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The Emergence of Cardiovascular Disease and Need For Lipid Screening in Youth

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PERMISSION

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Abstract

Cholesterol screening can be easily incorporated into well-child visits if health practitioners are comfortable ordering labs and caring for youth with lipid disorders. The newest recommendation made in 2011 by the National Heart, Lung, and Blood Institute (NHLBI) is to start lipid screening between age nine and eleven as this is the age most reflective of what the result will be as an adult (NHLBI, 2012). It also is the period that atherosclerosis is most accelerated. Screening is not recommended again until between the age of seventeen and eighteen as puberty is a time of stagnation. The only exception is if there is a strong family history of cardiovascular events. Examples are a parent with known hypertension, total cholesterol ≥ 240 mg/dL, or diabetes. This also includes parents, aunts, uncles, and grandparents who have had early cardiovascular disease as defined as younger than 55 years in males and 65 years in females. The top two ways to assess for hypercholesterolemia in youth are targeted screening and universal screening. Those who support universal screening do so because targeted screening makes it difficult to determine who should undergo cholesterol testing if the parent is unaware of their level or the parental health status is unknown in the case of parental separation, adoption, or death. Those who are in favor of targeted screening view universal screening as leading to over diagnosis and treatment.

Background

The purpose of this independent study is to evaluate the recommendations for cholesterol screening in children and adolescents as it pertains to age of initiation and whether it is recommended to screen based on a positive family history of cardiovascular events or if universal screening is the preferred method. This report does not seek to evaluate the frequency of testing or lipid parameters, but rather what the literature says about what the indications are for testing. The individual patient that spurred this discussion is a fairly healthy twenty-four year old male who presented for lipid screening. Upon testing it was noted that he had an elevated total cholesterol and low-density lipoprotein (LDL) level but based on his age and lifestyle it should not have come as any surprise. He was not doing much for aerobic activity, eating fast food one to two times a day, and binge drinking on the weekend. It is possible, but his levels are not indicative of familial hypercholesterolemia which affects between 1 in 200 to 1 in 500 children. For this reason this paper focuses on the debate of selective testing versus universal screening for the pediatric population. The literature review includes organizational guidelines for lipid testing with a specific focus on support and criticism of the 2011 National Heart, Lung, and Blood Institute guidelines and health providers' willingness to adopt it into practice (NHLBI, 2012).

Since hypercholesterolemia may go unrecognized for decades until the individual begins to experience health problems or upon autopsy, it is important to act when an individual is young when lifestyle modifications and pharmacotherapy are most beneficial. This is especially important with the emergence in obesity and sedentary lifestyle in youth today. Diagnosing hyper-cholesterolemia, in addition to hypertension, early will help decrease the number one cause of death in American adults: heart disease.

Case Report

The case report is based a twenty-four year old white male who comes to the Clinical Education Center at the request of his mother for a cholesterol check. There is a history of cardiovascular issues in the family. His father recently passed from a heart attack at forty-six years of age. His father had a history of hypertension and hypercholesterolemia. There are no known health issues noted in his mother. The patient's twenty-seven year old brother is on cholesterol medication. The patient has never had his cholesterol checked. He has been fairly healthy up to this point. The only medication he is currently on is Zyrtec as needed for allergic rhinitis. He has no known drug allergies. The patient's past surgical history includes a tonsillectomy and adenoidectomy at the age of four. The patient is a college student. He denies use of tobacco or illicit drugs and uses alcohol socially, which consists of one to two beers during the week and as much as four to five beers on the weekends.

Upon assessment the patient has no specific concerns. The review of systems is negative for any dizziness, headaches, change in vision, or change in hearing. The patient denies any shortness of breath at rest or with activity. History is negative for chest pain or palpitations; there is no change in skin or hair texture other than a bump on his left elbow and knee. There has been no drainage, redness, or itching associated with the lesions. The patient notes that he has gastroesophageal reflux disease for which he currently does not use pharmaceuticals. Symptoms are experienced once out of five meals. He admits that he eats fast food one to two times a day. He denies any concerns about his dietary habits as he exercises four to five times a week. His exercise consists of weightlifting forty-five to sixty minutes. Gastrointestinal review of systems is negative for nausea, vomiting, constipation, or diarrhea. The patient denies having any

increase in perspiration, thirst, or urination and is not aware of ever being tested for diabetes in the past.

A focused assessment is completed. The patient's vitals taken prior to the visit are as follows: blood pressure 110/54, heart rate 62, temperature 32.1 Celsius, height 6'1", weight 200 pounds. The patient's neck is supple with no presence of thyromegaly. Lung fields are clear with no use of accessory muscles or respiratory distress. Heart sounds are regular with no presence of murmurs, rubs, or gallops. The abdomen is soft, non-distended, and non-tender. The skin is not assessed, as this did not appear to be a concern for him and is unrelated to the purpose of the day's visit.

To assess for the patient's risk for cardiovascular disease a panel of labs are ordered: BMP, lipid panel, and liver panel. The BMP is normal with a serum glucose value of 86. The cholesterol level is 310 which is elevated; triglycerides are 140; high-density lipoprotein (HDL) is 60; low-density lipoprotein (LDL) is 209 which is elevated. A liver panel is ordered based on the patient's report of drinking more than the recommended two drinks for males; the results are within recommended range.

The patient's diagnosis is hypercholesteremia and he is started on 40 mg of Atorvastatin daily, which works, by decreasing overall cholesterol, triglycerides, LDL-cholesterol, and elevating HDL-cholesterol. There is the possibility of recommending lifestyle changes for a period of time prior to starting statin therapy, but based on the family history of cardiovascular disease and the patient's presentation of an elevated lipid panel, therapy is appropriate at the visit. He is educated that the medication may cause some nausea, vomiting, and cramping and if these occur he should call. It is recommended that the patient decrease fast-food intake to one to two times a week rather than daily and limit alcohol intake to two drinks per day. He should

follow up in three months or call sooner if he experiences adverse effects. Another recommendation that could be made is to engage in aerobic exercise in addition to the current weightlifting for cardiovascular fitness.

Review of Literature

Databases utilized include CINAHL, ClinicalKey, Google Scholar, and UptoDate. Some of the key terms utilized to narrow the search were “cholesterol” AND “children”, “familial hypercholesterolemia”, “cholesterol screening” AND “youth”. Limitations applied were those articles published in the United States within the last ten years.

The literature search is based on the twenty-four year old male patient included in the case study. The father, brother, and now the patient have hypercholesterolemia. The patient is an average size male with a BMI of 26.4, an acceptable blood pressure of 110/54, and is doing some strength training. He does have some unhealthy lifestyles that he needs to change, but based on the early onset of the hypercholesterolemia and the early onset of death in a family member it is reasonable to assume that the elevated lipid panel may be familial. If the patient had not come in at the request of his mother, he may not have had his fasting lipid panel checked until the recommended age of forty-five for males which may have been too late for this individual to do much in reversing his risk factors for cardiovascular health.

Prevalence of Hypercholesterolemia

Acceptable lipid values are those that were established from the early 1970s Lipid Research Clinical (LRC) Prevalence study that included a series of population based surveys offered in the United States and Canada as well as The United States National Health and Nutritional Examination Survey (NHANES). The NHANES is a program funded by the Centers for Disease Control and Prevention designed to assess the health and nutrition of adults and

children through physical examination and interview; the findings of these two studies are consistent with those of the National Heart, Lung, and Blood Institutes and the American Academy of Pediatric policy statement. According to the 2010 Centers for Disease Control and Prevention *Morbidity & Mortality Report,* as many as 20% of children between the ages of twelve and nineteen years have at least one abnormal lipid value. Abnormal values include a total cholesterol ≥200, a LDL level ≥130, non-HDL ≥145, elevated triglyceride ≥130, and a low HDL <40. Factors that contribute to hypercholesterolemia are an unhealthy lifestyle of sedentary lifestyle, alcohol consumption, and a fast-food diet, which also lead to childhood obesity. Unfortunately, this is the direction that the United States is heading as nearly one in three children is overweight or obese and is the number one health concern.

Hypercholesterolemia guidelines

The United States Preventative Services Task Force summary (2007) lists screening and treatment for lipid disorders in children and adolescents as a Grade I or insufficient evidence to recommend for or against any type of routine screening. In 2011, The National Heart, Lung, and Blood Institute published guidelines to reduce cardiovascular risk in children and adolescents. They recommend universal lipid screening and management once between nine and eleven years and again between seventeen and twenty-one years of age regardless of general health or cardiovascular disease risk. Lipid screening should start younger than nine and be completed between eleven and seventeen if there is a strong family history of cardiovascular events such as strokes, myocardial infractions, and acute coronary syndrome. There has recently been a move from focusing only on the LDL level to including triglycerides, non-fasting non-HDL, and HDL levels. This recommendation is given a B Grade. The Centers for Disease Control and Prevention (2010) and the National Lipid Association both support the 2011 National Heart,

Lung, and Blood Institute guidelines to do universal screening in children between nine and eleven. In 2011 the National Lipid Association developed guidelines for the diagnosis and treatment of familial hypercholesterolemia. Goldberg et al. (2011) lists the expert panel recommendations with universal screening at the above ages. Cholesterol screening should begin earlier if there is a family history of hypercholesterolemia or premature cardiovascular disease, but never later than the age of twenty.

Familial hypercholesterolemia

Both targeted screening and universal screening when done correctly will help diagnose familial hypercholesterolemia (FH). Chen and Hay (2015) and Ned & Sijbrands (2011) found that less than 20% of actual cases in the United States are diagnosed. Familial hypercholesterolemia is an autosomal co-dominant inherited disorder that is caused by one of over 1000 mutations of the LDL receptor gene and the gene for apolipoprotein B on the short arm of chromosome 19. Wiegman et al. (2015) recommend "diagnosis based on the presence of a elevated LDL-C level consistent with FH plus a family history of premature coronary heart disease and/or baseline high cholesterol in one parent and/or a FH-causing mutation". Ned et al. (2011) are also supporters of cascade screening. If history is not known diagnosis of FH can be completed by DNA testing (Wiegman et al, 2015). An alternative method is universal screening in childhood. McCrindle (2012a) found that sometimes lipid screening alone may be insufficient to detect all FH. The potential to detect all FH is improved when universal lipid screening is used together with cascade screening. As compared to the other articles that explore FH detection, McCrindle (2015) is not as quick to start statin therapy. The recommendation is to consider family history and additional risk factors because although treatment may slow down atherosclerosis it does not correct the metabolic defect.

Not all elevated cholesterol can be attributed to genetics so the goal is to determine how health practitioners are able to detect those children and adolescents who may have an elevated cholesterol level but no known family history possibly due to lack of testing in the adult or poor dietary intake and sedentary lifestyle of the child. The literature search reviewed recommendations from multiple sources in regards to whether providers should target patients that have a family history of elevated cholesterol levels or if all children should be tested starting at a certain age.

Target screening with a focus on family history and body mass index.

The gold standard for cholesterol screening is based off the 1998 Coronary Artery Risk Detection in Appalachian Communities (CARDIAC) Project that is an ongoing project in the state of West Virginia that was initiated to monitor "chronic disease risk factor surveillance, intervention, and research initiative… to combat the unacceptably high prevalence of heart disease, diabetes, and other chronic illnesses" (CARDIAC, 2016). Ritchie et al. (2010) review the 1998 project design, which compared reported family history of hypercholesterolemia and fasting lipid profiles of fifth-graders. Selective screening rather than universal screening was used for reasons that have been common among proposers of targeted screening: labeling of children, overuse of medications, and the cost of universal screening. Inclusion criteria were offspring of parents or grandparents with a documented coronary artery disease before the age of 55, offspring of a parent who has a cholesterol level of >240, or a family history that was unobtainable. A downfall of targeted screen as demonstrated by the CARDIAC project is that a large percentage of children with hypercholesterolemia may be missed. As a result, since 2000 the CARDIAC Project has offered a free universal screening to fifth-grade students in West Virginia public schools using a universal approach. In addition to screening 5th graders the

project has expanded to provide screening, education, and intervention for children 15 years and younger. In a way this study has led to the conception that universal screening should be the norm, as family history alone is not enough to determine the need for cholesterol screening.

One of the misconceptions that has led to targeted testing is that hypercholesterolemia is only elevated in those who are obese. Margolis et al. (2014) examine the frequency and results of lipid testing between 2007-2010 among children ages three and 19 whom had no known history of dyslipidemia or indication for testing based on other medical diagnoses. The conclusion was that both normal weight and obese children have abnormal lipid levels. Daniels and Greer (2008), deFerranti (2012), Kit et al. (2012) have found that although childhood obesity is an epidemic, lipid levels have declined. In fact, cholesterol results are similar if not improved in the obese child as compared to peers because excess weight may contribute more to metabolic syndrome and decreased insulin sensitivity rather than hypercholesterolemia.

Targeted screening is too aggressive.

Since the issuing of the 2011 National Heart, Lung, and Blood Institute guidelines and the endorsing of universal screening there has remained skepticism from parents and providers. Wilson et al. (2015) review the adopting of the 2011 National Heart, Lung, and Blood Institute guidelines. There was a three percent increase in testing after educating providers as compared to prior with an overall screening rate of 20.1%. This statistic is not uncommon as Dixon, Komblum, Steffen, Zhou, and Steinberger (2014) report that the 31% of pediatric providers were unfamiliar with the lipid screening guidelines and the majority uncomfortable caring for lipid disorders in this population.

Newman, Pletcher, and Hulley (2012), and Psaty and Rivara (2012), and Schroeder et al. (2012) share the feeling that guidelines are too aggressive in treating pediatric lipid levels. Often

times the child is started on a statin which currently lack studies in the pediatric population. Psaty et al (2012) consider statins a present hazard with no clear long-term risk-benefit profile. Potential complications of overprescribing statins are the potential to increase the incidence of myopathy, rhabdomyolyis, and Type II diabetes. An additional negative is that often times a child with an elevated LDL level will be placed on a special diet with fasting lipid panels to be repeated every six to twelve months indefinitely even if the lipid value becomes "acceptable". Schroeder and Redberg (2012) are unsupportive of the National Heart, Lung, and Blood Institute guidelines as well because of the unnecessary testing. Stressors for the child include unnecessary lab pokes, need to be fasting prior, and consequences of having a life-long "disease" label. There is also the fear that assigning labels may give the wrong impression that the child's eating is not "healthy" resulting in eating disorders, especially in young girls.

Schroeder et al. (2012) criticize the National Heart, Lung, and Blood Institute recommendations for universal lipid screening in children as it leads to over diagnosis and an additional $200 billion per year in medical costs. One reason for over diagnosis is that there is one set of cutoff numbers regardless of gender (Newman et al., 2012). It has been found that girls have higher lipid levels during the age of testing, but have a lower cardiovascular disease risk profile in ensuing decades. Evidence is also lacking in estimating the clinical benefit of screening and treatment in individuals as children versus later in life. Possible harms of diagnosing elevated cholesterol in a child is that it can cause obsession with food, anxiety, unnecessary lipid testing or visits with a dietician, or opposition from parents leading to noncompliance.

Targeted screening advantages.

McCrindle, Kwiterovich, McBride, Daniels, and Kavey (2012b) accuse Newman et al. (2012) of misrepresenting the National Heart, Lung, and Blood Institute guidelines. They argue

that the focus of the National Heart, Lung, and Blood Institute guidelines is not to find the asymptomatic patients and start treating them, but instead identify those who have familial hypercholesterolemia (FH) and never knew it so that they may get early treatment. In Nherera et al. (2010) "new cases diagnosed with FH gained 3.3 years of life at an average lifetime cost of $8,700 per year gained, with twenty-six myocardial infarctions prevented for every 100 persons treated". There is a contradiction in this article compared to Newman et al. (2012) in that Nherera et al (2010) state that studies have been completed with children who have FH and there is no difference in health perceptions and coping as compared to peers without a cholesterol diagnosis. As Nherera et al. (2010) explain the overall assumption by many people is that if there is a noted elevation in the lipid panel the child will be started on a medication, but in fact, based on studies the percentage of children placed on drug therapy is only 1%.

Daniels et al. (2008) support McCrindle (2012b) and Nherera et al. (2010) that targeted screening should be the preferred method. Daniels et al (2008) place the emphasis on the need to assess cholesterol based environmental risk factors rather than a genetic predisposition. They support testing all overweight children and those who use product such as tobacco and oral contraceptives, which have the potential to affect lipid levels. Daniels et al. (2008) believe the approach to treatment should be focused on non-pharmacologic intervention and that pharmacological intervention be reserved for those older than eight years of age unless the LDL concentration >500 as seen with the homozygous form for familial hypercholesterolemia.

Universal screening is preferred.

Universal screening is the recommended approach to identifying at risk children as endorsed by the National Heart, Lung, and Blood Institute. The revision of the guidelines in 2011 stems from the failed attempt to identify 60% of children and adolescents using targeted

screening based on family history alone. McNeal, Underland, Wilson, and Blackett (2013) present a summary of views on universal screening. Those in favor of the universal screening do so because early diagnosis allows for therapeutic lifestyle interventions for the individual and family system, which slows the progression of atherosclerosis, development of diabetes, and cardiovascular disease. Testing youth adds the benefit of identifying high-risk adults. Ritchie et al (2010) share the same belief that universal screening will allow for early diagnosis and treatment to prevent arterial disease. A non-HDL cholesterol screening is the test of choice as it can be collected in a non-fasting state, is superior to LDL in predicting cardiovascular disease as an adult, and was the best predictor of atherosclerotic lesions on autopsy (McNeal, 2013). An added benefit is that identifying a child at risk helps identify parents and first-degree relatives who may not have known that they had elevated lipid levels. Dyslipidemia is a modifiable risk factor for cardiovascular disease and when diagnosed early allows for lifestyle modification and pharmacological treatment. The goal of universal screening is not to start every child that has an abnormal lipid level on drug therapy, but more so to emphasis primary prevention in an effort to reduce morbidity and mortality as an adult.

Learning Points

- When deciding whether to adopt the National Heart, Lung, and Blood Institute guidelines into practice there must be a weighing of benefits versus harms based on the family history of the child in addition to whether anything will be done if the lipid panel comes back elevated. If there will be no change in the lifestyle of the child or if the parents or medical provider would not change how they care for the child than there would be no reason to assess at such a young age.

- There remains debate of whether targeted screening or universal cholesterol screening in children is the right guideline. The majority of people agree that if there is a strong family history of cardiovascular disease than it may be appropriate to screen when someone is young. Those who oppose the universal screening do so because we are submitting young healthy children who are asymptomatic to blood draws, the unnecessary burden of knowing that they have a risk factor for cardiovascular disease, in addition to not knowing what the cost of screening and treatment will be not only for that child, but for all children combined.
- Early treatment with lifestyle modification and/or medication will help the child adopt a healthier lifestyle and decrease adult morbidity and mortality rates. In order to achieve this goal, parents and providers need to be aware of lipid screening guidelines. The recommended initial screening test for children with cardiovascular risk factors is a fasting lipid profile usually between the age of two and eight years of age. Otherwise for universal testing the first draw should be between nine and eleven years of age.
- There is no particular level of cholesterol in children that predicts risk of adult cardiovascular disease. Risk of a cardiac event is based on a combination of factors: diet, exercise, use of alcohol, tobacco, and medications. As providers we need to be less focused on the numbers and more focused on lifestyle modifications especially as it pertains to youth.

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