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Report of the National Heart, Lung, and Blood Institute's Working Group on Obesity and Other Cardiovascular Risk Factors in Congenital Heart Disease Pemberton-Obesity in CHD WG Report

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Introduction

Obesity among North American youth has risen to epidemic levels and is expected to result in costly and burdensome health problems, most notably type 2 diabetes and premature coronary artery disease. In the 2001–2002 NHANES survey, 31% of children aged 6–19 were overweight, defined as body mass index (BMI) at the 85th–95th percentile, or obese (BMI \geq 95th percentile)¹. Recent research indicates that a significant portion of children with congenital

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heart disease (CHD) are also obese or overweight². While much has been written on obesity prevention and management of children with normal hearts3, little is known about how children with CHD will be affected.

The National Heart, Lung, and Blood Institute convened a *Working Group on Obesity and Other Cardiovascular Risk Factors in Congenital Heart Disease* in May, 2009 to address knowledge gaps, challenges and opportunities related to research, policies and the clinical care of children born with CHD who also have or are at risk for obesity and other cardiovascular (CV) risk factors⁴. The Working Group (WG) was composed of individuals with expertise in pediatric obesity and pediatric cardiology with the goals of summarizing the existing evidence on obesity and CV risk prevention and treatment in the CHD population, raising awareness of missing data and presenting data from "healthy" children with potential applicability to children with CHD.

Here we will discuss the prevalence of obesity, potential etiologic factors, possible sequelae, and obesity and CV risk management and treatment in patients with CHD. The recommendations of the WG will be presented.

Prevalence of obesity in CHD

There are no longitudinal data on weight trends in children with CHD and only recently have concerns been raised about obesity. In 2005, Stefan demonstrated that children with CHD whose activities are restricted are at particular risk for obesity⁵. The first large study to investigate obesity in children with CHD, published just two years ago, found that 26% of 1523 patients, seen in two large outpatient pediatric cardiology clinics, were overweight or obese². Patients who had undergone the Fontan palliative surgical procedure for single ventricle physiology fared slightly better, with 16% being overweight or obese. Systolic blood pressure percentile was significantly higher in the overweight/obese group compared to the normal weight group, illuminating the potential for long-term complications in this vulnerable population.

Pasquali et al. recently demonstrated that nearly 1/3 of patients 6–19 years old who had undergone the arterial switch operation or Ross procedure (both require reimplantation of coronary arteries) were overweight or obese⁶. These children had higher left ventricular mass and as in the general pediatric population, were more likely to have an obese parent (defined as BMI>30 kg/m²). Reported activity level and diet did not differ significantly from that of the normal weight population. Of note, inactivity was very common in the entire cohort.

Currently, there are more adults $(>1,000,000)^7$ than children with CHD and the number is expected to grow at about 5% per year8. Obesity is of great concern in adults with CHD with 54% having a BMI >25 kg/m^{2, 9}. The most common complications in adults with CHD are arrhythmia, heart failure, endocarditis, cardiac conduit obstructions, valve regurgitation and pulmonary hypertension¹⁰. Although little evidence exists to suggest how obesity may affect adults with CHD, it is reasonable that obesity will adversely influence at least heart failure and pulmonary hypertension in these individuals.

Etiology of obesity and CV risk in CHD

The development of obesity in children derives from a number of etiologic factors including biological and physiological (genetic predisposition and appetite), personal (physical activity and diet), environmental, societal and healthcare-related¹¹. While obesity has not been studied systematically in individuals with CHD, compelling contributing factors include nutrition and physical activity. The physiology of certain types of heart disease may affect CV risk.

Nutrition

For children with serious CHD, the battle to gain sufficient weight has traditionally begun in infancy. Heart failure, hemodynamic compromise and metabolic response to stress following cardiac surgery places additional burden on the neonate with limited metabolic reserves¹². Severity of the congenital defect and cyanosis appear to dictate both the energy requirement and the nutrient intake. From birth through the first two years of life, body weight, growth rates and energy intakes in children with CHD are often below the norm¹³.

Postnatal nutritional interventions aim to increase calories through supplemental feedings, alternative feeding methods and feeding protocols developed to promote weight gain12. In non-CHD infants, rapid growth has been associated with enhanced risk of obesity, diabetes, hypertension, CV disease and osteopenia in later life¹⁴. When small for gestational age (SGA) children were compared with normal birth weight children at age 4, they already had increased central adiposity and insulin resistance¹⁵. Key questions remain about how early feeding behaviors, increased caloric density early in life and dietary recommendations affect early growth patterns in children with CHD and whether families treat their child with CHD differently than usual care families.

Physical activity

The American Heart Association guidelines indicate that most children with CHD can be fully active, ¹⁶ but children with CHD are less likely to meet physical activity recommendations than their peers¹⁷. Behavioral factors appear to influence inactivity more than the severity of the condition. Self esteem and physical self concept are compromised in some children with CHD and may limit their inclination for activity¹⁸.

Children with CHD often lead sedentary lives even after their heart defect has been successfully treated. In a study of 144 children post-Fontan, aged 7–18, the mean self reported time spent in physical activity was 7 hours per week compared to 28 hours per week engaged in sedentary activities. However, accelerometry indicated that only 38% of study subjects actually met physical activity recommendations for children and adolescents¹⁹. Research has focused on measurements of exercise capacity (maximal heart rate or oxygen consumption) as indicators of cardiac performance. Children with CHD have normal peak heart rates $(189\pm12 \text{ bpm})^{20}$ but decreased peak oxygen consumption21, indicative of suboptimal fitness. The benefits and safety of exercise training for increasing fitness have been described for this population22 with increased fitness levels persisting over the long term23.

Children with CHD and their parents often self-limit exercise or sports²⁴ which may be unnecessary and even counterproductive. Children who are formally restricted from physical activity or competitive sports have a higher BMI over time⁵. Parental anxiety over the safety of physical activity might exceed their interest in promoting fitness. Less physical activity in childhood extends into adulthood where individuals again fail to achieve recommended levels of physical activity²⁵. It is daily physical activity which is closely associated with decreased risk for CV disease, obesity, diabetes and hypertension.

Pediatric cardiologists are frequently asked to provide recommendations for physical activity, but these may be inappropriately extrapolated from published guidelines for competitive athletics in children with heart disease²⁶, providing little practical advice for parents about more routine physical activity. Lunt and colleagues found that only 19% of young adult subjects with CHD received advice about physical activity²⁷. While guidelines exist for competitive sports participation in athletes with specific CV abnormalities²⁸ and for recreational activities in children with genetic heart conditions²⁹, none currently exist for safe physical activity for individuals with complex forms of CHD or for those whose hemodynamics are suboptimal.

Development of guidelines and consensus statements to encourage regular physical activity outside of competitive sports will require research to determine the type, duration and intensity of activity in which an individual with a particular cardiac lesion can participate safely³⁰.

Specific malformations and their treatment

CV risk may vary by type of heart defect. For example, it is possible that specific conditions where the coronary arteries are directly affected or altered surgically may confer greater risk for premature atherosclerotic coronary artery disease⁷. Coronary artery re-implantation at the time of transposition repair has been shown to result in abnormal coronary flow reserve³¹ and intracoronary ultrasound reveals that some patients develop intimal proliferation, a precursor to atherosclerosis³². Left-sided obstructive lesions may also be associated with accentuated CV risk. Coarctation of the aorta, even after repair, commonly is associated with systemic hypertension; aortic stenosis can be associated with left ventricular hypertrophy and diastolic dysfunction, known risk factors for adult-onset CV morbidity and mortality⁷. Interestingly, in a study of adults with CHD, no cyanotic patient had coronary artery disease, leading to the hypothesis that cyanosis may be protective³³.

Sequelae of obesity and CV risk factors in the patient with CHD

The relationship between childhood obesity and subsequent CV risk has been well described in children without CHD. These data suggest that the adverse effects of obesity on the patient with CHD include its potential impact on physiology, functional health status and quality of life.

Pathophysiologic sequelae

Obesity is associated with the presence or future development of hypertension, insulin resistance, dyslipidemia, increased inflammatory cytokines, sleep apnea, autonomic imbalance and abnormal cardiac remodeling34. In the obese individual without CHD, hypertension is often the result of increased fluid retention associated with an increased plasma volume and cardiac output35. Fluid retention is caused by activation of both the sympathetic nervous system and the renin-angiotensin-aldosterone system³⁶. The physiologic consequences of insulin resistance include altered lipid metabolism (increased triglycerides, decreased HDLcholesterol, and LDL-cholesterol particles that are small, dense and atherogenic)³⁷, altered vascular reactivity in both peripheral and coronary arterial beds38, non-alcoholic fatty liver39 and the development of type 2 diabetes. Obesity is also associated with an increase in the inflammatory cytokines known to be related to atherosclerosis and coronary artery disease 40. The autonomic imbalance associated with obesity includes withdrawal of parasympathetic tone and sympathetic predominance with a resultant reduction in heart rate variability and increased risk of atrial and ventricular dysrhythmias⁴¹. Finally, obesity is also associated with diastolic and systolic ventricular dysfunction, left ventricular hypertrophy and congestive heart failure^{42, 43}. All of these factors have potential adverse consequences for individuals with CHD, many of whom are already at risk for ventricular dysfunction, heart rate and rhythm disturbances, and overt heart failure.

Obesity might adversely affect an individual with CHD and is illustrated by the patient after Fontan repair for single ventricle. The current staged surgical approach, culminating in the Fontan procedure, results in passive systemic venous flow rather than active pumping of blood to the lungs, because the single ventricle must pump to the systemic circulation. An increase in fluid volume or sleep apnea associated with obesity would increase already elevated rightsided volume and filling pressures, leading to increased risk of edema and ascites. Increased inflammatory cytokines might enhance the thrombotic risk, or play a role in the pathogenesis of protein-losing enteropathy, a serious morbidity which occurs in approximately 5% of patients with Fontan physiology⁴⁴. The autonomic imbalance might lead to a further increase in the already significant risk of atrial rhythm disorders. Finally, obesity could exacerbate the diastolic dysfunction already seen in over 70% of children and young adults with the Fontan circulation⁴⁵.

But how the pathophysiology of CHD interacts with obesity and other CV risk factors is unknown. Patients with CHD have an abnormal myocardial substrate upon which these traditional CV risk factors are superimposed. Not only is the heart abnormally formed but the myocardium is subject to periods of cyanosis and ischemia-reperfusion during one or more surgical operations. However, a recent study demonstrated that atherosclerotic coronary artery disease in adult patients with CHD with no history of ischemic heart disease was associated with abnormal systolic and diastolic dimensions of the systemic ventricle³³. These findings, while preliminary, certainly suggest the potential implications of traditional CV risk factors in the setting of CHD.

Functional health status and quality of life

Research on the impact of obesity on functional health status and quality of life shows that when compared with lean children, obese children report poorer quality of life⁴⁶ and are more likely to have functional limitations. Young adolescents have more difficulties with depression, self-esteem and school and social functioning⁴⁷.

Children with CHD are at higher risk for behavioral and emotional problems⁴⁸ with neurologic deficits and behavioral abnormalities among the most concerning long-term morbidities. Neurodevelopmental impairments and exercise limitations are factors which may contribute to lower perceived quality of life for these children. The typical neurodevelopmental impairments observed in children with CHD include abnormalities in memory and higher order language function, visual-spatial relations, and executive function⁴⁹. Attention deficit disorder has also been found to occur at higher rates⁵⁰.

Obese children and adolescents are at increased risk for obstructive sleep apnea (OSA) which can lead to memory impairment⁵¹ and behavioral abnormalities52. While the effects of obesity and OSA have not yet been measured for patients with CHD specifically, the possible combination of obesity superimposed on this at-risk population is likely to lead to worsened school outcomes and a negative impact on quality of life.

Prevention and management of obesity and CV risk

Guidelines for children's daily energy requirements, nutrient intake, and physical activity levels have been published³. Much of this work is directly applicable to children with CHD and includes important recommendations to:

- Reduce excess energy intake through nutrient-dense, lower calorie food choices and promote specific eating behaviors associated with weight control (e.g. eating breakfast daily). In a British study, an approach to reduce sugar-sweetened beverages helped prevent obesity⁵³.
- Limit screen time and increase energy expenditure through at least 60 minutes of moderate to vigorous physical activity daily. Reduced screen time (i.e., television and video games), achieved through parent training or automated "TV Allowances," has been linked to obesity prevention⁵⁴. Home-based activity programs can increase physical activity in children with CHD by 90 minutes/week55. Reducing screen time can be as effective as increasing physical activity for the treatment of pediatric obesity56 and may be an appealing option for parents of children with CHD, who are concerned about intensive exercise.

The American Heart Association's Scientific Statement on CV risk reduction outlines treatment recommendations for individuals with CHD to include evaluation of diet, blood pressure, lipids, glucose, smoking and activity⁷. Strategies to reduce risk in children without CHD may be equally effective in children with CHD such as parent training in behavioral modification for prevention and management of obesity⁵⁷. Skills to identify target behaviors, self-monitor, set goals, and provide feedback have demonstrated moderate effect in the general population. Lasting interventions rely on the parent to model and facilitate healthy behaviors for the family, particularly for younger children who rely more on parental support⁵⁸. Guidelines and educational websites developed for all children are useful resources for recognition and management of CV risk factors in patients with CHD (Table 1). Additionally, parents see the internet as a helpful tool for learning about CHD⁵⁹ and the development of interactive, scientifically-accurate tools may help them to encourage appropriate activity for their children.

The health care provider's role in obesity and CV risk management

Both primary care providers and pediatric cardiologists can make valuable contributions to CV risk assessment and management in patients with CHD. The generalist has comprehensive knowledge of the family, familiarity with screening guidelines, experience with providing nutritional, physical activity and smoking cessation counseling, and proximity to the patient's residence for close follow up. Assets of the pediatric cardiologist include knowledge of the underlying cardiac condition, ability to perform exercise testing, familiarity with more sophisticated risk assessment and use of medications if needed, and the ability to provide exercise prescription. However, little time is devoted to CV risk assessment and management at most health care visits among both generalists and cardiologists whose endorsement of parental modeling of ideal lifestyle behaviors is essential to motivating family-based changes.

A poll of pediatric cardiologists to evaluate counseling on specific CV risk factors found that they believed that promotion of CV health was a more appropriate role for primary care providers than for pediatric cardiologists⁶⁰. Evaluation at two major pediatric heart centers found that practitioners failed to document obesity and/or weight counseling in >85% of their patients with heart disease².

Parents of obese or overweight children often perceive their child as being about the right weight, fueled in part by lack of attention to weight issues at health care visits. If the parent recalls a past expression of doctor concern about the child's weight, the parent is more likely to be concerned⁶¹. Anthropometry at every visit, accompanied by an explanation to the parent of the gap between a child's healthy weight and their current weight, can reinforce correct perceptions of weight and nutritional status.

Physicians often cite time as a barrier to counseling families. However, many office resources (e.g. handouts, assessment forms, etc.) are free and readily available on the web (Table 1). Activities that promote healthy nutrition and physical activity can be found in community settings as well. However, the link between the clinical encounter and the community resource may be weak or non-existent ⁶². Materials must be adapted for the child with CHD to address their unique physiological and social needs.

Recommendations from the WG

To address the research and training gaps and opportunities identified, the WG recommended that NHLBI:

1. Establish a collaborative process, with the Atherosclerosis, Hypertension and Obesity in the Young Committee and the Congenital Cardiac Defects Committee, both of the

American Heart Association's Council on Cardiovascular Diseases in the Young, to develop guidelines for the promotion of safe physical activity for children with CHD by lesion and to provide screening/counseling tools for healthcare providers. Since current practice may be too restrictive and may add to the health issue of obesity in this special population, this recommendation was viewed as a priority by the WG.

- 2. Support training of new specialists in preventive pediatric cardiology research and rehabilitation through already established funding mechanisms (training and fellowship grants) and encourage clinical research through Clinical Skills Development Cores established within the NHLBI's Pediatric Heart Network (PHN) and the new Childhood Obesity Prevention and Treatment Research Consortium. Despite a mandatory research year during fellowship training, few pediatric cardiologists have advanced training in clinical research methods. This might be addressed by promoting formal clinical research training prior to and during clinical fellowship and fostered by funding programs for such training and specialized centers/ programs to deliver that training.
- **3.** Support interdisciplinary research specific to the CHD population to address unexplored scientific areas, focused on solution-based initiatives over mechanistic inquiry, including discovery of:
 - **a.** optimal biomarkers and measures of obesity (which measures would be more sensitive and specific than BMI),
 - **b.** the best outcomes to measure,
 - **c.** parental/healthcare provider perceptions of obesity, activity risk and tolerance,
 - d. the impact of traditional risk factors in CHD,
 - e. obesity and CV risk prevention and management strategies,
 - f. the impact of nutrition and early feeding behaviors,
 - **g.** new insights gained from CHD pathophysiological models to inform the treatment and prevention of adult diseases and morbidities (e.g., the observation that patients with cyanotic heart disease tend to have minimal atherosclerosis to direct research efforts evaluating anti-atherogenic mechanisms), and
 - **h.** optimal levels for all CV risk factors in patients with CHD.
- 4. Facilitate research in the CHD population along the life continuum through collaborations between existing NIH-supported Networks (especially the Pediatric Heart Network and the Childhood Obesity Prevention and Treatment Research Consortium) and encourage utilization of the Clinical and Translational Science Award (CTSA) institutions/resources. A multi-institutional network of expertise of preventive cardiology and rehabilitation programs might be formed that is multidimensional and interdisciplinary, utilizes common databases, shares resources, and develops guidelines and educational/research programs. Opportunities should be pursued to develop linkages with non-CHD groups which are associated with an increase in CV risk, such as solid organ transplantation, childhood cancer survivors and patients with chronic infectious and inflammatory diseases.
- 5. Establish platforms for existing registries and support new registries to merge the data from CHD patients to be used for future research in obesity and CV risk.

Obesity and other CV risk factors are important health concerns for patients with CHD. With a coordinated effort aimed at increasing infrastructure, capacity and new knowledge, CV risk can be more effectively identified and addressed for patients with CHD.

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US Department of Agriculture	Weight and Obesity: Food and Nutrition Information Center:http://fnic.nal.usda.gov Smart Nutrition 101: http://www.nutrition.gov	Links to food pyramid, dietary guidelines, and information for clinicians, parents and children
US National Heart Lung and Blood Institute, National Institutes of Health	http://wecan.nhlbi.nih.gov	Nurrition and physical activity materials for clinicians, parents and community programs on childhood obesity prevention
US Department of Health and Human Services, Office of the Surgeon General	http://www.surgeongeneral.gov/obesityprevention/resources/index.html	Links to pediatric programs and resources for staying active and making healthy choices aimed at children, parents and health professionals
National Initiative for Children's Healthcare Quality	http://www.nichq.org/childhood_obesity/childhood_obesity_toolkit.html includes both materials and links	Management algorithm, screening surveys, prevention and intervention handouts
Centers for Disease Control Childhood Obesity	http://www.cdc.gov/HealthyYouth/obesity/index.htm	BMI calculator, intervention programs and risk behavior surveillance data
American Heart Association Childhood Obesity	http://www.americanheart.org/presenter.jhtml?identifier=3030490	Scientific statements, statistics and guidelines on subjects such as diet and physical activity.
American Public Health Association	http://www.apha.org/programs/resources/obesity/	Brochures, video clips, games, campaigns and recipes from various sources, compiled here
American Academy of Pediatrics	http://www.aap.org/healthtopics/overweight.cfm	Family and community resources and professional guidelines, policy statements and reports on obesity prevention.