ENERGY INTAKE AND EXPENDITURE IN

JAMAICAN CHILDREN 3 TO 6 YEARS

OF AGE WITH HOMOZYGOUS

SICKLE CELL DISEASE

BY

STEPHANY PAIGE PARKER

Bachelor of Arts

The University of Georgia

Athens, Georgia

1992

Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment for
the requirements for
the Degree of
MASTER OF SCIENCE
July, 1997

OKLAHOMA STATE UNIVERSITY
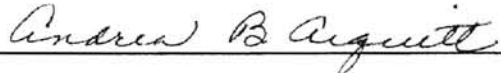
ENERGY INTAKE AND EXPENDITURE IN

JAMAICAN CHILDREN 3 TO 6 YEARS

OF AGE WITH HOMOZYGOUS

SICKLE CELL DISEASE

Thesis Approved:

_____
Thesis Advisor

_____

_____

_____
Dean of the Graduate College

ACKNOWLEDGEMENTS

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

ENERGY INTAKE AND EXPENDITURE IN JAMAICAN CHILDREN 3 TO 6

YEARS 0F AGE WITH HOMOZYGOUS SICKLE CELL DISEASE

Introduction

Sickle cell disease is an autosomal recessive blood disorder. Sickle hemoglobin (HbS) is an abnormal hemoglobin in which valine is inserted at position β^6 instead of glutamic acid which is present in normal hemoglobin (HbA). The term sickle refers to the sickled or crescent shape of red blood cells. Homozygous sickle cell disease (SS disease) refers to the inheritance of the abnormal sickle cell gene (HbS) from both parents.

Homozygous sickle cell disease is widespread affecting 8 of 100,000 people worldwide (1). There is a common misconception that sickle cell disease affects only people of African origin. Contrary to this belief, the disease also affects individuals from the Caribbean, Central America, South America, Turkey, southern Greece, Italy, Saudi Arabia, and eastern India (2). Migration of these people has led to the presence of the sickle cell gene throughout the world. Conditions in Jamaica are ideal for studies of sickle cell disease in that one in every 300 births is affected by SS disease (1).

1

Since sickle cell disease is a genetic disorder, the only cure at the present time is a bone marrow transplantation. This method is very risky in that 10% of the patients die from the treatment itself (3). For this reason, bone marrow transplants are only advised for those patients with severe complications which means that only 20% of sickle cell patients are suitable for the treatment (4). In addition to the risks posed by the method, the cost of the treatment cannot be afforded by most, especially those in developing countries where resources are scarce.

Treatments for sickle cell patients have improved. In the early 1970's patients had a 50% chance of surviving to adulthood, while today a child with sickle cell disease has a 90% chance of reaching adulthood (5). Despite improvements, sickle cell disease continues to cause significant morbidity and mortality during childhood. Infections and painful crises are frequent complications of children who have sickle cell disease. In a Jamaican cohort study, the mortality rate of children was reported as 10% in the first year of life, 5% in the second year of life, and 3% in the third (6). Approximately 20% of deaths in children are due to chronic organ failure (7).

In addition to the physical ailments suffered by children, sickle cell disease affects growth and development. Children with sickle cell disease exhibit deficits in height, weight, skeletal maturation and delayed puberty (8). Moreover, Knight and colleagues found that prepubertal height in Jamaicans was highly correlated with genotype differences in IQ (9). The impaired growth and mental development in sickle cell disease are similar to deficits found in children with chronic malnutrition and suggest that the nutritional status of children with sickle cell disease might also be impaired.

Research indicates that a relationship exists between nutrition and sickle cell disease (10, 11, 12). Nutritional factors might offer an explanation for the wide clinical variation observed in the course of the disease. Some sickle cell patients exhibit very mild clinical courses and have few hospital admissions while others have more severe clinical courses and are admitted to the hospital more frequently.

The physiologic synergism between malnutrition and infection has long been recognized. Malnutrition adversely affects an individual's ability to resist or respond to infection, and infection adversely affects an individual's ability to utilize energy and nutrients obtained from the diet (13, 14). Studies have shown that mortality is increased in individuals that are only moderately malnourished. In a study assessing nutritional status as a predictor of child survival, Schroeder and Brown found that mild to moderately malnourished children 6 to 60 months of age had 2.2 times the risk of dying than their better nourished counterparts while severely malnourished children had 6.6 times the risk of dying compared with their better nourished counterparts.

A number of macronutrient and micronutrient deficiencies have been suggested in sickle cell disease. However, inconsistent laboratory and anthropometric data have yielded conflicting results (10). At the present time, studies investigating associations between nutrition and sickle cell disease have been limited by the small number of patients studied and the selection of inappropriate controls.

In light of these shortcomings, this study was designed to evaluate genotype differences in the nutritional status of Jamaican children 3 to 6 years of age. The

genotypes to be compared are those of normal genotype (AA) and those with homozygous sickle cell disease (SS).

Objectives

The following research objectives were developed for the proposed study:

1. To determine a dietary assessment method suitable for use in Jamaican children 3 to 6 years of age.

2. To determine if the dietary intake of Jamaican children differs due to gender or homozygous sickle cell disease.

3. To determine if the resting energy expenditure of Jamaican children differs due to gender or homozygous sickle cell disease.

4. To determine if anthropometric measures of Jamaican children differ due to gender or homozygous sickle cell disease.

Hypotheses

The following hypotheses were developed for this study.

1. There will be no significant differences in dietary assessment methods.

2. There will be no significant differences in dietary intake due to gender or the presence of sickle cell disease.

3. There will be significant differences in measures of resting energy expenditure due to gender and the presence of homozygous sickle cell disease.

4. There will be a significant difference in anthropometric measurements due to gender and genotype.

Limitations

This study was conducted in the confines of a developing country. As a result, transportation was not always available at the needed times.

Jamaican children begin school at 3 years of age. Since the study subjects were 3 to 6 years of age, all were in school at the time the study was to be conducted. The construct of schools is not conducive to obtaining dietary data. Children often eat from venders on the street and following a child could interrupt normal eating habits. For this reason, the measurement of dietary intake took place from Friday to Sunday. Dietary intake may differ from Monday to Thursday. As a result, the dietary data obtained may not be indicative of usual eating habits.

In order to fully examine energy expenditure, physical activity levels should be examined. This study did not possess the resources to examine physical activity levels, further limiting the study.

Definition of Terms

Hemoglobin: a globular protein molecule composed of two pairs of polypeptide chains, each being folded around a pocket containing a heme molecule (15).

Sickle hemoglobin (HbS): a single point mutation where valine is inserted at position β^6 instead of glutamic acid that occurs in normal hemoglogin (15).

HbA: the normal hemoglobin gene (15).

Normal genotype (AA): refers to the inheritance of HbA from both parents (15).

Sickle cell trait (AS): the harmless carrier state acquired by the inheritance of one abnormal gene (sickle cell gene designated S) and one normal gene designated A (15).

Sickle cell disease: a generic term for disease states attributable to the presence of HbS. It includes all genotypes of sickle cell disease except the harmless sickle cell trait (15).

Homozygous sickle cell disease (SS disease): refers to the inheritance of the sickle cell gene from both parents (15).

Bone marrow transplantation: a method which has the potential to change the phenotype of SS patients to that of an AA or AS subject (15).

Eunochoid habitus: the physique of SS patients characterized by excessive growth of the long bones and infantile sexual organs (16).

Resting metabolic rate (RMR): the metabolic rate in the awake, resting, postabsorptive subject (17).

Gonadotropin: any hormone that stimulates the gonads (16).

Luteinizing hormone(LH): an anterior pituitary hormone causing secretion of female sex hormones by the ovaries or male sex hormones by the testes (16).

Follicle stimulating hormone (FSH): anterior pituitary hormone that causes growth of follicles in the ovaries prior to ovulation or promotes the formation of sperm in the testes (16).

CHAPTER II

REVIEW OF LITERATURE

Jamaica: Background Information

Jamaica is a middle ranked developing country located 145 kilometers south of Cuba and 160 kilometers west of Haiti in the northern Caribbean Sea. With a total land area of 11,000 square kilometers, it is about the same size as Connecticut and the third largest island in the Caribbean (Figure 1).

Kingston is the capital and urban center of Jamaica located on the east coast of the island. The city hosts over 600,000 of the country's population of 2,500,000. Migration to this urban center contributes to the city's poor transportation system. The majority of Jamaicans travel by buses that are overcrowded and do not run at scheduled times. Transportation problems are prevalent throughout the island and the conditions of the roads are poor.

English is the official language of Jamaica. However, when conversing in the home and in casual conversation, most Jamaicans speak Patois derived from English and African languages.

Jamaica's national motto "out of many, one people" reflects its multiracial composition. Ethnic divisions of the population include descendants of African (77%),

Figure 1. Map of the Caribbean Area.

The Caribbean

Afro-European (15%), East Indian (3%), Chinese (1%), and other (1%) origins (18). Nearly fifty percent of the population are under sixteen years of age.

Jamaica reports a literacy rate of 82% (18). Although education is compulsory to the age fourteen, thousands of working-class and middle class families are unable to afford fees to pay for books, supplies, and uniforms (18). As a result, some children take to the streets begging to help sustain the household or are left at home unattended while the bread winner is away .

The University of the West Indies is located in the Kingston area. However, few Jamaicans are able to afford tuition, and those who are able to afford fees are threatened by recent tuition hikes (18). Those who are able to obtain degrees seldom find gainful employment in Jamaica. Subsequently, many seek employment in North America or Europe and send money home to help support the family. The migration of Jamaica's highly educated has resulted in a serious deterioration of the economy's ability to produce goods and services (19).

Jamaica's tourist sector is the economy's most important foreign exchange earner. The white sand beaches along the northern and western coasts beckon tourists worldwide. However, the forecast for continued tourism is uncertain due to infrastructure limitations of airports, roads, harbors, and sanitation facilities (20). Jamaica's natural resources include bauxite, alumina, gypsum, and limestone. Mining of alumina and bauxite is the economy's second most important exchange earner.

Traditionally, agriculture was the mainstay of the Jamaican economy. More recently, the production of agricultural products such as sugar cane, bananas, coconuts,

and citrus fruits has declined due to competition from foreign producers, price fluctuations, and disease. Nonetheless, agriculture related activities still employ about 30% of the work force albeit wages are low. The future of the agricultural sector is uncertain as many farmers facing a credit crunch have failed to meet production projections (21).

Jamaica has experienced serious economic problems since 1993. High unemployment averaging 18.2%, inflation, depreciation of the Jamaican dollar, and labor unrest contribute to the recent increase in crime, especially in Kingston (18). Analysts warn that women workers, the heads of over 40% of Jamaican households, are bearing the brunt of unemployment with an unemployment rate over two times that of men. Consequently, many women find it difficult to provide the family with the basic essentials of food, clothing and shelter (22).

Less than 10% of Jamaica's population can afford the least expensive housing unit in urban areas (20). Thus, many settlements in these areas are squatter settlements, captured land settlements composed of make-shift housing with inadequate sewage facilities. The minimum wage for forty hours of work is J$750.00, the equivalent of U.S. $23.30. As a result, over one-third of the population live beneath the poverty line (20).

The decline in agricultural production, an increase in the cost of imported foods, and poor economic conditions contribute to food insecurity among the poor. A survey of Jamaican households indicated that the poor may spend as much as 80% of their income on food (23).

If economic conditions do not improve, serious health repercussions will be felt by Jamaicans in the near future. At the present time, however, Jamaicans enjoy a level of health higher than that of most developing countries. Life expectancy is 71 years and the infant mortality rate is 25/1000.

Chronic and degenerative diseases are the nation's biggest health problems. The leading causes of death are cerebrovascular accidents and coronary heart disease (24). AIDS is a growing problem in Jamaica and is for the most part socially unacceptable (25). In a study conducted in Montego Bay, 100% of prostitutes tested positive for HIV. Mortality rates of AIDS patients are high due to scarce resources and social ramifications (25).

Congenital abnormalities and perinatal morbidity are the leading causes of infant mortality in Jamaica (24). Other health problems of infants and children are diarrheal diseases, malnutrition, and iron deficiency anemia. The incidence of protein energy malnutrition has declined since the late 1980's, but room remains for improvement. Recent studies have shown that 6.9% of preschool children are moderately malnourished, and 1.2% are severely malnourished (24). Micronutrient deficiencies, such as deficiencies of vitamin A and iodine, which are common in developing countries are rare in Jamaica (26).

Jamaica's health care services are provided free or at a nominal charge to all citizens (27). Public health centers are located throughout each of the fourteen parishes with a mean distance of 2.4 miles from home to health care in all but one parish (28).

However, a number of health centers in rural areas are inaccessible to patients and staff due to poor road conditions.

Jamaica has experienced an overall decline in the quality of health care received in recent years (27). The shortage of family physicians, nurses, community health aides and domiciliaries continues to increase because of low wages offered them. Facilities are limited in resources. New equipment, medical supplies, and essential drugs are desperately needed in most health centers.

The History of the Sickle Cell Unit

The Sickle Cell Unit is located at the University of the West Indies in Jamaica. The clinic was started by Dr. Paul Milner who was astonished not only by the high frequency of sickle cell disease in Jamaica but also by longevity of the patients (29).

Today the Sickle Cell Unit functions with 3 main objectives.

1. To conduct research. The Sickle Cell Unit is funded primarily by the Medical Research Council, a British funded organization which supports a variety of medical research. The foci of research are to learn more about the natural history of sickle cell disease and to improve the management of complications associated with sickle cell disease. To date, research from the Sickle Cell Unit has produced 2 books and over 300 scientific papers.

2. To provide service. The Sickle Cell Unit located at the University of the West Indies operates daily and undertakes the management of most patients with sickle cell disease islandwide. Staff from the Sickle Cell Unit visit Black River Hospital and

Cornwall Regional Hospital monthly and provide services to patients living in those regions. Patients receive all services and most treatments free.

3. To provide education. Unit staff provide all undergraduate, postgraduate and some pediatric teaching of sickle cell disease. In addition, public education is provided by means of radio, television, newspaper, pamphlets, and lectures to local schools and colleges.

The Sickle Cell Unit serves over 5000 patients islandwide. The follow-up of these patients is good because of the cooperation and understanding of Jamaican patients coupled with the relatively well developed communication system.

Origin of the sickle cell gene

The sickle cell gene probably evolved because it renders some protection against faliciparum malaria during childhood. Early observations revealed that malaria occurred less frequently in individuals with the sickle cell gene (30). Additional observations noted that those children with the sickle cell trait who contracted malaria generally had uncomplicated clinical courses when compared to the clinical courses of those of normal genotype. Hence, the sickle cell trait (AS) most likely evolved in malarious regions (30). Migration and the slave trade lead to the presence of the sickle cell gene in non-malarious regions of the world. The sickle cell trait is harmless to the individual.

Homozygous sickle cell disease (SS disease) refers to inheritance of HbS from both parents. There is a 1 in 4 chance that a child will be born with SS disease if the parents have the sickle cell trait. The clinical course of SS disease is variable but often

severe. The deleterious effects of the disease are felt most by those living in developing countries where resources are scarce.

Homozygous Sickle Cell Disease and Growth

The adverse effects of sickle cell disease on growth and development have long been recognized. Washburn's report in 1911 was in all likelihood the study that generated research in the area of growth and development in sickle cell disease. In his report, he noted a delay of menarche to 18 years (31). In a subsequent study, Mason et al noted the slender build and poorly developed sexual traits of a 21 year old male patient (32). Since then studies have repeatedly documented not only deficits in physical development but also delays in sexual development.

Physical Development

Although deficits in height and weight are generally accepted, the age at which such deficits become noticeable varies (33-36). The lack of racially appropriate controls and the lack of appropriate height and weight standards make early studies of preadolescent growth difficult to interpret (33).

Provided that there are no complications in utero, infants with homozygous sickle cell disease generally exhibit normal birth weight and length (15, 33, 34). In general, growth deficits are recognizable by 4 to 6 months of age (15, 34). In a study comparing the growth and development of 14 newborns matched with appropriate controls, Kramer et al reported no deficits in weight or length until 5 or 6 months at which time in vivo

sickling begins (34). After this time, both weight and length deficits tended to increase with age.

In an attempt to determine whether height and weight deficits recognized in SS children were attributable to race differences or inappropriate standards, Whitten conducted a study comparing the growth of 48 SS children ranging from 2 to 13 years to their normal AA siblings (33). He reported that both SS children and AA siblings weighed less than standards for American white children. However, the mean ($\pm$ SD) percentile ranking for normal siblings was $41.4\pm$ 25.4 in contrast to 17.1 ± 17.4 for those with SS disease, indicating that SS children weigh less than both their normal siblings and normal white children (33).

Additional deficits in anthropometric measures have been observed in the United States (36-37). Significantly lower measures of height, weight, sitting height, calf and upper arm circumference in SS children as a group have been reported when compared to children of normal AA genotype (36). However, when analyzed according to sex, SS boys exhibited lower values than SS girls for all measures except height and sitting height beginning at 6 years of age. Observations noting gender differences in SS disease are not confined to this particular study. Possible gender related differences in the growth of children with SS disease have been postulated with greater deficits purported in male children with SS disease (38).

Data from Jamaica has indicated that children with SS disease exhibit more marked weight deficits than height deficits. Lowry reported that the weights of Jamaican

15

children were lower than local standards with the difference becoming significant at 10 years of age (39).

In contrast, Stevens et al reported both weight and height deficits in Jamaican children (35). The study subjects were participants of the Jamaican cohort study of sickle cell disease. The results indicated that mean weight in SS children decreased to less than that of AA controls before the first year of age with a significant difference in weight occurring at 12 months in girls and 21 months in boys (35). In both sexes, divergence of the two genotypes was evident by 2 years of age, with SS girls demonstrating greater deficits than SS boys. The deficit continued to increase with age, approaching 1 SD less than normal by 9 years of age. The significantly lower mean weight recognized in SS children continues throughout adulthood. However, the height of SS patients catches up to that of AA controls during adolescence and generally exceeds that of AA controls by about 20 years of age suggesting a delay in the skeletal maturation of SS children.

Perhaps the most distinguishing characteristics of SS adults are the abnormally long legs and above average height. A delay in skeletal development is thought to be the cause. The age at which bone retardation begins is variable but increases with age (39). Repercussions of skeletal delay are manifested during adolescence when delays of 4 or more years have been documented in Jamaica. Retardation in skeletal maturation during adolescence results in delayed epiphyseal closure and prolonged bone growth (29,36). Such abnormalities lead to the development of the characteristic eunoichoid habitus prevalent among SS adults (33, 35, 40).

Sexual Development

The delay in the onset of puberty is yet another abnormality recognized in SS adolescents. Specific mechanisms for the delay in puberty are unclear, however, possible mechanisms for the delay include constitutional delay in adolescence, hypogonadism and nutritional factors (41).

In 1945, Winsor and Burch designed one of the first studies to evaluate the body type of patients with SS disease (42). The study included six SS males 7-30 years of age and eight SS females 6-32 years of age. There were 10 controls for each SS patient. Nearly 75% of SS male subjects exhibited diminution in the amount of pubic hair when compared to AA controls, indicating that SS patients were at an earlier stage of puberty than AA controls. Meanwhile, females exhibited absolute or relative sterility. No abnormal breast development was recognized in the SS group. The results of this study are limited by the small sample size.

Olambiwonnu and colleagues set out to determine if sexual maturation was affected by serum gonadotropin (40). He reported that concentrations of luteinizing hormone (LH) were greater in SS children 5-10 years of age while there was no significant difference in luteinizing hormone between 11 and 16 years of age. The elevated concentration of LH is consistent with impaired gonadal function; however, since the concentration of follicle stimulating hormone (FSH) was not elevated in young SS subjects, he concluded that the impairment in gonadal function is merely transient and that the the difference in sexual maturation is temporary. He postulated that the delay in sexual maturation is a result of the variability in the rate of the maturation of the

hypothalamic-pituitary-gonadal axis rather than impaired gonadal function. This study was limited by the lack of racially appropriate controls.

The Jamaican cohort study has provided an opportunity to study sexual maturation over a longer period of time than previous studies. Singhal et al used patients in the cohort study to examine differences in adolescent growth according to the Tanner system of development (43). He reported that the first pubertal changes appeared later in both male and female SS patients than AA controls. First pubertal changes in male SS patients were evident at 12.8 ± 1.6(SD) years of age while the first pubertal stages were evident at 11.0 ± 1.2 (SD) years of age in AA adolescents. Similar differences in the onset of puberty were reported in females. The first signs of puberty were noticeable in SS females at 12.0 ± 1.8(SD) years of age while the first signs of puberty were noticeable by 10.1 ± 1.2(SD) years of age. Menarche was delayed in SS girls by an average of 2.3 years when compared to AA controls. Both the onset of puberty and menarche were highly correlated with height velocity. When differences in height were corrected between genotypes, there was no difference in the onset of puberty once again indicating that the difference in puberty is only temporary.

In sum, sexual maturation generally progresses in an orderly fashion although there is an average delay of 2 years in SS adolescents (37). In cases of extreme retardation of puberty, there may be underlying endocrine abnormalities (44). The determinants of the delay in sexual maturation for those transient deficits include nutritional factors and a high resting energy expenditure competing with the demands for growth (44).

Nutrition and Sickle Cell Disease

The data on the growth and development of children indicate that there may be an association between nutrition and growth deficits. Proposed mechanisms for nutrient deficiencies include decreased intake, intestinal malabsorption and increased metabolic rate.

Anorexia has been observed frequently in ill patients 2 to 8 years of age (46). However in steady state SS children appear to have adequate intakes when compared to the RDA (11, 38).

There is conflicting evidence concerning intestinal function in SS disease. Sindel et al reported that serum values of vitamin A and E were low in SS patients despite supplementation with these nutrients and proposed that the absorption of fat soluble vitamins is impaired in SS patients (45). Similarly, Gray et al reported that SS patients with higher intakes of protein than AA controls had lower levels of urine nitrogen (11). He proposed that protein malabsorption might account for the apparent differences between the two groups.

In contrast, studies examining the aspects of adequacy of digestion, motility, and morphology of the gastrointestinal tract indicate that these functions are normal (12, 46, 47). Rahbar et al examined oral glucose tolerance, xylose absorption, fat absorption and protein absorption in sixteen SS patients and eighteen controls 2 to 18 years of age. The results indicated that gastrointestinal digestion and absorption were essentially normal in SS patients. Moreover, jejunal biopsy tests from three patients did not show any abnormalities. Additionally, a case study of an SS male indicated that both fat excretion

and d-xylose absorption tests were within normal ranges (46). Furthermore, Heyman et al concluded that fat absorption and intestinal mucosal morphology, investigated by means of histological and electron microscopic exams of the small intestine, were normal in five growth retarded children with SS disease (12).

Although SS patients generally have normal dietary intakes and intestinal function, there is evidence that supports suboptimal nutrient intake as a result of increased metabolic demands. Erythropoietic hypertrophy and hyperdynamic circulation result in increased metabolic activity and might lead to increased requirements for protein and energy.

Erythrocyte lifespan of SS subjects is 10 days while the lifespan of erythrocytes in normal subjects is approximately 120 days. The marked destruction of erythrocytes must be accompanied by an increase in the production of erythrocytes (48). Serjeant calculated that hemoglobin synthesis increased from 6.25 grams/day in the normal subject to 40 grams/day in SS patients (15). The metabolic requirements of increased erythropoiesis might lead to increased energy needs.

Resting metabolic rate (RMR) is the major determinant of total daily energy expenditure. Elevated resting energy expenditure (REE) has been repeatedly documented in patients with SS disease (11, 48-51). Badaloo et al measured whole body protein turnover and resting metabolic rate in six SS Jamaican adults and six AA adults of similar age (50). The results indicated that the RMR of SS patients was 22% greater than AA controls. Moreover, nitrogen flux and protein degradation were significantly increased in SS patients when compared with AA controls.

Gray et al examined the energy expenditure of nine prepubertal SS patients and nineteen controls (11). The REE per kilogram of fat free mass was significantly greater in SS subjects than controls implying that the energy needs of SS patients are greater than controls. Furthermore, Singhal et al found that the RMR of 20 postpubertal adolescents was 19% greater than that of AA controls and postulated that the obvious growth deficits of SS children are a result of energy deficiency that could possibly be corrected with supplementation (49).

Regardless of the mechanism for increased metabolic demands, data suggest that children with SS disease may have increased nutritional needs beyond their normal intake (10). Prior studies of the nutritional needs of SS patients have either focused on macronutrients and the daily requirements for protein and energy, or micronutrients and their relationship to specific clinical features of sickle cell disease.

Macronutrients

Increased rates of tissue destruction and repair as well as frequent infections are among the important factors that might increase the needs for protein and energy in SS patients (15). In addition, the growth deficits, delays in sexual maturation, retarded bone age and lowered intelligence of SS patients could be considered adaptive responses to suboptimal nutrition, suggestive of malnutrition and supportive of increased energy needs.

The rate of both whole body protein synthesis and degradation have been reported to be two times greater in SS patients than AA controls (48). However, dietary intakes of

protein and energy were not reported as significantly different. Marked protein degradation not accompanied by increased intake suggests that SS patients are in a suboptimal nutritional state or compensate by decreasing levels of physical activity.

Further studies of adult patients suggest that SS patients have increased needs for dietary protein and energy. Enwonwu et al studied the effect of SS disease on protein and amino acid requirements (52). The diets, serum and urine of SS adults were compared to AA controls of similar age, sex, and socioeconomic status. The results indicated that protein and energy intakes were similar between the two, despite the 21% lower total concentration of fasting plasma indispensable amino acids in SS patients. There was not a difference in dispensable amino acids. Urinary excretion of amino acids was less in SS patients than AA controls despite the twofold greater urinary volume in SS patients. Consequently, the difference in plasma indispensable amino acid concentrations was not attributed to increased urinary loss, but to greater flux and use in tissues. The plasma free amino acids differences found in SS patients are consistent with protein-energy deficiency and suggest that the dietary intakes are not sufficient to maintain adequate protein nutritional status in SS patients.

Warrier et al studied protein status of 34 SS children and 23 controls without growth deficits (53). Similar mean levels of albumin and transferrin were reported in SS children and AA controls, while significantly lower mean levels of retinol binding protein and retinol-prealbumin were reported in SS children (53). The degree of height and weight deficits in SS children correlated with levels of prealbumin. The SS children without significant height and weight deficits had higher levels of prealbumin than those

with mild to moderate growth retardation suggesting that the apparent growth deficits of SS patients are a result of some degree of malnutrition. The degree or presence of protein energy deficiency in SS patients is controversial but is most likely a mild to moderate deficiency.

Supplementation trials have suggested that increased protein and calorie intakes result in a rapid sustained increase in growth rate and improved clinical course (12, 54). These studies support the idea that nutrition intervention may improve growth in SS patients as well as minimize complications associated with the disease. Protein-energy deficiency in SS patients is most likely complicated by concurrent deficiencies of several important vitamins and minerals.

<div align="center">Micronutrients</div>

Over the past 20 years, deficiencies of a variety of micronutrients have been linked to specific clinical features of SS disease (10).

<u>Zinc</u>

Zinc deficiency has been implicated in the pathogenesis of certain sickle cell related problems such as growth deficits, impaired healing of leg ulcers, abnormal sexual development and defects in the immune system (10). Biochemical evidence of zinc deficiency has included decreased levels of zinc in plasma, erythrocytes and hair (58). Supplementation trials have been conducted in an attempt to establish a relationship between zinc and the clinical features of SS disease (56, 57). Twenty seven SS patients 14-24 years of age receiving supplements of zinc over a year showed increases in height,

body weight, and serum testosterone demonstrating the effect of zinc on growth (55). In contrast, other studies examining zinc status in SS patients have shown no evidence of zinc deficiency and concluded that additional factors such as diet and socioeconomic class are the reasons for differences in zinc status among SS patients and that zinc supplementation is not needed for all SS patients (56, 58).

Folate

Accelerated erythropoiesis recognized in SS disease results in an increased use of folate. Observations of patients with SS disease indicate that folic acid stores may be compromised resulting in the need for daily folic acid supplements (46). Contrasting observations indicate that folate supplementation is only needed when dietary availability is insufficient and that the indiscriminate use of folate supplements might lead to a deficiency of cobalamin (58).

Other B vitamins

The roles of vitamin B_6 and riboflavin have been examined to determine if supplementation is of therapeutic benefit to SS patients (60, 61). These vitamins, however, have not been implicated in growth deficits.

Antioxidants

Research in SS disease indicates that the red cell membrane has an increased sensitivity to oxidant stress. The characteristic acceleration of erythrocyte membrane peroxidation leads to shortened red cell survival (62). Sickled red blood cells are more susceptible to oxidizing agents than are normal red blood cells.

Reports of the antioxidant status of SS patients are inconsistent. The roles of vitamin E, vitamin C, and carotenoids in disease severity have been investigated but they have not been implicated in growth deficits (62-65).

Iron

Iron deficiency has been presumed to be of benefit to SS patients because it reduces the likelihood of polymerization of deoxygenated hemoglobin (29). In addition, treatment of iron deficiency has been shown to increase the number of irreversibly sickled cells. Despite iron's importance in growth and development, few studies have examined the role of iron deficiency in homozygous sickle cell disease. Further research in this area is needed.

CHAPTER III

VALIDATION OF CAREGIVER WEIGHED INTAKE METHOD FOR

USE WITH JAMAICAN CHILDREN 3 TO 6 YEARS OF AGE

Stephany Parker, Atul Singhal, Barbara Stoecker, and

Graham Serjeant

From the Medical Research Council Laboratories (Jamaica) and The Department of

Nutritional Sciences Oklahoma State University, Stillwater,Oklahoma 74078

Abstract

Objective The purpose of this study was to determine a dietary assessment method

suitable for the examination of energy, protein, carbohydrate, and fat intake of children 3

to 6 years of age in a developing country.

Design Dietary intake from one meal was determined using caregiver reported 24 hour

recall and weighed intake method. Foods recorded using these methods were compared

with those recorded by unobtrusive observers.

Subjects/setting Twenty two children 3 to 6 years of age were recruited from the patient list of the sickle cell unit of the University Hospital of the West Indies located in Kingston, Jamaica.

Main outcome measures Protein, carbohydrate, fat and energy values obtained by 24 hour recall and weighed intake method were compared by paired *t* tests with those values obtained by observation, the criterion for actual intake.

Statistical analyses performed Descriptive statistics, paired *t* tests, and Pearson's correlations.

Results There were no significant differences between observed intake and weighed intake. The 24 hour recall tended to overestimate all dietary components. Significant differences existed for all dietary components obtained by 24 hour recall except that of protein.

Applications/Conclusions The weighed intake method was the method of choice for use in the dietary assessment study at the sickle cell unit in Kingston, Jamaica and should be considered a viable method for future studies assessing the intakes of children in households with several feeders.

Introduction

Accurate dietary assessment of children living in developing countries is hindered by unsatisfactory dietary assessment methods and nonscientific settings (1). The dietary assessment method used most often in developing countries is surrogate reported 24 hour recall. The frequency of its use can most likely be attributed to three factors. First, it is a

relatively inexpensive method. Second, it is quick to administer and third, it does not alter usual diet. However, a well-known problem of this method is that of underreporting or overreporting (2, 3). A factor not often taken into consideration in developing countries is that respondents are likely to overreport intake as proof of economic success (4).

In addition to reporting errors, the construct of the family in developing countries is likely to impede the use of 24 hour recall. The frequency of extended family members residing in one household increases the number of feeders in the family Quite often, cousins, aunts, grandparents and inlaws reside within the same household and are all responsible for feeding children (5). In such situations, the recall of several members of the household must be reliable which places further limitations on the use of 24 hour recall.

The weighed intake method is seldom used in less developed countries. Advantages of this method are that it does not depend on memory and several members of the household can be trained in its use. Few studies have been conducted validating the use of surrogate reported 24 hour recall and weighed intake method in preschool subjects in developing countries (6-11). Unobtrusive observation is generally considered the best tool for validating these methods (12).

This study used unobtrusive observation to validate surrogate reported 24 hour recall and weighed intake method for use in a preschool population in Kingston, Jamaica. Estimates of protein, carbohydrate, fat, and energy were compared.

28

Subjects and Methods

The study subjects included twenty two boys and girls 3 to 6 years of age recruited from the sickle cell unit of the University Hospital of the West Indies. The subjects included patients and their siblings, relatives, or neighbors living in the Kingston corporate area who were to become part of a larger study assessing the diet of children with homozygous sickle cell disease. The subjects included 11 children with homozygous sickle cell disease, 8 children of normal genotype, and 3 children with the sickle cell trait. The protocol was approved by the Institutional Review Boards of the University of the West Indies and Oklahoma State University. Signed parental consent was obtained prior to subject participation.

For each subject dietary assessment of one meal was obtained using three methods: weighed intake, observed intake, and 24-hour recall. The weighed records were obtained using portable electronic scales accurate to ± 2g. Subjects were visited in their homes the day before caregivers were to begin the record (Day 0).

On Day 0, primary caregivers were given a demonstration of the scales and asked to try the scales themselves. If any errors were made, they were instructed in the use of the scales again and asked to repeat the method until no errors were made. Caregivers were left written instructions and a booklet for recording foods and weights. They were then asked what time the child usually ate and informed that a healthworker would be returning the following day (Day 1) to make sure that the scales were working properly. The caregivers were instructed not to alter the eating habits of the child or to wait for the health worker if the child was hungry.

On Day 1 the health worker returned during mealtime to observe the use of the scales. The health worker recorded in a separate booklet the weights of foods eaten. If any errors were made on the part of the caregiver, the health worker weighed the foods and recorded the measure without correcting the caregiver's record. Before leaving the home, the health worker advised caregivers of mistakes made and instructed them in the proper use of the scales. Caregivers were then informed that a different health worker would be returning the next day (Day 2) during mealtime.

On Day 2 a health worker who was not involved in the observation on Day 1 visited the household to observe a meal and conduct a 24-hour recall. Caregivers were asked to remember foods that were weighed on the previous day (Day 1). Standard measuring cups, spoons and household utensils were used to estimate portion sizes. Each family was visited for a total of three days.

Protein, carbohydrate, fat, and energy intake were calculated using Nutritionist IV (version 3.5.2, 1994) modified for use in the Caribbean by the Caribbean Food and Nutrition Institute located at the University of the West Indies. Local recipes and foods commonly consumed were added to the database

Statistical Methods

Means and standard deviations for each energy nutrient were calculated for observed, caregiver reported 24 hour recall and caregiver weighed intake method. Two tailed paired t tests were performed and differences were declared significant when $p<.05$. Pearson's correlations were calculated between observed intake and weighed intake.

Results

Complete observed, 24 hour recall, and weighed intake were obtained for 14 subjects. It was not possible to obtain a 24 hour recall for 8 subjects because the caregiver was not present at the time the 24 hour recall was to be conducted. For this reason, the results are presented separately, with one group (Group 1) for whom all methods were obtained and another (Group 2) for whom only observed method and weighed intake were obtained.

Table 1 outlines the means and standard deviations of the observed, 24 hour recall, and weighed intake methods for Group 1. The results indicate that there was no significant difference between any of the observed dietary components and the weighed intake dietary components. Significant differences did exist however between the observed method and 24 hour recall method for each of the dietary components except protein. Caregivers tended to overestimate all of the dietary components when using the 24 hour recall method.

Pearson's correlation coefficients were calculated between the observed intake and weighed intake. The results indicate that a strong correlation exists between the observed values and weighed intake with $0.92 \leq r \leq 0.99$ for all dietary components ($p < 0.0001$).

The observed and weighed intake data for Group 2 are outlined in Table 2. Means and standard deviations for Group 2 are very similar to those of Group 1. No significant differences existed between observed and weighed dietary components.

Pearson's correlations coefficients for Group 2 (n=8) indicated a very high correlation between the observed and weighed intake with $0.95 \leq r \leq 1.00$ (p< 0.001, for all).

Discussion

The results of this study indicate that data obtained by the weighed intake method are very similar to those obtained by observation, the criterion for actual intake. The ability to train several members of the household to use the scales is the most likely explanation for the advantage of this method. The major disadvantage of the weighed intake method is that it could alter the feeding behavior of caregivers and consequently, alter the nutrient intakes of children. However, weighed intakes were completed for all subjects while 24 hour recalls were completed for only 14 subjects.

Previous studies have indicated limitations in the use of surrogate reported 24 hour recall (3, 6-8). The present study supports these findings. One possible explanation for incomplete recall data from the observed meal is the number of feeders present in the household. Responsibility for feeding young children varies from siblings to grandparents to non-blood related members of the household. Frequently, obligations of feeders outside of the household render it impossible to retrieve 24 hour recall information without intervening in the lifestyles of households. This is evident in the present study in that no 24 hour recall information was attainable for 36% of the participants because the feeder was absent at the time the recall was to be conducted.

A further limitation of 24 hour recall is that it relies on memory (13, 14). The results of this study indicate that feeders consistently overestimated dietary intakes of the

32

subjects. Overestimation is a problem commonly encountered with 24 hour recall (4). However, such extreme overestimation of all dietary components warrants further exploration. It is possible that caregiver overreporting might be a result of their values placed on body size. Overreporting in developing countries has been attributed to values of "bigness" (15). Body size may be an indicator of one's socioeconomic success in many developing countries and may be the reason for such overreporting of energy intakes in the present study.

Due to the limitations of the 24 hour recall and the strong agreement between the weighed and observed dietary data, the weighed method was chosen as the method most suitable for the examination of dietary intakes of preschoolers in Kingston, Jamaica.

Applications

The relationship between nutrition and health make dietary assessment a necessary component of research studies. The need for better dietary assessment of children is a worldwide problem (11, 16-20) In order to attain accurate dietary data, validation studies must be conducted to determine a method suitable for the population to be studied.

Although the 24 hour recall method is often used as a means of dietary assessment, this study found that it was not a reliable method for use with Jamaican preschoolers. The lifestyles of the population to be studied were not conducive to 24 hour recall measures provided by one caregiver; this scenario is likely in many households worldwide due to the increasing number of single headed households and women in the workplace.

The weighed intake method compared most closely to observed intake. Training several members in its use provides an advantage and the weighed intake should be considered as a viable method in future research studies with preschoolers.

References

(1) Buzzard JM and Sievart YA. Research priorities and recommendations for dietary assessment methodology. *Am J Clin Nutr.* 1994;59(suppl):275S-280S.

(2) Block G. A review of dietary assessment methods. *Am J Epidemiol.* 1982;115:492-505.

(3) Piwoz EG, Creed De Kanashiro H., Lopez De Romana G, Black RE, and Brown KH. Potential for misclassification of infants' usual feeding practices using 24-hour dietary assessment methods. *J Nutr.* 1995;125:57-65.

(4) Cassidy CM. Walk a mile in my shoes: culturally sensitive food-habit research. *Am J Clin Nutr.* 1994;59(suppl):190S-197S.

(5) Scrimshaw SCM and Hurtado E. Rapid Assessment Procedures for Nutrition and Primary Health Care: Anthropological Approaches to Improving Programme Effectiveness. Tokyo, Japan: The United Nations University;1990.

(6) Baranowski T, Sprague D, Baranowski JH, and Harrison JA. Accuracy of maternal dietary recall for preschool children. *J Am Diet Assoc.* 1991;91:669-674.

(7) Bash CE, Shea S, Arliss R, Contento IR, Gutin B, Irigoyen M, and Zybert P. Validation of mother's reports of dietary intake by four to seven year old children. *Am J Public Health.* 1990;81:1314-1317.

(8) Eck LH, Klesges RC, and Hanson CL. Recall of a child's intake from one meal: Are parents accurate? *J Am Diet Assoc.* 1989;89:784-789.

(9) Livingstone MBE, Prentice AM, Coward WA, Strain JJ, Black AE, Davies PSW, Stewart CM, Mckenna PG, and Whitehead RG. Validation of estimates of energy intake by weighed dietary record and diet history in children and adolescents. *Am J Clin Nutr.* 1992;56:29-35.

(10) Klesges RC, Klesges LM, Brown G, and Frank G. Validation of the 24-hour dietary recall in preschool children. *J Am Diet Assoc.* 1987;87:1383-1385.

(11) Crawford PB, Obarzanek E, Morrison J, and Sabry ZI. Comparative advantage of 3-day food records over 24-hour recall and 5-day food frequency validated by observation of 9- and 10-year-old girls. *J Am Diet Assoc.* 1994;94:626-630.

(12) Simons-Morton BG and Baranowski T. Observation in assessment of children's dietary practices. *J Sch Health.* 1991;61:204-207.

(13) Dwyer JT, Krall EA, and Coleman KA. The problem of memory in nutritional epidemiology research. *J Am Diet Assoc.* 1987;87:1509-1215.

(14) Davidson FR, Hatek LA, and Altschul AM. Towards accurate assessment of children's food consumption. *Ecol Food Nutr.* 1985;18:309-317.

(15) Cassidy CM. The Good Body: When Big is better. *Med Anthropol.* 1991;13: 181-213.

(16) Wynder EL. The need for frequent and better dietary assessment of children. *Prev Med.* 1990;19:489-490. Editorial.

(17) Bingham SA, Gill C, Welch A, Cassidy A, Khaw KT, Sneyd MJ, Key JA, Roe L, and Day NE. Comparison of dietary assessment methods in nutritional epidemiology: weighed records v. 24 h recalls, food-frequency questionnaires and estimated diet records. *Br J Nutr.* 1994;72:619-643.

(18) Krall EA, Dwyer JT, and Coleman KA. Factors influencing accuracy of dietary recall. *Nutr Res.* 1988;8:829-841.

(19) Pelto G. Methodological Issues in Nutritional Anthropology: report of a workshop. *Food Nutr Bull.* 1981;3:21-28.

(20) Harbottle L and Duggan MB. Dietary assessment in Asian children - a comparison of the weighed inventory and diet history methods. *Eur J Clin Nutr.* 1993; 47: 115-112.

Table 1. **Comparison of three methods for assessing one meal dietary intakes of Jamaican preschoolers.**

dietary component	observed	24 hour recall	weighed
energy (kcal)	272 ± 92^a	$451 \pm 282^*$	284 ± 86
protein (kcal)	35 ± 21	70 ± 89	36 ± 21
carbohydrate (kcal)	154 ± 80	$236 \pm 156^*$	158 ± 79
fat (kcal)	81 ± 53	$145 \pm 131^*$	83 ± 50

[a]Mean $\pm$ standard deviation, n=14

[*]Different from observed, p<0.05

Table 2. Comparisons of observed and weighed one meal dietary intakes of Jamaican preschoolers from whom 24 hour recall could not be obtained.

dietary component	observed	weighed
energy (kcal)	254 ± 153^{a}	267 ± 148
protein (kcal)	35 ± 40	36 ± 40
carbohydrate (kcal)	142 ± 90	151 ± 86
fat (kcal)	77 ± 77	77 ± 77

[a]Mean $\pm$ standard deviation, n=8; no means were different, ($p>0.05$).

CHAPTER IV

ENERGY INTAKE AND EXPENDITURE IN JAMAICAN PREPUBERTAL

CHILDREN WITH HOMOZYGOUS SICKLE CELL DISEASE

Stephany Parker, Atul Singhal, Graham Serjeant and Barbara Stoecker

Medical Research Council, The University of the West Indies, Jamaica and The

Department of Nutritional Sciences, Oklahoma State University

Stillwater, Oklahoma 74078

Abstract

Dietary intake and resting energy expenditure were examined in 41 patients with homozygous sickle cell (SS) disease and 31 age-, sex-, and socioeconomic- matched control subjects with normal hemoglobin (AA). For resting energy expenditure (REE) there was a significant interaction between genotype and gender. The SS male patients exhibited values 25% greater than AA males, while SS females exhibited values only 10% greater than AA females. Total energy intake of energy was not significantly different by genotype or gender. Although there were few anthropometric differences,

male patients exhibited more marked deficits than female patients. As a result, it is postulated that increased energy expenditure not accompanied by increased intake will lead to significant deficits in later years and that the more marked anthropometric deficits in SS males are a result of the greater elevation in REE than SS females.

Introduction

The adverse effects of homozygous sickle cell (SS) disease on growth and development have long been recognized. Children with sickle cell disease exhibit deficits in height, weight, sexual maturation and skeletal maturation (1-8). Although the determinants for such deficits are possibly multifactoral, research has suggested that an increased metabolic rate may be partly responsible (9-12). Rates of resting energy expenditure (REE) are reportedly elevated as a result of increased erythropoiesis, protein turnover, tissue destruction and repair as well as frequent infections (13). Despite reports of increased metabolic demands, dietary intakes of SS patients are similar to those of normal hemoglobin (AA) genotype and adequate according to the Recommended Dietary Allowances. The RDA, however, was not devised to meet the needs of sick children.

Studies of resting energy expenditure of adolescent and adult patients with SS disease indicate that REE is increased (11,12). Increased energy expenditure not accompanied by increased dietary intake is likely to retard the physical growth and development of children with SS disease. At the present time only two studies have examined energy metabolism and dietary intakes in prepubertal children with SS disease (9, 10). Both indicated that the resting energy expenditure of SS children was higher than

that of AA controls. The dietary data from these studies are conflicting. Gray et al reported that protein and energy intakes were more than that of controls while Salaman et al reported similar intakes. The validity of these studies is limited by the relatively small sample sizes. Furthermore, no studies have examined energy expenditure in SS patients during times of critical growth.

The purpose of this study is to determine whether the dietary intake and energy expenditure of children 3 to 6 years of age with homozygous sickle cell disease differ from those of children with a normal hemoglobin genotype matched for age, sex and socioeconomic status. The study was approved by the Institutional Review Boards of the University of the West Indies and Oklahoma State University. Signed parental consent was obtained prior to participation in the study.

Subjects and Methods

Subjects The study subjects were recruited from the patient list of the sickle cell unit located at the University of the West Indies in Jamaica. At the time of the study there were 178 children of the desired age range attending the sickle cell clinic. Since the study was to be conducted in Kingston, only those patients living in the Kingston corporate area were eligible for the study. There were 72 SS patients between 3 to 6 years of age on the list that resided in the Kingston area.

Forty one SS children were recruited and thirty one AA controls were recruited from the households of SS children. Thirteen controls were siblings of SS patients

attending the sickle cell unit. Control subjects were similar with respect to age, sex and socioeconomic status. Socioeconomic status was scored using indices of overcrowding (people/ room), sanitation (toilet type and location), availability of electricity, water and appliances (14).

Each subject underwent a clinical history to exclude those with a diagnosis or chronic disease other than SS disease. Controls were excluded if hemoglobin levels were 2 SD below the Jamaican norm and treated if necessary. All subjects were clinically well for at least 2 weeks prior to the study.

Measurement of Dietary intake. For each subject, dietary assessment was obtained using 3 day weighed intake. Weighed records were obtained using portable electronic scales (OHAUS LS5000) accurate to $\pm$ 2g. Subjects were visited in their homes the week caregivers were to begin the record and instructed in the use of the scales. Healthworkers visited daily to ensure proper use of the scales. Nutrients were calculated using Nutritionist IV (version 3.5.2, 1994) modified for use in the Caribbean by the Caribbean Food and Nutrition Institute located at the University of the West Indies.

Measurement of Resting Energy Expenditure. REE was determined from measurements of oxygen consumption and carbon dioxide production using the Douglas bag method of open circuit indirect calorimetry (12). All subjects were fasted overnight in a metabolic ward. Subjects were lying comfortably on a couch in a supine position. The ambient room temperature was 22-25° C. RMR was calculated using the method of Weir (15). The mean of two RMR measurements was expressed as $MJ \cdot kg^{-1} \cdot d^{-1}$.

Anthropometry. Height was measured to the nearest 0.1 cm on a Harpendon wall

mounted stadiometer (CMS Instruments Ltd., London). Weight was measured to the nearest 0.1 kg in light clothing but without shoes on a beam balance scale (Detecto Ltd., Brooklyn). Skinfold thickness was measured to 0.1 mm on the left side of the body at biceps, triceps, subscapular and suprailiac sites using Harpendon skinfold calipers (Holtain Instruments Ltd., Crymmych, UK). Arm and wrist circumference were measured to 0.1 cm using a nonstretchable measuring tape. All measurements were taken by a single observer.

Biochemical Analysis. Hematologic indices were measured using a Coulter plus 4 counter (Coulter Electronics Inc., Hialeah FL). Genotype was determined by hemoglobin electrophoresis.

Statistical Methods. Comparisons of anthropometric, hematologic, dietary intake and energy expenditure data were made in a 2 x 2 factorial design using generalized linear model procedure to explore possible gender and genotype differences. A *P* value of 0.05 or less was considered significant. All analyses were performed using SAS (SAS Institute, Cary, NC).

Results

Relevant anthropometric and clinical features of SS patients and controls are summarized in Table 1. Although there was a trend for SS patients to weigh less and be shorter than AA controls, the difference did not reach significance for either SS males or SS females. However, male patients had significantly lower ($p<0.05$) sum of skinfold measures and arm and wrist circumferences than male controls, while SS females

43

exhibited significantly lower values than AA females for arm and wrist circumferences, but not sum of skinfold measures. As expected, total hemoglobin values of both SS males and SS females were significantly less than AA controls.

The indices of socioeconomic status indicated that both SS males and SS females were similar to AA controls with respect to socioeconomic status (Table 2).

Mean dietary intake values are expressed in Table 3. Total energy intake, protein, carbohydrate, and fat values were examined. There were no significant differences in the total energy, protein or fat intakes of the two groups. There was, however, a significant interaction between genotype and sex for carbohydrate. In males there was a significant difference in the grams of carbohydrate consumed with SS males consuming significantly less. There was not a significant difference in female subjects. Both groups consumed less total energy than recommended by the Caribbean Dietary Allowances (15). SS females consumed approximately ≅92% of the recommended energy allowance while AA controls consumed approximately ≅91% of that recommended. Meanwhile, SS male patients consumed ≅81% of the Caribbean Allowances while AA males consumed approximately ≅90% of that recommended.

Although differences in REE were not significant when expressed on a whole body basis for males or females, when expressed per unit of body weight (MJ $kg^{-1}d^{-1}$), the REE of SS males was ≅25% greater ($p<0.05$)than AA controls (Table 4). The REE (MJ $kg^{-1}d^{-1}$) of SS females was ≅10% greater than AA controls, but this difference was not significant. When REE was expressed in relation to metabolic mass (MJ $(wt^{0.75})^{-1}$ d^{-1}), SS males exhibited values ≅19% ($p<0.05$) greater than controls.

44

When REE was expressed in terms of metabolic mass, there was not a significant difference between females. There was not a significant genotype difference in the mean respiratory quotient (RQ) for either sex. When energy intake was viewed in relation to need, the mean ratio for SS males was significantly lower ($p<0.05$) than AA males but there was not a significant genotype difference in the mean ratio values of females.

Discussion

Previous studies of REE in children are limited despite the fact that it represents the largest component of total energy expenditure (13,15). To our knowledge, this is the first study to examine genotype differences in the resting metabolic rate of children 3 to 6 years of age.

The present study did not find significant genotype differences in height or weight of either gender. Patients were very closely matched with controls with respect to socioeconomic status which may explain the similar heights and weights. Although the differences were not significant, mean heights and weights of SS patients tended to be less than AA controls. The resting energy expenditure results of the present study are in concert with those of previous studies (9-12, 17). This study reveals that rates of energy expenditure in steady-state males with SS disease were considerably higher than rates of males with normal genotype children. The REE results of SS females were only slightly elevated. This finding is in agreement with a previous report of the Jamaican cohort study which found more marked increases in the REE of male adolescents than female adolescents (12).

Despite increased REE, the total energy intakes of SS patients were not increased in this study. Furthermore, when the ratio of energy intake was viewed in relation to expenditure, the ratio was significantly greater in AA males than SS males. It is interesting that in this study, although the REE of SS females was elevated, the difference was not significant. There was a significant genotype difference in the REE of males and the anthropometric measures of SS males were more affected than SS females. These observations indicate that the growth of SS males may be more affected as a result of greater increases in REE. Modebe Ifenu reported similar gender related differences in anthropometric measures with males being more affected (18). In addition, the increased energy expenditure in SS males not accompanied by increased intake, might be the reason that SS males experienced increasing deficits in height and weight with age, while the growth deficits in females were less pronounced (6). In a previous study of prepubertal children, McCormack and colleagues reported that SS boys exhibit lower values than SS girls for all anthropometric values from the age of six (4). The mean age of subjects in our study was $\cong 4$ years. Perhaps mean height and weight differences in this group will become more pronounced in later years.

Factors influencing variation in the energy expenditure in children include body composition and gender (19,20). REE is usually greater in smaller individuals (10). Furthermore, males tend to have greater REE than females.

The mechanism for increased energy expenditure in sickle cell patients remains unclear, but the increase cannot be explained solely by disease, since all SS children were in steady-state. Possible mechanisms for elevated REE include increased hemoglobin

synthesis and increased rates of protein turnover. Previous studies suggest that SS patients exhibit a twofold increase in protein turnover (10,13). Moreover, protein is an important structural component of hemoglobin and therefore increased protein use results to meet the accelerated demand for hemoglobin synthesis in SS patients (13). This study did not find significant genotype differences in the protein intakes of either male or female subjects. Therefore, SS patients are not likely compensating for increased protein use by increasing intake. At the present time, gender differences in rates of hemoglobin synthesis and protein turnover have not been extensively examined. Perhaps, hemoglobin synthesis and protein turnover are more accelerated in SS males than females.

Even though physical activity levels are the most variable component of energy expenditure (21), levels of physical activity were not examined in this study. It is possible that SS children save energy by reducing levels of physical activity. Furthermore, it is conceivable that there may be genotype as well as gender differences in physical activity levels.

Although this study did not note significant genotype differences in height and weight, such deficits are likely to increase with prolonged increased energy expenditure not accompanied by increased intake. A recent study indicated that prepubertal SS children use $\cong$ 58% more protein and $\cong$ 47% more glutamine than AA subjects (10). Furthermore, nutritional supplementation in older SS patients has been shown to accelerate growth as well as improve the clinical course of patients with sickle cell disease (22). These findings suggest that growth deficits might be preventable with supplements. Supplementation studies of patients with other conditions (congenital heart

disease, cystic fibrosis, inflammatory bowel disease, and AIDS) in which resting energy expenditure is increased have shown that supplementation is valuable in improving not only growth but also the clinical course of the specific disease (23-27).

Further studies are needed to examine the effects of dietary supplementation on growth and development in children with sickle cell disease. In view of the gender differences noted in this study, supplementation studies should be designed not only to examine the effect of supplementation on SS children, but also to examine differences in gender response to supplementation.

References

1. Whitten CF. Growth status of children with sickle cell anemia. Amer J Dis Child. 1995: 102:101-110.

2. Booker CR, Scott RB, and Ferguson AD. Studies in sickle cell anemia XXII. Clinical manifestations of sickle cell anemia during the first two years of life. Clin Pediat. 1964; 3:111-114.

3. Jiminez CT, Scott RB, Henry WL, Sampson CC, and Ferguson AD. Studies in sickle cell anemia XXVI. The effects of homozygous sickle cell disease on the onset of menarche, pregnancy, fertility, pubescent changes, and body growth in negro subjects. Amer J Dis Child. 1966; 111: 497-504.

4. McCormack MK, Dicker L, Katz SH, Caleb M, McDaniels J, Humphrey A, et al. Growth patterns of children with sickle cell disease. Human Biol. 1976; 48: 529-437.

5. Kramer MS. Rooks Y, Washington LA, and Pearson HA. Pre- and postnatal growth and development in sickle cell anemia. J Pediatr. 1980; 96:857-60.

6. Phebus CK, Gloniger MF, Maciak BJ. Growth patterns by age and sex in children with sickle cell disease. J Pediatr 1984; 105: 28-33.

7. Stevens MVG, Maude GH, Cupidore L, Jackson H, Hayes RJ, Serjeant GR. Prepubertal growth and skeletal maturation in children with sickle cell disease. Pediatrics 1986; 78: 124-32.

8. Athale UH, Chintu C. The effects of sickle cell anemia on adolescents and their growth and development-lessons from the sickle cell anemia clinic. J Trop Pediatr 1994; 40: 246-52.

9. Gray NT, Bartlett JM, Kolasa KM, Marcuard SP, Holbrook CT, Horner RD. Nutritional status and dietary intake of children with sickle cell anemia. Am J Pediatr Hematol Oncol 1992; 14: 57-61.

10. Salman EK, Haymond MW, Bayne E, Sager BK, Pitel WP, and Darmaun D. Protein and energy metabolism in prepubertal children with sickle cell anemia. Pediatr Res 1996; 40: 34-40.

11. Badaloo A, Jackson AA, Jahoor F. Whole body protein turnover and resting metabolic rate in homozygous sickle cell disease. Clin Sci 1989; 77: 93-97.

12. Singhal A, Davies P, Sahota A, Thomas PW, Serjeant GR. Resting metabolic rate in homozygous sickle cell disease. Am J Clin Nutr 1993; 57: 32-4.

13. Enwonwu CO. The effect of sickle cell anemia on protein, amino acid, and zinc requirements. Food and Nutr Bull 1989; 11: 71-8.

14. Statistical Institute of Jamaica. Jamaica survey of living conditions 1990. Kingston, Jamaica: Statistical Institute of Jamaica, 1990.

15. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949; 109: 1-9.

16. Caribbean Food and Nutrition Institute. Recommended Dietary Allowances for the Caribbean. CFNI Press, 1993.

17. Odonkor PO, Addae SK, Apatu RS, Yamamoto S. Basal metabolic rate and serum thyroid hormone levels in adolescent sickle cell patients. IRCS Med Sci 1982; 10: 302.

18. Modebe O, Ifenu SA. Growth retardation in homozygous sickle cell disease: Role of calorie intake and possible gender-related differences. Am J Hematol 1993; 44: 149-54.

19. Carpenter WH, Poehlman ET, O'Connell M, Goran MI. Influence of body composition and resting metabolic rate on variation in total energy expenditure: a meta-analysis. Am J Clin Nurt 1995; 61:4-10.

20. Goran MI, Kaskoun M, Johnson R. Determinants of resting energy expenditure in young children. J pediatr 1994; 125:362-7.

21. Rising R, Harper IT, Fontvielle AM, Spraul M, Ravussin E. Determinants of total daily energy expenditure: variability in physical activity. Am J Clin Nutr 1994; 59:800-4.

22. Heyman MB, Vichinsky E, Katz R. Growth retardation in sickle cell disease treated by nutritional support. Lancet 1985; 2: 903-6.

23. Shepherd R, Cooksley WGE, Cooke WDD. Improved growth and clinical, nutritional, and respiratory changes in response to nutritional therapy in cystic fibrosis. J Pediatr 1980; 97: 351-7.

24. Barton JS, Hindmarsh PC, Scrimgeour CM, Rennie MJ, Preece MA. Energy expenditure in congenital heart disease. Arch Dis Child 1994; 70: 5-9.

25. Tomezsko JL, Stallings VA, Kawchak DA, Goin JE, Diamond G, Scalin TF. Energy expenditure and genotype of children with cystic fibrosis. Pediatr Res 1994; 35: 451-60.

26. Kaplan AS, Zemel BS, Neiswender KM, and Stallings VA. Resting energy expenditure in clinical pediatrics: Measured versus prediction equations. J Pediatr 1995; 127: 200-5.

27. Murphy MD, Ireton-Jones CS, Hilman BC, Gorman MA, and Liepa GU. Resting energy expenditures measured by indirect calorimetry are higher in preadolescent children with cystic fibrosis than expenditures calculated from prediction equations. J Am Diet Assoc 1995; 95:30-3.

Table 1. Anthropometric and clinical characteristics by gender of prepubertal Jamaican children with sickle cell disease and controls.

	SS Females (17)	AA Females (14)	SS Males (20)	AA Males (16)
Age	4.2 (0.3)[1]	4.2 (0.3)	4.1 (0.2)	4.2 (0.2)
Weight (kg)	16.6 (0.9)	17.6 (1.0)	16.3 (0.5)	17.2 (0.7)
Metabolic weight (wt $^{0.75}$)	8.2 (0.3)	8.6 (0.4)	8.1 (0.3)	8.4 (0.3)
Height (cm)	107.9 (2.5)	109.8 (2.8)	105.8 (1.5)	107.9 (2.2)
Wrist circumference (cm)	10.8 (0.2)*	11.6 (0.2)	10.9 (0.1)*	11.8 (0.2)
Arm circumference (cm)	15.5 (0.4)*	16.7 (0.4)	15.6 (0.2)*	16.7 (0.4)
Sum of skinfolds (mm)	20.8 (1.0)	20.8 (1.0)	18.8 (0.6)*	21.5 (0.9)
Body Mass Index (kg/m^2)	14.2 (0.3)	14.5 (0.3)	14.5 0.2)	14.7 (0.3)
Total hemoglobin (g/100 ml)	7.9 (0.3)*	11.5 (0.2)	7.5 (0.2)*	11.8 (0.3)

[1] Mean ± SEM
* Significantly different from controls ($p<0.05$)

Table 2. Indices of socioeconomic status by gender of prepubertal Jamaican children with sickle cell disease and controls.

	SS Females (18)	AA Females (14)	SS Males (23)	AA Males (17)
Social amenity rating	15.1 (0.9)	14.5 (0.5)	14.9 (0.7)	15.5 (0.5)
People per room	2.2 (0.3)	2.4 (0.3)	2.2 (0.4)	2.8 (0.5)

[1] Mean ± SEM

There were no significant differences ($p>0.05$) for all.

Table 3. Three day dietary intake data by gender of prepubertal Jamaican children with sickle cell disease and controls.

Dietary Component	SS Females (18)	AA Females (14)	SS Males (23)	AA Males (17)
Energy (MJ)	6.2 (0.2)	6.2 (0.2)	6.1 (0.2)	6.75 (0.3)
Protein (g)	44 (2.9)	47 (3.2)	47 (2.2)	54 (3.5)
Carbohydrate (g)	234 (7.1)	217 (8.3)	217 (8.7)*	243 (14.5)
Fat (g)	45 (2.9)	47 (3.1)	48 (2.7)	50 (2.5)

[1] Mean ± SEM

* Significantly different from controls ($p<0.05$)

Table 4. Resting energy expenditure differences by gender of prepubertal Jamaican children with sickle cell disease and controls.

	SS Females (15)	AA Females (13)	SS Males (20)	AA Males (15)
Respiratory Quotient	0.77 (0.02)[1]	0.84 (0.04)	0.81 (0.02)	0.86 (0.05)
REE (MJ/D)	5.13 (0.28)	5.09 (0.42)	5.70 (0.22)	5.10 (0.24)
REE (MJ·kg^{-1}·d^{-1})	0.32 (0.01)	0.29 (0.05)	0.35 (0.01)*	0.28 (0.01)
REE (MJ·kg$^{-.75}$·d^{-1})	0.64 (0.02)	0.59 (0.03)	0.70 (0.03)*	0.59 (0.02)
Ratio of energy intake to REE (MJ/D)	1.27 (0.06)	1.30 (0.10)	1.09 (0.05)*	1.40 (0.09)

[1] Mean ± SEM
* Significantly different from controls ($p < 0.05$)

CHAPTER V

SUMMARY, IMPLICATIONS, AND RECOMMENDATIONS

Summary

The purpose of this study was to examine genotype differences (homozygous sickle cell disease vs. normal hemoglobin genotype) in the nutritional status of Jamaican female and male children 3 to 6 years of age. Differences in anthropometric measures, dietary intake, and energy expenditure were examined. Forty one patients with homozygous sickle cell disease, attending the Sickle Cell Clinic located at The University of the West Indies, and 31 age-, sex- and socioeconomic- matched controls with normal hemoglobin were included in this study. It was not possible to obtain all measurements for all patients. Measures of resting energy expenditure required that both the subject and parent stay overnight in a metabolic ward. At times, parents were unable to stay because of obligations at home or work.

Although SS patients tended to be smaller than controls, the differences were not significant except for arm and wrist circumferences. When analyzed according to gender, males exhibited more marked deficits than females, but height and weight differences remained insignificant. It is possible that significant genotype differences in weight and height were not found because patients were very closely matched to controls with respect

to age and socioeconomic status. Furthermore, 13 of the controls were siblings of SS patients, and all but 8 of the controls were related to SS patients. However, concern remains for the more marked differences in male patients. Male SS patients had significantly lower anthropometric measures than did SS females. For example, there was not a significant difference in the sum of skinfolds when analyzed as a group, but when analyzed according to gender, SS males had significantly lower scores ($p<0.05$), while there was no genotype difference in the scores of females.

The age at which growth deficits appear in SS children varies, and it is generally agreed that such deficits increase with age. It is possible that the differences between the groups in this study will increase with time, especially since there were significant genotype differences in the resting energy expenditure. Examination of three day food records indicated that the dietary intakes of SS patients and AA controls were quite similar. Furthermore, the intake of both groups was less than that recommended by the Caribbean Dietary Allowances. The energy intake of both groups is likely an overestimate, since intakes were recorded over the weekend when Jamaican families tend to eat more (unpublished observation). As discussed in Chapter I, it was impossible to obtain dietary records from children during the week because children begin school at the age of three. Consequently, dietary records were confined to Friday to Sunday. Children seldom attend school on Fridays for cultural reasons. Furthermore, teacher planning days are often on Fridays.

The fact that the energy intakes of SS patients were similar to AA controls is of concern since SS patients exhibited a REE 17% greater than AA controls. When

analyzed according to gender, the REE of male SS patients was 25% greater than male controls while the REE of female SS patients was approximately 10% greater. The elevation in REE has been documented in adolescent and adult patients as well.

How then are SS children coping with increased rates of energy expenditure? Perhaps SS children are less physically active than their normal counterparts and conserve energy in this manner. To date, the physical activity levels of SS children has not been studied.

In summary, children with SS disease have greater resting energy expenditures while dietary intakes are similar to AA controls. Male SS children appear to be more affected than female SS children. Elevated REE not accompanied by increased energy intake will most assuredly lead to greater growth deficits in later years. Documentation of delayed sexual maturation and bone growth in other studies supports this postulation.

Implications

The following implications are presented as a result of this research:

1) Health care professionals, especially doctors and nurses, working with sickle cell patients should be educated about the importance of nutrition for growth.

2) Health care professionals in turn should emphasize the importance of adequate nutrition to parents.

3) Improving the nutritional status of sickle cell patients will likely improve their quality of life by improving certain psychosocial aspects of the disease. Often Jamaican children with sickle cell disease are not included in games and activities with other

children because they are small or considered sick. Improving growth could ameliorate this problem. Furthermore, since nutrition is related to immune status, the clinical course of the disease might improve if care is taken to promote optimal nutrition thereby decreasing the number of days that a child is absent from school due to illness. Fewer absences could improve interactions with other children resulting in improved self image of the child with sickle cell disease.

Nutrition Education for Parents of Children with Sickle Cell Disease

1) Nutrition education for parents should emphasize the importance of providing small frequent meals as well as nutrient and energy dense snacks.

2) The importance of nutrition during times of illness should be emphasized to parents. Children should eat during times of illness.

Recommendations for Further Research:

1) Gender differences in resting energy expenditure and growth should be examined closely.

2) Levels of physical activity should be examined in patients with SS disease to determine if physical activity is related to growth or if levels of physical activity are related to genotype.

3) Supplementation trials should be carried out in an effort to determine if increased energy intake has an effect on the growth and clinical course of SS patients.

REFERENCES

1. Health Information. http://www.housecall.com/databases/ami/convert/000527.html

2. Med Access. http://www.medaccess.com/h_child/sickle/sca_01.htm

3. Platt OS, Brambilla OJ. Bone Marrow Transplantation in Sickle·Cell Disease. New England Journal of Medicine. 1996; 335: 253-54.

4. Lee A, Thomas P, Cupidore L, Serjeant B, Serjeant G. Improved Survival in Homozygous Sickle Cell Disease: Lessons From a Cohort. British Medical Journal. 1995; 31: 1600-1602.

5. Blatt JR. Sickle Cell Disease. The Gene Letter. 1996; 1.

6. Cruikshank J, Beevers D. Ethnic Factors in Health and Disease. London: Butterworth and Company. 1989: 103-113; 140-142.

7. http://www.whs.wjusd.k12.ca.us/research/Sickle%20cell%20anemia.html

8. Singhal A, Morris J, Thomas P, Dover G, Higgs D, Serjeant G, Factors Affecting Prepubertal Growth in Homozygous Sickle Cell Disease. Archives of Disease in Childhood. 1996; 74: 502-506.

9. Knight S, Singhal A, Thomas P, Serjeant G. Factors Associated with Lowered Intelligence in Homozygous Sickle Cell Disease. Archives of Disease in Childhood. 1995; 73: 316-320.

10. Reed J, Redding-Lallinger R, Orringer E. Nutrition and Sickle Cell Disease. American Journal of Hematology. 1987; 24: 441-455.

11. Gray N, Bartlett J, Kolasa K, Marcuard S, Holbrook C, Homer R. Nutritional Status and Dietary Intake of Children with Sickle Cell Anemia. The American Journal of Hematology/Oncology. 1992; 14: 57-61.

12 Heyman M, Vichinisky E, Katz R, Gaffield B, Hurst D, Castillo R, Chiu D, Kleman K, Amman A, Thaler M, Lubin B. Growth Retardation in Sickle Cell Disease Treated by Nutritional Support. Lancet; 1985; 2: 903-906.

13. Pelletier D. The Potentiating Effects of Malnutrition on Child Mortality: Epidemiologic Evidence and Policy Implications. Nutrition Reviews. 1994; 52: 409-415.

14. Schroeder D, Brown K. Nutritional Status as a Predictor of Child Survival: Summarizing the Association and Quantifying its Global Impact. Bulletin of the World Health Organization. 1994; 72: 569-579.

15. Serjeant GR. Sickle Cell Disease. 2nd ed. New York, N.Y.: Oxford University Press. 1994.

16. Guyton A. Textbook of Medical Physiology. Eighth Edition. Philadelphia, PA: W. B. Saunders Company. 1991.

17. Lee R, Nieman D. Nutritional Assessment. St. Louis, MO. Mosby Year Book Inc. 1996.

18. U.S. Department of State. Background Notes of Jamaica. Bureau of Public Affairs. Washington, D.C., 1994.

19. U. S. Department of State. Background Notes of Jamaica. Bureau of Public Affairs. Washington, D.C., 1990.

20. The World Bank. Jamaica: Economic Issues for Environmental Management. Library of Congress. Washington, D.C., 1993.

21. The National Peace Corps Association. World View. 1996; 9:3.

22. Klak TH, Hey JK. Gender and State Bias in Jamaican Housing Programs. World Development. 1992; 20:212-227.

23 Fraser HA. Household Food Security. Caribbean Preparatory Meeting for the International Conference on Nutrition. 1992: 111-114.

24 Feifer CN. Maternal Health in Jamaica. World Bank Working Paper, No. 539. Washington D.C., 1987.

25. FAO and WHO. Caribbean Regional Food and Nutrition Profile. Caribbean Preparatory Meeting for the International Conference on Nutrition. 1992: 15.

26. Sinha D. Changing Nutritional Patterns of the Caribbean Population and Their Implications for the 1990's and Beyond. Caribbean Preparatory Meeting for the International Conference on Nutrition. 1992: 81-95.

27. Lavey V, Palumbo M, Stern SN. Health Care in Jamaica: Quality Outcomes, and Labor Supply. World Bank Working Paper No. 116. Washington, D.c., 1995.

28. Bailey W, Phillips DR. Spatial Patterns and Health Services in the Kingston Metropolitan Area. Social Science and Medicine. 1990; 30:1-12.

29. Serjeant G. Clinic and Cohort Handbook. 1996.

30. Allison AC. Protection Afforded by Sickle-Cell Trait Against Subtertian Malaria. Br Med J. 1954, 1:290-294.

31. Washburn R. Peculiar Elongated and Sickle Shaped Red Blood Corpuscles in a Case of Severe Anemia. Virginia Medicine Semi Monthly. 1911; 15: 490-493.

32. Mason K, Grandison Y, Hayes Y, Serjeant B, Serjeant G, Vaidya S, Wood W. Postnatal Decline of Fetal Haemoglobin in Homozygous Sickle Cell Disease: A Relationship to Parental Haemoglobin F Levels. British Journal Of Haematology. 1982; 52: 455-463.

33. Whitten C. Growth Status of Children with Sickle Cell Anemia. American Journal of Diseases of Children. 1961; 102: 355-364.62. Serjeant GR. Natural History and Determinants of Clinical Severity of Sickle Cell Disease.Current Opinion in Hematology.1995,2:103-108.

34. Kramer M, Rooks Y, Washington L, Pearson H. Pre and Postnatal Growth and Development in Sickle Cell Anemia. The Journal of Pediatrics. 1980; 96; 857-860.

35. Stevens M, Maude G, Cupidore L, Jackson H, Hayes R, Serjeant G. Prepubertal Growth and Skeletal Maturation in Children with Sickle Cell Disease. Pediatrics. 1986; 78: 124-132.

36. Mckormac M, Dicker L, Katz S., Caleb M, McDaniels J, Humphrey A, Buchert E, Lubin B. Growth Pattern of Children with Sickle Cell Disease. Human Biology. 1976; 48: 429-437.

37. Jiminez C, Scott R, Henry N, Sampson C, Ferguson A. Studies in Sickle Cell Anemia: The Effects of Homozygous Sickle Cell Disease on the Onset of Menarche, Pregnancy, Fertility, Pubescent Changes, and Body Growth in Negro Subjects. American Journal of Diseases of Children. 1966; 111; 497-504.

38. Modebe O, Ifenu S. Growth Retardation in Homozygous Sickle Cell Disease: Role of Calorie Intake and Possible Gender Related Differences. American Journal of Hematology. 1993; 44: 149-154.

39. Lowry MF, Desai P, Ashcroft MT, Serjeant BE, and Serjeant GR. Heights and weights of Jamaican children with homozygous sickle cell disease. Human Biology. 1977; 49: 429-436.

40. Olambiwonnu N, Penny R, Frasier S. Sexual Maturation in Subjects with Sickle Cell Anemia: Studies of Serum Gonadotropin Concentration, Height, Eeight, and Skeletal Age. The Journal of Pediatrics. 1975; 87: 459-464.

41. Platt O, Rosenstock W, Espeland M. Influence of Sickle Hemoglobinopathies on Growth and Development. New England Journal of Medicine. 1984; 311: 7-12.

42. Winsor T, Burch G. The Habitus of Patients with Sickle Cell Anemia. Human Biology. 1944; 16; 99-113.

43. Singhal A, Thomas P, Cook R, Wierenga K, Serjeant G. Delayed Adolescent Growth in Homozygous sickle cell Disease. Archives of Disease in Childhood. 1994; 71: 404-408.

44. Singhal A, Gabay L, Serjeant G. Testesterone Deficiency and Extreme Retardation of Puberty in Homozygous Sickle Cell Disease. West Indies Medical Journal. 1995; 44: 20-33.

45. Sindel L, Baliga B, Bendich A, Mankad V. Nutritional Deficiencies Associated with Vitamin E Deficiency in Sickle Cell Patients; The Effect of Vitamin Supplementation. Nutrition Research. 1990; 10: 267-273.

46. Alperin J. Folic Acid Complicating Sickle Cell Anemia. Archives of Internal Medicine. 1967; 120: 298-306.

47. Rahbar F, Scott R, Jily P. Studies in Sickle Cell Anemia: Preliminary Observation on Gastrointestinal Digection and Absorption. National Medical Association. 1973; 69: 103-104.

48. Badaloo A, Jackson A, Jahoor F. Whole Body Protein Turnover and Resting Metabolic Rate in Homozygous Sickle Cell Disease. Clinical Science. 1989; 77: 93-97

49. Singhal A, Davies P, Sahota A, Thomas P, Serjeant G. Resting Metabolic Rate in Homozygous Sickle Cell Disease. American Journal of Clinical Nutrition. 1993; 57: 32-34.

50. Badaloo A, Singhal A, Forrester T, Serjeant G, Jackson A. The Effect of Splenectomy for Hyperspleenism on Whole Body Protein Turnover and Resting Metabolic Rate and Growth in Sickle Cell Disease. European Journal Of Clinical Nutrition. 1996; 50: 672-675.

51. Salman E, Haymond M, Bayne E, Sager B, Wilsanen A, Pitel P, Darmaun D. Protein and Energy Metabolism in Prepubertal Children with Sickle Cell Anemia. Pediatric Research. 1996; 40: 34-40.

52. Enwonwu C. The Effect of Sickle Cell Anemia on Protein Amino Acid, and Zinc Requirements. Food and Nutrition Bulletin. 1989; 11: 71-77.

53. Warrier R, Kuvibidila S, Gordon L, Humbert J. Transport Proteins and Acute Phase Reactant Proteins in Children with Sickle cell Anemia. Journal of the National Medical Association. 1994; 86: 33-39.

54. Vichinsky E, Heyman M, Hurst D, Chiu D, Gaffield B, Thompson K, Kleman K, Lubin B. Nutrition in Sickle Cell Anemia. Pediatric Research. 1984; 18S: 930.

55. Prasad A, Cossak Z. Zinc Supplementation and Growth in Sickle Cell Disease. Annals of Internal Medicine. 1984; 100: 367-371.

56. Abshire T, English J, Githens J, Hambridge M. Zinc Status in Children and Young Adults with Sickle Cell Disease. American Journal of Disease of Childhood. 1988; 142: 1356-1359.

57. Muskiet FA, Muskiet FD, Meiborg G, Schemer J. Supplementation of Patients with Homozygous Sickle Cell Disease with Zinc, $\propto$-Tocopherol, Vitamin C, Soybean Oil, and Fish Oil. American Journal of Clinical Nutrition. 1991; 54: 736-744.

58. Kapu M, Fleming A, Ezem B. Plasma Zinc in Sickle Cell Anemia. Lancet. 1976;1: 920.

59. Carmel R, Johnson C. Cobalamin Deficiency in Sickle Cell Disease: A Survey with Implications for Routine Folate Supplementation. Blood. 1995; 86S; 644.

60. Ajayi O, Ipadeola T. Clinical Trial of Riboflavin in Sickle Cell Disease. East African Medical Journal. 1993; 70: 418-421.

61. Natta C, Reynolds R. Apparent Vitamin B6 Deficiency in Sickle Cell Anemia. American Journal of Clinical Nutrition. 1984; 40: 235-239.

62. Lachant N, Davidson W, Tanaka K. Impaired Pentose Phosphate Shunt Function in Sickle Cell Disease: A Potential Mechanism for Increased Heinz Body Formation and Lipid Peroxidation. American Journal of Hematology. 1983; 15: 1-13.

63. Phillips G, Tanganey C. Relationship of Plasma $\propto$-Tocopherol to Index of Clinical Severity in Individuals with Sickle Cell Anemia. American Journal of Hematology. 1992; 41: 227-231.

64. Tatum V, Chow C. Antioxidant Status and Susceptibility of Sickle Erythrocytes to Oxidative and Osmotic Stress. Free Radical Research. 1996; 25: 133-139.

65. Natta C, Machlin L. Plasma Levels of Tocopoherol in Sickle Cell Anemia Subjects. American Journal of Clinical Nutrition. 1979. 32; 1359-1362.

APPENDIXES

APPENDIX A

SOCIAL AMENITIES RATING QUESTIONAIRRE

Survey of Living Conditions

1. Housing

    _____ Board   _____ Block   _____ Other

2. Number of rooms in house _____

3. Number of people in house _____

4. Density   _____

Social Amenities Rating

Circle those that apply.

Water Supply

Piped in home	3
Piped in yard	2
Stand pipe	1
Tank in yard	2
From stream	1

Electricity and Appliances

Electricity	2
Refrigerator	3
Radio	1
Television	4
Phone	3

Toilet

Flush	2
Pit latrine	1

Total Score   _____

APPENDIX B

DIETARY INTAKE DIRECTIONS AND RECORD FORMS

3 Day Food Diary

Name_____

Address_____

Date of birth_____   Phone_____

Directions for Using the Food Diary

1. Try not to move the scales once they have been placed in your home.

2. To turn the scales on press the button marked on/off,

3. Put the plate on the scale.

4. Press the button marked on off. The scale should now read 0 g.

5. Put one food on the plate.

6. Write the weight of that food on the paper in the column marked amount served.

7. Press the button again so that the scale reads 0 g. Now put the next food on the plate

and record the weight.

8. Continue in this way. Always make sure that the scale reads 0 g before you put a new

food on the plate.

9. You must record everything that your child eats.

10. Record only one food item per line.

11. Be as specific as possible when describing the food item eate: the way it was cooked

(if it was cooked) and the weight of the food.

12. Include brand names when possible. For example, " Lasco Whole Milk" or "Maggi

Chicken Soup".

13. Include the method that was used to prepare the food item – for example: fried

chicken, stew peas, boiled green bananas, fried dumpling.

14. For canned foods, include the liquid in which it was canned, for example: mackerel in

tomato sauce.

15. Report only the portion that was actually eaten – you must weigh the amount that was

left over. To record the amount left you must first put the food on another plate.

    a. Press the button marked on/off.

    b. Put the plate on the scales

    c. Press the button so that the scale reads 0g.

    d. Now put one food on the plate. Write down the weight in the column marked

       amount left.

    e. Press the button so that the scale reads 0g. Now put the next food on the plate and

       record the weight in the same way.

    f. Continue in this way until there is no food left.

16.   Record drinks too. Press the button marked on /off.

    a. Put the cup on the scale. Press the button so that the scale reads 0g.

    b. Pour the liquid into the cup. Now write down the weight in the space marked

       amount served.

17. If your child does not drink the entire amount you must record the amount left. To do

this follow these instructions:

    a. Pour the drink in another cup.

    b. Press the button to turn the scale on.

c. Place an empty cup on the scales. Press the button so that the scale reads 0g.

d. Pour the left over liquid into the cup.

e. Record the amount left in the space marked amount left.

18. Do not change your child's eating habits during the period that you keep this diary. This is very important since we must know the exact amount of food that your child is eating.

If you need assistance at any time be sure to call me at one of the numbers given to you.

Time	Food Item and Method of Preparation	Amount Served	Amount Left

Friday

Name_____   Date_____

Time	Food Item and Method of Preparation	Amount Served	Amount Left

Saturday

Name_____ **Date**_____

Time	Food Item and Method of Preparation	Amount Served	Amount Left

Sunday

Name_____ Date_____

Time	Food Item and Method of Preparation	Amount Served	Amount Left

APPENDIX C

RECOMMENDED DIETARY ALLOWANCES FOR THE CARIBBEAN

Summary of Recommended Dietary Allowances of Nutrients for use in the Caribbean[a], Revised 1993

Age	Gender	Body Weight	Energy[b]		Protein[c]	Fat Soluble Vitamins			Water Soluble Vitamins							Minerals					
		kg	kcal	MJ	g	Vit A Re[d] µg	Vit. D[e] µg	Vit. E[f] mg α-TE	Thiamin mg	Riboflavin mg	Niacin[g] mg	Vit. C mg	B6 mg	Folac in[h] µg	Vit. B12 µg	Ca mg	Mg mg	Fe[i] mg	Na[j]	K[j] mg	Zinc mg
0-3 mths	MF	4.5	520	2.18	9	350	10	3	0.3	0.4	4	25	0.1	40	0.3	400	50	6	120	500	5
4-6 mths	MF	7.0	700	2.90	13	350	10	3	0.3	0.4	5	25	0.1	40	0.3	400	50	6	120	500	5
7-9 mths	MF	8.5	810	3.40	14	350	10	4	0.4	0.4	5	30	0.2	60	0.3	500	60	10	200	700	5
10-11 mths	MF	9.6	960	4.03	14	350	10	4	0.5	0.4	7	50	0.2	60	0.3	500	60	10	200	700	5
1-3 years	M	13.5	1390	5.81	16	400	10	6	0.6	0.7	9	60	0.3	100	0.8	500	150	10	225	1000	10
	F	12.9	1295	5.42	15	400	10	6	0.5	0.6	9	60	0.3	100	0.8	500	150	10	225	1000	10
4-6 years	M	19.7	1800	7.53	22	400	5	7	0.7	1.0	12	60	0.3	100	0.9	500	200	10	300	1400	10
	F	18.6	1625	6.79	21	400	5	7	0.7	0.9	11	60	0.4	100	0.9	500	200	10	300	1400	10
7-9 years	M	26.7	2070	8.66	27	400	2.5	10	0.8	1.2	14	60	0.4	100	1.0	600	250	10	400	1600	10
	F	26.6	1825	7.64	27	400	2.5	10	0.7	1.0	12	60	0.7	100	1.0	600	250	10	400	1600	10
10-14 years	M	45.0	2450	10.22	45	500	2.5	10	1.0	1.3	16	60	0.7	200	1.5	700	300	12	500	2000	15
	F	45.0	2065	8.66	45	600	2.5	8	0.8	1.1	13	60	0.8	200	1.5	700	250	15	500	2000	12
15-18 years	M	60.0	2720	11.38	57	600	2.5	10	1.0	1.3	18	60	0.7	200	1.5	900	350	12	500	2000	15
	F	55.0	2190	9.18	52	600	2.5	8	0.9	1.1	15	60	0.8	200	1.5	900	250	15	500	2000	12
19-29 years	M	70.0	2970	12.44	53	650	2.5	10	1.2	1.3	20	60	0.7	200	1.5	700	350	10	500	2000	15
	F	60.0	2200	9.23	45	560	2.5	8	0.9	1.1	15	60	0.8	200	1.5	700	250	15	500	2000	12
30-60 years	M	70.0	2870	12.02	53	650	2.5	10	1.1	1.3	19	60	0.7	200	1.5	700	350	10	500	2000	15
	F	60.0	2160	9.04	45	560	2.5	8	0.9	1.1	15	60	0.8	200	1.5	700	250	15	500	2000	12
>60	M	70.0	2295	9.60	53	650	2.5	10	0.9	1.3	15	60	0.7	200	1.5	700	350	10	500	2000	15
	F	60.0	1835	7.68	45	560	2.5	8	0.7	1.1	12	60	0.8	200	1.5	700	250	15	500	2000	12
Pregnancy			+285	+1.0	+6	660	5.0	10	+0.1	+0.3	+2	+10	0.8	+200	2.3	1000	+20	30*	500	2000	15
Lactation	0-6		+500	+2.0	+11	960	5.0	12	+0.2	+0.5	+3	+10	0.8	+100	2.0	1000	+50	15	500	2000	19
	6+					960	5.0	11	+0.2	+0.5	+3	+10	0.8	+100	2.0	1000	+50	15	500	2000	16

[a] The allowances represent daily amounts of energy and nutrients sufficient for the maintenance of health in nearly all people in the Caribbean.

[b] BMR x PAL (Physical Activity Level) for 10 year olds and above

[c] Adapted from WHO based on egg protein assuming complete digestibility, but adjustment may be necessary for diets based on high vegetable protein.

[d] R.E. + Retinol Equivalents. 1 µg RE= 1 µg retinol (3.3 IU) or 6 µg β carotene (10 IU)

[e] 1 µg =40 IU

[f] α-tocopherol equivalents; 1 mg d-α-tocopherol = 1 α-TE

[g] NE (niacin equivalent) = 1 mg Niacin or 60 mg tryptophan

[h] Expressed as free folate activity

[i] Based on 15% absorption for diets containing 14-20% of energy from food from animals

[j] NRC (USA) values. Sodium values are minimum requirements; total day's intake should not exceed 1600-2000 mg.

* Supplementation may be required

APPENDIX D

INSTITUTIONAL REVIEW BOARD

APPROVAL FORM

OKLAHOMA STATE UNIVERSITY
INSTITUTIONAL REVIEW BOARD
HUMAN SUBJECTS REVIEW

Date: 09-19-96   IRB#:   HE-97-014

Proposal Title: IS THERE A RELATIONSHIP BETWEEN HOMOZYGOUS SICKLE CELL DISEASE AND PROTEIN ENERGY MALNUTRITION?

Principal Investigator(s): Barbara Stoecker, Stephany Parker

Reviewed and Processed as: Expedited

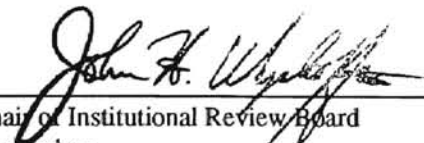**Approval Status Recommended by Reviewer(s):** Approved

ALL APPROVALS MAY BE SUBJECT TO REVIEW BY FULL INSTITUTIONAL REVIEW BOARD AT NEXT MEETING, AS WELL AS ARE SUBJECT TO MONITORING AT ANY TIME DURING THE APPROVAL PERIOD.
APPROVAL STATUS PERIOD VALID FOR DATA COLLECTION FOR A ONE CALENDAR YEAR PERIOD AFTER WHICH A CONTINUATION OR RENEWAL REQUEST IS REQUIRED TO BE SUBMITTED FOR BOARD APPROVAL.
ANY MODIFICATIONS TO APPROVED PROJECT MUST ALSO BE SUBMITTED FOR APPROVAL.

Comments, Modifications/Conditions for Approval or Disapproval are as follows:

Signature: Date:March 4, 1997

Chair of Institutional Review Board
cc: Stephany Parker

79

VITA

Stephany Paige Parker

Candidate for the Degree of

Master of Science

Thesis: ENERGY INTAKE AND EXPENDITURE IN JAMAICAN CHILDREN 3 TO 6
YEARS OF AGE WITH HOMOZYGOUS SICKLE CELL DISEASE

Major Field: Nutritional Sciences

Biographical:

Personal Data: Born in Kingsmountain, North Carolina, August 16, 1969, the
daughter of Mary Jane Beck and John David Parker.

Education: Graduated from Dublin High School, Dublin, Georgia, in June of
1987; received Bachelor of Arts degree in Anthropology from The University
of Georgia, Athens, Georgia in March of 1992; completed requirements for the
Master of Science Degree at Oklahoma State University in July of 1997.

Professional Experience: United States Peace Corps Volunteer, Jamaica, July
1994 to August 1996; Nutrition Assistant, the Ministry of Health, August 1994
to May 1995; Nutrition Reasearcher, the Sickle Cell Unit of the Medical
Research Council Laboratories, The University of the West Indies, Mona
Campus, May 1995 to August 1996; Teaching Assistant, Department of
Nutritional Sciences, Oklahoma StateUniversity, August 1996 to present.