

**UNIVERSITY OF ZAMBIA  
SCHOOL OF MEDICINE**

THESIS  
M. MED  
(PAEDIA)  
MUT  
2004  
C.1

**RELATIONSHIP BETWEEN ARTERIAL  
ELASTICITY AND BIRTH WEIGHT IN ZAMBIAN  
CHILDREN**

00278430



**DR. ANTHONY MUTITI BSc H.B MB.ChB**

**2004**

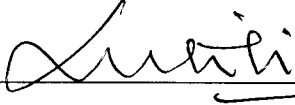
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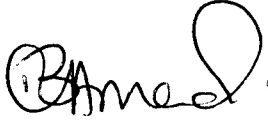
***Submitted as part fulfillment of the requirement for Masters of Medicine  
degree in the Paediatrics and child health.***

## **DECLARATION**

I declare that this dissertation represents my own work and has not been presented even in part to any forum or university other than the University of Zambia.

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## APPROVAL

This dissertation of Anthony Mutiti is approved as partial fulfillment of the requirements of the award of the Masters of Medicine Degree in Paediatrics and child health by the University of Zambia.

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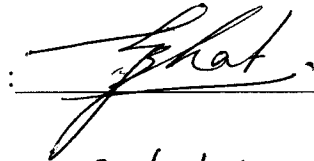
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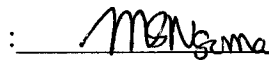
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## **DEDICATION**

This project is dedicated to all the children of Zambia, my mother Constance, my wife

Mwaka and my daughter Mambwe. These people are my life.

## **ACKNOWLEDGEMENTS**

I wish to thank the following people for their great contribution towards this project; Professor Steve Greenwald for his overall role in providing the necessary knowledge and equipment, which made this project possible

Drs Beatrice Amadi and Paul Kelly for their guidance and providing the necessary logistical support (and funding) which made it possible to conduct this study.

Dr Isaac Zulu for his assistance during the formulating the research proposal.

Mrs. Chilinda who was my assistant during the study for her total dedication during the study period.

Max Katubulusha, Mrs. Njovu and Mr. Phiri for the excellent support, which they rendered to me at the time of the data collection.

Lisa Laban for helping type this manuscript.

All the teachers and pupils at Twinkle star, Eagles Nest and Lord's Way schools for their kindness and the excellent assistance rendered during the time I was conducting my research.

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## LIST OF ACRONYMS

BMI	Body mass index
CAT	Category
DPB	Diastolic blood pressure
IUGR	Intrauterine growth retardation
MAP	Mean arterial pressure
PWV	Pulse wave velocity
PWV-F	Pulse wave velocity-femoral artery
PWV-R	Pulse wave velocity-radial artery
PWV-T	Pulse wave velocity-tibia (leg arteries)
SBP	Systolic blood pressure

## ABSTRACT

The objective of the study was to determine the effect of birth weight on blood pressure and arterial stiffness in childhood.

This was a cross sectional retrospective study involving 143 children from low to medium income areas of Lusaka, aged from 5 to 8 years old with mean age 6.78 years. It was conducted in 2002 between October and December. The information of birth weight, which is an index of intra uterine growth, was obtained from the children's under five cards. Blood pressure and pulse wave velocities were then measured and compared with the birth weights.

After adjusting for current weight, subjects in the lower birth weight category had the highest systolic blood pressure. A rise by 3.72mmHg (95% CI; 0.992-6.321) was observed for each kilogram decrease in the birth weight. The diastolic blood pressure was poorly associated with the birth weight. The association between the birth weight and the pulse wave velocity was not demonstrated in this study, though a weak but not statistically significant inverse relationship, was observed in the 8-year-old category.

All age groups had similar relationships; however the magnitude was highest in the older age category.

In conclusion the study has shown that birth weight was strongly inversely related to the systolic blood pressure in Zambian children. This supports the hypothesis that intrauterine environment may partly determine the elastic properties of blood vessels.

# Chapter 1

## 1.0. INTRODUCTION

### 1.1.0. General Background

The mechanical properties of the large elastic arteries have been the subject of continuing interest to physiologists and engineers for well over a century.

However, during the last fifteen years the subject has attracted the attention of clinicians as it has become more widely recognized that the compliance of the conduit arteries is a major determinant of pulse pressure and hence the pulsatile workload of the heart.<sup>1</sup> This interest has been encouraged by the development of non-invasive methods for measuring arterial elasticity.<sup>2</sup> At the same time it has become clear that the response of the vascular system to changes in pressure and flow due to aging and disease usually involves alterations in the dimensions, composition and properties of the affected vessels.<sup>2</sup> This implies that changes in vascular elasticity may indicate changes in the general state of health of the cardiovascular system, and therefore elasticity measurements will provide an effective means of assessing these changes.<sup>3</sup>

Of the many methods for measuring vascular elasticity that have been developed the simplest and most suitable for routine vascular assessment are based on the idea along a blood vessel segment pulse wave velocity (PWV) is inversely proportional to the square root of volume compliance of that segment. In other words, the stiffer the artery, the higher the PWV.<sup>3</sup>

A novel method for measuring PWV has been developed over the past few years. Briefly, the propagation velocity of the pressure wave traversing an artery (generated by the beating heart) is measured by detecting optically by two probes placed on the skin at two sites over the vessel under investigation.<sup>3</sup> Knowing the time taken for the waves to travel between the two sites and their separation the pulse wave velocity maybe determined. The average stiffness of the vessels between the two sites is proportional to the square root of the wave velocity.

A number of validation experiments have been carried out and there is now good evidence that this novel method is reliable, repeatable and gives PWV values that agree well with older techniques such as Doppler Ultra sound.<sup>3, 4</sup> This has led to the conclusion that this method provides a simple and reliable complement to existing techniques for the non-invasive measurements of arterial compliance.<sup>3</sup> It's portability, cheapness and reliability make it particularly suitable for large-scale epidemiological studies in children.

### **1.1.1. Reasons For Measuring Arterial Elasticity In Children**

There is strong epidemiological evidence of an association between growth retardation in utero and higher than average blood pressure in middle age.<sup>4</sup> As a possible mechanism for this association it has been proposed that, in fetuses whose growth is retarded, there is impairment in the synthesis of elastin during a critical period of blood vessel development, which may be associated with in intra-uterine growth retardation.<sup>5</sup>

As a result of the elastin deficiency, the compliance of the conduct arteries is reduced. Decreased conduct artery compliance causes increased pulse pressure, thus imposing a

greater than normal peak load on the left ventricle. This leads to the development of left ventricular hypertrophy, impaired coronary arterial perfusion, hypertrophy of the arterial wall, increased peripheral resistance and a consequent increase in mean blood pressure.<sup>5</sup>

Once established, the elastin deficiency cannot be corrected due to the low turnover of this protein and the tendency for vascular smooth muscles preferentially to synthesize collagen when subjected to increased levels of mechanical stress.<sup>5</sup> Over time, the gradual loss of elastin that accompanies aging and its replacement with collagen will tend to amplify the increase in blood pressure.<sup>1, 2</sup>

It has previously been shown that growth retardation in utero is associated with stiffer than normal conduit arteries in middle age.<sup>6</sup> These results raise several interesting questions. For instance: do these growth-retarded babies have stiffer than normal vessels, and if so, is it possible to treat them before the vascular system has lost its ability to adapt by remodeling? Compliance measurements on a population of growth-retarded babies in Europe are in progress. It is hoped these might help to answer the first of these questions. To answer the last question, a large –scale epidemiological study on a population of babies, children and adults of varied nutritional status has to be carried out. As a first step of more manageable proportions, measurements of blood pressure and pulse wave velocity on a population of children from various backgrounds was performed with the immediate aim of determining, if there is a relationship between the birth weight of these children and the elasticity of their aorta and femoral arteries.

### 1.2.0.Literature Review

A relationship between low birth weight and higher than normal blood pressure in adult life has been strongly demonstrated.<sup>4</sup> It has been shown that people who were thin or short at birth, or proportionately small, have persistent elevation of blood pressure.<sup>7</sup> This finding suggests that intra uterine growth retardation may have an effect on the development of the cardiovascular system.<sup>6, 8</sup> Barker et al in their study in Herfordshire in 1992 and 1993 found that there was an increased prevalence of a condition associating obesity with hypertension and non-insulin dependant diabetes mellitus in people who were small at birth.<sup>9-10</sup> David et al, in a study of Swedish men aged 18 years showed that systolic blood pressure was independently inversely associated with birth weight for gestational age.<sup>11</sup> Similarly another longitudinal study of those aged 5-37 years, found the strongest association between birth weight and systolic blood pressure to be in the age group 15-19 years.<sup>12</sup>

A study of Israeli conscripts aged 17 years, similar in design to the study by David et al reported the same correlation.<sup>13</sup> However, the association noted earlier may be obscured in adolescents and young adults due to disturbances in tracking of blood pressure.<sup>14</sup>

Several other studies in children have also demonstrated a similar relationship.<sup>15-17</sup> Godfrey et al in a study of children in Zimbabwe found weak inverse relation between the birth and the systolic pressure.<sup>16</sup> These results were similar to the finding by Whincup et al.<sup>15</sup> However, the magnitude of this association in childhood studies is not as strong as that found in studies involving older children and young adults. This could suggest that the effect of birth weight on blood pressure is amplified from infancy to older age.<sup>1,2</sup>



In humans, low birth weight, and disproportion in head circumference, length, weight and placental weight, are markers of nutrients.<sup>18,19</sup>

In fetal life the tissues and organs of the body go through what are called 'critical' periods of development during which rapid cell division occurs.<sup>18</sup> Experimental studies in animals have established the principle that stimuli at the critical periods of early life can have permanent effects on a range of physiological processes, a phenomenon termed fetal programming.<sup>19</sup> Studies in rats, have shown that fetal under- nutrition causes persistent elevation of blood pressure as well as persistent changes in the composition arteries.<sup>20,22</sup> Several epidemiological studies further consolidate the evidence that under-nutrition in utero leads to persisting changes in blood pressure, cholesterol metabolism, and insulin responses to glucose.<sup>14, 23-25</sup>

Intrauterine growth retardation [IUGR] is a common problem both locally and worldwide. According to WHO low birth weight is defined as birth weight less than 2.500g or below the 10<sup>th</sup> percentile for gestational age.<sup>26</sup> Aetiological factors include chronic maternal illness (e.g. Hypertension, pre-eclampsia, maternal drug use, malnutrition), congenital infections due to, for instance, cytomegalovirus, Toxoplasmosis and human immunodeficiency virus.

Neonatal outcome of IUGR due to fetal under nutrition, is usually good and mortality is low.<sup>27</sup> The catch- up growth is rapid in the first three months of life and attains normal growth curves by age of 1 year. Long-term complications include hyperactivity, clumsiness and poor concentration.<sup>27, 28</sup> Children with IUGR have an increased risk for developing hypertension later in life as shown by numerous studies discussed earlier.

The facts from these studies point to a need for paediatricians to carefully follow up children with a history of IUGR or small for gestational age with the objective of documenting postnatal catch-up, preventing excessive weight gain and to advocate for normal and well balanced diets.

## Chapter 2

### **2.0. OBJECTIVES OF THE STUDY**

#### **2.1.Main Objective.**

To determine the relationship between birth weight and the elasticity of the aorta and femoral arteries in Zambian children.

#### **2.2.Specific Objectives.**

1. To determine the effect of birth weight on blood pressure in childhood.
2. To determine the effect of birth weight on arterial stiffness.

## **Chapter 3**

### **3.0.MATERIALS AND METHODS**

#### **3.1 The Research Design**

This was a cross-sectional study of school children aged between 5 and 8 years in Lusaka and was conducted between October and December 2003.

#### **3.2 Study Subjects And Site**

143 subjects aged from 5-8years were recruited in the study. By random sampling 10 schools were selected but authority was only obtained from 3 church run primary schools. These schools have very similar characteristics and serve mainly low to medium income families of the church members and the neighborhood. They enroll classes from nursery to grade 4, with the age of the pupils ranging from 2-10 years. All the parents of children whose age fell within the study requirement were contacted and invited to participate. Information sheets and consent forms were sent through the school head teacher. Those who needed more information were met in person. 260 parents agreed to their children included in the study out of 350 invitations sent. Of these only 143 children were included in the study.

#### **3.3.Inclusion Criteria**

1. Children with known birth weight
2. Consent from parents

### **3.4. METHODS**

#### **3.4.0. Blood pressure measurements**

The children were examined in a room provided by the school. They were evaluated in groups of 4 pupils. A teacher assisted in order to calm the children and once the child was calmed and relaxed, blood pressure was measured using a mercury sphygmomanometer.

Systolic and diastolic blood pressures were recorded.

#### **3.4.1. Pulse wave velocity measurements.**

The compliance of the large arteries was determined by using two compliance probes (proximal and distal). A uni-modal electrocardiograph is used as the proximal probe, which remains fixed while the distal probe is placed over the carotid artery in the neck, and then over the radial artery at the wrist referred to as the arm segment. Recordings are done for 30 seconds respectively and the data recorded. The procedure is repeated twice; firstly with the distal probe placed over the femoral artery just below the inguinal ligament. And secondly, with the distal probe placed below the medial malleolus of the tibia. The readings are recorded by a computer program, which then calculates the transit time of the pulse wave generated from the heart to the various points where the distal probe is placed. Measurement between the sternal notch and the various points where the distal probe was placed are done using a measuring tape and fed into the computer program that in turn is able to determine the pulse wave velocity.

The height of each child is measured using a stadiometer and recorded in centimeters. All children are weighed in kilograms using an electronic scale.

The birth weight (kg) and date of birth of each was obtained from the children's under five cards. The parents gave information on the period of gestation.

All the data was entered on a standard questionnaire (appendix)

### **3.5. Ethical issues**

The research and ethics committee of the University of Zambia approved the study.

The school authorities granted permission to use the schools and confidentiality was observed in the handling of the information obtained.

### **3.6. Data analysis**

The data was entered and analyzed on Epi Info-v6 computer software.

Statistical analysis included analysis of variance and multiple linear regression analysis.

### **3.7. Limitation of the study**

1. The sample size was very small. A larger sample size would have been more conclusive. In a few instances the data was so scanty that it was very difficult to compare within the categories.

# Chapter 4

## 4.0. RESULTS

A Total of 143 children from three schools in Lusaka were examined. Only 120 of these were included in the analysis because the other 23 had no birth weights recorded on their children’s card. The chart below shows the age distribution of the study subjects.

Chart1

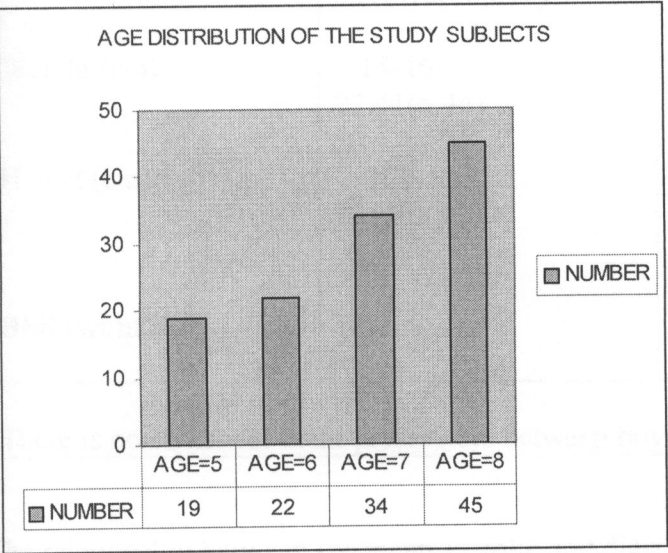
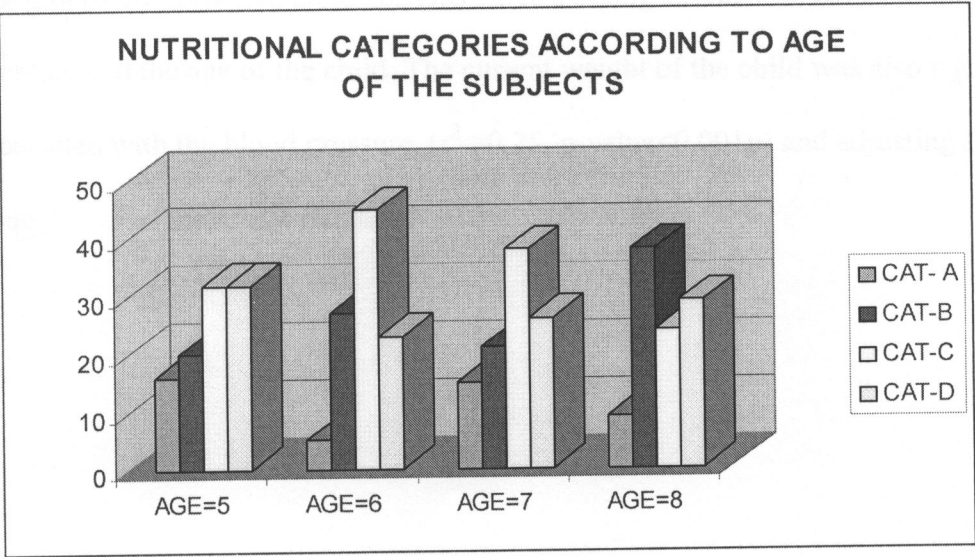


Chart 2



Nutrition categories based on the child’s birth weight; CAT-A= Birth weight >2500g  
CAT-A= Birth weight >2500g; CAT-B= Birth weight 2500-2999g; CAT-C= Birth weight 3000-3499g; CAT-D= Birth weight >3500g

**Table1a shows the anthropometric data of these children.**

	Boys range/ mean (SD)[N=54]	Girls range/ mean (SD)[N=66]	Total range/ mean (SD)[N=60]
Age (years)	5-8 6.78(1.44)	5-8 6.95(1.04)	6.87(1.09)
Birth weight (g)	1500-4500 3098.10(662.90)	2000-4200 3103.00(562.70)	3100.55(612.80)
Weight (cm)	15-46 23.41(5.44)	17-40 24.41(5.67)	23.90(5.555)
Height (cm)	102-138 121.70(8.71)	102-141 124.64(8.28)	123.17(8.495)
BMI (wt/ht <sup>2</sup> )	16.0	15.71	15.86
There is no statistical in all parameters between boys and girls, p-value = 0.5542			

The relationship between the mean systolic and diastolic blood pressure in the various age groups are shown in table 1b. There was a strong association between the blood pressure and the age of the child. The current weight of the child was also significantly associated with the blood pressure, ( $r^2=0.25$ , p-value<0.001p) and adjusting for this was done.



**Table 1b. The relationship between blood pressure, pulse wave velocity and the sex of the child.**

	Boys range/ mean (SD)[N=54]	Girls range/ mean (SD)[N=66]	Total range/ mean (SD)[N=60]
Systolic blood pressure (mmHg)	85-110 93.80(7.705)	75-130 104.92(10.21)	99.36(8.958)
Diastolic blood pressure (mmHg)	55-70 62.04(5.453)	55-70 61.51(4.721)	61.78(5.087)
Pulse wave velocity- carotid (ms <sup>-1</sup> )	0.970(0.315)	1.005(0.295)	0.988(0.305)
Pulse wave velocity- radial (ms <sup>-1</sup> )	4.954(0.842)	5.139(0.820)	5.046(0.831)
Pulse wave velocity- femoral (ms <sup>-1</sup> )	3.228(0.674)	3.251(0.484)	3.240(0.597)
Pulse wave velocity- femoral (ms <sup>-1</sup> )	4.469(0.501)	4.816(0.541)	4.642(0.521)
P-value = 0.4619			

Table 1b shows the association between systolic blood pressure (and diastolic blood pressure) and gender. There was no significant difference in blood pressure in relation to gender and hence no adjustment was necessary.

**Table 2. Association between systolic blood pressure (SBP) and diastolic blood pressure (DBP), and birth weight (500g Intervals), according to the age.**

Birth weight (g)	No of Subjects	Mean SBP (mmHg)	Mean DBP (mmHg)
Age=5			
<2500	3	91.67	60.00
2500-2999	4	89.09	62.73
3000-3499	6	90.08	63.33
3500+	6	87.00	62.00
age=6			
<2500	1	85	60.00
2500-2999	6	85.53	58.93
3000-3499	10	86.50	59.50
3500+	5	86.25	57.50
age=7			
<2500	5	98.00	62.00
2500-2999	7	95.25	61.75
3000-3499	13	94.46	60.70
3500+	9	97.86	62.86
age=8			
<2500	4	101.25	65.00
2500-2999	17	95.50	62.25
3000-3499	11	94.80	63.18
3500+	13	90.00	60.00
p-value		<0.001	0.209

Table 2 shows that blood pressure was lower in children with higher birth weights in most age groups. There was an overall significant inverse association between the birth weight and the systolic blood pressure ( $r^2=0.25$ ,  $p\text{-value}<0.001$ ), after adjusting for the current weight.

An increase in blood pressure of 3.72mmHg (95% CI:0. 992-6.321) was observed for each kilogram fall in the birth weight.

A similar association was observed with the diastolic pressure however this was statistically insignificant (p-value=0.209). An increase in birth weight by 1kg was associated with a fall of 0.92mmHg(95%CI:0. 524-2.359) in the diastolic blood pressure. Current weight did seem to confound with the diastolic blood pressure. Overall, the age did not significantly affect the relationship between the birth weight and the blood pressure.

**Table3a. Association between pulse wave velocities of the aorta (PWV-F), radial (PWV-R), and leg arteries (PWV-T). Age 5and 6**

Birth weight (g)	No of Subjects	Mean MAP (mmHg)	PWV-F (ms <sup>-1</sup> )	PWV-R (ms <sup>-1</sup> )	PWV-T (ms <sup>-1</sup> )
Age=5					
<2500	3	70.56	3.397	5.167	5.183
2500-2990	4	71.51	3.740	5.735	5.330
3000-3499	6	72.22	3.627	5.483	4.667
3500+	6	70.33	3.480	5.405	4.707
p-value			0.600	0.720	0.122
Age=6					
<2500	1	68.33	3.210	5.100	4.600
2500-2990	6	67.80	3.066	5.048	4.568
3000-3499	10	68.50	3.460	5.636	4.674
3500+	5	67.16	3.608	4.884	4.980
p-value			0.310	0.820	0.210

**Table3b. Association between pulse wave velocity of the aorta (PWV-F), radial (PWV-R), and leg arteries (PWV-T) Age 7and 8**

Birth weight (g)	No of Subjects	Mean MAP (mmHg)	PWV-F (ms <sup>-1</sup> )	PWV-R (ms <sup>-1</sup> )	PWV-T (ms <sup>-1</sup> )
Age=7					
<2500	5	74.00	3.002	4.940	4.570
2500-2990	7	72.89	2.471	4.581	4.387
3000-3499	13	71.67	3.293	4.841	4.510
3500+	9	74.53	3.058	5.328	4.648
p-value			0.700	0.420	0.730
Age=8					
<2500	4	77.08	2.800	4.638	5.445
2500-2990	17	73.33	3.052	4.984	4.828
3000-3499	11	73.76	3.145	4.936	4.812
3500+	13	70.00	3.432	4.874	4.800
p-value			0.50	0.590	0.090

Table 3 compares of the birth weight with the pulse was velocities. Except for the 8year old subjects there was no significant correlation between the birth weight and the pulse wave velocity obtained in children. In the age group = 8 there was a drop of 0.114ms2(95%CI;0. 257-0.057) per 1kg rise in the birth weight. There was no significant difference in the mean arterial pressure for subjects with differing age groups.

## Chapter 5

### 5.0.DISCUSSION

#### 5.1.Study population

The study included 143 children of which only 120 were analyzed due to incomplete data. The children were evenly matched for gender as there was no significant differences in the variables (p-value 0.509), however during data analysis adjustment of the blood pressure for the current weight of the child was made because the current weight of the child was significantly associated with the systolic blood pressure (p-value<0.001).

The majority of the children in the study were 7years and above (66%) with the 8 year old category having the highest number. This probably explains why it was much easier to analyze the data for the 7 and 8-year-old groups than in the 5 and 6 year olds were data was very scanty.

The children were further subdivided into nutritional categories based on their birth weights. Those with birth weights less than 2500g(low birth) were put in category A, while category B and C included children with birth weights within the normal range, that is 2500 to 2999g and 3000 to 3499g respectively. The children who were large as babies with birth weights above 3500g were put in category D.

There was no information about the gestational age of the children; as a result the effect of gestational age on the blood pressure of these children was not evaluated. It has been shown however, that there is no significant relationship between blood pressure and gestation age adjusted for age.<sup>16</sup>

Most of the children were of good nutrition status .The average BMI of the children in the study was 15.86

## **5.2.Birth weight and systolic blood pressure**

The blood pressure of 120 school children aged between 5 and 8 years were then compared with the birth weights. By categorizing the children into various birth weight categories it was shown that birth weight was inversely related to the corrected systolic blood pressure and decrease of 3,72mmHg(95%CI;0. 992-6.321) occurred with each kilogram rise in birth weight after adjusting for current weight. This association has been replicated in many studies all over the world.<sup>6-17</sup> However the strength the association varied from study to study. Studies in children by Whincup et al and Godfrey et al reported 1.83 and 1.73mmhg rise for each kg respectively. However, Mahmoud et al. in their study of subjects aged between 8 to 24years showed a decrease by 3.7mmHg(95%, CI; 1.1 to 6.3) for every kilogram increase in birth weight.<sup>17</sup> This shows great variability in the magnitude of the relationship. In adult studies values of 5mmhg rise for each 1kg drop in birth weight have been reported.<sup>29</sup> The association in this study was observed in all age groups, meaning that the changes in vessel wall characteristics resulting from intra-uterine growth retardation can be noticed by 5years of age .The relationship was noted to be stronger in the 8 years category demonstrating to some extent that this association may be progressively amplified in child hood and older age.

## **5.3.Diastolic blood pressure and birth weight**

The diastolic pressure did not show significant association with birth weight (p-value 0.210). This is consistent with the findings in other studies.<sup>29</sup>

#### **5.4.Pulse wave velocity and birth weight**

Concerning the pulse wave velocity measurements, there was poor correlation between the birth weight and the pulse wave velocities except in the 8 years age. In this age group there was a weak association with  $0.114\text{ms}^{-1}$  (95% CI; -257 to -0.0557) decline for each 1 kg increase in birth weight, though this was statistically insignificant (p-value 0.09). This result may mean that the vessel characteristics are still unchanged. This is further supported by the finding of insignificant differences in the mean arterial pressures, which have a direct bearing on the vessels compliance. However the sample size was too little to draw meaningful conclusions.

## **Chapter 6**

### **6.0. CONCLUSION AND RECOMMENDATIONS**

#### **6.1 CONCLUSION**

This study shows that Zambian children who are small for gestational age are at risk of developing hypertension later in life.

The study therefore supports the hypothesis that elevated blood pressure and arterial stiffness are partly programmed by under nutrition in utero and the changes are already apparent by early childhood. It also shows that this hypothesis may be true for Zambian children and that such evidence is already apparent by 5years of age. However it is very important to note that the data was not adequate to draw meaningful conclusions.

As hypertension is a major cause of morbidity and mortality in Zambia, this risk factor must be further evaluated and considered in the aetiology of hypertension.

#### **6.2. RECOMMENDATIONS**

1. A large-scale study should be conducted in Zambia for more conclusive data.
2. The children's under-five card should include the birth weight but also gestation age, occipito-frontal circumference and length at births. This will allow health-workers and paediatricians to correctly assess intra-uterine growth.
3. Blood pressure measurements and interpretation should be done routinely at all health centers. Health centers therefore need to be equipped with paediatric sphygmomanometers. This will allow children at risk to be picked up and intervention measures instituted as early as possible.



4. Children who are small for gestation age, should be followed-up, initially for catch –up growth, then later for blood pressure tracking. They should be advised appropriately about the other risk factors of hypertension and the need for a healthy diet should be emphasized.

## REFERENCES

1. Nicholas W.W. and O' Rourke, MF. Structural changes in arteries with age, McDonalds Blood flow in arteries, 1998. Anord; London P.356-376
2. Glasgow, S. Intimal hyperplasia, vascular modeling and the restenosis problem. [Review]. Circulation 1994;89:288-2891.
3. Greenwald S. E. Denyer. H.T, Adnsobeh M.S., Non-invasive measurement of vascular compliance by a photoplethysmography technique SPIE proceeding, 1997-2970-89-97.
4. Law, C.M, Shell, A.W, Is blood pressure inversely related to birth weight? The strength of evidence from system review of Literature. Hyperten, 1996-14:935-941.
5. Martyn. C.N and Greenwald S.E. Impaired synthesis of elastin in the walls of the aorta and large conduit arteries during early development may be an initiating event in the pathogenesis of systemic hypertension, Lancet, 1997-350:953-955.

6. Martyn, C.N Barker, D.J.P, Jespersen, S. Greenwald, S.E. Osmond, C and Berry, C. Growth in utero, adult blood pressure and arterial compliance. British heart journal, 199-73:116-121.
7. Law C.M, Swiet M. Osmond C, Initiation of hypertension in utero and its amplification throughout life BMJ 1993-306:24-7
8. Edwards C.R.W, Bennediktson R, Lindsay. Dysfunction of the glucocorticoid barrier: Link between fetal environment and adult hypertension? Lancet 1993-341:355-7
9. Barker D.PJ, Gluckman PD, Godfrey K.M Harding J. Owen J.A Robinson J.S: Fetal nutrition and cardiovascular disease. The Lancet 1993-341:938-1941.
10. Barker D.P; in fetal and infant origins of adult disease (DJP Barker, Ed), p.342. Brit med. Pul London 1992
11. David A. Leon, Malin Johnson and Finn Rasmusseu, Am. J. Epidemiology Volume number 152, 7:597-604,2000
12. Uiterwaal C.S Anthonys, Launder L.J. Birth weight, growth and blood pressure; an annual follow up study of children aged 5 years through to 21 years. Hypertension, 1997-30:267-71



13. Laor. A. Stevenson D.K, Shemer J. et al. Size of material nutrition status in pregnancy, and blood pressure at age 17: population based analysis B.M.J 1997-315:449-53.
14. Macintyres, Watt. G. West P. Correlates of pressure in 15 years olds in the west of Scotland. J Epidemiol community health 1991-45; 143-7(abstract)
15. Whincup.P.C. D, Papacosta O., Walker M. Birth weight and blood pressure cross sectional and longitudinal relations in child hood. BMJ 1995-311:773-776
16. Godfrey W. Irvin E. Noel S. Weiss, Bruce M. Psaty. Arch Dis Child fetal Neonatal Ed 199-F119-F122 (September)
17. Mahmoud Z. Claire B. Edith L. Gerard St and Pierre D. Hypertension, 1996-27:339-345.
18. Widdowson E.M. Mc Cance R.A. A reviews: New thought on growth. Paediatric Res 1975- 9: 154-6
19. Mc Cance R.A Widdowson E.M. The determinants of growth and form Proc. London; 1974-185:1-17

20. Langley S.C Jackson, A.A. Increased systolic blood pressure in adult rats induced by fetal exposure to maternal low protein diets. Clin. Sci. 1994-86:217-22
21. Greenwald S.E, Berry C.L and Ramsey R.E. The static elastic properties and chemical composition of the aorta in spontaneously occurring and experiment induce hypertension. The effect of an antihypertensive drug. British journal of experiment pathology, 1985-66-642.
22. Osmond .C., Baker D, JP. Winter PD, Fall C.H.D, Simmonds S.J. Early growth from cardiovascular disease in women BMJ-BMJ 1993-397: 1519-24
23. Forsen T, Erickson J.G, Tuomilehto J, Teramo K, Osmond C Baker DPJ).  
Mother's weight in pregnancy and coronary heart disease in a cohort of Finnish men: Follow up study BMJ. 1997-315:837-840.
24. Hales C.M, Barker D.P.J, Clark P.M.S. Cox L.J. Fall C.H.D, Osmond C. Winter P.D. Fetal and infant growth and impaired glucose tolerance at age. BMJ 1991-303 1991 1019-22.
25. Lithell H.O, Mc Keigue PM, Berglund L, Mohsen R., Lithell UB, Leon D.A  
Relation of size at birth to non-insulin dependent diabetes and insulin concentration in men aged 50-60 years. BMJ 1996-312: 406-10

26. Dunn P.M. The search for perinatal definitions and standards. *Acta paediat, Scand Suppi-1985- 3:716.*
27. Lippert E, Lee K., Gartner L.M, Grellong B. Determinants of neurobehavioral outcome on low-birth weight infants. *Paediatrics* 1981-67: 502-5
28. Robertson C.M, Etches. P.C, Kyle. I.M. Eight –year school performance and growth, small for gestational age infants: a comparative study with subjects matched for birth weight or gestational age. *J. Paediatric.* 1990-116: 1926
29. Barker D.J.P, Osmond C, Golding J, Kuh D, Wadsworth MEJ, Growth in utero, blood pressure in childhood and adult life and mortality from cardiovascular disease. *BMJ* 1989-298:564-567

**APPENDIX**

**A.CONSENT FORM**

TITLE: Relationship Between Arterial Elasticity and Birth weight in Zambian Children

I/We..... the parents/guardians  
of..... Aged..... agree that he/she can be included  
in the above named study .in this study his/her blood pressure and the speed of her pulse  
will be measured using a special instrument placed over the skin by the doctor. Secondly,  
we shall provide the doctor with the child’s children’s clinic card and if possible his birth  
record. The child will also be examined to asses his/her general health and if any  
problems are noted the doctor will appropriate advice.

Note: the information provided will be handled with strict confidence.

SIGNATURE.....

WITNESS.....

DATE.....

## **B. STUDY INFORMATION SHEET.**

### THE STUDY

We have found out that children who are very small at birth have a higher than average blood pressure later in adulthood. This probably is because growth retardation in the unborn child alters the formation of the walls of the blood vessels. We want to know if children with low birth weight have different blood pressure characteristics,

For this reason we want to perform measurements of blood pressure and the speed of their pulses on a population of Zambian children that we can see if there is any relationship between their birth weight and the elasticity of their blood vessels.

### INVITATION

You and your child have been invited to take part in this study in which your child's blood pressure and pulse will be measured.

### WHY HAS YOUR CHILD BEEN CHOSEN?

The reason you have been asked is because your child's age falls in the age group we want to study and also the weight at birth is known.

### WHAT IS INVOLVED

1. If you agree to enter your child in the study, you will be asked to give us your antenatal card if available and the child's under five card which we will examine and give back to you. You will also be asked to tell us if your child was born at the expected time or earlier than expected. You will also tell us where your child was born and the day the child was born.



2. The child's blood pressure will be taken by a doctor and the nurse. This is not painful at all and will be in a form of a game with the child. No injections are involved.

WHAT ARE THE POSSIBLE BENEFITS AND DISADVANTAGES OF TAKING PART?

- Your child's blood pressure will be known
- If any abnormalities are detected your child will receive thorough medical evaluation and if necessary treatment by a specialist.
- There are no disadvantages except for the inconvenience of time.

Thank you for taking time to consider this study for your child. Please ask any questions and let us know if there are things you do not understand or would like more information about.

C.QUESTIONNAIRE

Relationship between Arterial Elasticity and Birth weight In Zambian Children.

1. Name..... Study number...
2. School.....
3. Consent obtained from.....
4. Relation to child.....
5. Address.....
6. D.O.B..... Sex: M / F BWT.....
7. Number of children.....Position.....D.O.B of previous child.
8. Gestational age.....Term.....Premature.....No. of weeks.....
9. Mode of delivery SVD..... C/S.....
10. Sopped breast feeding.....
11. Age in months:
12. Weight.....kg. height:..... cm.
13. Blood pressure:.....mmhg.....mmhg
14. Probe separation: Carotid.....mm  
Radial.....mm  
Femoral.....mm  
Dorsalis pedis.....mm
15. General examination:

Pallor: .....

LAD: .....

RR .....

Condition of the mouth.....

Condition of the skin.....
16. Urinalysis

SG: .....

2025010

Sugar: .....  
Blood: .....  
Proteins .....  
Ketones .....  
Leucocytes .....

17. CVS

Precordial activity:.....  
Exam (auscultation).....  
S1 .....  
S2 .....  
Added sounds

18. Referral to specialist yes/no