life span. Scientific breakthroughs in the basic, clinical, and epidemiological sciences reveal how different stressors and exposures during what are now termed "critical" or "sensitive" periods of development can affect growth, tissue differentiation, and physiologic set points that influence an individual's response to metabolic, physiologic, emotional, and environmental challenges throughout life. In light of this explosion of new scientific data about the importance of the early years for lifelong health and development, general pediatricians will have to play an increasing role in addressing childhood antecedents to adult cardiovascular diseases (CVDs).

A growing body of research demonstrates that many of the most common and costly adult chronic health conditions (ie, obesity, hypertension, dyslipidemia, DM, and metabolic syndrome) have their origins in childhood. In utero initialization of metabolic pathways and early childhood priming of behavioral response patterns can lead to overt pathology in the future. Landmark retrospective epidemiological cohort studies, such as one conducted by David Barker and colleagues in Hertfordshire, England, used birth and early nutrition records to demonstrate how nutritional insults to the fetus during pregnancy influence CVD rates decades later. (1)(2) These and related studies also show similar birth weight–related risk gradients for hypertension, stroke, and DM. The transmission of risk across the placenta is not limited to alterations in maternal nutrition, but also has demonstrated how high levels of maternal stress can

Abbreviations

CVD: cardiovascular disease
DM: diabetes mellitus
IDF: International Diabetes Federation
LCHD: Life Course Health Development
NCEP: National Cholesterol Education Program

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result in differences in child and adolescent nervous system functioning.

Although the connection between early experiences and exposures and the development of adult chronic disease is becoming better understood, the effectiveness and appropriateness of different types of early intervention is just beginning to be elucidated. Nonetheless, it is increasingly apparent that interventions that have the potential to prevent chronic disease as well as augment adult health might need to start early in life, so as to address childhood and adolescent risk and protective factors that can influence an individual's lifelong health trajectory. More is being learned about the role that the pediatrician can play in recognizing, influencing, and redirecting these developing health trajectories by reinforcing positive behaviors, providing psychosocial support, responding to risk factors or "red flags" with interventions (pharmacologic or otherwise), and playing an active role in preventing diseases that could prove debilitating or lethal in adulthood.

Life Course Health Development

Current concepts of health have evolved and expanded significantly from early notions of health as merely a state of being free of disease. The 2004 Institute of Medicine Report on *Children's Health, the Nation's Wealth* defined health as the following:

"Children's health is the extent to which individual children or groups of children are able or enabled to (a) develop and realize their potential, (b) satisfy their needs, and (c) develop the capacities that allow them to interact successfully with their biological, physical, and social environments." (3)

In addition to this new developmental definition of health, the *Children's Health, the Nation's Wealth* report proposes a life course framework for how health develops across the life span. Life Course Health Development (LCHD) is shaped by the dynamic and continuous interaction between biology and experiences that is framed and influenced by dynamic developmental contexts over the lifetime. (4) Synthesizing evidence from several fields of scientific inquiry, the LCHD model suggests that

- Health development is influenced by the dynamic interactions of risk with protective and promoting factors nested in several different contexts, including socioeconomic, psychological, genetic, and cultural influences, as well as the health care system itself (Fig 1).
- Sensitive and critical periods of heightened developmental plasticity means that certain risk, protective, and promoting factors have greater influence during these periods and are potentially more amenable to intervention. Although many critical and sensitive periods of development occur prenatally and during the early years, research on brain development during adolescence has highlighted the importance of this period to future psychological development and mental health.
- Multiple interacting pathways account for variations in trajectories of health development.
- Optimizing lifelong health depends on a long-term strategy of enhancing protective and promoting factors and minimizing or eliminating risks through clinical and preventive interventions targeting individuals and populations.
- Optimal health trajectories can be facilitated by minimizing risk factors that cause stress and maximizing health-promoting protective factors (Fig 2).

By focusing more attention on sensitive and critical periods of development, the LCHD framework recognizes the importance of developmental plasticity as an adaptive process that evolution has selected to promote survival, biological fitness, and reproductive success. Because developmental plasticity focuses on life-course strategies to optimize the biopsychosocial capacity to survive and reproduce, some response patterns may enhance reproduction fitness but impair longevity. This effect is especially true if environmental conditions change strikingly between conception and adulthood.

With the modern life expectancy of humans living in developed countries now being twice as long as their Paleolithic ancestors, the harmful effects of poor long-term biobehavioral influences are becoming more apparent. Adaptive anticipatory strategies, such as catch-up growth after prenatal undernutrition, makes adaptive sense for the individual to grow and develop so as to be able to reproduce. (5) Although preventing small-for-gestational age infants can have benefits, interventions to augment prenatal diets to increase birth weights may run the risk of unintended consequences, such as increased adiposity in childhood, DM, and certain kinds of malignancies.

A basic premise of LCHD is that optimal health development can be facilitated by reducing the stresses and strains that are induced by specific risks and increasing the protective factors and other conditions that promote the best possible functioning. Stresses occur when environmental influences and experiences disrupt normal patterns of functioning, either through acute shocks, especially during sensitive periods, or a chronic weathering process that grinds away at adaptive response patterns that are in place to guard against external threats and disruptions. Placing demands on developing biobehavioral systems and exceeding their normal capacity to

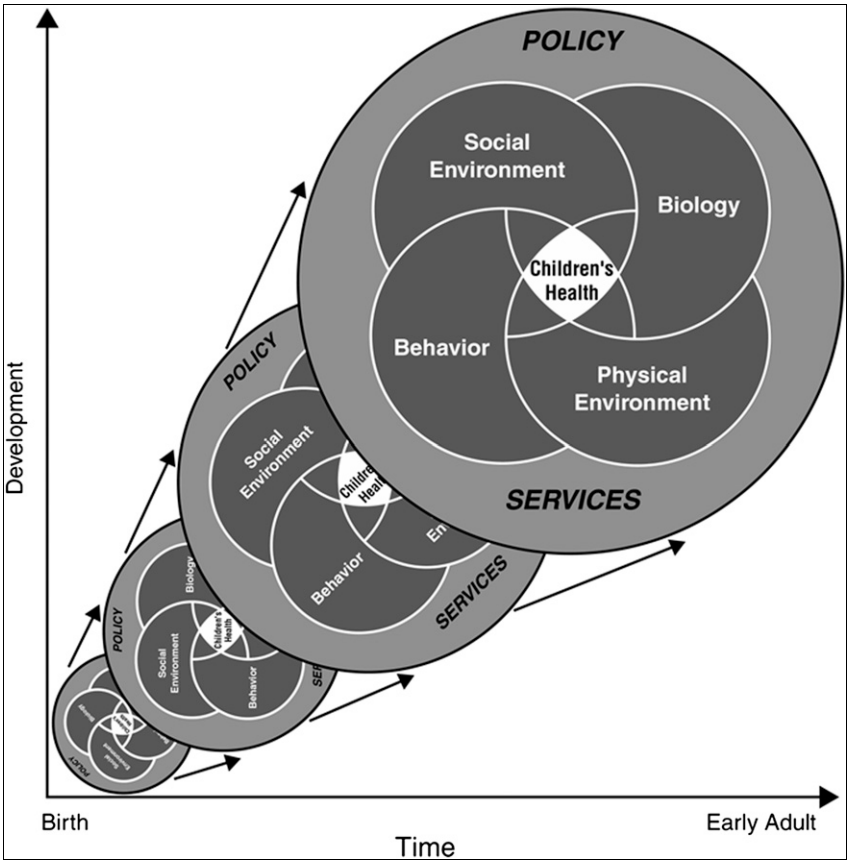

Figure 1. A new model of children's health and its influences. (Reprinted with permission from Institute of Medicine. *Children's Health, the Nation's Wealth*. Washington, DC: National Academies Press; 2004.)

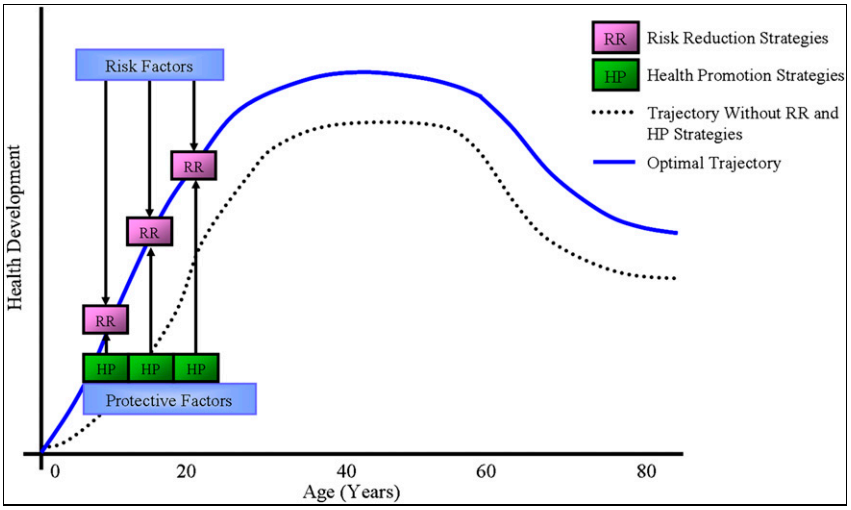

Figure 2. Health development trajectories. (Reprinted with permission from Halfon N, Inkelas M, Hochstein M. The health development organization: an organizational approach to achieving child health development. *Milbank Q.* 2000;78(3):447–497.)

respond adaptively induces a range of developmental responses that can be beneficial over the short term, yet lead to longer-term response patterns that are detrimental to lifelong health. (6)

One of the most important and ubiquitous stresses that children experience is the stress associated with living in poverty or experiencing socioeconomic disadvantage. A series of longitudinal studies conducted in the United Kingdom, New Zealand, and Scandinavia have demonstrated that children who experience socioeconomic disadvantage are more likely to have major depression, high levels of inflammation (as measured by C-reactive protein), hypertension, obesity, elevated total cholesterol concentrations, high levels of glycosylated hemoglobin, and low maximum oxygen consumption. One recent study from New Zealand indicated that adverse childhood experiences associated with childhood disadvantage accounted for ~30% of these clustered metabolic risks when these children became young adults. (7) Retrospective studies conducted in the United States regarding adverse childhood experiences have linked the number of adverse experiences to the prevalence of coronary artery disease, hypertension, alcoholism, and illicit drug use decades later.

Growing research on gene-environment interactions is providing valuable information about specific genetic susceptibilities and the specification of environmental exposures and experiences that are likely to induce genetic expression. Well-recognized examples of such markers, such as the breast cancer genes and the apolipoprotein E gene for late-onset Alzheimer disease, are being joined by new genetic markers that are associated with many other outcomes. In addition

to identifying markers of future diseases, many life-course health-development studies are identifying biological and behavioral markers that represent the expression of a particular developmental pathway. A combination of these genetic, biological, and behavioral markers will be used increasingly to develop risk profiles, permitting better targeting of specific interventions, as well as the development of population-based prevention strategies.

Pediatrician's Role in Preventing Adult CVD

The pediatrician can play several important roles in addressing the developmental antecedents of adult CVD. As a clinician who can recognize and intervene to reduce risk, it is important for pediatricians to be aware of childhood risk factors for CVD that are amenable to intervention. Although there are many reasonably straightforward and generic recommendations for reducing risk and promoting health, such as general recommendations that emphasize appropriate nutrition, exercise, and daily activities, there are many areas in which the evidence for what constitutes an appropriate early intervention is less clear.

Over the next several years, as more evidence emerges about the connection between childhood risks and later diseases, pediatricians will be called on to play an important role as interpreters of this information for parents and families, highlighting not only what we know about the causes of adverse adult health outcomes, but also what families can do to disrupt chains of associated risks, creating conditions for more optimal health trajectories.

Because prevention and health-promotion strategies come in both individual and population-based formats, pediatricians can play an important role in advising parents about what kinds of programs and approaches they might want to adopt at home, and which community-based resources are likely to be reliable purveyors of appropriate interventions. At a population level, pediatricians also can play an important role advocating for evidence-based school- and community-focused prevention and intervention programs that can play an important role in diminishing risks and promoting healthy behaviors.

In the next section, we consider several different adult cardiovascular conditions in which the developmental pathways are emerging, and where the early antecedent risks have been defined well enough to permit recommendations for specific interventions.

CVD

More than 80 million adult Americans (one in three) have CVD (hypertension, coronary artery disease, heart failure, stroke), with ~47% of these persons being older than 60 years. CVD is the most common cause of death in the United States. Although cancer-related deaths slightly exceed deaths related to CVD for persons ages 45 to 74 years, deaths caused by CVD are more than twice as frequent as cancer-related deaths for persons older than 74 years.

Metabolic Syndrome

The term metabolic syndrome refers to the clustering of risk factors for CVD and type 2 DM. The International Diabetes Federation (IDF) definition of metabolic syndrome is central obesity with a waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women and the presence of at least two of the following four clinical risk factors:

1. Blood pressure (BP) ≥130 mm Hg systolic or ≥85 mm Hg diastolic or drug treatment for hypertension;
2. High-density lipoprotein (HDL) cholesterol level <40 mg/dL (1.0 mmol/L) in men or <50 mg/dL (1.3 mmol/L) in women or treatment for lipid abnormalities;
3. Triglyceride level ≥150 mg/dL (1.7 mmol/L); and
4. Fasting plasma glucose level ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 DM.

An estimated 47 million US residents have metabolic syndrome, with the highest prevalence in Mexican American individuals (32%) and the lowest prevalence in white individuals (24%). Persons with metabolic syndrome have a higher risk of developing DM and CVD and have a higher risk of death from CVD.

In 2007, the IDF convened a consensus panel to define the metabolic syndrome in children and adolescents, (8) as a follow-up to the IDF consensus worldwide definition of the metabolic syndrome in adults that was published in 2005. In summary, the IDF states that metabolic syndrome should not be diagnosed in children younger than 10 years of age, although weight management for children who are obese should be strongly encouraged. For adolescents ≥16 years, the adult criteria for metabolic syndrome should be applied. For children between 10 and 16 years, the criteria are generally the same as those for adults, except that waist circumference must be >90th percentile, and the HDL cholesterol level must be <40 mg/dL (1.0 mmol/L) in both boys and girls (as one of the four possible clinical risk factors).

Obesity

Adults with a BMI between 25 and 29.9 are considered overweight, and those with a BMI ≥30 are considered obese. For children and adolescents between the ages

of 2 and 19 years, overweight is defined as a BMI ≥85th percentile and <95th percentile, and obesity is defined as a BMI ≥95th percentile for children of the same age and sex. In addition, in 2007, an Expert Committee further recognized a third cutoff at the 99th percentile, which indicates severe obesity in children and adolescents. Although the standard Centers for Disease Control and Prevention BMI growth charts stop at the 97th percentile, the Expert Committee report includes a table of 99th percentile cutoff points by age and gender. The recommendations for prevention and treatment of childhood obesity are available in the Expert Committee report, which is published in a 2007 supplement to *Pediatrics*. (9)

Overweight in adolescence can result in immediate adverse effects on health before adulthood. In addition, most overweight teenagers continue to have an elevated BMI in young adulthood, with studies estimating that 80% of overweight adolescents become obese adults. The effect of adolescent overweight on future adult CVD is projected to be substantial even in young adulthood and will continue to rise in middle age. The expected higher rates of hospitalizations, procedures, disability, long-term use of medications, and premature death in a working-age population that would otherwise be at low risk for CVD could be dramatic.

As the obesity epidemic unfolds, more attention has been placed on the early life programming of obesity and related metabolic syndromes, as well as other environmental factors that may play a role. Maternal weight gain during pregnancy and excessive postnatal feeding with enriched formulas, especially in children who are small for gestational age, have been implicated in higher weight-for-height growth trajectories. (10) Recent studies suggest that the metabolic syndrome is far more common among children and adolescents than previously reported and that its prevalence increases directly with the degree of obesity, with rates of 39% in moderately obese and 50% in severely obese children in one study. Each element of the syndrome worsens with increasing obesity—an association that is independent of age, gender, and pubertal status. (11)

Hypertension

Hypertension affects one in four adults worldwide, and poorly controlled hypertension is the leading cause of death globally. Hypertension is more prevalent in non-Latino black persons and older persons than in the general population. Approximately 67% of patients older than 60 years and more than 75% of patients older than 80 years have hypertension. The following recommendations for the screening and management of pediatric hypertension come from the latest (2004) report from the National High Blood Pressure Education Program Working Group on high BP in children and adolescents. (12)

Hypertension is defined as average systolic BP (SBP) or diastolic BP that is ≥95th percentile for gender, age, and height on more than three occasions.

- Prehypertension in children is defined as average SBP or diastolic BP levels that are ≥90th percentile but <95th percentile.
- As with adults, adolescents with BP levels ≥120/80 mm Hg should be considered prehypertensive.
- A patient with BP levels >95th percentile in a physician's office or clinic, who is normotensive outside a clinical setting, has "white-coat hypertension." Ambulatory BP monitoring is usually required to make this diagnosis.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure from 2003 defines prehypertension as a BP level that is ≥120/80 mm Hg and recommends the application of preventive health-related behaviors, or therapeutic lifestyle changes, for individuals having SBP levels that exceed 120 mm Hg. (13) It is recommended also that, as with adults, children and adolescents with BP levels ≥120/80 mm Hg but <95th percentile should be considered prehypertensive. The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure should be released in 2012.

Children older than 3 years who are seen in medical care settings should have their BP measured at least once during every health care episode. Children younger than 3 years should have their BP measured in special circumstances (Table 1).

High BP in childhood had been considered a risk factor for hypertension in early adulthood; however, primary (essential) hypertension is now identifiable in children and adolescents. Primary hypertension in childhood usually is characterized by mildly elevated BP and often is associated with a positive family history of hypertension or CVD. Children and adolescents with primary hypertension frequently are overweight. Data on healthy adolescents obtained in school health-screening programs demonstrate that the prevalence of hypertension increases progressively with increasing BMI, and hypertension is detectable in ~30% of obese children (BMI ≥95th percentile). The strong association of high BP with obesity and the marked increase in the prevalence of childhood obesity indicate that both hypertension and prehypertension are becoming a significant health issue in the young.

Secondary hypertension is more common in children than in adults. The possibility that some underlying disorder might be the cause of the hypertension should be considered in every child or adolescent who has elevated BP; however, the extent of an evaluation for detection of a possible underlying cause should be individualized for each child. Very young children, children with moderately elevated BP, and children or adolescents with clinical signs that suggest the presence of systemic conditions associated with hypertension should be evaluated more extensively, as compared with those having mild hypertension.

Indications for antihypertensive drug therapy in children include secondary hypertension and insufficient response to lifestyle modifications. Recent clinical trials have expanded the number of drugs that have pediatric dosing information. Pharmacologic therapy, when indicated, should be initiated with a single drug. Acceptable drug classes for use in children include angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, β-blockers, calcium channel blockers, and diuretics. The goal for antihypertensive treatment in children should be reduction of BP to <95th percentile unless concurrent conditions are present, in which case BP should be lowered to <90th percentile.

In adults, hypertension typically is a lifelong condition. Most patients with hypertension will need to remain on medications for the rest of their lives. Given the known long-term adverse consequences of untreated or undertreated hypertension, most adults understand and accept this fact. Although the long-term consequences of untreated hypertension in children are unknown, one could presume that these consequences are likely to be similar to those in adults. In addition, because no data are available on the long-term effects of antihypertensive drugs on growth and development, a definite indication for initiating pharmacologic therapy should be ascertained before a drug is prescribed.

At present, many of these children are referred to pediatric cardiologists or nephrologists to begin medications. As a growing number of children with obesity are identified as having primary hypertension, however, general pediatricians will need to gain the knowledge and skills to be comfortable with prescribing antihypertensive medications.

Dyslipidemia

"Dyslipidemia" refers to a pathologic imbalance in the levels of low-density lipoprotein (LDL) cholesterol, HDL cholesterol, and triglycerides, and is well recognized as a risk factor for adult CVD. Studies have shown that children with elevated cholesterol levels continue to have elevated cholesterol into adulthood. More important, treating childhood dyslipidemia may help prevent or reduce the risk of adult CVD and reduce the atherosclerotic burden later in life.

The National Cholesterol Education Program (NCEP) established guidelines in 1992 for screening and treating pediatric hyperlipidemia. (14) In 2011, the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents released its summary report, which includes a revised screening guideline for dyslipidemia based on reviewing and grading of the latest evidence. (15) The Expert Panel concluded that use of family history of premature CVD for targeted screening for dyslipidemia in children missed 30% to 60% of children with dyslipidemias. Thus, the Expert Panel now recommends universal screening of non-fasting non-HDL cholesterol in children 9 to 11 years old (prior to onset of puberty) and again in individuals 17 to 21 years. Targeted screening should occur in children

Table 1. When to Measure Blood Pressure in Children <3 Years Old

History of prematurity, very low birth weight, or other neonatal complication requiring intensive care
Congenital heart disease (repaired or nonrepaired)
Recurrent urinary tract infections, hematuria, or proteinuria
Known renal disease or urologic malformations
Family history of congenital renal disease
Solid organ transplant
Malignancy or bone marrow transplant
Treatment with drugs known to raise BP
Other systemic illnesses associated with hypertension (eg, neurofibromatosis, tuberous sclerosis)
Evidence of elevated intracranial pressure

Reprinted with permission from The Fourth Report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics.* 2004;114(suppl 2):556.

2 to 8 years old and adolescents 12 to 16 years old with two fasting lipid profiles (between 2 weeks and 3 months apart, results averaged) for the risk factors listed in Table 2.

Once lipid values have been obtained, the Expert Panel used NCEP-established cut points for total cholesterol and LDL concentrations in children and adolescents, and the Bogalusa Heart Study for non-HDL cholesterol (Table 3). The Expert Panel further identified cut points for lipid levels in young adults that are distinct from those used in adults of all ages in the most recent NHLBI adult guidelines, Adult Treatment Panel III ("Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults").

Initial treatment includes lifestyle changes, such as diet and exercise. The Expert Panel identified and graded age-specific recommendations in the Cardiovascular Health Integrated Lifestyle Diet (CHILD-1) for children with identified dyslipidemia, overweight and obesity, risk-factor clustering, and high-risk medical conditions that might require more intensive dietary change. (13) For children with dyslipidemia with persistently elevated LDL cholesterol or triglyceride levels after a 6-month trial of CHILD-1, specific dietary restrictions on saturated fats and dietary cholesterol are made (CHILD-2).

All children under 10 years of age for whom medication for dyslipidemia is being considered should be cared for in conjunction with a lipid specialist. For children 10 to 21 years old, those with an average LDL cholesterol level of ≥ 250 mg/dL should be referred directly to a lipid specialist. Otherwise, treatment with medication is based on an assessment of lipid levels in conjunction with associated risk factors or conditions (a more detailed discussion is available on pages S28–S30 of the Expert Panel summary report (15).

The recommended initial medication therapy for dyslipidemia in children and adolescents are the 3-hydroxy-3-methyl-glutaryl coenzyme A reductase inhibitors (statins). The statins are generally well tolerated and result in 20 to 50% lowering of cholesterol, depending on the dose used. Adverse effects of statins are related to increased hepatic transaminase levels and also elevations of creatine kinase, which may be associated with rare but clinically important episodes of rhabdomyolysis. There is also a concern about the potential of statin medications to be teratogenic, so they are not recommended for women who are pregnant, seeking to become pregnant, or breastfeeding. Patients should be monitored with periodic measurement of liver transaminase and creatine kinase levels. Patients should also be instructed to report symptoms of muscle aches or cramping.

The AAP recommendations are based on the best available evidence and may be altered as new thinking evolves. Readers are advised to stay current on AAP policies regarding this and other clinical topics. While the new lipid screening recommendations may be challenging for primary care pediatricians to espouse, it is incontrovertible that the rising rate of childhood obesity will have a deleterious effect on the future health of children in this country. Primary care pediatricians are in a critical position to intervene as early as possible to optimize children's cardiovascular health.

DM

Type 2 DM accounts for 90% to 95% of DM worldwide and has a more insidious onset than type 1. Patients with type 2 DM usually are older than 40 years and typically overweight or obese. Because of increasing obesity rates in the young, type 2 DM is becoming more common in teenagers and older children.

Table 2. Risk Factors for Targeted Cholesterol Screening in Children and Adolescents

Screen children between 2 and 8 years of age and adolescents between 12 and 16 years of age who:

1. **have a moderate- or high-risk medical condition (Table 1)**
2. **have other cardiovascular risk factors (diabetes, hypertension, BMI ≥ 95th percentile, or smoke cigarettes) or**
3. **have a family history of early CVD or severe hypercholesterolemia. Of note, a significant family history includes:**
   - **a. parent or grandparent who at <55 years for males or <65 years for females had suffered a myocardial infarction or sudden death, had undergone a coronary artery procedure, or who otherwise had evidence of coronary atherosclerosis, peripheral vascular disease, or cerebrovascular disease**
   - **b. parent with total cholesterol ≥ 240mg/dL or known dyslipidemia**

Data from Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Summary Report. *Pediatrics.* 2011;128;S213–S256.

Table 3. **Cut Points for Lipid Levels in Children, Adolescents, and Young Adults**

Category	Acceptable, mg/dL	Borderline-High, mg/dL	High, mg/dL
Children and Adolescents			
Total cholesterol	<170	170–199	≥200
LDL cholesterol	<110	110–129	≥130
Non-HDL cholesterol	<120	120–144	≥145
Triglycerides			
0–9 y	<75	75–99	≥100
10–19 y	<90	90–129	≥130
Young Adults (20–24 y)			
Total cholesterol	<190	190–224	≥225
LDL cholesterol	<120	120–159	≥160
Non-HDL cholesterol	<150	150–189	≥190
Triglycerides	<115	115–149	≥150

Reprinted with permission from Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Summary Report. *Pediatrics.* 2011;128;S13–S256.

The pathogenesis of type 2 DM involves the dual defects of insulin resistance and relative insulin deficiency. Patients at risk for type 2 DM initially develop insulin resistance alone, accompanied by augmented pancreatic insulin secretion. Because of the resulting hyperinsulinemia, plasma glucose levels are maintained in the normal range. In most patients, however, pancreatic β-cell function ultimately declines, with deterioration of endogenous insulin secretory capacity over time.

The increased incidence of type 2 DM diagnosed in the pediatric population has been associated with the epidemic of obesity. The Centers for Disease Control and Prevention and the National Institutes of Health have funded a national childhood DM registry, the multicenter SEARCH for Diabetes in Youth Study, which estimates that 3600 youth will be newly diagnosed with type 2 DM annually in the United States (compared with 15,600 new cases of type 1 DM). (16)

Well-designed studies from Europe indicate that type 2 DM remains a rarity in these populations, accounting for only 1% to 2% of all DM cases. In contrast, although the SEARCH study data identified that type 2 DM in youth is predominantly occurring in high-risk ethnic groups, type 2 DM accounts for 15% of all DM cases among non-Latino white adolescents aged 10 years or older in the United States. (17)

Risk factors and screening recommendations for type 2 DM are found in Table 4 and include obesity, sedentary lifestyle, intrauterine exposure to maternal DM, and low birth weight. In addition, the rates of DM are ~60% higher in girls than boys. The mean age of diagnosis for type 2 DM is midpubertal, from 12 to 16 years. (17)

Measuring C-peptide levels and anti-glutamic acid decarboxylase antibody levels are helpful in differentiating between types 1 and 2 DM. In general, patients with type 2 DM have an elevated fasting C-peptide level and do not have antibodies to anti-glutamic acid decarboxylase. It is also recommended that screening for the comorbidities and complications of DM (including urine microalbumin measurement and fasting lipid profile) be performed at the time of diagnosis.

Lifestyle changes always are indicated in patients with type 2 DM. Despite the lack of successful obesity prevention and treatment programs, aggressive lifestyle modification is widely recommended for all children who are at risk for overweight or are overweight, have risk factors for type 2 DM, have impaired glucose tolerance, or have already been diagnosed as having type 2 DM. Weight loss or prevention of weight gain is the best way to prevent type 2 DM among children with risk factors for the disease. The AAP recommends supporting breastfeeding, promoting healthy eating habits and physical activity, and discouraging sedentary activities, such as watching television. (19)

Patients presenting with mild hyperglycemia (126–200 mg/dL) and glycosylated hemoglobin level <8.5% or an incidental diagnosis of type 2 DM can be treated initially with therapeutic lifestyle changes in combination with metformin, the only drug approved by the Food and Drug Administration for pediatric patients with type 2 DM. Metformin, a biguanide, decreases hepatic glucose production and increases insulin-mediated glucose uptake in peripheral tissues, primarily muscle tissue. A child who presents with severe hyperglycemia (>200 mg/dL), glycosylated hemoglobin level >8.5%, or ketosis should be treated initially with insulin to achieve metabolic control. (20)

Metformin is associated with disturbances in the gastrointestinal tract and, on rare occasions, with lactic acidosis. A modest amount of weight loss is a desirable side effect. Metformin should not be given to a child with type 2 DM and ketosis because it may precipitate lactic acidosis. Metformin should be started, however, once the child recovers from ketosis after treatment by rehydration and with insulin. Insulin should be added whenever glucose control cannot be achieved after 3 to 6 months of metformin therapy. (20)

Table 4. Recommendations for Screening for Type 2 DM in Children

Children who meet the following criteria should be screened for DM beginning at age 10 years or at onset of puberty (if puberty occurs at a younger age). Screening should occur with either a fasting plasma glucose measurement or 2-hour oral glucose tolerance test, and should occur every 2 years. (18)

- Obese or at risk for overweight (BMI >85th percentile for age and sex; or weight for height >85th percentile; or weight >120% of ideal [50% percentile] for height)

PLUS having any TWO of the following risk factors:

- Family history of type 2 DM in first- or second-degree relative
- Race/ethnicity (Native American, African American, Latino, Asian or Pacific Islander)
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome)
- History of DM in the mother or gestational DM during the child's gestation

Adapted from American Diabetes Association. Standards of medical care in diabetes 2011. *Diabetes Care*. 2011;34(suppl 1):S15.

Type 2 DM has a significant prevalence of comorbidities already present at the time of diagnosis. It is recommended that BP measurement, a fasting lipid profile, microalbuminuria assessment, and dilated eye examination be performed at the time of diagnosis. Additional problems that may need to be addressed include polycystic ovary disease and the various comorbidities associated with pediatric obesity, such as sleep apnea, hepatic steatosis, orthopedic complications, and psychosocial concerns. (21) The American Diabetes Association consensus statement on this subject (18) provides guidance on the prevention, screening, and treatment of type 2 DM and its comorbidities in young people.

For children or youth with type 2 DM who are found to have persistently elevated BP, angiotensin-converting enzyme inhibitors should be considered for the initial treatment of hypertension, following appropriate reproductive counseling owing to the potential teratogenic effects of these agents. The goal of treatment is a BP consistently <130/80 or <90th percentile for age, gender, and height, whichever is lower.

For children or youth with type 2 DM who have elevated LDL cholesterol after normalization of glucose levels, treatment should be initiated to lower the LDL cholesterol level. Initial therapy should consist of optimization of glucose control and medical nutrition therapy by using a Step 2 American Heart Association diet aimed at a decrease in the amount of saturated fat in the diet. After the age of 10 years, the addition of a statin in patients who, after medical nutrition therapy and lifestyle changes, have LDL cholesterol >160 mg/dL (4.1 mmol/L), or LDL cholesterol >130 mg/dL (3.4 mmol/L) and one or more CVD risk factors, is reasonable. The goal of therapy is an LDL cholesterol value <100 mg/dL (2.6 mmol/L).

Summary

- Through research in the prevention and treatment of adult diseases, it has become clear that many adult diseases have their origins in childhood. As illustrated in this review, these antecedents are largely a function of the nutrition, physical activity, and habits of developing children.
- There is also increasing evidence that chronic and toxic levels of stress can play a significant role not only in the development of mental and behavioral conditions but in the developmental pathways that lead to a number of chronic physical health conditions.
- Internists, family medicine physicians, and medicine-pediatrics physicians generally are comfortable managing patients with a number of cardiovascular risk factors or conditions. Although pediatric clinical guidelines have recommended universal screening for hypertension since 1977 and targeted screening for dyslipidemia since 1992 and type 2 DM since 2000, this screening is not yet common practice in general pediatrics.
- As the population of children and youth with risk factors for metabolic syndrome – hypertension, dyslipidemia, and type 2 DM – increases as a result of the obesity epidemic, pediatricians will have to screen routinely, and diagnose and treat these conditions in the primary care setting.
- Pediatric residency programs and continuing medical education programs will have to provide knowledge and clinical training in the management of these conditions before primary care pediatricians are comfortable treating children and youth with multiple cardiovascular conditions.

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Parent Resources From the AAP at HealthyChildren.org

The reader is likely to find material to share with parents that is relevant to this article by visiting this link: http://www.healthychildren.org/English/health-issues/conditions/heart/pages/heart-disease.aspx.

PIR Quiz

This quiz is available online at http://www.pedsinreview.aappublications.org. NOTE: Beginning this past January, learners can take *Pediatrics in Review* quizzes and claim credit online *only*. No paper answer form will be printed in the journal.

New Minimum Performance Level Requirements

Per the 2010 revision of the American Medical Association (AMA) Physician's Recognition Award (PRA) and credit system, a minimum performance level must be established on enduring material and journal-based CME activities that are certified for *AMA PRA Category 1 Credit™*. In order to successfully complete 2012 *Pediatrics in Review* articles for *AMA PRA Category 1 Credit™*, learners must demonstrate a minimum performance level of 60% or higher on this assessment, which measures achievement of the educational purpose and/or objectives of this activity.

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1. Which of the following is a feature of metabolic syndrome in adolescents, as defined by the International Diabetes Federation?
   - A. Height >70 inches
   - B. High-density lipoprotein level >60 mg/dL
   - C. Low-density lipoprotein level <100 mg/dL
   - D. Postprandial glucose level >150 mg/dL
   - E. Waist circumference >40 inches
2. You are evaluating a 12-year-old girl at a health supervision visit. Her BMI is 24 kg/m^2, which is between the 90th and 95th percentiles for her age. How would you classify her weight status?
   - A. Normal body weight
   - B. Obese
   - C. Overweight
   - D. Severely obese
   - E. Underweight
3. A 10-year-old boy comes in for a health maintenance visit. The 2011 guidelines recommend that he should be screened for dyslipidemia, even in the absence of risk factors, by obtaining which of the following measurements?
   - A. HDL cholesterol
   - B. LDL/HDL ratio
   - C. Non-fasting, non-HDL cholesterol
   - D. Total cholesterol
   - E. Triglycerides
4. You are working at a health fair for your community junior high and high schools. Which of the following children should be screened for type 2 diabetes mellitus at this time?
   - A. A 13-year-old white girl with BMI 85% and a father with hypertension
   - B. A 15-year-old white girl with BMI 95% and no additional risk factors
   - C. A 15-year-old African American boy with BMI 75% and no additional risk factors
   - D. A 16-year-old Latino boy with BMI 95% and a mother with type 2 diabetes mellitus
   - E. A 17-year-old African American girl with BMI 75% and a grandmother with high cholesterol
5. A 2-year-old boy is being seen for a health maintenance visit. Which of the following factors would induce you to measure his blood pressure?
   - A. African American race
   - B. Father has hypertension
   - C. Mother has diabetes mellitus
   - D. Repaired Tetralogy of Fallot
   - E. Weight at 90th percentile

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