Chapter Twelve

Newborns, Infants, and Grown-up Children (Adolescents): Embers of Researches, Ideas, and Advancement

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Acknowledgment

Wherefore seeing we also are compassed about with so great a cloud of witnesses, let us lay aside every weight, and the sin which doth so easily beset us, and let us run with patience the race that is set before us.

Hebrews 12.1

Ladies and gentlemen, I will like to end this lecture by expressing my sincere gratitude to the Vice Chancellor, Ahmadu Bello University and the entire university community, not only for the singular honour of giving this lecture, but also for providing an environment that is conducive for learning, research, practice, growth and development and for running the race. I am not too sure of where I would be without this great university. I must thank the VC especially for encouraging the regular presentation of inaugural lectures in the university. I can only say the name and sweet memory of Ahmadu Bello University, Zaria, this intellectually and physically gigantic institution, will remain with me till I breathe my last.

I must appreciate my Dean, Professor AG. Bakari, for committing the Faculty of Medicine, one of the greatest Faculty (if not the greatest), to regularly take part in the inaugural series. Mr. Dean, I remember our days as neighbors in Gaskiya, when we were "growing up". Thank you for nominating me to represent the Department of Paediatrics of Ahmadu Bello University.

I thank all my colleagues, senior, junior and contemporary, and all postgraduate (resident) doctors in my department, for the support enjoyed over the years. There is no way I could come so far without you. I also thank my colleagues and friends in other departments, both medical and non-medical for their being there when needed. I must make mention of Professor JO. Hambolu who persistently prod me to move on along the carrier ladder. I pray that the Almighty God will continue to prosper all your ways.

I must acknowledge my alma mater, the University College Hospital/University of Ibadan, for turning me into a medical doctor in the first place.

I thank my parents for having me. It is one thing to give birth to a child, it is another issue to nurture the child. This is one huge area we have problems with in Nigeria and it should be of great concern for anyone with any positive outlook for the future of our great country, which can truly be great in the real sense of the word.

I thank you, my wife, Mrs. Olufunmilayo Rebecca Ogunrinde, Mama T, for your love and support; for being there during the struggle to make headway in academic affairs, and indeed, in other areas of my life and wellbeing. I thank my children, Olwatobiloba, Oluwadara and ModupeOluwa. They have made everything worthwhile and have pushed ahead, and still pushing, like normal offspring.

I thank all the children I have come across, and still encountering, who are unfortunately labelled as patients. I will like to label them as my children. Unfortunately, a significant number of them are no longer with us on this side of the divide by virtue of myriads of problems they faced at the time of dire needs.

> Long live Nigeria, the good name inspiring the title of this lecture and actually is the title. Long live Ahmadu Bello University, the birthplace of so many great ideas, in itself the gestational product of a great mind. Long live the Department of Paediatrics, one of the best in the country, the handiwork of great teachers and great colleagues. Thank you, ladies and gentlemen, for your patient and kind attention.

> *I returned, and saw under the sun, that the race is not to the swift, nor the battle to the strong, neither yet bread to the wise, nor yet riches to men of understanding, nor yet favour to men of skill, but time and chance happeneth to them all"*
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> ***Ecclesiastes 9:11***

Introduction

The Vice Chancellor, Ahmadu Bello University, Zaria, the Deputy Vice Chancellor (Academics), the Deputy Vice Chancellor (Administration), the Registrar, the University Librarian, the Bursar, Dean Faculty of Medicine, Deans of other Faculties, Directors of Institute, Heads of Department, senior Professors (my teachers),

other highly esteemed Professors, members of academic and non-academic staff, students, other members of the university community, ladies and gentlemen.

I thank the Almighty God, Maker of heaven and earth, God of Abraham, Isaac and Jacob, the Beginning and the End, for this wonderful opportunity offered me to give my inaugural lecture as a professor of Paediatrics. I return all glory and adoration to Him.

I will like to start this lecture by letting people know why I chose Paediatrics as a field of interest. I have an inkling that some in the audience may want to know why. It is proper to let you know. Until I graduated from the Medical School (now College of Medicine), University College Hospital, Ibadan, I had no clue as to what I was going to be apart from being a medical doctor and be able to heal sick people, hopefully. As a medical student, I was too busy learning medicine to actually recognize the patients. It was a hectic schedule and there were occasions when I doubted if it was possible to complete the medical education. However, during my internship year in UCH, Ibadan, when the practical aspects of medicine rather than theory were now routine the patients swam into sharp focus. The order of my internship in the four clinical departments was Paediatrics, Obstetrics/Gynecology, Medicine and lastly Surgery. Without trying to deride anyone and bearing in mind that first impression may be influential, I found the patients in the Department of Paediatrics to be very friendly and very forthright. They have this eagerness to get well soon and get back to the routine of life as quickly as possible. Very importantly, children hardly have overt psychiatric manifestations and psychiatry was my worst subject as a medical student. In fact, the day I watched a young man in Aro Psychiatry Hospital, Abeokuta, being given the electroconvulsive therapy (a kind of shock therapy) I knew I was never going to be a psychiatrist. The thrashing about and convulsions induced in the young man had a severe negative impact on me. During my internship, I soon grew tired of the very complex natures of adult symptoms, many of which had no organic basis and probably reflected cultural bias. I have heard of people having headaches, but it was new when the headache went round the head seven times, then travelled to the shoulder, stayed there for three days, move back to the head, and it would go on and on. Whereas an adult would still like to stay in bed and be pampered even when he

is 95% healed, at 50% a child is already trying to get out of bed to start playing. What a fantastic way to demonstrate healing. While I had frowning and complaints from adults one was helping, from children it was always crying (not from anger) to be followed on many occasions by those beautiful smiles that are still quite rewarding. When I started out as a lecturer and paediatrician in 1997, in addition to the teaching, I was entrusted with the care of children in the following areas: nutrition, cardiology and pulmonology, and sickle cell disease. Later I got more involved in the care of children with cancers (oncology). Over the years I settled into paediatric haematology (the branch of paediatrics devoted to the study of blood, blood-producing tissues, and diseases of the blood) and paediatric oncology (the branch of paediatrics that deals with the study and treatment of malignant tumors).

What is Paediatrics?

Paediatrics is the sole discipline concerned with all aspects of the well-being of infants, children, and adolescents, including their health; their physical, mental, and psychological growth and development; and their opportunity to achieve full potentials as adults. [1] The word *paediatrics* means "healer of children"; it is derived from two Greek words: pais "child" and iatros "doctor, healer". [2] As paediatricians, we are concerned not only with particular organ systems in the body of the child, but also with environmental and social influences, which have a major impact on the physical, emotional and mental health and social well-being of children and their families. [1] Children are among the most vulnerable and disadvantaged members of society and their needs require special attention. The age range defining children varies but it is from birth and to, usually, 18 years of age. There are occasions when a paediatrician is called upon to assess the suitability of the scheduled birth of a newborn-to-be, while still in the uterus, to determine if the baby is matured enough to survive outside the womb. In this case the lower age limit defining our patients may shift to the left side of day one. The entire purpose of paediatrics is the advancement of the well-being of children. Paediatricians must be advocates for the individual child and for all children, irrespective of culture, religion, gender, ethnicity, race, or of local,

state or national boundaries. Children, ordinarily, cannot advocate for themselves. [1]

Historical Perspective

Paediatrics as a medical specialty, when compared to other areas of medicine is relatively new, coming into existence just under two centuries ago with the campaign of Francesco Fede (1832-1913), a professor of paediatrics at the University of Naples. [3] However, ancient medical literature includes write-ups concerning children, many of which are still relevant today. For instance, Ibn Qayyim al-Jawziya (1292-1350) from Damascus wrote a child-rearing manual called Tuhfatul Mawdud bi Ahkam al-Mawdud (A gift to the loved one regarding the rulings of the newborn), in which care of the newborn is discussed. [3] The Ebers Papyrus, written about 1552 BC and unearthed in 1872, discussed, among other topics, breastfeeding, a cure for worms, and treatment of eye diseases. [4] Writings of Hippocrates (c. 400 BC) covered cephalhaematoma, hydrocephalus, clubfoot, worms, diarrhoea, asthma and mumps. [4] Galen (c. AD 200), Greek philosopher, surgeon and physician, wrote of ear discharge, pneumonia, and intestinal prolapse, and described a disorder that corresponds to rickets, a disease that is found only in children. [4] In 1583, Hieronymus wrote what was described as the first important printed book about children, entitled *De Morbus* Pusiorum (disease of the little boy). Thomas Syndeham (1624-1689) wrote on scarlet fever, measles, small pox, epilepsy, rickets, teething fever, scurvy and the chorea we now know as St. Vitus Dance. By the late 1700s and early 1800s, the need to attend specifically to the care, development, and the diseases of children became more apparent, and specialization in paediatrics evolved particularly in Germany and France. [4] Some of the oldest traces of paediatrics can be discovered in Ancient India where children's doctors were called *kumara bhrtya*. [2,3]

Paediatrics in Nigeria

Before the advent of orthodox medicine in Nigeria traditional medicine was established. This was practiced by, among others, "specialist" birth attendants. These practitioners did not share

knowledge and kept their skills closely guarded family secrets to protect their means of livelihood. [5,6]

Some of the measures that were used to try to improve or mitigate childhood mortality in those very early days included: [5]

1. The use of charms (or juju) to protect against witchcraft;
2. Use of cow's urine to arrest convulsion, and the bodily application of hot objects to revive the unconscious victims of convulsion;
3. The use of cow dung for the treatment of the umbilical cord of the newborn;
4. Infanticide was used as a means of ridding the society of congenital malformations; part of the congenital malformation apparently included twinning in some parts of the country.

Of course, we now know to a good extent that these are injurious practices. Unfortunately, many of these practices are still commonplace in the country. According to my teacher, Professor AM. Yakubu, [5] modern scientific medicine was introduced into Nigeria by the Portuguese for the their traders and sailors coming to the West Coast of Africa as far back as the 15th Century. Gradually over time, Nigerians started to enjoy these services. In Nigeria, the path towards emergence of paediatric care by paediatricians has been long and tortuous but by the time of our independence in 1960 there were general hospitals and some elements of specialist care like the Massey Street Hospital in Lagos. [5,6] Massey Street Hospital is actually the first children's hospital in Nigeria. [5] According to Yakubu, Nigerian pioneer paediatricians were/are Drs. Animashaun, Ajenifuja, Fadahunsi and Ekpechi. Tertiary paediatric clinical services started in UCH, Ibadan and later in LUTH, Lagos. [5]

The first academic Department of Paediatrics was established in the University College Hospital, Ibadan.

Postgraduate training in Paediatrics started in Nigeria in 1969.

Paediatrics in Zaria

In Ahmadu Bello University, the Department of Paediatrics was created in the Faculty of Medicine in 1969 when the pioneer

batch of medical students entered into the clinical years of their training. [5] Prior to this time, children were admitted into the female wards of the hospital. The first head of department was Professor Sinette, an African American. He was succeeded after a brief period by Professor Richard Dobbs, an Englishman. The academic staff then comprised of foreigners, mainly Americans and British. [5] The first Nigerian head of the Department of Paediatrics, Ahmadu Bello University, was Professor MB. Abdurrahman, whom I have the honor of knowing tangentially, and also of learning from, both in person and from reading some of his many writings. The late Professor Kunle Ijaiya, a former Dean of the Faculty of Medicine, took over from Professor Abdurrahman. Then came Professor AM. Taqi, Professor AM. Yakubu (a former Dean of the Faculty of Medicine and a one-time Chief Medical Director of Ahmadu Bello University Teaching Hospital, Zaria) and Professor WN. Ogala (a former Deputy Dean of the Faculty of Medicine, ABU, and presently a member of the Board of ABUTH, Zaria). I have the honor of working closely with the last two, in their own right doyens of paediatrics in Nigeria and abroad. Under their guidance (and that of Professor HA. Aikhionbare, also a former Dean of the Faculty of Medicine) the Department of Paediatrics of our University has grown into, and remains, one of the best in the country. Under their tutelage I have become what I am today.

The Newborn and the Infant

The Newborn

The birth of a child, after 40 weeks of complex development in the uterus, can be described as traumatic, indeed, very traumatic. It is traumatic for the mother (hopefully with pleasant memories) and for the newborn who, thankfully, is oblivious of what is happening. The management of this point in time (the starting line of life's race) goes a long way in shaping the future of the child as an individual, as a member of the society and as a productive workforce. Poor attention at this critical period, and during the first 28 days of life, both in the hospital and community settings in Nigeria, contribute significantly to morbidity (quality of life) and mortality (decreased life span). A baby aged between one and 28

days is referred to as a neonate. Many years ago we published a case of gishiri cut that inflicted severe damage to the scalp of a neonate.[7] Up till that point in time virtually all the complications arising from this traditional practice were reported in the mothers.[8,9] Harrison described the rare complication in which the mother's bladder and urethra were completely divided, the peritoneal cavity opened, and the foetus injured.[9] But the type of foetal injury was not described. Ours was the first clear cut recorded instance of a direct harm to the baby (Picture 1). The "gishiri" cut is the local equivalent of episiotomy, a cut that is normally applied to the opening of the birth canal to facilitate birth of the head of the baby. Episiotomy requires the skilled used of a special pair of scissors. In the case just mentioned a long knife or razor blade was probably used and by a traditional birth attendant with no training in dealing with complicated births.[10] This apparently caused inadvertent injury to the baby. Apart from the deep laceration, the baby was brought with copious pus production from the wound. It was also noted that the cut was just one or two centimeters from the anterior fontanel. Fortunately, the baby made a full recovery with the administration of potent antibiotics and staff dedication of those days and was discharged after 11 days. The sad aspect was the fact that the baby had to spend 11 of the first 14 days of his life on admission, which cannot be described as a good start in life. Many mothers, for various reasons, some of which may be considered valid, still prefer to give birth at home without skilled supervision and within relatively unhygienic conditions.[11] When there are confounding variables like precipitate labour the results may be catastrophic. A nine-day old baby boy once presented to us with 8 days history of right-sided scalp swelling, 6 days of intermittent fever and excessive crying.[12] The child was delivered at home after a precipitate labour (unusually rapid labour and birth). At the time of birth the mother did not notice any abnormality. There was no skilled birth supervision. On the second day a swelling was noticed on the right side of the head and on the third day the baby had a traditional uvulectomy. When seen, the child was quite sick with pus coming out of his "eyes" and had this big swelling on the right side of his head which made him more irritable when touched. (Picture 2). Initial thought was that blood must have collected in that part of his

head after the precipitate labour and was most likely infected. Despite antibiotics given intensively through his vein the swelling started discharging pus which was not foul-smelling and did not grow any organism on culture. The baby eventually had a minor surgery to evacuate the pus and spent 22 days in the hospital. Here again, the first month of his life was spent sick from preventable illness. Not really the kind of start one would want in life. These are just two lucky fellows having access to medical care, even if their presentations were late.

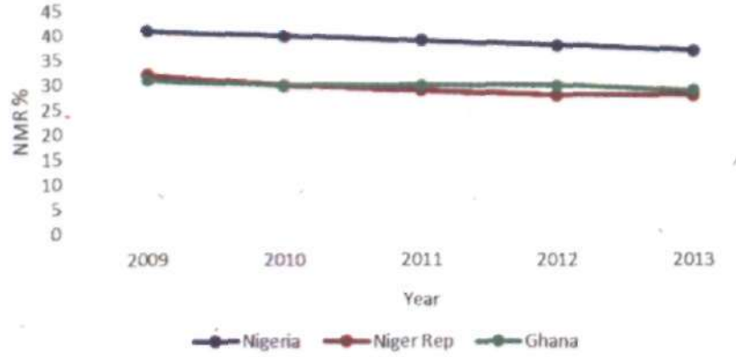
The neonatal period is critical with the baby undergoing rapid transition from intrauterine to extrauterine existence. Birth defects usually become quite manifest and take their toll. The constant supply of nutrition the child was exposed to prior to being born will now be supplied in an intermittent fashion. The child is now exposed to a hostile environment instead of the clean and cozy intrauterine space. Infections may become established and overwhelm the immature immune system of the newborn. Infections constitute a common cause of ill-health in the newborn as we showed in a prospective study designed to identify bacterial causes of neonatal sepsis in ABUTH, published in 2008. In the study we found that 30.4% of babies born within our facility requiring special baby care and 38.0% of babies born outside but admitted into our hospital had culture-proven blood infection (bacteraemia). [13] It is pertinent to note that there was no significant difference in the proportions of these babies with culture-proven infections and this points to the high risk of neonatal sepsis in our setting. Not surprisingly, we found *Staphyloccus aureus* to be the commonest causative organism in out-born babies while streptococcal species were the most frequent in the inborn group of babies.

Neonatal mortality rate (NMR) is the number of neonates or newborn dying before reaching 28 days of age, per 1,000 live births in a given year. Neonatal health is a sensitive indicator of national development. [11]

In 2013, globally, NMR represented 44% of all deaths in children aged less than 5 years. [14] In Nigeria, as at 2011, one-quarter of all U-5 deaths occur in the newborns, approximately 241,000 babies per year. [11] NMRs have been declining gradually in Nigeria but, remains unacceptably high compared to some sister African

countries (Figure 1). [15] As at 2011, Nigeria is said to contribute about 8% of global neonatal deaths. This is obviously unacceptable.

Figure 1. Trends in NMR in selected sub-Saharan countries



It is very likely that the figures being reported are gross underestimations as registration of births and deaths is not mandatory in the country. As such, there would not be any accurate data from the community and figures being quoted would represent institutional data; these often do not necessarily reflect what is going on in the community. Reasons for the relatively high NMRs in the country include:

i. Poor antenatal care, in terms of inadequate availability (equity of distribution) and low utilization of facilities. Only 6 of 10 expectant mothers seek antenatal care from trained medical personnel. [16]
ii. Poor maternal status. Many mothers (including expectant mothers) are poorly nourished, stunted, overworked, and with such conditions as illiteracy and anaemia. Early child bearing and closely spaced pregnancies also negatively affect maternal status. [17]
iii. Unskilled and unsafe birth practices. Many, if not most, of the deliveries in the rural areas of Nigeria are attended to by traditional birth attendants as in the days of old. Almost 40% of women in Nigeria give birth with just a family member or

no skilled attendant present. [11] The proportion of home births in northwestern Nigeria is 90%. [11] Due to their lack of training, these TBAs are unskilled in modern practices and are dangerous. Some factors like inadequate cord care, letting the baby stay wet and cold, discarding colostrum and feeding other foods are prevalent in the setting of unsupervised delivery and contribute significantly to early neonatal death.

iv. Dearth and inequitable distribution of paediatricians (and other doctors and health workers) between urban and rural settings.
v. Severe infections, like tetanus and neonatal sepsis, which tend to occur at home and contribute massively to unrecorded mortality.
vi. Birth asphyxia, trauma and injuries.
vii. Congenital abnormalities of varying severity.
viii. Poor management of the first few minutes of life: not starting appropriate feeding as soon as possible after birth, keeping the wet baby including the unnecessary need to bath the baby immediately after birth, and inappropriate cord care.

These are just a few examples of the myriad of problems faced by newborns in Nigeria and contributing to high NMR in the country, and in the developing nations of the world. Problems such as obtaining money for treatment, distance to health facilities and having to take transport to such facilities are some of the many difficulties by women describing the difficulty with accessing healthcare. [16]

Some factors predisposing the newborn to infections, and thus high risk of mortality, that we identified in Zaria included: [18]

i. Lack of antenatal care,
ii. Prolonged rupture of membranes,
iii. Prolonged labour,
iv. Preterm delivery, and
v. Perinatal asphyxia.

Good antenatal care can prevent the major causes of neonatal mortality in Nigeria – neonatal tetanus, malaria and maternal anaemia. [16] It has been estimated that up to two-thirds of newborn deaths could be prevented if skilled health workers perform effective health measures at birth and during the first week of life. [11]

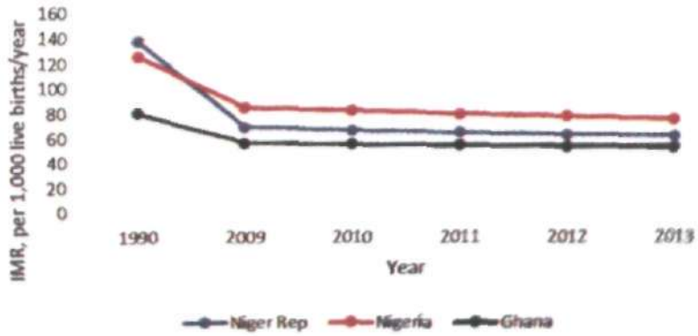
As was pointed out earlier, some issues that contribute to the poor management of the first few days and weeks of life include weak health infrastructure and harmful cultural and traditional practices. Hopefully, these harmful practices have reduced in frequency of occurrence. It has been estimated that up to 70% of newborn deaths could be averted if essential existing health interventions can reach all Nigerian women and newborns. [11] Healthy home practices and community-based care, which are possible to improve, could save over 90,000 babies a year. [11]

The Infant

Who is an infant? An infant, in the context of *Homo sapiens*, is the very young of human. The word infant comes come from the Latin word *infans* which means unable to speak or speechless. For the purpose of this lecture an infant is a child aged between 1 and 12 months.

The death of a baby before his or her first birthday is called infant mortality. The *infant mortality rate* is an estimate of the number of infant deaths for every 1,000 live births in a given year. This rate is often also used as an indicator to measure the health and well-being of a nation, because factors affecting the health of entire populations can also impact the mortality rate of infants. [19,20] Presented in Figure 2 is the infant mortality rates of Nigeria, Niger Republic and Ghana, two of our close neighbours. Compared to the 1990 figures all three countries have reduced IMR, Niger Republic by 56.6%, Nigeria by 41.3%, and Ghana by 35.0%. This is far short of the 66% reduction we are supposed to witness by next year which should see figures like 46 coming out Niger Republic, 42 from Nigeria, and 26 from Ghana. These are figures all nations agreed to under the Millennium Development Goals which I will touch on briefly shortly.

Figure 2. Trends in IMR in some selected African countries



Incidentally, causes of or contributors to IMR in Nigeria are mostly preventable or treatable conditions like: malaria, diarrhoea, pneumonia including pulmonary tuberculosis, measles, HIV, and malnutrition (undernutrition, particularly in Nigeria). Even though I mentioned malnutrition last, it actually sits on top of the pile as it contributes directly and indirectly to more than 55% of IMR and under-5 mortality in the country. On its own, severe malnutrition is a prominent killer of children. When it occurs, it will also lower the child's immunity and predispose the child to severe forms of infections and other medical conditions. Infections will reduce the appetite of the children reducing their intake and worsening the malnutrition. Infections and other medical conditions may also cause a child not to absorb nutrients adequately via his intestine, or they may increase the child's metabolic requirement and effectively make a "normal" meal inadequate. When other medical conditions co-exist with severe malnutrition in a child, the outlook for the child is grim. It has been shown that malnutrition is an independent risk factor impacting on higher mortality and morbidity in hospital-admitted children, increasing hospital stay and cost. [21] Malnutrition in children typically develops during the period from 6 to 18 months of age, when growth velocity and brain development are especially high. [22] So, feeding in the first year of life become a very important issue. We should not forget the popular saying, "you are what you

eat". It is particularly poignant in children as they would grow up to make what Nigeria would be in the future.

It is not uncommon for paediatricians to come across mothers complaining of their infants not feeding properly. Of course, feeding must start as early as possible after the birth of the child. It is highly recommended that feeding should commence within one hour of birth. [11,23] It has been shown by several studies that breast milk only is sufficient in the first six months of life. This has led to the defining of exclusive breastfeeding and its promotion. A lot of efforts have been put into promotion of EBF with the introduction of the Baby-Friendly Hospital Initiative in 1991. Ahmadu Bello University Teaching Hospital, Zaria, is a recognized and certified baby-friendly hospital. There are many benefits of EBF, some of them proven, some speculative; but all so important as to make the use of EBF highly recommended, if not enforceable for a developing nation in need of optimal adults. The beneficiaries of exclusive breastfeeding include the infant (obviously), the mother, the father, the community, and the nation. The benefits to the infant include provision of anti-infective components to guard against common killer conditions like diarrhoea, lower and upper respiratory tract infections. It promotes strong physical and emotional bonding between child and mother. It is the only natural food carefully designed for the newborn and in the early months of life, it is free, available whenever, wherever needed by the baby and always at the right temperature. There is no need for utensils and, therefore minimal or no risk of contamination of the baby's food. Breast milk reduces the risk of constipation in the first few months of life, it reduces the lifelong risk of conditions like obesity, type-2 diabetes mellitus, asthma, eczema. It is being speculated that it may protect against some childhood cancers and that it confers superior intelligence quotient in children. For the mother, exclusive breastfeeding promotes uterine involution, promotes family spacing by provide contraception during the period of breastfeeding, reduces the risk of developing breast and ovarian cancers. Breastfeeding is "cheap", it saves money for all stakeholders and helps keep the environment clean. Breast milk has no perfect substitute. It is a completely balanced diet able to provide all nutrients and calories in the right amount for six months. It is more complex than any meal one can think of as pictures 3 and 4 demonstrate.

Exclusive breastfeeding is defined as the feeding of a newborn, on demand, with only breast milk, and nothing but breast milk, for at least 8-12 times in 24 hours for the first 6 months of life. The use of physician-prescribed medication or supplements does not invalidate this definition. Sadly, studies have shown low rates of EBF in Nigeria and in Zaria. For instance, Audu and Ogala [24] found that the proportion of infants having EBF fell from 70.7% at 0-6 weeks of age to 14% at 5-6 months. Okolo et al., [25] working in JUTH, found none of 310 rural Savanna women practicing of EBF. Ogunrinde et al [26] found a despairingly low 47.4% EBF rate at 0-3 weeks of age and this more than halved to 20% at around 6 months. Reasons for this poor performance include the uncertainty surrounding the practice of EBF and the belief that giving water (or some other fluids, depending on culture) relieves pain, prevents and treats common cold and constipation, soothes fretfulness and quenches thirst. The situation is compounded by suggestion that some health workers may also promote this belief. [27,28]

Studies done mostly outside Nigeria had suggested that under various climatic conditions babies do not need supplemental water in the first 6 months of life to maintain water balance. For instance, in Lahore, Pakistan, it was demonstrated that babies were able to appreciably concentrate their urine when water restricted. The authors concluded that 2-4 month-old breastfed, healthy infants showed no signs of dehydration if additional water was not given during the summer month. In Benin, Edo State, Eregie showed that there was no significant difference in rates of micturition in exclusively and partially breastfed neonates. [29] When there is water deprivation there is a resultant rise in plasma osmolality and this would stimulate the release of the antidiuretic hormone leading to the formation of progressively more concentrated urine as the body attempts to preserve water. This increasing urine concentration may be detected by measuring the urine specific gravity as Ogunrinde GO & Alegbejo JA did and reported in 2005. [26] We set out to find out if supplemental water may be needed in the first six months of life in children living in the Guinea Savanna, our region of location. The study covered part of the dry season extending from March to September 1998 thereby capturing part of the dry season ending May of the same year. Meteorological data were collected from the

Meteorological Section of the Department of Soil Science, Institute for Agricultural Research, Ahmadu Bello University, Zaria.

The season was characterized by an average environmental temperature of 35.5 °C and a relative humidity range of 11.4% to 45%. The average temperature was 31.1 °C in the wet season and the relative humidity ranged from 76.6% to 87.6%. During the study period, 47 of 122 randomly selected infants aged less than 6 months were being exclusively breastfed, giving an overall EBF rate of 38.5%. Twelve of the remaining infants on supplemental water were also receiving other food items and were excluded from further analysis; so that only infants receiving either EBF or water and breast milk were studied.

An interesting finding to support the "baby is thirsty" issue is the observation that during the wet season 34 (53.1%) of babies received only breast milk. This proportion fell significantly to 28.3% (13 of 46 babies) in the dry season.

One of our findings was that while 47.6% of water-supplemented infants were delivered at home only 19.1% of EBF infants were similarly delivered ($p = 0.0039$). It is obvious that health workers are very important at promoting good health practices; even though at 19.1% water-supplementation rate among EBF infants there is still a lot of room for improvement in the education and work attitude of health workers.

We also found some evidence in the study to suggest that formal education of mothers goes a significant extent in promoting ideal infant feeding methods.

Grown-Up Children (Post-Infancy Children)

This is a big group of children. They can be categorized as those under 5 years (usually referred to as under-5), the pre-pubertal children (from 6 years to about 10-12 years) and the adolescents (from 10-12 years up to 19 years). These subcategories of children have very distinct biological, cognitive and social characteristics. But time and fate that determined my areas of practice and experience would not allow the distinction of these groups in my lecture. Let me say in the past two decades, a lot of attention had been put on the under-fives and we are presently seeing the positive outcomes of the many programs put in place to improve mortality and morbidity. Many more children are now surviving into the

second decade of life and programmes are now springing up to consolidate on these gains and build the foundation for a greater tomorrow. [30]

Unfortunately, the reduction in child morbidity and mortality has not been evenly spread with sub-Saharan countries witnessing a plateauing or reversal of progress. [31] The programmes aimed at reduction of childhood deaths and morbidity have been basically of two type: short-term, disease-specific initiatives and more general programmes of health care that are people-centred and community-based. [31] The disease-specific technology-dependent interventions have been met with both failures (malaria eradication programme) and successes (smallpox eradication, poliomyelitis eradication). The people-centred community-based programmatic interventions have their own difficulties arising from the wide areas needing intervention and meagre resources available. There is, of course, need for interventions to be scientifically sound. There are now efforts to coalesce these two types of interventions.

Diarrhoeal disease remains a significant health problem globally, coming second only to pneumonia as a cause of death in under-5 children. [32] In 2004, WHO and UNICEF jointly recommended the use of newly formulated low osmolarity oral rehydration salts and zinc supplementation in the treatment of childhood disease. [33] About 159-300 mg/kg/day of zinc is lost in diarrhoeal stools by children, and zinc supplementation has been shown to reduce duration of diarrhoeal episodes by 9-23% and stool frequency by 18-39%. [34,35]

According to UNICEF, it is not enough simply to expand the delivery of packages of low-cost, proven interventions: behavioural, institutional and environmental impediments that can impede access must also be addressed as part of the scaling up process. Families and communities are key to achieving the goals set for managing diarrhoeal disease by making the new recommendation routine practice in the home and health facilities. [33] A few years after the recommendation we decided it was pertinent to determine the degree of empowerment of home caregivers as far as the treatment of diarrhoeal disease was concerned. [36] We studied 4,386 caregivers. We noted a low literacy rate of less than 30% in both males and females. More than 70% of male caregivers were farmers while a significant higher proportion of females were housewives. Despite

the low literacy rates a good proportion correctly identified suggested causes of diarrhoea in children. Fifty-nine percent associated diarrhoea with suboptimal hygienic conditions, contaminated food and water. A further 10% linked diarrhoea with various infections including measles, malaria and human immunodeficiency virus infection.

Table I. Causes of diarrhoea identified by caregivers of under-5 children with diarrhoea

Suggested causes of diarrhoea	Frequency (%)
Contaminated food/water	649 (29.9)
Poor hygiene/sanitation	615 (28.4)
Teething	411 (19.0)
Infections	215 (9.9)
Inadequate breast milk/malnutrition	146 (6.7)
Malaria	121 (5.6)
Houseflies	11 (0.5)
Total	2168 (100.0)

In the study, less than 1% (2/4386) were able to correctly state the four rules of home management of childhood diarrhoeal disease; a majority of caregivers 56.7% were totally ignorant of the rules with the proportion being significantly higher in males. Seizing the opportunity of this lecture to spread the message, the rules are:

1. Give the child more fluids than usual. If oral rehydration salts solution is available this should be given to the child. Oral rehydration solutions, in addition to treating dehydration, can also prevent dehydration. Indeed, the prevention of dehydration should be the primary goal of the home management of childhood diarrhoeal disease. If ORS is not available fluids such as gruel, soup or rice water may be given. If the child is tolerating feeds well clean and safe water should be encouraged. In a child still on breast-milk breastfeeding should continue on a more frequent basis and each episode for longer period. If a child is on EBF ORS should be added. But note that a child on EBF hardly develops diarrhoea.
2. Give zinc supplementation. It has been demonstrated that zinc decrease the duration and severity of diarrhoea. It also boost the child's immune system and helps in lengthening

the interval between episodes of diarrhoea and promoting child health.

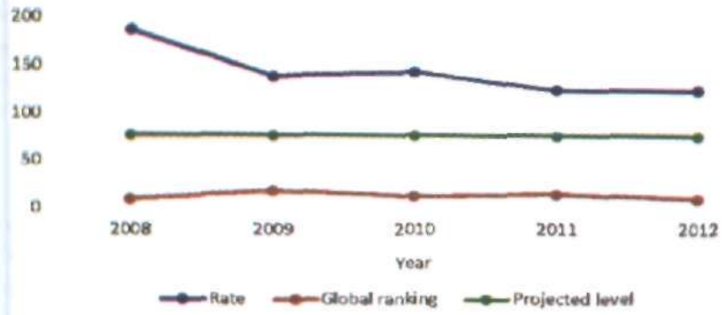
3. Continue to feed the child. There is a common and pervasive misconception in the country not to feed a child that is having diarrhoea. This is a very harmful practice as it deprives the child of the fluids, calories and nutrients needed to fight off infections
4. Know when to return or report to the clinic or health facility. When the child is passing many stools (say >5 times daily), child is very thirsty or has sunken eyes, has fever or a poor appetite, the caregiver should know it is time to seek medical advice.

The awareness of these rules should improve the outcome of diarrhoeal disease in the country and bring us to a situation when diarrhoea would become a nuisance, even in children, instead of a killer disease it is today. The proper implementation of these rules will go a long way in reducing the unnecessary, and sometimes harmful, treatment given to the children. In our study, we found 36.1% of caregivers gave antibiotics to their children with diarrhoea as first line treatment. This not only amounted to a waste of resources (as we know that 95% of diarrhoeal episodes are caused by viruses) but may contribute to worsening of the diarrhoea and incidence of resistance in medical cases where the antibiotics are actually needed. During the study, the caregivers were provided with 10-day supplies of dispersible zinc tablets to give to administer to the children. The rate of adherence to the 10-day regimen was 75.5% with male caregivers doing a better job at ensuring the children received the zinc supplementation. At an international conference in Liberia in 2009, ours was the only oral presentation on zinc supplementation in diarrhoea disease and it resulted in a recommendation on the use of zinc in the communiqué.

The international community in 2000, endorsed the eight millennium development goals (MDGs). These eight MDGs were established following the Millennium Summit of the United Nations

in 2000, following the adoption of the United Nations Millennium Declaration, to address the pervasive poor health status in mostly developing countries of the world. Each goal has specific targets and dates for achieving those targets. As far as reducing under-5 mortality rate Nigeria has been described as being off track. For Nigeria to meet MDG 4, the country must attain a two-thirds reduction in the U5MR from 230 per 1000 live births in 1990 to 76 by 2015. [11] The year 2015 is definitely around the corner and we are among the 10 countries with the worst U5MR global (Figure 3). There is urgent need to scale up activities aimed at promoting health of the Nigerian child.

Figure 3. Trend in under-5 mortality rate in Nigeria



Sickle Cell Anaemia

The Vice Chancellor, Sir, let me turn my attention to sickle cell anaemia, a disorder I have been treating for the past 17 years. It is a disorder that affect all age groups in childhood, including adolescents. Sickle cell anaemia (SCA) is a disorder of the haemoglobin contained in red blood cells that form the major component of blood, and essentially confers blood with its red colour. The major function of haemoglobins is to transport oxygen from the lungs to the body tissues where it is utilized in metabolism of nutrients, and to carry carbon dioxide in the opposite direction. Sickle cell anaemia is one of the many diseases of haemoglobin and they are referred to as haemoglobinopathies . There are basically two types of haemoglobinopathies: those that have altered structures

resulting in qualitative haemoglobinopathies; and those that have a reduced production of haemoglobin resulting in quantitative haemoglobinopathies. Sickle cell anaemia is an example of qualitative haemoglobinopathy. Sickle cell anaemia is a genetic disease and it occurs if an individual inherits the sickle cell genes, one from each parent. The gene is estimated to be present in one of every four Nigeria, [37,38] and this contributes to making SCA the commonest genetic disease in the country.

The sickle cell gene confers some protection against malaria in individuals with just one copy of the gene and a normal human haemoglobin gene. [38] These individuals are described as carrier of the sickle cell gene and are protected to some extent from the severe manifestations of malaria. It is likely that by selective pressure these individuals increased in number. This longevity is not duplicated in their offspring who tend to die at a young age. This pattern of increased longevity on one side of the coin and decreased life span on the other side has been described as a *balanced polymorphism*, an attempt to balance for gene loss that occurs with the early demise of children with phenotype SS.

Burden of Sickle Cell Anaemia

It is estimated more than 300,000 babies are born with severe forms of hemoglobinopathies worldwide each year. While 75% of all patients with SCD live in sub-Saharan Africa, Nigeria alone accounts for more than 100,000 new births every year, [39] representing about 2% of babies born in the country. In sheer numbers, Nigeria has the largest burden of sickle cell disorders in the whole world. [40]

The incidence and impact of SCA in Nigeria, and other developing tropical nations, is likely to grow in the future as improvement in hygiene and nutrition occur, and reduction in infections resulting in reduced childhood mortality allowing babies with severe haemoglobin disorder to survive long enough to present to health facilities for diagnosis and treatment. [41] As noted by Molineaux et al, apparently melancholically, "there is no other known inherited disorder present at such high frequency in a large population and of comparable severity as sickle cell anaemia in Africa." [42] They continued, "With the rising standards of living and

control of malaria, sickle cell anaemia will become an immense medical, social and economic problem throughout the continent." If the selective force of malaria were to be removed it would take many generations for the frequencies of these conditions to fall significantly. [41] With a trait carrier rate of about 25% and an estimated population size of 170 million people there would be approximately 42.5 million, mostly healthy, Nigerians having a copy of the sickle cell gene. This number of carriers far exceeds the population of every other African country and, indeed, of several of them put together. [40] There is a significant proportion of mortality in children with SCD. In Garki District of Kano State in 1979, for instance, 2.1% of babies born had SCA. This prevalence was maintained in the first year of life but fell drastically to 0.4% by 4 years and 0.05% over the age of 9 years. [42] SCA has major social and economic and psychological implications for affected children and their families. It places a heavy burden on the already strained health sector of the country. SCA may explain the phenomena of the "abikus" and the "ogbanjes" in certain part of the country. The psychological stress in families with repeated child death is better left to imagination.

Pathophysiology of Sickle Cell Anaemia

The acquisition of the genes means that the red blood cells in the child start synthesizing a qualitatively different type of haemoglobin called the sickle haemoglobin. All haemoglobins are soluble in water including the sickle haemoglobin. But when HbSS gives up its oxygen it becomes insoluble in water and starts to come out of solution in a process that is referred to as polymerization or gelling. This polymerization is not an instantaneous event and it takes a while for the process to progress significantly to cause disturbance in shape, rheology and function. When haemoglobin polymerization has progressed significantly in the erythrocyte, the cell changes shape into the characteristic sickle shape, become harder and less deformable, and becomes stickier and attaches to the wall of the blood vessel very easily. The abnormally shaped, less deformable and sticky red cells will now cause obstruction to the free flow of blood, not unlike the traffic situation occurring in the Kwangila area of Zaria on a daily basis. The interruption of blood

flow to parts of the body results in ischaemia and hypoxia which, if not addressed in a timely fashion will lead to more permanent injuries and loss of function. The most common manifestation of this process is the unpredictable and severe pains that sufferers of SCA experience, some at an unbearable frequency. The pain had been described as being far worse than that being experienced in the labour of childbirth. [43]

Fortunately, many of the red cells will make it back to the lungs long before there is extensive polymerization, acquire oxygen and revert back to the soluble state. However, the repeated cycle of sickling and un-sickling will ultimately damage the cells with resultant failure to come out of the sickled shape. These kind of cells are called irreversibly sickled cells. The cell membranes of these cell are damaged beyond what the body system can repair and they have to be removed from the body. The removal of these cells is much more than is seen in the removal of senescent cells of people with phenotype AA and results in two prominent features of SCA, namely pallor and jaundice.

One area of the body where it is specifically designed that blood flow would be slow is in the core of the kidneys. In the core of the kidney, called the medulla, is a countercurrent concentrating mechanism that helps the mammalian body preserve water with the passage of concentrated urine. This part is made up of parts of the loop of Henle (basically the tube in the kidney that transmit forming urine), the vasa recta (intricate blood vessels surrounding the vasa recta), both with fluids (glomerular filtrates and blood) flowing in opposite directions, and the surrounding supporting tissue of the kidney. There is extreme hypertonicity and extremely sluggish blood flow in this region; therefore, this is a very hostile condition to red cells containing sickle haemoglobin. They give up their oxygen as is expected, are subject to prolonged passage in a very hypertonic environment. They, therefore, become sickled and clog up vascular passages in the kidney which suffer irreparable damages.

Microangiopathic studies of sickle cell kidneys reveal gross lesions of the vessels of the renal medulla, with almost complete absence of vasa recta in sickle cell anaemia; and reduced number of vasa recta and loss of normal bundle architecture in sickle cell trait and sickle cell HbC disease. [44] The findings, according to the authors, suggest that the basic lesion in sickle cell nephropathy is

obliteration of vasa recta leading to the observed abnormalities in concentrating function.

A study carried out in Zaria and reported in 2007 explored an aspect of this school of thought. [45] We suspected that if, indeed, there was diminished ability to concentrate urine there should be an increased prevalence of bedwetting in children with SCA as was demonstrated in Lagos by Akinyanju and co-workers. [46] A case-control study of 360 children with SCA aimed to determine the prevalence and describe the pattern of nocturnal enuresis (bedwetting) in this type of haemoglobinopathy.

It was revealed that 150 (47.1%) of them, aged 5-12 years were bedwetting. This was significantly higher than the 17.7% (42 of 237) control children with nocturnal enuresis. The majority in each had never stopped bedwetting in their lives, so, they are considered to have primary enuresis. After the age of 84 months the prevalence of bedwetting in control children dropped rapidly to zero while it virtually plateaued in children with SCA, and dropped slowly after the age of 144 months. The oldest child with SCA and enuresis was 202 months (16 years and 10 months). It is known in normal children that males are more predisposed to enuresis than girls. This is confirmed in the Zaria study where 27 of 106 (25.5%) boys and 15 0f 131 (11.5%; $p = 0.008$) had enuresis. The reasons for this have not been established but slower developmental maturity and increased physical activities in boys leading to increased exhaustion at night are speculated. Even though the same pattern was observed in children with SCA the difference did not attain statistical significance. In 63 (42.0%) of the 150 enuretic children with SCA, the home caregivers perceived the bedwetting as being abnormal, even though only 6.4% attributed it to the effect of SCA. Among the caregivers of "normal" children only 9 (21.4%) thought of the bedwetting their children were experiencing as abnormal.

Table II. The caregivers adduced various reasons for the bedwetting in their wards.

Reasons for enuresis	Frequency (%)
Too much fluids	54 (19.1)
Too much sleep	51 (18.0)
Delayed development	34 (12.0)
Weather	33 (11.7)
Ill-health apart from SCA	24 (8.5)
SCA	18 (6.4)
Laziness	18 (6.4)
Familial	15 (5.3)
Don't know	12 (4.2)
Others	24 (8.5)

These reasons, which probably reflect beliefs and possible remedies, are worrisome. Obviously, majority would probably want to deny their wards adequate sleep and water. The withholding of fluids, which was being practiced by 9% of caregivers is alarming, as liberal fluid intake is at the cornerstone of the management of SCA. Of note is the fact that only three caregivers rightly thought that enuresis is a medical problem that requires the attention of health workers. The aetiology of enuresis is multifactorial although no definite cause has been established. It is possible that whatever the underlying causes are in the normal population, they are probably also operational in children with SCA. On top of these, children are known to develop hyposthenuria, an inability to adequately concentrate their urine, very likely the result of the virtual total destruction of their vasa recta. Children with SCA have a mean urinary output that is 53% greater than that of children with haemoglobin phenotype AA. [47] This additional factor may partly explain the greater prevalence of enuresis in them and also probably obliterate the known gender difference that happen in the "normal" population.

A maturational lag has been suggested as a cause of nocturnal enuresis and may be a factor in SCA-related bedwetting. Delay in pubertal changes is known in SCA and this may be related, in part, to SCA-related injury to the central nervous system. In our study, we did observe that children with SCA started walking at a significantly older age compared to controls. Motor achievement is

known to correlate with appropriate myelination and brain growth. Even though most caregivers of children with SCA thought enuresis as not being abnormal, the methods employed in amelioration may be harmful to the children. Withholding fluids in hyposthenuric children, for instance, may rapidly lead to significant dehydration with dire consequences. Scolding and/or spanking may add to the significant psychological burden being experienced by these children. It is also suggested that health workers involved in the management of children with SCA should be more proactive in the management of enuresis as fear of stigmatization of family and child may be a reason why they do not seek medical attention.

In a recent study, carried out in ABUTH, we demonstrated that 8.1% of children with SCA have significant bacteriuria, which is evidence of urinary tract infection in them. [48] The commonest causative organism was *Escherichia coli*, a major facultative inhabitant of the large intestine. The study also suggested that urinary tract infection is an important trigger of crisis as it occurred in 20.7% of children in sickle cell crises compared to the 2.2% in those that are well and said to be in steady states. Urinary tract inf ections in children with SCA, whether symptomatic or not, may ultimately lead to chronic kidney injury, compounding the direct insults of SCA on the kidney. All these data suggest the importance of closely monitoring kidney functions in children with SCA in order to facilitate early detection of kidney dysfunction and prompt institution of treatment designed to halt or slow disease progress.

Sickle cell anaemia, being a blood disorder, affects virtually all organs of the body to varying extent. We were able to show some mild liver derangement in children aged 1 – 14 years with SCA in Zaria in a recent case-controlled study. [49] We found that bilirubin (total, conjugated and conjugated), alkaline phosphatase levels were significantly increased in children with SCA. The derangements were mild apparently because only children with SCA who were in steady states were studied. There is need for further studies to enunciate the significance of the elevated aspartate alanine transaminases ratio noted in our study. It has been suggested that this elevation in ratio in the absence of non-alcoholic liver disease should point to the presence of cirrhosis. [50]

Table III. Liver function test profiles in children with sickle cell anaemia and controls

Liver function test profile (mean±SEM) among children with SCA according to age group										
Age group	*n*	TB (µmol/l)	CB (µmol/l)	UCB (µmol/l)	ALT (IU/l)	AST (IU/l)	ALP (KAU/l)	TP (g/l)	ALB (g/l)	AST/ALT
I (<5 years)	21	49.53±8.66	16.21±2.21	33.32±7.25	30.24±3.37	57.76±3.78	157.32±10.13	51.88±1.22	36.21±2.01	2.68±0.19
II (5-9 years)	20	46.92±5.13	16.12±1.65	30.80±3.96	24.87±2.91	54.58±5.23	163.47±15.70	53.16±1.35	37.84±1.71	2.70±0.15
III (10-14 years)	19	42.63±5.50	14.06±1.76	28.56±4.19	20.18±4.41	47.81±4.82	163.91±11.38	53.19±1.26	39.63±1.90	2.44±0.19
F-value		0.245	0.364	0.178	1.211	1.171	2.829	0.366	0.723	0.714
P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05	>0.05

n: Sample size, TB: Total bilirubin, CB: Conjugated bilirubin, UCB: Unconjugated bilirubin, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, TP: Total protein, ALB: Albumin, AST/ALT: De Ritis ratio, SEM: Standard error of mean

Liver function test profile (mean±SEM) among controls according to age group										
Age group	*n*	TB (µmol/l)	CB (µmol/l)	UCB (µmol/l)	ALT (IU/l)	AST (IU/l)	ALP (KAU/l)	TP (g/l)	ALB (g/l)	AST/ALT
I (<5 years)	21	21.67±2.14	4.71±0.83	17.77±3.43	25.53±4.67	56.47±4.85	116.92±12.29	76.47±2.06	37.15±0.91	2.47±0.20
II (5-9 years)	20	19.38±1.36	4.36±1.66	17.40±2.00	23.16±2.20	50.18±5.01	95.38±12.56	78.94±1.87	39.80±1.46	2.16±0.21
III (10-14 years)	19	17.91±1.96	4.27±1.07	13.55±1.35	18.13±1.54	37.91±5.42	149.26±19.83	78.36±3.62	38.64±1.28	1.84±0.12
F-value		0.799	0.056	0.307	1.598	1.642	4.087	0.292	1.418	1.230
P value		>0.05	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05	>0.05	>0.05
Post-hoc										
Grp I vs. II		-	-	-	-	-	*P*<0.05	-	-	-
Grp I vs. III		-	-	-	-	-	*P*<0.05	-	-	-
Grp II vs. III		-	-	-	-	-	*P*<0.05	-	-	-

Grp: Group, *n*: Sample size, TB: Total bilirubin, CB: Conjugated bilirubin, UCB: Unconjugated bilirubin, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, TP: Total protein, ALB: Albumin, AST/ALT: De Ritis ratio, SEM: Standard error of mean

Blood transfusion forms an integral part of management of sickle cell disease and is also an established route of transmission of diseases, such as HIV, especially in underdeveloped countries lacking properly organized blood transfusion services. Blood transfusion may become necessary in children with SCA when they develop:

1. Severe anaemia secondary to malaria, other infections, haemolytic, sequestration and aplastic crises.
2. Vaso-occlusive phenomena like stroke, acute chest syndrome and priapism.

Depending on the severity and persistence of the above complications, blood transfusion may be used on a chronic basis to forestall recurrence of the complications.

We, therefore, screened 55 children with sickle cell disorder for antibodies of the human immunodeficiency virus, a topical blood transmissible infection that makes blood transfusion the more risky. Their mean age 68.5 ± 37.0 months. More than half (54.5%) had history of hospital admissions, mostly one admission each. We found almost half of the children with history of blood transfusion. [51] Incidentally, almost of these children with positive history had the blood transfusion outside Ahmadu Bello University Teaching Hospital. It is noteworthy that there are only two teaching hospitals in Zaria with the other one (Veterinary Teaching Hospital, ABU) not offering clinical services to human beings.

Sad as it may be, but fortunately, only one child with SCA had evidence of HIV infection. The infection was not acquired from the parents (they were seronegative 5 years after the birth of the child). The child had three blood transfusion, one of which was outside ABUTH. The same child had multiple intramuscular injections outside the walls of the teaching hospital. The low incidence of HIV seropositivity is unacceptable as it portend great risk in this group of children. Part of the solution would be to lower the prevalence of HIV disease in the nation, if not eliminate it, reduce the risk posed by the window period, and reduce the need and the use of blood in the management of sickle cell disease.

Blood donation and transfusion programme in Nigeria is mainly non-voluntary, remunerated, and family or family-

replacement dependent. This situation has been shown to pose significant risk of blood-transmissible infections, especially to those that cannot avoid blood transfusion in their treatment. A goal of making at least 80% of blood donations in Africa benevolent, voluntary and non-remunerated by 2012 was set by the Regional Strategy for Blood Safety of World Health Organization Regional Committee for Africa. A blood donation and transfusion programme coordinated at national or zonal levels as being advocated by WHO would probably go a long way to ensure adequate availability of high quality blood and blood products, especially in resource-limited settings. Nigeria is a signatory to the World Health Assembly Resolution, WHA 28.72 of 1975, which requires each member state to develop a nationally coordinated blood transfusion service, based on voluntary, non-remunerated blood donation. [52]

The management of sickle cell disorder should start as early as possible in life to effectively reduce morbidity and mortality. It was shown that early treatment with penicillin coupled with parental education resulted in significant reduction in adverse events in sickle cell disease. This had led to the introduction of neonatal screening and diagnosis of sickle cell anaemia, a concept that has not caught on in Nigeria probably due to lack of facilities and awareness of such rather than unwillingness to embrace it on the part of parents. It may also point to the unwillingness of policymakers and policy implementation to commit scarce resources to what might be thought of as a "no-problem" area. Whether we like to accept it or not, sickle cell disease has come to be with us for a long time to come. We have shown that as early as the second year of life significant reduction in height and weight occurs in children with SCD compared to those blood phenotype AA/AS. There is also evidence of zinc deficiency in children with sickle cell anaemia by the third year of life, and probably disturbed zinc metabolism and homeostasis.

There are many clinical effects of SCD in the body and a complete list is beyond the scope of this lecture. Suffice it to mention that because it is a haematological disorder and therefore affects virtually all bodily systems and organs.

We found in a study carried out in ABUTH, Zaria that children with sickle cell anaemia have reduced height and weight compared to children with blood phenotype AA/AS. [53] The deficits

in height and weight started early in life and tended to become more pronounced with advancing, probably a consequence of ongoing unabated insult. This could be a reflection of the disease severity, inadequate health-seeking practice or inadequate health care delivery.

There are many mechanisms speculated for the various manifestation of SCD, some are obvious and others not so.

We tried to ascertain if zinc deficiency existed in children with SCA and if the deficiency could account for some of the deficit in anthropometric measures noted in these children. [53] There are many body specimens that could be used to determine zinc deficiency. The most commonly studied specimen is the serum but this is known to be influenced by recent events, such as recent ingestion of zinc-rich foodstuff, such as beef, dairy products, spinach and nuts.

One of the richest store of zinc in the body is the red blood cell (erythrocytes) but it is thought that the zinc in these cells may not be metabolically available. We decided to use erythrocyte zinc since it is known that this storage accumulates over time. We felt this would be a more appropriate sample to look at as one of the parameter, height, being studied increases over a long time. We found that, aside the anthropometric deficits, children with SCA also had significantly lower erythrocyte zinc levels than children phenotype AA. We also found that whereas height and erythrocyte zinc concentration are positively correlated in children the AA phenotype no such relationship exist in children with SCA. Of course, we know that children with SCA are constantly destroying their red cells at a rate that occurs in other children with the AA/AS phenotypes. This would mean that a lot more zinc is circulating free in their plasma and therefore more likely to be excreted by the kidneys. Coupled with this is the known fact that the kidneys are also affected in SCD and therefore do not effectively filter the plasma with resultant loss of nutrients, including zinc, in the urine. It would, therefore, appear that children with SCA may need to have zinc supplementation to prevent such effect as growth retardation, increased susceptibility to infections and hypogonadism. Indeed, studies have shown that zinc supplementation resulted in improved growth patterns, increased affinity of the sickle haemoglobin for

oxygen without alteration of the Bohr effect, improved androgen levels in patients with testicular failure, and healing of ulcers. We felt there is need for further studies of zinc in SCD to determine the significance, if any, of the element in disease mechanism.

Clinical Manifestation of Sickle Cell Anaemia

Children with SCA usually suffer from episodes of serious illness described as crises. There are four of them, namely the vasoocclusive, the haemolytic, the aplastic and the sequestration crises. The most frequent is the vasoocclusive crisis, it results in severe painful episodes mostly requiring the attention of physicians, and is in its own class, the non-anaemic crisis, as it does not manifest with anaemia. The other three all give rise to anaemia by different mechanisms and are grouped together as the anaemic crises. The aplastic crisis is a particularly serious condition as the mechanism responsible for red blood cell production is temporarily shut down. The commonest organism responsible for this form of crisis is reported to be the Parvovirus B19. The virus is also implicated in the causation of the other three types of crisis in children with SCA.

In Kaduna State, we found 204 of 239 children aged 1-15 years had positive IgG to Parvovirus B19 giving a seroprevalence rate of 85.4%, with the highest seroprevalence rate in 10-12 year olds. [54] In Lagos, Iwalokun et al found 61.2% of individuals with SCA having IgG Parvovirus B19 antibodies and 64.2% non-SCA with the antibodies in their serum. [55]

In the United States of America, Smith-Whitley and coworkers found just 30% of their 633 children with IgG to the virus. [56] However, a significant number of their seronegative cohort subsequently seroconverted with an incidence rate of 11.3 per 100 patient-years.

The virus does not recognize socioeconomic borders as more than 80% of children in these groups showed evidence of previous infection with the organism. Apart from the transient red cell aplasia, Parvovirus B19 causes some other disease conditions in sickle cell disorder, including splenic and hepatic sequestration, acute chest syndrome, stroke and nephrotic syndrome.

Even though there is significant tissue damage in SCA at an early age pharmacodynamics of some drugs, at least pyrimethamine-

sulphadoxine, do not seem to be impaired to any significant extent as we showed in a recent study of children with SCA in Ile-Ife. [57] I will not bother you with details of that study as it was technical to a very good extent. Our study did show that children with SCA absorbed and metabolized this drug as would children without SCA. Pyrimethamine-sulphadoxine is an antimalarial fixed-combination antimalarial drug that is still useful in the prophylactically and curatively in Nigeria, even though it has been discontinued in countries like the United States of America.

Malaria is one of the most important public health problems in the world, particularly in the sub-Saharan region contributing significantly to childhood mortality and morbidity. [58] In Nigeria, it accounts for over 25% of under-5 mortality while children aged more than 5 years (about 24 million of the) have 2 to 4 attacks annually (Nigerian Federal Ministry of Health Report 2002). It is widely believed that malaria is the reason why we have SCA in the first place. People who are carriers of the trait, as well as heterozygotes of other inherited haemoglobin disorders, enjoy some protection from the severe forms of malaria. This protection is lost in those that have SCA. In actual fact, malaria is the commonest trigger for crisis in SCA. [59] So, not only do they suffer directly from having malaria, they also suffer the crises that malaria provokes in them.

Prevention of Sickle Cell Anaemia

Because malaria is an important issue in the disease process of sickle cell disorder, prophylactic or preventive antimalarial drugs form a cornerstone of management. Antimalarial drugs used for chemoprophylaxis include proguanil (Paludrine®), pyrimethamine (Daraprim®) and mefloquine. Proguanil (daily dosing) and pyrimethamine (weekly dosing) are the two commonest regimens. These prescriptions may not necessarily be effective due to poor compliance with or adherence to prescription; or to drug resistance. A reason for poor adherence include exorbitant prices of the drugs. In Zaria, for instance, we prescribe daily doses of proguanil for extended periods of time between clinic visits. I was reliably informed by a pharmacist that parents hardly buy supplies for more

than a week or two and do not usually come back for a refill. Yet, in the name of drug-resistant malaria new and more expensive antimalrial drugs are being developed and imported into the country. However, we have shown in studies carried out in Zaria that the careful and proper use of existing antimalarial drugs still offer considerable hope in the effective management of malaria.[60,61,62]

As pointed out earlier on, we should be seeing more individuals with sickle cell disorder in Nigeria as the prevalence of contemporary leading causes of childhood mortality reduces. This is bound to happen and is happening as a result of improvement in hygiene, nutrition and infection control. As a result of such demographic changes, the impact of inherited haemoglobin disorders is being felt all over the Indian subcontinent and in many parts of Asia, and this will undoubtedly be the case in sub-Saharan Africa as it undergoes a similar transition. [63] Evidence of our improving infection control capacity is the speed and the effectiveness with which the country resolved the Ebola issue with resultant certification of the country as Ebola-free by the World Health Organization on the 20th October 2014, about 4 months when it was brought into the country. As far as Ebola virus disease is concerned, Nigeria is the cynosure for the world, especially the Western countries trying to cope with the disease.

Is there anything that can be done to forestall this projected increase in sickle cell disorder? I am not sure we can do much. A much touted proposal is to put a programme in place to prevent individuals with sickle cell trait from marrying each other. One of my teachers, seated in this gathering, once asked me what my take on this was. I will repeat my answer. I do not accept this proposition because I believe it will create more problems for us as a nation. I believe that following through on this programme will create a social upheaval of seismic proportion. It will create a caste system in the country and establish more room for stigmatization. If such a programme is officially adopted, the typical Nigerian family with an HbAA son or daughter will most likely refuse the introduction of the S gene into the family lineage through marriage to a carrier of the trait. This is not to say young adults with the trait should not be advised on individual basis on the choice of appropriate marriage partners. Vice Chancellor, Sir, ladies and gentlemen, I am not against mass education on the subject matter but it should be done

carefully and sensitively. The solution to sickle cell anaemia, I believe, is to remove the "advantage" that persons with the SCA trait enjoy. It is desirable to remove this "advantage" as it will result in economic prosperity to the country. This "advantage" is malaria. There is strong evidence that the high frequency of sickle cell and α-thalassaemia genes have been maintained by exposure of population to malaria. [64] It is well established that malaria is one single vitally important cause of lack of development in Africa, Nigeria inclusive. It does so by hampering innate drive, reducing economic and educational output and development, and by extracting a heavy financial tag for treatment and prevention. [65] The perceived risk of contracting malaria has been suggested to negatively affect decisions related to investment, trade and crop choice and to impose a sizeable longer term costs by slowing economic growth in malarious countries and widening the gap between them and the rest of the world. [66] Malaria encourages capital flight from Africa.

Of course, we can decide to toe the line of Cyprus, as was attempted by a military governor in Oyo State. [40] In Cyprus, a country with a population of about 1.1 million (2010 estimation), there was a problem with β-thalassaemia that is inherited just like SCA and requires the inheritance of two genes. In an effort to reduce the incidence of newborns with two mutations associated with β-thalassaemia, and acting on a recommendation from the WHO in 1973, the Cypriot government established a compulsory carrier screening and counseling which was actively supported by the Orthodox Church of Cyprus. Although two carriers are free to marry, a research, that is yet to be published {Beck}, suggests that they are unlikely to do so anymore. According to the research the compulsory screening and counseling for thalassaemia is one of the most successful public health programs, but that it violates all existing ethical norms. It is obvious that this program is successful because it violates the bioethical rules formulated by the international agencies and associations of geneticists.

Among the Cypriots, the testing is basically compulsory, not voluntary. It is driven by an epidemiological approach to the population, not the individual as the fundamental unit. Counseling is directive, not non-directive. The result is eugenic, that is, fitted solely for the production of good offspring.

In this instance, an adaptive culture has ignored international bioethical norms – in the name of health and prosperity. [67] However, the programme met with initial resistance in the form of denial and falsification of results of phenotype screening. [40] Nigeria is a more complex country and I foresee a lot of problem if we decide to formalize screening for sickle cell trait.

Screening is usually targeted at two populations. Newborns can be screened for early diagnosis and intervention. It has been established that early commencement of medical care coupled with early education of parents result in fewer mortality attributable to SCA and improved quality of life. Of course, results of the screening at this age can be used for later reproductive decisions. Adolescents and young adults are screened basically for reproductive reasons. There is no direct evidence, however, that individual genetic counseling by itself significantly alters reproductive behaviour or the incidence of births of infants with haemoglobin disorders. [68] So, the question should be, can we improve our surroundings and environment so as to reduce the prevalence of adverse factors causing us so much discomfort in this country?

Cancers in Children

I cannot bring this lecture to a close without a brief mention of another area of interest. An area where progress in terms of meaningful research and development has been very difficult. I once did a presentation on childhood cancer and was amazed at the bewilderment of the audience at the mere thought of a child having cancer. Yes, children do have cancers. There are some significant differences between the cancers of children and those of adults, however.

1. Cancers in adults tend to occur in tissues or organ systems that have been exposed to one or more environmental insults, e.g. skin, lung, gastrointestinal tract, cervix and rectum. Those of children arise from such tissues as lymph nodes, blood, muscles, kidney and brain which are usually deep structure not in contact with the environment.
2. Compared to adult epithelial tumours, an extremely small fraction of paediatric cancers appear to be explained by known environmental exposure, such as ionizing radiations, chemicals and drugs used to treat cancers.

3. Unlike in adults where the risk of cancer increases with age, a relatively wide age range occurs in paediatric malignancies. There are two age peaks in children, early childhood and adolescence. During the first year of life, cancers described as embryonal tumours are the commonest. They become rarer as the child ages. Bone malignancies and Hodgkin disease and gonadal germ cell malignancies occur more frequently in the older child.
4. Children tolerate chemotherapy better and respond more to it than adults.

Cancer is a very important cause of childhood mortality, even in Nigeria. Its significance as a non-communicable disease is bound to rise, just like sickle cell anaemia, when we start to get the handle on communicable diseases.

We (Ogunrinde GO, Musa HH, Olorukooba AA, Musa H) have looked at the pattern of childhood cancer in Zaria, before the Haematology/Oncology Unit was established in the Department of Paediatrics. [69] The study was an audit of the first two years of operation at the permanent site of the teaching hospital in Shika. The clinical department moved from Tudun Wada to its present location in 2005.

Between 2005 and 2007 81 children (7.6% of childhood admission) with malignancies were identified, 74 (91.4%) had established histological diagnosis. The age distribution by sex revealed that virtually all affected children were aged between 1 and 12 years.

Table III: Sex and age distribution of children with cancers

Age (yrs)	Male	%	Female	%	Total	%
<1	1	2.6	0	0.0	1	1.4
1-5	18	46.2	15	42.9	33	44.6
6-12	19	48.7	18	51.4	37	50.0
>12	1	2.6	2	5.7	3	4.1
Total	39	100.0	35	100.0	74	100.0

In the years under study the four commonest childhood cancer in decreasing order were retinoblastoma, Burkitt's lymphoma,

acute lymphoblastic leukaemia and nephroblastoma. A mention must be made of the high rank of Burkitt's lymphoma. It is a tumour more commonly seen around 7 years of age, has been linked to the Ebstein Barr Virus and malaria, and therefore more commonly found in tropical Africa. It used to be the commonest childhood cancer in Zaria (Wammanda et al. unpublished). Another recent study in Zaria by Adewuyi, Ogunrinde and others confirmed retinoblastoma as the commonest childhood malignancy. [70] This apparently changing pattern became noticeable after the movement of the hospital to its permanent site in 2005. The reasons are not clear presently but it could be due to ongoing demographic transition. A report from Ilorin spanning 28 years of histological data showed Burkitt's lymphoma as the leading type of malignancy in children. [71] Incidentally, the authors did not disaggregate their data by year so it is unknown if there is a trend in the study. Other reports continue to show Burkitt's lymphoma as the commonest type of childhood, with retinoblastoma either second or third commonest. [72] A report from Enugu suggested the possibility of the increased incidence of nephroblastoma and retinoblastoma [73] while in Jos rhabdomyosarcoma was found to be commoner than Burkitt's lymphoma. [74] In our first series it was revealed that chemotherapy (the use of anti-cancer drugs) on its own represented 63.5% of treatment modality and was overall in 73.0% in combination with either surgery or radiotherapy. Unfortunately, only 5 (10.6%) of 47 children completed their courses of drugs. In the case of acute lymphoblastic leukaemia the course of therapy may last as long as two years.

The outcome for childhood malignancies was, and continues to be, poor. We were able to discharge, after the first few cycles of drugs, only 47.3%. There was an unacceptably high 29.7% hospital-based mortality. Eleven (14.8%) either left against medical advice or absconded. Overall, 74.2% of children that were discharged were lost to follow up. These are statistics that can be improved upon if studies are encouraged to find out the real reasons for the poor performance. One obvious reason is the advanced stages of cancer Nigerian children present with. Even studies would be needed to establish why parents present their children with strange symptoms late to the hospital. Then, we would be able to match internationally acceptable survival rates. As a result of the study we reported in

2004 we did recommend the establishment of an organized oncology unit in the Department of Paediatrics, staff training in oncology and funding of research and patient care. I am happy to report that there is a unit of Haematology and Oncology in my department, staff training has picked up. We are still having huge problems when it comes to contemplative research in paediatric oncology. Incidentally, our diagnostic capabilities are light years away from optimal.

Conclusion

The subspecialty of Paediatrics has a come a long way since its inception in the country in the 1960s. However, when compared to what is happening internationally, including in sister sub-Saharan countries, we have still a long way to go. There is need for intensive and focused manpower development, need for more contemplative and in-depth researches in order to give our children, the obvious future of our great nation, a better beginning in life. We need to make informed decision and this will depend on the availability of qualitative studies in Paediatrics.

Bibliography

1. Stanton BF, Behrman RE. The field of Pediatrics. In Kliegman R, Stanton B, St. Geme III J, Schor N, Behrman R, editors. Nelson Textbook of Pediatrics.: Elsevier Saunders; 2011. 1-13.
2. Wikipedia. [Online].; 2001 [cited 2014 October 23. Available from: HYPERLINK "http://en.wikipedia.org/wiki/Pediatrics" http://en.wikipedia.org/wiki/Pediatrics .
3. Colón AR, Colón PA. Nurturing children: a history of pediatrics: Greenword Press; 1999.
4. Luecke Jr. PE. The history of pediatrics at Baylor University Medical Center. BUMC Proceed. 2014; 17: 56-60.
5. Yakubu AM. *Child health care in Nigeria: historical background.* Niger J Paediatr. 2012; 39: 1-6.
6. Ajenifuja B. Paediatrics health care in Nigeria: yesterday, today and tomorrow. Niger J Paediatr. 2011; 38: 146-58.
7. Ogala WN, **Ogunrinde GO**. An unusual birth injury as a complication of traditional obstetric practice. Niger Med Pract. 1988; 16: 93-4.
8. Tahzib F. Epidemiological determinants of vesico-vaginal fistulas. Br J Obstet. 1983; 90: 387-91.
9. Harrison KA. Obstetric fistula: one social calamity too many. Br J Obstet. 1983; 90: 385-6.
10. Yola AI. Yankan gishiri (salt cut). Intl J Obstet Trauma. 2011; 1.
11. Federal Ministry of Health. Saving newborn lives in Nigeria: newborn health in the context of the Integrated Maternal, Newborn and Child Health Strategy. Countdown to 2015. Abuja: Federal Ministry of Health, Save the Children, Jhpiego; 2011.
12. **Ogunrinde GO**, Ogala WN, Ameh EA, Onalo R, Lukong CS. Subgaleal abscess in the newborn: a case report. Ann Pediatr Surg. 2006; 2: 48-9.
13. Onalo R, **Ogunrinde GO**, Olayinka AT, Ogala WN, Adama SA, Ega B. Bacterial agents of neonatal septicaemia: a prospective study in Zaria. Niger J Paediatr. 2008; 35: 1-6.
14. [Online]. [cited 2014 October 26. Available from: HYPERLINK "http://www.who.int/maternal_child_adolescent/epidemiology/en/" http://www.who.int/maternal_child_adolescent/epidemiology/en/ .
15. The World Bank. [Online].; 2014 [cited 2014 October 26. Available from: HYPERLINK "http://data.worldbank.org/indicator/SH.DYN.NMRT"

http://data.worldbank.org/indicator/SH.DYN.NMRT .

16. World Health Organization. WHO Nigeria. [Online].; 2007 [cited 2014 October 29. Available from: HYPERLINK "http://www.who.int/pmnch/activities/countries/nigeria/en/index1.html" http://www.who.int/pmnch/activities/countries/nigeria/en/index1.html .
17. World Health Organization. Neonatal and perinatal mortality: country, regional and global estimates. ; 2006.
18. Onalo R, Ogala WN, **Ogunrinde GO**, Olayinka AT, Adama SA, Ega B. Predisposing factors to neonatal septicaemia at Ahmadu Bello University Teaching Hospital, Zaria. Niger Postgrad Med J. 2011; 18: 20-5.
19. Centers for Disease and Prevention. Infant Mortality - Maternal and Infant Health - Reproductive Health. [Online].; 2014 [cited 2014 October 30. Available from: HYPERLINK "http://www.cdc.gov/reproductivehealth/maternalinfanthealth/infantmortality.htm" http://www.cdc.gov/reproductivehealth/maternalinfanthealth/infantmortality.htm .
20. UN Inter-agency Group for Child Mortality Estimation (UNICEF, WHO, World Bank, UN DESA Population Division). [Online].; 2014 [cited 2014 October 30. Available from: HYPERLINK "http://www.childmortality.org" http://www.childmortality.org .
21. Correia MITD, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through multivariate model analysis. Clin Nutr. 2003; 22: 235-9.
22. WHO. Guidelines: updates on the management of severe acute malnutrition in infants and children. Geneva: World Health Organization; 2013.
23. World Health Organization. Early initiation of breastfeeding. [Online].; 2014 [cited 2014 November 17. Available from: HYPERLINK "http://www.who.int/elena/titles/early_breastfeeding/en/" http://www.who.int/elena/titles/early_breastfeeding/en/ .
24. Audu LI, Ogala WN. Exclusive breast-feeding rates in Zaria. In Abstracts 29th Annual Conference of the Paediatric Association of Nigeria; 1988.
25. Okolo SN, Adewunmi YB, Okonji MC. Current breast-feeding

knowledge, attitude and practices of mothers in five rural communities in the Savannah region of Nigeria. J Trop Pediatr. 1999; 45: 323-6.

26. **Ogunrinde GO**. Alegbejo JO. Pattern of urine specific gravity in exclusively breastfed and water-supplemented infants. Sahel Med J. 2005; 8: 60-4.
27. Martines JC, Rea M, Zoysa I. Breast-feeding in the first six months. BMJ. 1992; 304: 1068-9.
28. Guttman N, Zimmermann DR. Low income mother's view on breastfeeding. Soc Sci Med. 2000; 50: 1457-73.
29. Eregie CO. Observations on urinary frequency in exclusively breast-fed neonates. East Afr Med J. 1998; 75: 576-8.
30. United Nations Children's Fund. State of the World's Children. ; 2011.
31. Claeson M, Waldman RJ. The evolution of child health prograames in developing countries: from targeting disease to targeting people. Bull WHO. 2000; 78: 1234-45.
32. United Nations Children's Fund and World Health Organization. Diarrhoea: why children are still dying and what can be done. ; 2009.
33. United Nations Children's Fund and World Health Organization. WHO/UNICEF Joint Statement: Clinical management of acute diarrhoea. [Online].; 2004 [cited 2009 12 20. Available from: HYPERLINK "http://www.afro.who.int/cah/documents/intervention/acute_diarrhoea_joint_statement.pdf" http://www.afro.who.int/cah/documents/intervention/acute_diarrhoea_joint_statement.pdf .
34. Sur D, Dutta P, Bhattacharya S. Zinc supplementation in diarrhoeal disease. Postgrad Doc Afr. 2003; 25: 31-33.
35. The Zinc Investigators' Collaborative Group. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. Am J Clin Nutr. 2000; 72: 1516-1522.
36. **Ogunrinde GO**, Raji T, Owolabi MO, Anigo K. Knowledge, attitude and practice of home management of childhood diarrhoea among caregivers of under-5 children with diarrhoeal disease in northwest Nigeria. J Tro Pediatr. 2012; 58: 143-6.
37. Nnaji GA, Ezeagwuna DA, Nnaji IJF, Osakwe JO, Nwigwe AC, Onwurah OW. Prevalence and pattern of sickle cell disease in

premarital couples in southeastern Nigeria. Niger J Clin Pract. 2013; 16: 309-14.

38. **Ogunrinde GO**, Onimoe GI, Inglis R, Onalo R. Haemoglobinopathies. In Ameh E, Bickler S, Lakhoo K, Nwomeh B, Poenaru D, editors. Paediatric surgery: A comprehensive text for Africa. Seattle: Global HELP Organization; 2012. 34-9.
39. Global Health. CDC Global Health - Nigeria - Sickle Cell Disease. [Online].; 2012 [cited 2014 November 4. Available from: HYPERLINK "http://www.cdc.gov/globalhealth/countries/nigeria/what/scd.htm" http://www.cdc.gov/globalhealth/countries/nigeria/what/scd.htm .
40. Akinyanju O. [Online]. [cited 2014 November 7. Available from: HYPERLINK "www.sicklecellfoundation.com/Nat%20Burden%20SCD.pdf" www.sicklecellfoundation.com/Nat Burden SCD.pdf .
41. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Organ. 2001; 79: 704-12.
42. Molineaux L, Fleming AF, Cornille-Brogger R, Kagan I, Storey J. Abnormal haemoglobins in the Sudan savanna of Nigeria. III. Malaria, immunoglobulins and antimalarial antibodies in sickle cell disease. AnnTrop Parasitol. 1979; 73: 301-10.
43. Wang Z, Wilkie D, Molokie R. Neurobiological mechanisms of pain in sickle cell disease. Hematology. 2010; 2010: 403-8.
44. Statius Van Eps L, Pinedo-Veels C, Vries G, De Konig J. Nature of concentrating defect in sickle cell nephropathy. Lancet. 1970; 295: 450-2.
45. **Ogunrinde GO**, Zubair RO, Mado SM, Musa S, Umar LW. Prevalence of nocturnal enuresis in children with homozygous sickle cell disease in Zaria. Niger J Paediatr. 2007; 34: 31-5.
46. Akinyanju O, Agbato O, Ogunmekan AO, Okoye JU. Enuresis in sickle cell disease. Prevalence studies. J Trop Pediatr. 1989; 35: 24-6.
47. Addae S, Konotey-Ahulu FID. lack of diurnal variation in sodium, potassium and os
48. molal excretion in the sickle cell patient. Afr J Med Sci. 1971; 2: 349-59.
49. Yauba MS, Aikhionbare HA, **Ogunrinde GO**, Bugaje MA.

Significant bacteriuria in children with sickle cell anaemia in a Nigerian tertiary hospital. Niger J Paediatr. 2014; 41: 350-3.

50. Akuyam SA, Anaja PO, **Ogunrinde GO**, Abubakar A, Lawal N, Ya'uba SM, et al.. Liver function test profile of Nigerian children with sickle cell anaemia in steady state. Niger J Basic Clin Sci. 2014; 11: 13-19.
51. Williams AL, Hoofnagle. Ratio of serum aspartate to alanine aminotransferase in chronic hepatitis. Relationship to cirrhosis. Gastroenterology. 1988; 95.
52. **Ogunrinde GO**, Keshinro MI, Ige SO. HIV seropositivity in children with sickle cell disease. Ann Afr Med. 2005; 4: 104-6.
53. Federal Ministry of Health, Abuja. [Online].; 2006 [cited 2014 November 7. Available from: HYPERLINK "www.nbts.org.ng/images/nationalbloodpolicy.pdf" www.nbts.org.ng/images/nationalbloodpolicy.pdf .
54. **Ogunrinde GO**, Yakubu AM, Akinyanju OO. Anthropometric measures and zinc status of children with sickle cell anaemia in Zaria. Niger J Paediatr. 2000; 27: 64-9.
55. Ujo H, Mamman AI, Aliyu A, **Ogunrinde GO**. The sero-prevalence of Parvovirus antibodies among children with sickle cell anaemia in Zaria. Afr J Cln Exper Microbiol. 2012; 13: 74-8.
56. Iwalokun BA, Iwalokun OI, Hodonu SO. Seroprevalence of parvovirus B19 antibodies and evidence of viremia among Nigerian patients with sickle cell anemia. J Biomed Res. 2013; 27: 272-82.
57. Smith-Whitley K, Zhao H, Hodinka R, Kwiatkowski J, Cecil R, Cecil T, et al.. Epidemiology of human parvovirus B19 in children with sickle cell disease. Blood. 2004; 103: 422-7.
58. Ademisoye AA, Soyinka JO, Onyeji CO, Adeodu OA, Solomon S, **Ogunrinde GO**. Effects of sickle cell anaemia on the pharmacokinetics of sulphadoxine and pyrimethamine in children. Intl J Pharm Pharm Sci. 2012; 4: 169-72.
59. **Ogunrinde GO**, Ogala WN, Bugaje MA. Cerebral malaria in Zaria. A review of 50 cases. In Niger J Paediatr; 1999; Sokoto. p. 62.
60. Konotey-Ahulu FID, Serjeant G, White JM. Treatment and prevention of sickle-cell crisis. Lancet. 1971; 298: 1255-6.
61. Adagu SI, Lege-Oguntoye L, Okoyeh JN, Ogala WN, **Ogunrinde GO**. Preliminary investigation in vivo/in vitro sensitivity of Plasmodium falciparum to quinine in Zaria. West Afr J Pharm Drug Res. 1990/91; 9/10: 68-70.

62. Adagu SI, Okoyeh JN, Lege-Oguntoye L, Ogala WN, **Ogunrinde GO**, Faji JT, et al.. Efficacy of a 3-day oral regimen of quinine in an area of northern Nigeria with low-grade resistance of Plasmodium falciparum to chloroquine and sulphadoxine-pyrimethamine. J Trop Med Hyg. 1995; 98: 296-8.

63. Okoyeh JN, Lege-Oguntoye L, Ugbode RO, **Ogunrinde GO**. Responses of multi-drug Plasmodium falciparum to mefloquine in Nigerian children. Trop Med Intl Health. 1997; 2: 319-24.

64. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bull World Health Organ. 2001; 79: 704-12.

65. Weatherall J, Clegg J, Kwiatkowski J. The role of genomics in studying genetic susceptibility to infectious disease. Genome Res. 1997; 7: 967-73.

66. Gallup JL, Sachs JD. The economic burden of malaria. Am J Trop Med Hyg. 2001; 64 (Suppl): 85-96.

67. UN Millennium Project 2005. Coming to grips with malaria in the new millennium. , Task Force on HIV/AIDS, Malaria, TB, and Access to Essential Medicines, Working Group on Malaria; 2005.

68. Cyprus: how one nation's culture influences its genes. [Online].; 2010 [cited 2014 October 21. Available from: HYPERLINK "http://www.geneletter.com/cyprus-how-one-nations-culture-influences-its-genes-16/" http://www.geneletter.com/cyprus-how-one-nations-culture-influences-its-genes-16/ .

69. Bowman JE. Is a national program to prevent sickle cell disease possible? Am J Pediatr Hematol Oncol. 1983; 5: 367-72.

70. **Ogunrinde GO**, Musa HH, Olorukooba A, Musa A. Trend of childhood malignancies seen at Ahmadu Bello University Teaching Hospital, Zaria. In Book of Abstracts, Annual General Meeting and Scientific Conference, Paediatric Association of Nigeria; 2008; Lagos. p. 31-2.

71. Adewuyi SA, Musa H, Samaila MOA, **Ogunrinde GO**, Ameh EA, Popoola OB. Pattern of paediatric solid cancers seen in Radiotherapy and Oncology Department, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. Niger Postgrad Med J. 2013; 20: 120-4.

72. Omotayo JA, Duduyemi BM, Buhari MO, Anjorin AS. Histological pattern of childhood solid tumour in Ilorin: A 28-year retrospective review. Am J Med Sci Med. 2013; 1: 105-9.

Shehu UA, Adegoke SA, Abdulsalam U, Ibrahim M, Oyelami OA, Adeodu OO. Pattern of childhood malignant tumours in two tertiary hospitals in Nigeria: comparative study . Niger J Paediatr. 2013; 40: 175-8.

73. Ocheni S, Bioha FI, Ibegbulam OGEIJIAN. Changing pattern of childhood malignancies in Eastern Nigeria. West Afr J Med. 2008; 27: 3-6.

74. Tanko NM, Echejoh GO, Manasseh NA, Mandong MB, Uba AF. Paediatric solid tumours i n Nigerian children: a changing pattern? Afr J Paediatr Surg. 2009; 6: 7-10.

Picture 1



Picture 2



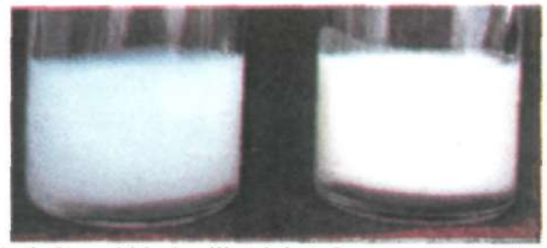
Picture 3



Colostrum (left) and matured milk (right)

Source: http://www.drpaul.com/breastfeeding/colostrum.html. Retrieved 2011-10-26

Picture 4



Foremilk (left) and hind-milk (right). *Source: Tonicthebrown*