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Since 1975

BLOOD DISORDERS AND TRANSFUSION MEDICINE

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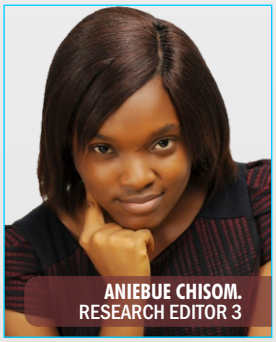
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Editorial

It's a great privilege and honour to present the 2014 edition of MEDIKKA, the international journal of the University of Nigeria Medical Students to us. The University of Nigeria Medical Students Association has come a long way, since 1975, to carry on MEDIKKA from one generation to another, despite the multifarious challenges it's been confronted with. From the time of inauguration of this year's MEDIKKA editorial board, it seemed an onerous task chiefly because of the halt in production of the journal for the past three years which is attributed to the problems its mother association faced; coupled with the quest for a well-seasoned publication as most of the students think a journal is mind-numbing from 'first principle'. It's vital we appreciate that a journal is purely intended to be an avenue for access to first-hand research information, referencing, and motivation for further research. It's no news that well-conducted research is vital to the success of global health endeavours and the medical profession by extension.

The focus for this year's edition of MEDIKKA is on the blood subject matter which we narrowed down to blood use in medicine (transfusion) and pathologies (disorders). This stems from manifold debates on the use of blood especially in the tropics, and blood disorders which are gradually coming into limelight as facilities to make more accurate diagnosis are becoming increasingly available. However, this is not to say we have made an exhaustive presentation on the subject matter. We only created a platform for further research and exploration to the best of our abilities and within the limited time we had to make this publication a reality. Lest I forget, funding for research and technical supplies is a major encumbrance to students and on that note, I wish to implore our alumni, organizations and well-wishers to rise up to this challenge and assist as much as possible.

The list for acknowledgments and appreciation is inestimable. We are indeed grateful to everyone, whom through their support-financially and otherwise, made this publication a success story. On behalf of the editorial board, I wish to start by thanking our chief editorial consultant: Prof Iheanyi Okpala, who despite his busy schedule found time to give us guidance as regards a student journal. I appreciate Dr. Onyeakusi Emeka, an alumnus of the University of Nigeria Medical School, who from far away Texas-USA took it up as a matter of great responsibility to ensure that we have the right orientation of what a standard journal should be. I also wish to express my immense gratitude to Professor Jonathan Azubuike, the Chairman of the Medical and Dental Council of Nigeria, who founded the vision for MEDIKKA and gave us the necessary audience we needed despite his scores of engagement. I will not fail to thank Dr. Nwachukwu Ugwunna and Dr. Enoch Uche notably for their contribution. I will ever remain indebted to Uzoma, Chukwuebuka an associate editor, with whom I kept late nights on most days to collate the articles satisfactorily.

Finally, to my editorial team, I wish to express my profound gratitude for playing your part in the production of this work. You will attest to the fact that the sacrifices we made, the solidarity we have demonstrated and the training we acquired on this platform will stand the test of time.

One thing is certain: It can only get better!

Respectfully yours,

Okoye, Onyedikachukwu Michael
Editor-in-Chief
MEDIKKA 2014 edition

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The following categories of manuscripts are accepted for publication:

- ***Research Articles***: Original research concerning any aspect (e.g. aetiopathogenesis, epidemiology, diagnosis, management and prevention) of disease. Animal research contributions of relevance to human health are also welcome. Abstract required. (Maximum 4,000 words)
- ***Review Articles*** including meta-analyses: Detailed systematic and critical evaluation of the literature on a specified clinical problem. Reviews should include information such as type of studies and the selection process. (Maximum 3,500 words)
- ***Short Communications and Case Reports:*** These may be unique case reports, clinical experiences and short reports of original research. (Maximum 1,500)

All articles are subjected to peer-review by the ***MEDIKKA*** Board of Editorial Consultants and/or invited assessors.

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Papers should be type-written (original copy) with double spacing throughout, except for quotations. On a sheet separate from the text, the following should be typewritten:

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- Title of Article/Paper
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- Tables and Illustrations
- Key words for indexing (three to six)
- Original and Research articles should contain an abstract of 150-200 words.

The Editor reserves the right to shorten and/or correct the articles received (in consultation with the Editorial Consultants) without altering the subject matter of the articles.

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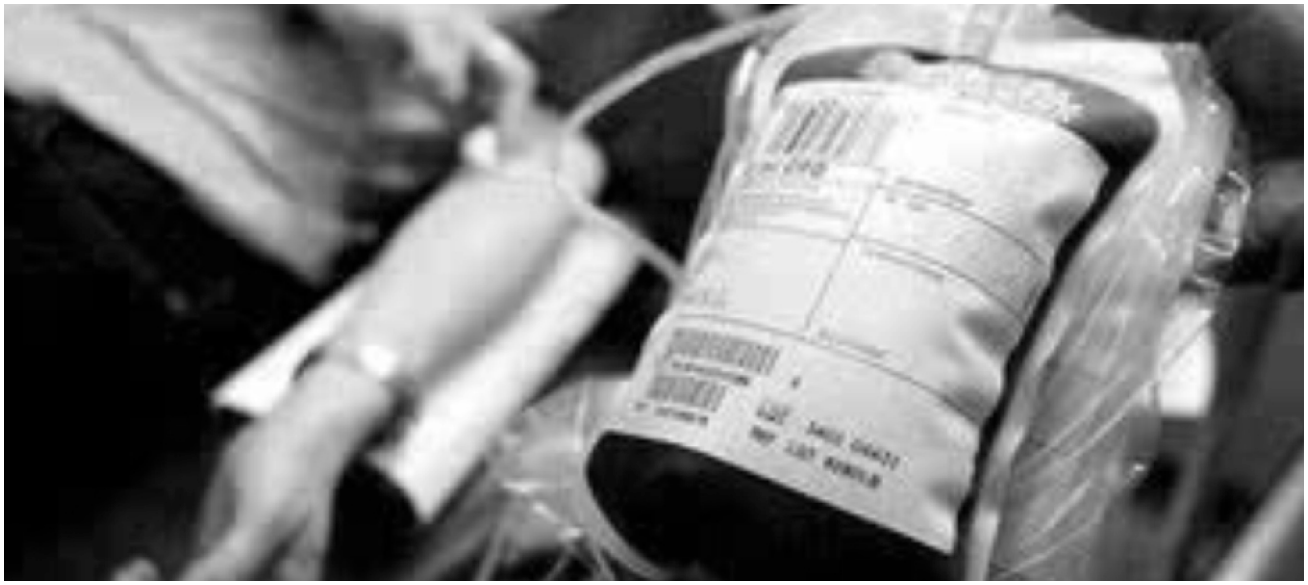

KNOWLEDGE, ATTITUDE AND PRACTICE OF BLOOD DONATION AMONG UNDERGRADUATES IN ENUGU METROPOLIS

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**At the time of writing, were 5th year clinical students of College of Medicine, UNEC*

ABSTRACT
This is a study of the knowledge attitude and practice of blood donation among undergraduates in Enugu State.
The study was carried out using self-administered questionnaires. 280 questionnaires were distributed, collected and analyzed.
The study revealed that 96.1% of the students heard about blood donation at one point or the other. It is also revealed that 96.4% know about blood screening before donation. Despite this knowledge, only 19.6% of our respondents have donated blood before and 45.4% is for their relatives.

Tackling the issue of blood scarcity in our banks therefore rests to a greater extent on explicitly educating the youths on the importance of blood donation and disabusing their minds of the perceived side effects of blood donation because they contribute largely to the bulk of donors in the society and 97.9% said they will donate if educated appropriately.

GENERAL INTRODUCTION
Blood donation is the only way of acquiring blood to meet emergency requirements in cases of road traffic accidents, complications of pregnancy and childbirth, various anemic disorders and surgical emergencies among others.
Blood is the most donated tissue in medical practice and a veritable tool in many live-saving situations when used judiciously. In spite of the rapid and remarkable conquest and breakthrough of medical science today, there is still no ideal substitute. Blood is only manufactured by human beings and human donation is the only way of acquiring blood to meet emergency requirements in cases of road traffic accidents, complications of pregnancy and childbirth, various anemic disorders and surgical emergencies among others. Blood donation is the act of giving one's blood so it can be transfused into another for therapy.
Globally, 80 million units of blood are donated each year but only two million units are donated in sub-Saharan Africa where the need is enormous.1 In Nigeria, although half of the population in the country is medically fit for donation, only four in a thousand are voluntary blood donors.2

World Blood Donor Day, celebrated on 14 June every year, serves to raise awareness of the need for safe blood and blood products and to thank voluntary unpaid blood donors for their life-saving gifts of blood. With the slogan "Give the gift of life: donate blood", this year's campaign (2013), the 10th anniversary of World Blood

Donor Day, will focus on the value of donated blood to the patient, not only in saving life, but also in helping people live longer and more productive lives.3
Since infectious diseases can be transmitted through blood transfusion, there is need to source blood from a low risk population. The first step towards blood safety is to encourage voluntary, non-remunerated and regular blood donors who will donate blood at least once or three times a year.
In Nigeria, the estimated blood requirement amounts to about 1.5 million units of blood.4
Obviously, this target is not met. A baseline data survey was conducted in August 2005 by Nigerian national Blood Policy shows that about half a million units of blood were collected from private and public sources in the previous one year. This is grossly inadequate for a country of about120 million people. 5
A national baseline data survey on blood transfusion conducted in August, 2005 revealed that in the public sector, 25% and 75% respectively were commercial and replacement donors while voluntary non-remunerated donors were negligible. In the private sector, the reverse was the case, with 75% and 25% respectively being commercial and replacement donors while voluntary donors were insignificant.6This ugly trend should not be allowed to hold sway any longer as this practice carries a significant risk of transfusion related complication and transfusion transmitted infections.

STATEMENT OF PROBLEM
A visit to our blood banks revealed that this valuable resource “blood” is in short supply while demand is on the increase. Should we fold our hands and watch this happen? The truth is that we don't know who among us will need blood the next minute.

METHODOLOGY
A cross sectional descriptive study was carried out in four tertiary institutions in Enugu state. These institutions were selected by random sampling method among the tertiary institutions in the state. They are:
University of Nigeria, Enugu Campus Enugu State University of Science and Technology.
Institute of Management and Technology, Enugu.
Enugu State College of Education Technical.

The respondents were regular student of the chosen institutions above. Simple random sampling method was used to select the students. The basis for selection was not dependent on age, sex, or height.

RESULTS
Age of respondents: The highest distribution (66.2%) was seen in the 20-24 age bracket. The lowest was seen in the 30-34 age bracket. The mean age of our respondents was 22 and the standard deviation 0.511.

Sex of respondents: Most of our respondents (64.6%) were females.

Religion of respondents: The majority of our respondents (96.1%) were Christians.

Marital status of respondents: 93.2% of our respondents were single while 6.8% were married.

Institution of study: Most of our Respondents were from the University of Nigeria Enugu Campus.

Knowledge of blood GROUP: Most of our respondents 83.2% already knew their blood group. 31% of our respondents think it is not necessary to know their blood group while 26% don't have time for it.

Knowledge of practice of blood donation: 96.1% have heard about blood donation before. 43.9% of our respondents heard about blood donation from the hospital while 18.6% heard from television and radio. 65.4% of our respondents know of a blood donation center. 53.9% of our respondents believe one can donate blood twice in a month. 96.4% of our respondents already know that there should be screening before donation. Most of our respondents (60.0%) think both the donor and the recipient should be screened while 37.9% believe only the donor should be screened before blood donation. Some knowledge exists among our respondents on the screening of blood for HIV I & II, Hepatitis and for blood group compatibility while little knowledge exists about screening blood for cytomegalovirus, sickle cell disease and malaria. Most of our respondents (63.9%) think one can benefit from donating blood while 30% do not know if one can benefit from it or not. Most of our respondents (43.2%) gave the benefit of donating blood as to save lives.50.0% of the respondents agreed that major surgery requires blood donation. Most of our respondents (48.2%) think that menstruating women can donate blood. Most of our respondents, (45.0%) think this age bracket, 19-30 years, can donate blood. Most of our respondents (88.6%) agreed that they were fit to donate blood.

Most of our respondents (84.3%) agreed that they can donate blood to anyone in an emergency.
Most of our respondents (75%) disagreed that they are only interested in donating blood to known persons.

Most of our respondents (87.9%) disagree that they only donate blood because they will be paid at the end of the day.
Most of our respondents (80.4%) stated that they have never donated blood before.
Most of our respondents (56.4%) would love to be recruited as a voluntary non-remunerated blood donor.

DISCUSSION OF FINDINGS

The highest percentage of age distribution recorded (66.2%) was in the age class 20-24 years. An appreciable number 28.1% was also found to be in the range of 25-29 years. Very few 3.6% of our respondents were of the age bracket of 30-34 years.

There is a difference in the gender respondents. There were more females in the institutions of study. We had up to 64.6% of females. This agrees with the general belief in the society that there are more females than males
A large chunk of our respondents were found to be Christians 96.1% which reflect the religion of the easterners. 1.1% of the Christian respondents were of the Jehova's Witnesses, a denomination that strictly condemns blood donation.

An overwhelming majority 93.2% of our respondents are single. This in fact is a plus, because they would not have to obtain permission from their parents or spouse, which is one of the hindrances to blood donation.

Most of our students were from the University of Nigeria Enugu Campus 53%. This was because they had most of their students around (health students) at the time this research was made because of a University strike.
About the knowledge of blood group, 83.2% knew their blood group, while 16.8% did not know their blood group. Out of the 16.8% that do not know their blood group, 31% said it was not necessary to know their blood group, 26% did not have time for it, 17.8% did not know where to do it, while 24.9% did not donate because of their cultural belief.

A large percentage of our respondents (96.1%) knew about blood donation which is an important step towards blood donation. We went further to ask their source of information. 18.6% heard it through the television or radio and 2.1% knew through the newspaper. This is poor. This means that the media should be encouraged to create more awareness to undergraduates about blood donation. Worthy of note is the fact that 43.9% of our respondents got to know about blood donation in the hospital. This shows that the hospital staffs are really interested in encouraging people towards blood donation. 2.5% of our respondents were informed by their family relatives. This differs from the findings of K.K. Agbour et al who found out that 93.3% of his respondents have heard about blood donation and received information mainly from friends and the media.

On knowledge of any blood donation centre, 65.4% of our respondents know at least a blood donation centre in Enugu Metropolis. 34.6% said they do not know of any blood donation centre. This situation is rather unacceptable, because this group of people represent a significant amount that would have added to our blood bank centre. Even amongst those that knew of blood donation centres, 40.7% knew only about ESUT while 23.6% knew about UNTH. Only about 8.2% knew about National Blood transfusion Centre, Enugu while 6.8% knew about Annunciation Specialist Hospital and 1.8% knew about Mother of Christ hospital.

It was cheering to observe that 53.9% of our respondents donated blood twice in a year, 30.4% thrice every year, 10% once every year and 1.8% four times every year.

Most of our respondents 96.4% knew that blood should be screened before donation. This is a positive finding as they know one can actually get infected from blood and blood products. A mere 3.6% claim they do not know about screening of blood prior to donation.
On who is to be screened prior to donation, 60% of respondents think both the donor and the recipient need to be screened, while 37.9% think only the donor should be screened. This results show a good level of awareness on the need to screen blood. We also asked further questions on what is screened for. 25% knew about blood group, 25% knew about HIV I/II, 7.9% about hepatitis, about malaria parasites, 2.1% about sickle cell disease 5.7% knew about malaria parasite. 3.9% knew all the above diseases that should be screened for.
63.9% of our respondents think that one can benefit from donating blood while 2.1% do not see any benefit derived from donating

blood, while 3.9% had no response to this question. Of those who think there is a benefit in blood donation, a large chunk of our respondents (43.2%) donated blood to save life, 6.1% donated blood as a service to humanity, 2.1% believed they will be blessed by God, another 2.1% donated because they want to save the sick, while 1.8% donated blood so that they can be paid.

About the conditions that needed blood donation, 50% of our respondents said major surgeries, 19.3% said child birth, 18.9% said bleeding from injury, while 19.3% chose all the conditions.

About 93.6% of our respondents believed that pregnant women, hypertension, diabetics and menstruating women can donate blood to other people. 48.2% believed that menstruating women can donate blood. 6.4% , 10.7% and 10.4% of our respondents believed that pregnant women, diabetic and hypertensive women respectively can donate blood. This calls for more education of undergraduates on the criteria for blood donation.

When asked about the age groups that can donate blood, 45% of our respondents believed the ideal age for blood donation are between 19-30 years, while 32.1% believed 31-44 years could only donate blood. 2.1% believed that those between 15-18 years are eligible to donate blood. 10% believed that blood donation is for those between 45-65. 10% believed all ages are qualified to donate. These results show a good level of awareness on the acceptable age ranges for blood donation.

Concerning attitude towards blood donation, 88.6% of our respondents felt that they were medically fit to donate blood, while 11.4% felt that they were medically unfit to donate blood. This buttresses the fact that one has to be psychologically fit before he/she can donate blood. This supports the findings of Alam Magbool and Bourham El Din Masalmeh, where 38.3% of their respondents considered themselves not fit for blood donation.

65.4 of our respondents said they were not afraid of donating blood, while 34.6% said that they were afraid of donating blood. We probed further to ascertain their fears, 42% said they did not have enough blood while 12.8% were afraid of medical problem afterwards. 25.6% said they will get sick if they donate blood, while 15.3% do not donate because of fear of needle prick.

Also, 73.6% said they look forward to donating blood in future, while 16.8% deferred from donating blood in future.

80% of our respondents said they always disclose correct information about their health status before donation while an appreciable percent 10.4% say they don't. This casts aspersions on the safety of some of our blood donors and thus calls for proper scrutiny of prospective donors by the blood donation centers.

49% of our respondents did not donate blood due to fear. 20% did not donate because of HIV screening. 10% said they have no reason for not donating blood, 7.8% said they might faint after donation while another 6.2 % said they might feel ill after donation. 4.2 % said they were not physically fit and healthy. 3.2% donated because they wasn't to help the patient while 2.8% said they are not sure they have enough to donate. However, 44.6% of our respondents said that their fears have changed their attitude towards blood donation. this is an important finding. These fears largely contributes to non-donation but largely does not affect their view about blood donation being life saving. This result is supported by the study of K.K. Agbour et al, in Lome Togo who found that among his 300 respondents, only 95 persons were donors. The reason for non-donation was mainly related to the fear of catching diseases especially HIV and the fear of knowing the result of one's HIV test.

Furthermore, in attitude towards blood donation, we found something interesting. 84.3% of our respondents say they can donate blood to anyone in case of an emergency while 15.7% said they cannot. 25% said they can only donate blood to persons who are known to them, while 75% said they can donate blood to anyone irrespective of the fact that they are not known to them.

59.3% said they will donate blood always and when the need arises while 38.9% said they will always donate blood.

A mere 12.1% of our respondents said they would only donate blood to get paid while 87.9% said they are not interested in the financial benefit accruable to blood donation. This supports the findings of Olaiya M. A., Alakija W., Ajala W., Olatunji R. O. that some group of donors prefer to be rewarded financially. 97.9% of our respondents said if they were educated on the importance of blood donation, they will donate regularly and about 2.1% believed further education would not improve their frequency of donation. This supports the finding of Wiwanik it in his study in Thailand. He found that the attitude of the subject only significantly correlate with the

level of education. He therefore proposed that blood donation should be taught repeatedly at any educational level including the school system.

On the practice of blood donation, 19.6% of our respondents have donated blood at least once in their life time while a whopping 80.4% have never donated blood. 57.9% said it is because nobody has asked them to donate. This is an interesting finding because about 98.6% of our respondents have heard about blood donation. This shows that knowledge of blood donation does not actually translate into blood donation. 45.4% of the donors said they donated for a relative or friend, 18.6% said it was for money, 29.3% donated voluntarily. 34.6% still have fear for donation while 73.6% look forward to blood donation.

These figures are in consonance with the findings of Karakkamandapam Sabu in South India, among 410 respondents, 64.1% were voluntary donors, 31.1% had donated for relatives or friends and 1.9% donated for relatives or friends and 1.9% donated blood for money.

Most of respondents 10.4% only donate blood once yearly, 6.1% donate twice, and 7.9% donate three times in a year. Only about 8.6% donate four times in a year. This shows a good knowledge of the maximum number of times one should donate blood in a year. 10.4% of our respondents last donated blood over a year ago, 12.9% donated less than 6 months ago, 3.9% donated less than 3 months ago and 3.6% less than 1 month ago. The fact that most of them donated over a year ago which could mean two years or even three years ago revealed some sort of inconsistency as regards blood donation.

Most of our respondents 6.1% said they go to donate blood at the University of Nigeria Teaching Hospital, 7.9% at Mother of Christ Specialist Hospital and 6.1% at Annunciation Specialist Hospital. 8.67% at Enugu State Teaching Hospital. Still on the practice of donation, 55% of our respondents said they would not continue in the act of blood donation, a situation that is really worrisome. 37% of them sited health reasons as being the cause. Another 19.2% cited religious reason. 27.4% said it was because of no reason. A mere 11.4% said they were afraid of donating blood. 56.4% of our respondents said they would continually donate blood so long as they are fit and would like to be recruited as a voluntary non-remunerated blood donor.

CONCLUSION

From the study, it can be gathered that there is a great knowledge among the students of the terminology 'Blood Donation' Most of them knew about blood screening before donation and even the person screened and what are to be screened. However, this knowledge did not translate into greater blood donation among these students.

Many number of students cited fear as being the main reason for non-donation especially fear of being detected as HIV positive. Some of the other reasons they gave include: not being sure of having enough blood to donate, not being physically fit and healthy, fear of fainting and being sick after donating blood. These reasons clearly show that the general knowledge of students on blood donation needs to be broadened. There appear not to be a significant influence of financial reward, religion and parents on the practice of blood donation among undergraduates in Enugu metropolis. Most of our respondents who are donors donate voluntarily while a few others donate only when the need arises i.e. to a friend/relative, in emergencies etc.

RECOMMENDATIONS

From the results and from the foregoing conclusion, we can draw the following recommendations on the ways to improve on the practice of blood donation among our undergraduates.

Improved and consistent education

There is need for widespread and spirited education of the youths on the importance of blood donation. Most of these youths have a biased view about donation and correction of these views would lead to improved practice of blood donation. The education of these should also be consistent.

Incorporation of blood donation education in our secondary school and University curricula

When these students are taught in-depth on the importance of blood donation, most of them would see the need to constantly donate blood.

Incentives for donors

Though the youths are encouraged to donate voluntarily, the fact that these ones need to be motivated cannot be overemphasized. This would make them look forward to donation subsequently. These motivations can be in cash or kind.

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NEONATAL JAUNDICE

KNOWLEDGE, ATTITUDE AND TREATMENT PRACTICES AMONG MOTHERS ATTENDING CLINICS AT THE UNIVERSITY OF NIGERIA TEACHING HOSPITAL, ITUKU-OZALLA, ENUGU.

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INTRODUCTION

Neonatal morbidity and mortality remain very high in the developing countries of sub-Saharan Africa, Asia and Latin America 1, and one of the important contributors to this is neonatal jaundice (NNJ).2-4
Jaundice due to unconjugated hyperbilirubinemia is also the most common clinical problem requiring medical attention in newborns in many parts of the world.2
Jaundice refers to the yellow coloration of the skin and the sclera (whites of the eyes) caused by a raised level of bilirubin in the body, a condition known as hyperbilirubinemia. 5 It's a common disorder worldwide and account for 75% of hospital re-admissions in the first week of life.6,7
Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life and about 10% of breast fed babies are still jaundiced at 2 month.5 For most babies, jaundice is not an indication of an underlying disease, and this early jaundice (termed 'physiological jaundice') is generally harmless.
Bilirubin is mainly produced from the breakdown of red blood cells. Red cell breakdown produces unconjugated (indirect) bilirubin, which circulates mostly bound to albumin although some is 'free' and hence able to enter the brain. Unconjugated bilirubin is metabolized in the liver to produce conjugated (direct) bilirubin, which then passes into the gut and is largely excreted in stool.
Unconjugated bilirubin can penetrate the membrane that lies between the brain and the blood (blood-brain barrier) and it is potentially toxic to neural tissues (brain and spinal cord). Entry of unconjugated bilirubin into the brain can cause both short-term and long-term neurological dysfunction (bilirubin encephalopathy). The term kernicterus is used to denote the clinical features of acute or chronic bilirubin encephalopathy, as well as the yellow staining of the brain associated with the former. Fortunately however, these complications can be avoided by the appropriate use of phototherapy and exchange blood transfusion to control serum bilirubin levels.

In order to achieve this, mothers must be able to recognize the condition and refer affected babies to the right places for prompt care and management. More often than not, action as well as treatment practices taken by these care providers are influenced not only by their knowledge, but also by their attitude towards the condition.
Since babies and mothers are discharged early, the ability of the mothers to recognize NNJ becomes important in order to prevent its progression and significantly reduces the morbidity and mortality due to the condition.
A study done with 255 mothers in Port Harcourt revealed that 225(88.2%) were aware of jaundice; 75(33.3%) and 50(22.2%) believed that eating too much groundnut in pregnancy and mosquito bite respectively were the main causes while 55(24.4%) answered it was due to mismatch of mother and baby's blood. 114(50.7%) and 60(26.7%) wrongly believed that the exposure to sunlight and use of glucose drinks respectively were the main forms of treatment and 50(22%) knew brain damage as a possible complication.8
Early intervention plays a key role in the prevention of the adverse outcomes resulting from neonatal hyperbilirubinemia. Early post-natal discharge from the hospital requires that parents should be able to recognize and seek prompt medical attention for it. This study was therefore designed to assess the knowledge, attitude and treatment practice of mothers attending clinics at the University of Nigeria Teaching Hospital, Ituku-Ozalla as regards neonatal jaundice, with the view of providing background data as basis for planning necessary health education intervention.

MATERIALS AND METHODS

Study area

The study was carried out in Enugu, Nigeria. Enugu is the capital city of Enugu state (created 1991 from the old Anambra state) and is geographically located in latitude 7N and 6 S of the equator at an altitude of 29.23m above sea level. It shares boundaries with Abia and Imo state to the south; Ebonyi state to the east, Benue state to the Northeast, Kogi state to the Northwest and Anambra state to the west. It has a total of 17 local government areas and population of 3,267,837 as at 2006 census. It also is one of the major cities of Nigeria which is a sub-Saharan African country and as such one of the developing nations of the world.21

Study design
This was descriptive cross-sectional study type.

Study population
Mothers who visit the immunization clinics of the Institute of Child Health (ICH) as well as mothers who attend Antenatal clinics, all of the University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, Enugu.

UNTH is a tertiary health care facility situated in Enugu state. The immunization clinics were held on all days of the week with exception of Tuesdays and Fridays, under the supervision of the Director of ICH, department of Pediatrics. Antenatal clinics were held every day of the week (Monday-Friday) with patients who were registered under the five firms of the department of Obstetrics and Gynecology.

RESULTS
Two hundred and sixty (260) questionnaires were distributed; 247 was retrieved but 240 were filled correctly, giving a response rate of 95%.

- Majority of the women were aged 25-29years and had tertiary education. Most of the women were married and professionals
- 81.7% of the respondents are aware of neonatal jaundice while 15.8% are not aware.
- 55% of the respondents got to know jaundice through the hospital/health workers while 1.3% of the respondents knew the condition from Church.
- Yellowness of the sclera of the eye was the commonest symptom identified by the women while the least was arching of the back
- 125(52.1%) know infections like malaria as a cause of NNJ while 3(1.3%) know drinking of cold water to be a cause.
- 76(31.7%) do not know any complications of jaundice while 8(3%) attribute deafness as a complication.
- 115(47.9%) attribute appearance of baby as an effective method of detection of jaundice.
- 129(53.8%) attribute exposure to sunlight as an effective method of treatment while 2(0.8%) attribute it to suspension of feeds.

DISCUSSION
From the study, it was found that 196(81.7%) were aware of neonatal jaundice. Thus a high level of awareness about NNJ was shown in this study, which was in keeping with findings from similar studies in Benin and Port Harcourt with 334(85.9%) and 225(88.2%) of the mothers respectively being aware of the condition.8,18
A majority of the respondents who affirmed awareness of NNJ had their source of information from hospital workers 132(55%), while very few had theirs from the mass media, school or church. This was similar to the findings in the study done in Benin, South Western Nigeria6 and in Port Harcourt8, where a very little proportion of the mothers had their source of information from the mass media, school or from books. This therefore implies that the mass media, which ought to play a key role in disseminating information has failed to do so seeing that health talks in the antenatal clinics alone will not be sufficient to reach the mothers in the community because only about 58% of pregnant women in Nigeria receive antennal care from skilled providers while only 35% of women in Nigeria give birth in Health facilities.24
One hundred and twenty five (52.1%) of the respondents attributed infections like malaria as a cause of jaundice;3(1.3%) thought it to be attributed to drinking cold water. Studies from Benin showed that 156(40.1%) of respondents attributed infections as a cause18 which was contrary to that found in Port-Harcourt where the mothers believed that eating too much groundnut during pregnancy and mosquito bites were the main causes of NNJ.8
The commonest sign of NNJ in our study was yellowing of the sclera of the eye (72.9% of the respondents). 3.8% were also aware of seizure. In the study in Benin, 116(29.8%) accounted for seizure and 205(52.7%) did not know any sign of jaundice.18
Seventy-six (31.7%) of respondents did not know any complication of NNJ, while 70(29.2%) knew neonatal death as a complication. The study in Benin showed that 225(57.8%) of the respondents knew death of baby as a complication while 128(33%) knew no complication.8
As regards effective diagnosis and treatment, 115(47.9%) respondents could detect jaundice by appearance of the baby.
One hundred and twenty nine (53.8%) and eighty (33.3%) respondents wrongly believed that exposure to sunlight and glucose water/drink was an effective treatment of jaundice while 29(12.1%) did not know any treatment. This is in keeping with a similar study done in Port Harcourt where 114(50.7%) and 60(26.7%) wrongly believed that exposure to sunlight and use of glucose drinks respectively were the main forms of treatment.8
From the study, a greater percentage of the mothers 148(61.7%) believed that neonatal jaundice should be treated in the hospital while 4(1.7%) believed that neonatal jaundice should be treated with traditional medicine. This is similar to study done in Benin were 335(86.1%) respondents were of the opinion that jaundiced baby should be taken to the hospital.133(55.4%) of the respondents agreed that they will accept phototherapy as a mode of treatment if their babies developed neonatal jaundice while 28(11.7%) rejected phototherapy. Some of the respondents who rejected phototherapy gave reasons like blindness resulting from the procedure. In the study done in Benin, 374(96.1%) of the mothers accepted phototherapy as a method of treatment if their babies had the condition.8
Finally, 94(39.2%) of our

respondents accepted exchange blood transfusion as a mode of treatment while 75(31.3%) did not accept attributing it to reasons such as transmission of HIV infection, religious background. The study done in Benin showed that 324(83.3%) of the respondents agreed that they would accept exchange blood transfusion as a treatment for NNJ.8

CONCLUSION AND RECOMMENDATION

In conclusion, the study revealed that mothers attending clinics in the University of Nigeria Teaching Hospital, Ituku-Ozalla, had a relatively high level of awareness of neonatal jaundice, but borderline knowledge of the condition. The following recommendations are hereby made:

Seeing that knowledge gaps existed among the respondents, the primary and major tool for combating this is IMPROVED HEALTH EDUCATION, which would involve;

* The mass media being used actively as part of the health communication plan (seeing that the mass media played very little role in the dissemination of information from the study). This has the advantage of reaching a large number of persons, in addition to providing continuing reminders and reinforcement.
* The Church and religious centers being involved in educating the mothers and fathers on the symptoms and signs of NNJ, seeing that from the study they played very little role in doing this. We also know that in many places messages carried by them are believed.
* Hospitals and health facilities intensifying their work on educating mothers, with special attention to clarifying misconceptions on the use of sunlight exposure and glucose water/drink in treating jaundice. Other important causes of neonatal jaundice other than malaria (blood group incompatibility; G6PD deficiency - where camphor balls could be a precipitating factor for jaundice in this group) should be aware to the mothers. Pictures depicting the hazards of practicing wrong forms of treatment should be displayed in the hospital.

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PERCEPTION, ATTITUDE AND PRACTICE OF CERVICAL CANCER SCREENING AMONG HIV-POSITIVE WOMEN IN ENUGU STATE

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INTRODUCTION

Cervical cancer is the commonest genital tract cancer and has most of its burden in developing countries where according to WHO 2008, there were more than 530,000 new cases of cervical cancer worldwide and over 90% of the cases were recorded in developing countries [1]. Majority of the cases present in the late stages when available treatments are ineffective. The scenario is entirely different in developed countries where cervical cancer has been reduced as a result of efficient cervical screening programme. This is because it has been identified that no form of cancer better documents the remarkable effects of screening, early diagnosis and curative therapy on the mortality rate than does cancer of the cervix [2]. The value of cervical cancer screening in reducing the risk of cervical cancer and mortality has been established and the risk of developing cervical cancer can be reduced by 80% through regular screening [3]

Several studies show that HIV positive women have increased risk of developing cervical cancer [4,5,6]. In sub-sahara African countries where HIV is pandemic, cervical cancer has become a major public health challenge. This forms the basis for our study.

DEFINITION OF TERMS

Cervical cancer: Is a malignant neoplasm arising from cells originating in the cervix uteri [7]

* *Cervical screening:* Is a way of preventing cervical cancer from developing, and diagnosing the disease at an early precancerous stage. There are several methods of cervical screening [7]

* *Papanicolaou test:* Also called Pap smear, Pap test, cervical smear or smear test. It is the commonest cervical screening used to detect potentially precancerous and cancerous process in the transformation zone of cervix. The test was invented by and named after the prominent Greek doctor; GeorgiosPapanicolaou[7]

* *Transformation zone:* This is a zone where the epithelium of the uterus (columnar epithelium) and that of the vagina (non-keratinized stratified squamous epithelium) meet. The zone is constantly changing due to hormonal change. The transformation zone is the site where pre-malignancy and malignancy develop (Gynaecology by Ten Teachers) [7]

* *Human Papillomavirus (HPV)*: Is a virus from papillomavirus family that is capable of infecting humans. [7]

* *Human Immunodeficiency Virus (HIV):* Is a lentivirus (slowly replicating retrovirus) that causes acquired immunodeficiency syndrome (AIDS) a condition in humans in which failure of the immune system allows life threatening opportunistic infections and cancer to thrive. [7]

PREVALENCE

Globally, cervical cancer is the 5th most common cancer in women with approximately 471,000 new cases diagnosed each year. Several studies have established that 80% of the new cases of cervical cancer are in developing countries [4]. In Nigeria, the burden of cervical cancer is unknown mainly because of lack of statistics or under-reporting [8]. After a study by Ugwu E.O et al at UNTH Enugu between 2000 - 2009 on the Pattern of Gynaecological cancer in UNTH Enugu Southeastern Nigeria, cervical cancer was by far the commonest gynaecological cancer constituting 78% of all the cases [9]

In a Northern American multi cohort collaborative prospective study by Alison G et al done on the incidence of cervical cancer among HIV positive women, the incident rate for HIV positive and HIV negative women were 26 and 6 per 100,000 person –years respectively[10]. This also agrees with the work by Dim et al at UNTH Enugu, on the Prevalence of Cervical Squamous Intraepithelial Lesion among HIV positive women in Enugu, Southeastern Nigeria between December 2007 and March 2008 using HIV negative women control. The prevalence for HIV positive and HIV negative women were respectively 12.6% and 4.6%. [11]

AETIOLOGY/RISK FACTORS

Several studies show that over 99% of cervical cancer is due to the human papilloma virus. However, Haverkos H.W in his work on Multifactorial etiology of cervical cancer; A Hypothesis, reported that HPV can be found in a growing population of patient with cervical cancer approaching 100% but is not found yet in every patient with the disease [12]. This shows a multifactorial cause for cervical cancer. Other risk factors

include [7]:
Having sex at an early stage
Having other sexually transmitted infections
Multiple sexual partners
Smoking
Long term use of contraceptive pills
Having a weaken immune system

BACKGROUND TO THE RESEARCH PROBLEM

The incidence of cancers was common before the HIV epidemic in some African countries but their incidence increased dramatically with rise in the national HIV prevalence [13]. The association between HIV and invasive cervical cancer is complex with several studies now demonstrating an increased risk of pre- invasive cervical lesion among HIV infected women. The reason identified for this increased burden of cervical cancer on HIV positive women is immunosuppression leading to HPV- HIV coinfection [7]. Despite the fact that more than 80% of cervical cancer cases are in developing countries, only 5% of women there have ever been screened for cervical abnormality (WHO 2006).[1]

SCREENING METHODS

The main aim of the screening is to detect the premalignant lesion. Screening and early detection helps in reducing the mortality due to cervical cancer. The following methods are commonly used:
Conventional cytology (Pap smear): This is regarded as the gold standard in developed countries [14]. The sample collected are smeared and viewed under the microscope. It has about 72% sensitivity and 94% specificity.[14]
HPV – Testing: The sensitivity ranges from 88% to 97% and specificity is about 73% to 93% [14]
Visual Inspection: In areas where Pap smear screening is not available or affordable, visual inspection of the cervix using acetic acid (VIA) is used. This gives acetowhite which indicates the malignant cells. Also Lugol's iodine can also be used for visual inspection (VILI) and precancerous lesion can be seen with naked eyes. Sensitivity of VIA has been shown to be between 47-62% [14]. VIA offers significant advantages over Pap smear in low resource setting particularly in terms of increased screening coverage, improved follow up and requirement of fewer specialized personnel and less infrastructure. With VIA, Public Health systems can offer cervical screening in more remote and less equipped health care settings and achieve higher coverage [14].

METHODOLOGY

This study was a descriptive cross-sectional survey that was conducted at AIDS Preventive Initiative in Nigeria (APIN clinic) of University of Nigeria teaching hospital Ituku/Ozalla, Enugu State.The study area was chosen using simple random sampling, a type of probability sampling method .APIN clinic was formerly known as President Emergency Plan for AIDS Relief (PEPFAR clinic).The hospital is located in Nkanu West local government area of Enugu State. Enugu State is one of the pioneer tertiary health centre and leading hospital in Southeast Nigeria. It is one of the few designated by the federal government of Nigeria for management of people living with HIV/AIDS and it offers free antiretroviral therapy.

The adult antiretroviral clinic of the hospital was started on February 2002 and is fed by VCT clinic as well as referrals from other health institutions. The hospital is the only government hospital within Enugu State that has functional voluntary counselling and Testing (VCT) clinic and is the personnel training site for few other VCT sites in the state and beyond.

Formal approval for the study was obtained from the Research Ethics Committee of University of Nigeria teaching hospital Ituku/Ozalla. Participation of the patients was voluntary and only those who give consent after the purpose of the study has been explained to them participated in the study.

RESULTS

Here is the analysis of the result carried out on the Perception, Attitude and Practice of cervical cancer screening among 150 HIV positive women attending APIN clinic.

The result obtained from this study showed that there is an increasing practice towards cervical cancer screening among HIV positive women compared with previous studies.

		Respondents	Percentage(%)
Age(years)	21-24	7	4.7%
	25-29	29	19.3%
	30-34	41	27.3%
	35-39	26	17.3%
	40-44	20	13.3%
	45-49	7	4.7%
	50-54	9	6.0%
	55-59	4	2.7%
	>59	7	4.7%
TOTAL	**150**	**100%**	

Marital status	Married	86	57.3%
	Single	28	18.7%
	Divorced	0	.0%
	Widowed	33	22.0%
	Separated	1	.7%
	Co-habiting	2	1.3%
TOTAL	**150**	**100%**	

Occupation	Teacher	15	10.0%
	House wife	17	11.3%
	Civil servant	21	14.0%
	Trader	53	35.3%
	Doctor	1	0.7%
	Health worker	1	0.7%
	Others	42	28.0%
TOTAL		**150**	**100%**

Employment status	Employed	32	21.3%
	Unemployed	49	32.7%
	Self employed	68	45.3%
	Pensioners	1	0.7%
TOTAL		**150**	**100%**

Highest level of education	No formal education	9	6.0%
	Primary education	46	30.7%
	Secondary education	70	46.7%
	Tertiary education	25	16.7%
TOTAL		**150**	**100%**

TABLE 2
PARTICIPANTS RESPONSE ON DIAGNOSIS OF HIV

When were you diagnosed of HIV?	Respondents	Percentage (%)
2-4 years ago	60	40.0%
5-7 years ago	35	23.3%
8-10 years	29	19.3%
Others	26	17.3%
TOTAL	150	100%

40% of the women were diagnosed of HIV 2-4 years ago.
Others here include those tested within this year and above10 years.

TABLE 3: KNOWLEDGE OF CERVICAL CANCER AMONG HIV POSITIVE WOMEN IN ENUGU

Are you aware of cervical cancer?	Response	%
YES	54	36%
NO	96	64%
TOTAL	**150**	**100**

TABLE 4: KNOWLEDGE OF PAP SMEAR TEST AMONG HIV POSITIVE WOMEN IN ENUGU

Have you heard of Pap smear test?	Respondents	%
YES	35	23.3%
NO	115	76.7%
TOTAL	**150**	**100**

TABLE 9: CERVICAL CANCER IS MORE COMMON TO WOMEN WHO ARE HIV POSITIVE

	Respondents	%
Strongly agree	9	6.0%
Agree	12	8.0%
Not sure	97	64.7%
Disagree	15	10.0%

TABLE 10 WOMEN WITH MULTIPLE SEXUAL PARTNERS ARE MORE PRONE TO CERVICAL CANCER

	Respondents	%
Strongly agree	25	16.7%
Agree	15	10.0%
Not sure	89	59.3%
Disagree	17	11.3%

TABLE 6: PRACTICE OF CERVICAL CANCER SCREENING

Have you done cervical cancer screening?	Respondents	Percentage (%)
YES	8	5.3%
NO	142	94.7%
TOTAL	**150**	**100**

TABLE 11 PARTICIPANTS RESPONSE ON THE REASON WHY THEY HAVE NOT DONE PAP SMEAR DESPITE BEING AWARE

	Count	%
Couldn't afford it	9	32.1%
Fear of the result	6	21.4%
Don't feel susceptible to Cervical cancer	6	21.4%
No doctors request	5	17.9%
Religious belief	2	7.2%
TOTAL	28	100

Out of the 28 respondents who know about pap smear and have not done the test despite being aware, one respondent had two reasons for not doing the test

Table 12: ATTITUDE OF SUBJECTS TO CERVICAL CANCER SCREENING

Attitude to cervical cancer screening	Respondents	%
Willing	128	85.3%
Not willing	22	14.7%
TOTAL	150	100

Table13: PARTICIPANTS REASONS FOR DOING THE TEST IF AVAILABLE AND ACCESIBLE

	Respondents	%
To know if i have the cancer	106	82.8%
For health purpose	17	13.3%

Table 14: PARTICIPANTS REASONS FOR AVOIDING THE TEST EVEN WHEN AVAILABLE AND ACCESSIBLE

	Respondents	%
Don't think i have it	6	27.3%
I don't wish to have it	2	9.1%
Extra burden	4	18.2%
Have done cervical surgery	2	9.1%
Fear of the result	8	36.4%
TOTAL	22	100%

DISCUSSION

Data from 150 subjects seen at the APIN clinic UNTH were collected and analyzed using SPSS.

The age distribution showed that more of the respondents were women between the ages of 30-34 years. Out of 150 respondents 148 (98.7%) were Christians and majority were married. The highest level of education of majority of the respondents (46.7%) was secondary education while 9 (6.0%) had no formal education. This is in line with works of Dim et al in which 43.8% of the respondents had secondary education while 11.5% had no formal education18.

The study showed that 36% of respondents were aware of cervical cancer and 23.3% (35) of the respondents were aware of pap smear. This finding does not agree with the works done by Dim et al and Rabiuinq which 2.8% and 16% of respondents respectively were aware of pap smear 18,5. 27 out of 35 respondents (77.1%) had not done the pap smear test despite being aware . this does not correspond with the results of the work done by Rabiu in which 68.75% of the respondents had not done the pap smear test despite being aware (5)

Of these respondents, cost hindered (33.3%) from doing the test. This agrees with the work by Ezechi et al in which 35.2% of the respondents did not do the test because of cost.

Also, 22.2% of the respondents who had not done the test despite being aware attributed it to fear of the result, reaffirming the work by Collins Wamosa of Kenya in which 22. 1% of the respondents had not done the test due to fear of the result . 7.4% of the respondents had not done the test despite being aware because of their religious belief which is not in keeping with the study by Ezechi et al in which 14% of the respondents had not done the test due to their religious belief (6)

From the study, 128 (85.3%) of the respondents were willing to do the pap smear test. However, in separate works done by Ezechi et al and Dim et al 79.5% and 96.0% of the respondents respectively were willing to do the test (6,4)

Out of the 22 (14.7%) respondents who were not willing to do the pap smear test, 8 (36.45) attributed it to fear of the result while others gave their reasons as 'extra burden" (18.2%) "Don't think 1 have it" (27.3%) , "don't wish to have it" (9.1%) and I have done cervical surgery" (9.1%)

Finally, 5.3% (8) of the respondents have had cervical screening done which respondents 22.86% of the respondents that were aware of cervical screening test. 94.7% (142) respondents have not done the pap smear test. However , studies done by Ezechi et al and Dim et al showed that 9.1% and 9.4% of respondents respectively who were aware of cervical cancer, screening had done the pap smear test .

Of the 8 respondents who had done pap smear test, 7 (87.5%) were done based on doctor's recommendation although in a related work by Rabiu et al 12.5% of the pap smear tests were recommended by doctors.

CONCLUSION AND RECOMMENDATIONS

In conclusion, the study revealed that most HIV positive women are not aware of cervical cancer and cervical cancer screening. nonetheless, very few HIV positive women have done the test for cervical cancer screening. Cost and the fear of the result were the major limiting factors for not doing the test among the few women who were aware of the pap smear tests. However 128 (85.3%) of the respondents were eager to undertake the test if facilities are available and accessible

Based on our findings, we recommend that:

- Awareness campaign on cervical cancer and cervical cancer screening should be intensified among HIV positive women via mass media, seminars, etc
- Cervical cancer screening should be included as a routine test for HIV positive women
- Cost of cervical cancer screening should be subsidized by the government and donor agencies to enhance the practice
- Pre and post cervical cancer screening counseling should be done to reduce the fear of outcome of the result.
- Other cheaper methods of cervical cancer screening such as visual inspection using Acetic acid and Lugol's iodine should be promoted
- More health personnel's should be recruited and trained on skills required for carrying out cervical cancer screening

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NUTRITIONAL ASSESSMENT OF CHILDREN AGED 6-12 YEARS IN A RURAL AREA IN ENUGU STATE

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ABSTRACT

Nutrition is a fundamental pillar of human life health and development across the entire life span. From the earliest stages of fetal development, at birth, through infancy, childhood, adolescence, and into adulthood and old age proper food and good nutrition are essential for the survival, physical growth, mental development, performance and productivity, health and well-being.
(FAO/WHO;1992 WHO,2000)[1].Nutritional status shows the balance between the intake of nutrients and expenditure of energy from these nutrients. An imbalance results in over nutrition or under nutrition. The study was conducted in Akegbeugwu community in Nkanu west LGA of Enugu state. A total of 262 questionnaires were collected and analyzed using the statistical package for social sciences (spss) 17.0 version. A total of 262 school children (male 52%, females 48%) were involved in the study. The mean values of measured attributes were age 7.33years, weight 28.12kgheight 126.43cm. The dietary intake of the subjects showed that carbohydrates formed the largest portion of (52%) of the dietary intake of the children on daily basis. About 23.13% of children were able to complement their carbohydrate intake with proteins and 7.2 % included fats and oil. Proteins made up the bulk of the deliberately denied food (20.9%). The socioeconomic attributes of the parents (fathers) of the selected children showed that the majority of them (27.1%) were farmers followed by traders (13.0%) and civil servants (10.7%); others included vocational and manual workers and those that have no specific socioeconomic activities. Majority of the test children parents were of the socioeconomic class 111b.

In conclusion, the anthropometric results show that the mean height for age and weight for age values of the majority of children were within the normal range when compared with the CDC and WHO reference standards(within +2SD and -2SD of the mean of the reference population). No specific signs of micronutrient deficiency or severe protein energy malnutrition were found on physical examination. The prevalence of acute malnutrition among children aged 6-12years in Akegbeugwu from our study was 2.67% while that of chronic malnutrition viz a viz stunting was 1.91%.

Though the result suggested that the prevalence of malnutrition is very low in the study area, there is still need for public health measures(health education, women empowerment, food supplementation) to improve the nutritional status of children especially in the rural areas.

INTRODUCTION

Evidence have shown that physical growth and cognitive development in children are faster during early years of life, and that by the age of four years, 50% of the adult intellectual capacity has been attained and before thirteen (13) years, 92% of adult intellectual capacity is attained.

World nutrition day-'right to food' is on 16th October of every year. It is an occasion which has brought about an understanding of this topic which unites everyone on this planet.

STATEMENT OF THE PROBLEM

Forbes (1987) estimated that over 40 million children worldwide are malnourished, while WHO (2002) and FAO (2004) estimated that 852 million people are malnourished worldwide with most (815 million) living in developing countries[2]
Evidence has shown that 4% of the total children born in developing countries die of malnutrition before they are five (5) years old and that most affected are usually children of illiterate parents in low socioeconomic brackets that have low purchasing power in the economy[3]. It is also very common in conditions of severe famine ,drought, war, civil unrest and may be due to lack of knowledge on part of mothers who are the care givers.
At the millennium summit in September 2000, the United Nations re affirmed its commitment to working toward a world in which sustaining development, eliminating poverty and hunger would have the highest priority. Nutritional problems certainly creates a huge human and economic concern.

RATIONALE OF THE STUDY

There are several studies investigating the problem of malnutrition amongst children in different parts of Nigeria. However, scanty information exist regarding malnutrition amongst children living in rural areas in Enugu.
Furthermore, most previous studies are focused on children under five (5) years in neglect of school age children.
The present study evaluates the prevalence and cause of under nutrition and/or over nutrition among children aged 6-12 years living in a rural community in Enugu. We think that such data are essentially important from public health standpoint as they would provide reliable basis for instituting appropriate strategies to identify and combat factors associated with nutritional abnormalities in children.

LITERATURE REVIEW

A good number of studies abound to show the extent to which the world and by extension Nigerian children are suffering from malnutrition and hunger;
-according to Geoffrey Njoku et al, Nigeria has the 4th highest number of underweight children in the world (behind India, Bangladesh and Pakistan.)
-Geoffrey in the same work categorically stated that there are estimated to be over two million children suffering from severe and moderate acute malnutrition in the country (Nigeria) and most of them are in the north[4].
In addition to this mind bugging statistics Karen Allen in July 2012 estimated that one in 7 children won't survive to see their fifth birthday in Nigeria and malnutrition is a huge factor[5].
In 2008, Nigeria demographic and health survey recorded that about 19% of the children in the North West zone were acutely malnourished (13.9% in national average) and required outpatient therapeutic care in the course of a year[4].
In a work done by Agbanu Emeka evaluating PEM in Enugwu Ukwu general hospital from (1985-1990), he found that out of 12,781 children admitted during that period, protein energy malnutrition cases numbered 470(3.68%)of the total patients admitted. The highest incidence from his study occurred between the months of June and august; the results also showed that more males than females suffered from PEM. The ratio is 2:1; male: female ratio respectively. The study also revealed the role of position In the family on the incidence of PEM as 91 children (19.36%) affected were 1st born in their families, 54 children (11.49%) in the middle birth order and 325 children (62.15%) were last born[6]. Another study done by Sebanjo et al in 2007 done in a rural Nigerian community showed the prevalence of protein energy malnutrition to be 20.5%[7].
Even more distressing is the discovery that worldwide the scourge of malnutrition is still raging as rural poverty portal declares over 800 million people go to bed hungry every day including 300million children and every 3.6sec, a person dies of starvation and most of those who die are children under age 5, while every year 6 million children die from malnutrition before their 5th birthday[8].

OBJECTIVES OF THE STUDY

1. To determine the prevalence of malnutrition in school children in the area.
2. To find out the feeding habit of children in the rural areas.
3. To establish the relationship between socioeconomic classes, parents educational level and nutritional status.
4. To ascertain the effect of position in the family and family size on the nutritional status of children.

METHODOLOGY

Children aged between 6-12 years in Akegbeugwu community, Nkanu West L.G.A, of Enugu state. The study was a descriptive epidemiological study also known as a survey study. An estimated sample size of 275 was gotten. The selected children were administered questionnaire (interviewer administered questionnaire), several physical parameters were accessed and the parents were also interviewed. Instruments used included bathroom scale calibrated rule, questionnaire, pen touch and calipers

RESULTS AND DISCUSSION OBJECTIVE 1

The study showed that the prevalence of under nutrition was 2.67% while the prevalence of over nutrition was 0%, while the prevalence of stunting was 1.91% and gigantism was 1.14% using WHO and CDC growth charts and 3rd and 97th percentile as cut off.
It is clear from the above stated valued that the prevalence of

malnutrition in children aged 6-12 years in Akegbeugwu where we studied is very low. This is not totally strange as a previous study by Sebanjo I.O et al 2007 discovered that the prevalence of under nutrition, wasting and stunting in the rural area they studied were 23.1%, 9% and 26.7% respectively. Our values though were much lower than theirs ,we suppose that the variance might indicate that standard of living of an average Nigerian rural dweller has increased over the past five years or that the rural area we studied are actually more developed than theirs.
This result also proves that residence in a rural area does not necessary imply paucity of food or a high prevalence of malnutrition because as a matter of fact these foods are produced in large quantities in rural areas and all that is needed is an enlightened/informed rural dweller for the nutritional needs of children to be met.

OBJECTIVE2
From our study, children ate mostly carbohydrate which accounted for 51.1% of breakfast 50.7% of lunch and 53.4% of dinner. This was comparable to a study by Okeke E.C 1996, where he found starchy staple food were mainly consumed by 100% of the respondents.

From our study children that ate carbohydrate+protein+fat and oil in the morning had the highest height as their average height was 1.34m and compared to those that ate only carbohydrate whose average height was 1.31m thus confirming the importance of food variability.

Also from our study protein constituted approximately 4.92% of breakfast, 6% of lunch and 2.2% of dinner, but constituted 20.9% of foods deliberately denied. This might not be unconnected with beliefs that proteins make children become thieves.

OBJECTIVE3
From our study, 90% of test children mothers and 89.2% of test children fathers were of the class 111b-V level of social stratification using the classification by the department of preventive and social medicine, institute of child health university of Ibadan.

Also from our study, there seemed to be a better correlation between mother's socioeconomic status and weight and height of their children compared with that of fathers. childen that have mothers as civil servant weighed 19% more than children of the least weighed occupational group, whereas children whom their fathers were civil servants weighed 12% more than children of the least weighed occupational group.

OBJECTIVE 4
From our study there was no correlation between nutritional status and academic performance.

OBJECTIVE 5
We noticed that the middle birth order (3rd to 4thPOSITION) lagged behind in weight and height when compared to other birth orders.

SUMMARY
In summary, we have been able to ascertain that the prevalence of under nutrition was low, about 2.67% of children in the area, the children ate more of carbohydrate containing food. Protein was the most common food taboo.
Some of the factors the study noted to influence malnutrition includes food variability, socioeconomic class of parents especially that of mothers and position in the family.
We did not find any relationship between poor nutritional status and academic performance, number of siblings, and deworming activities.

RECOMMENDATION
1. Health education to convey the information of the importance of food variability on nutritional status of children.
2. Government should empower women in order to improve their socioeconomic status and the way the society view them since women are very important in achieving our aim of ensuring adequate nutrition in children.

ACKNOWLEDGMENT
We acknowledge God's guidance during the course of this study. We want to express our heartfelt gratitude to our parents for providing us with emotional and financial support, our project supervisor Prof D.F.E Nwagbo for his untiring efforts and directives throughout the course of this work.

We will also like to thank the staff of community central school Akegbeugwu and central primary school Akegbeugwu, and the staff of Augustine Nnamani library UNTH oldsite. Finally, we appreciate Miss Okechukwu Chidubem and Miss Amaka Okafor for their assistance in the field work.

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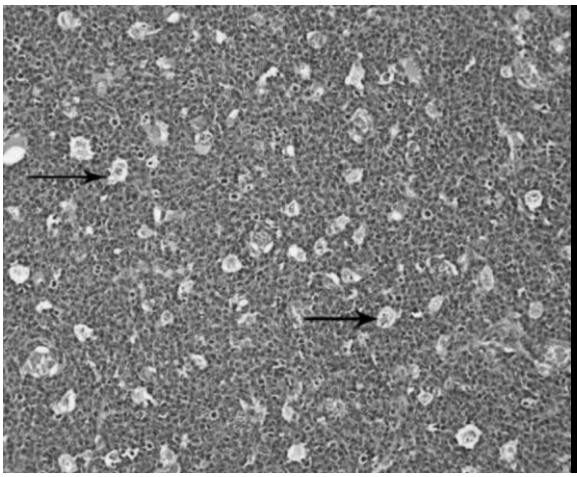

A TYPICAL AFRICAN BURKITT LYMPHOMA CASE IN AN 8-YEAR OLD NIGERIAN GIRL PRESENTING WITH MULTIPLE JAW TUMORS AND ABDOMINAL MASSES - A case report.

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ABSTRACT
Burkitts lymphoma is named after Denis Person Burkitt, who mapped its peculiar geographical distribution across Africa1.It's a high grade monoclonal B-cell neoplasm and has two major forms, the African form and the non-endemic (sporadic) form. It's also a childhood neoplasum, which is seen in adult patients1. The African form most often involves the maxilla and the mandible. The involvement of the abdominal organs, such as the kidneys, ovaries, or retroperitoneal structures, is slightly less common. In contrast, the sporadic form usually involves abdominal organs, the most common involvement being the distal ileum, caecum, or mesentery and less common involvement of other abdominal organs, pelvic organs and facial bones1.
We present a case of an 8year old Nigerian girl who was seen in our pediatric oncology department on 19/04/2005 with complaints of toothache, jaw swelling, and eye swelling all of one-week duration. Fine needle aspirate cytology confirmed a Burkitts lymphoma. She was commenced on cytotoxic chemotherapy as appropriate with dramatic results, after the first course.

KEY WORDS Burkitts
Lymphoma, Multiple facial /jaw masses, Females, Types, African Burkitts, Sporadic, Fine needle aspirate cytology.

CASE REPORT
We present an 8year old Nigerian female who was seen in our pediatric oncology unit on 19/04/2005.with complaints of
(1) Toothache 1/52.
(2) Jaw swelling 5/7
(3) Eye swelling 5/7
The patient was well until a week prior to presentation when she developed toothache, which was gnawing in nature, intermittent, non-radiating, worse at night and relieved by analgesics. The pain was severe enough to disturb her sleep. Two days later the patient also developed a swelling on the right jaw and left eye. The jaw swelling was initially small but progressively increased to about thrice its original size within the next five days. There was an associated history of loosening of teeth, the left eye swelling was also associated with redness and mucoid nasal discharge. She first presented at the state specialist hospital from where she was referred to us for definitive management.
On examination she was acutely ill looking, pale, there was a generalized lyphadenopathy involving the submandibular, axillary, inguinal, and cervical groups of nodes, all of which were firm, non-tender, mobile and measured 1cmby 1cm.
Eye: Purulent discharge from both eyes, proptosis of the left eye.
Mouth: Loose right upper incisors and canines. Swelling over the maxilla 8cm by 8cm in the largest diameter, firm, non-tender, non-erythematous, immobile, not attached to over lying skin. Swelling over the left maxilla is about 6cm by 8cm firm, non-tender, immobile, not attached to overlying skin.
Central Nervous System: Conscious and alert. Neck supple, Tones and reflexes were all normal.
Cardiovascular System: Pulse rate 104/min, regular moderate volume, Heart sounds S1, S2
Chest: Respiratory rate 26/min, Trachea central, Percussion note –resonant. Breath sounds vesicular.
Abdomen: Full and tense, Hepathomegaly of 5cm,firm, non-tender. Spleen 8cm, Kidneys not palpable.

ASSESMENT: Burkitts Lymphoma Stage D.

INVESTIGATIONS DONE
(1) Abdominal ultrasound scans.
(2) Full blood count.
(3) Electrolytes /Urea /Creatinine in Blood.
(4) Fine Needle Aspirate Cytology.
The child was subsequently placed on antibiotics and analgesics.
Abdominal Scan Result. Normal liver, pancreas, kidneys, multiple hypoechogenic foci in the spleen and Para aortic regions suggestive of multiple lyphadenopathies. Conclusion was abdominal lymphoma with infiltration of the spleen and Para aortic nodes.

Electrolyte/Urea result.
Urea 8mg/dl. Sodium 132mmol/l, Potasium 3.3mmol/l, cloride 95mmol/l, Bicarbonate20mmol/l.
Full Blood Count Result. Packed Cell Volume 35%, Mean Corpuscular volume 85fl,Mean Corpuscular Hemoglobin Concentration 32%, Mean Corpuscular hemoglobin 27pg,Platelets 876,000/ml, White Blood Cell Count 10,100/ml, Neutrophils 71%, lymphocytes21%, others 8%.
Fine Needle Aspirate Cytology Result See picture 1showed typical starry sky patterns, with proliferation of uniform intermediate sized lymphocytes having multiple nucleoli, punctuated by normal macrophages.
She was placed on
(1) Cyclophosphamide 1mg/m2 .850mg Day 1.
(2) Oncovin 1.2mg/m2. 1.22mg Day 1.
(3) I.V.Methotrexate 15mg/m2 13mg/day. Days 2and 3.
(4) Tabs Prednisolone 40mg/m2.for 5/7translating to 20mgmorning, 10mg noon, 10mg nocte. daily for 5/7.
(5) Intrathecal Methotrexate 15mg/m2.13mgDays 1and 4.
Before discharge facial masses were markedly reduced and cytotoxic drugs were well tolerated without tumor lysis syndrome. Proptosis was also almost completely abated. See pictures 2 and 3, which were pictures of the patient before and after chemotherapy.
Abdomen was full soft with hepatomegaly receding to 4cm,spleen was just tipped.
Another assessment of Burkitts Lymphoma in remission was made following response to chemotherapy.

DISCUSSION

Typical African Burkitts lymphoma involves the maxilla and mandible as in this case. The involvement of the para aortic nodes as well as the spleen and liver shows that the disease was not an early presentation contrary to the impression given by the history. This is typical of most malignancies presenting our environment because of poverty, ignorance and inaccessibility of good health care facilities. The gut was characteristically spared. Burkitts Lymphoma appears to be endemic in our environment where the mean age of presentation is about 7years1.Exact figures in our environment is not well established, but studies are currently going on in this respect.
Burkitts lymphoma is a very fast growing tumor. Systemic chemotherapy is the treatment of choice for this aggressive disease in all its stages. The overall survival rate of Burkitts lymphoma depends upon the stage of the disease at initial diagnosis. In this case bone marrow biopsy was not done as an initial assessment, which is a major factor in staging and prognosis, as involvement carries an obvious poor prognosis. This was presumably to avoid further delay in the face of obvious ultrasonographic evidence of abdominal involvement. Patients with localized disease responds well to chemotherapy and also have an excellent survival rate. Patients with disseminated disease respond less well to chemotherapy and have less favorable survival rate. So far this patient has done well despite her advanced disease and has just had her second course of chemotherapy without sequaele. Both spleen and liver were normal in size and all facial masses have completely resolved.
Cyclophosphamide therapy alone has been curative for 80% of children from Africa with localized early stage disease. However, combination chemotherapy as in this case has markedly improved treatment results, especially in patients with extensive disease. Short -duration intensive, alkylator based mutagenic reagents are necessary for patients with extra nodal tumors and for all patients with the sporadic form of the disease. Of particular importance is the rapid administration of several cycles to prevent tumor regrowth2, 3.For patients with extensive disease, a long term survival of 70%-80% can now be achieved with intense chemotherapeutic regimens.

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Figures below shows patient before and after treatment.

HAEMOPHILIC EMERGENCIES IN CHILDREN

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INTRODUCTION

Emergency conditions could occur in both children and adults. We commonly discuss this in children because they are peculiar regarding emergencies in haemophilia. They may be the first index case in a family lineage and as such no preventive or anticipatory management may be put in place leaving them at risk of bleeding into dangerous sites resulting in life-threatening manifestations. This is commonly seen during delivery when traumatic or instrumental delivery may result in intracranial bleed. Those that were already known haemophiliacs, because they are children may not be able to restrain themselves from traumatic play activities commonly seen in children with potential risk of bleed into dangerous sites. All these put children with haemophilia at risk of emergencies.

DEFINITION

Haemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII) (in haemophilia A) or factor IX (FIX) (in haemophilia B). Some books still describe haemophilia C which is deficiency of factor XI. The deficiency is the result of mutations of the respective clotting factor genes.

Overview of Haemostasis

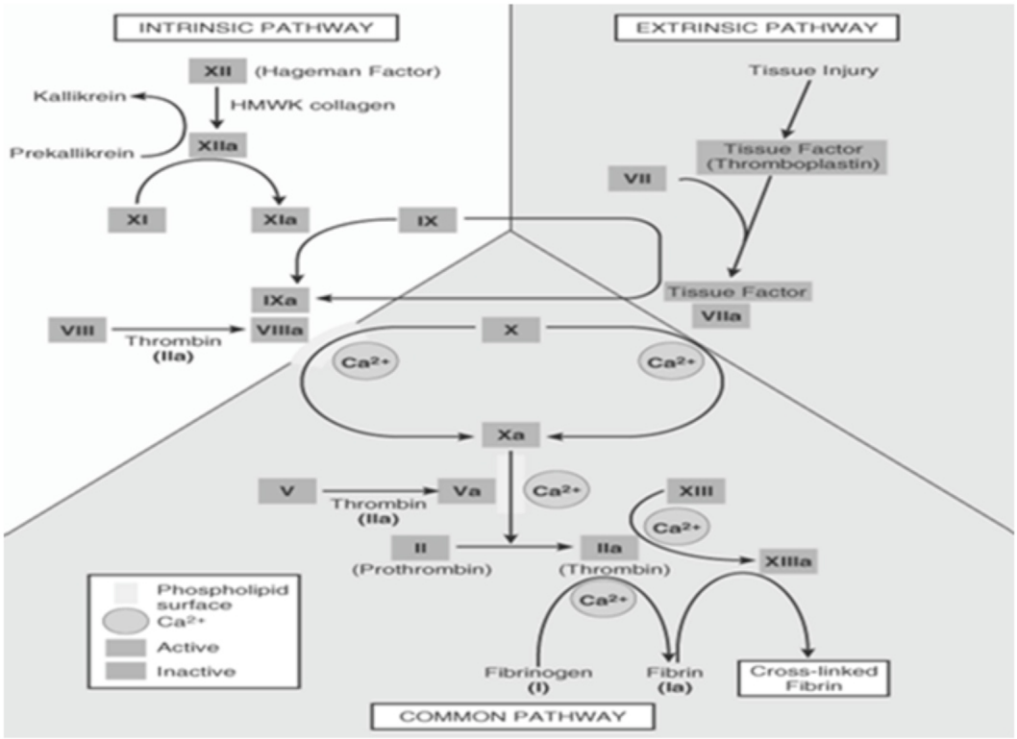
To understand haemophilia (which is a bleeding disorder caused by deficiency of coagulation factor),it is needful to first understand how coagulation factors are important in the clotting process during injury. During a vascular injury, three factors are put in place to secure haemostasis and stop bleeding. In sequential order, these include:

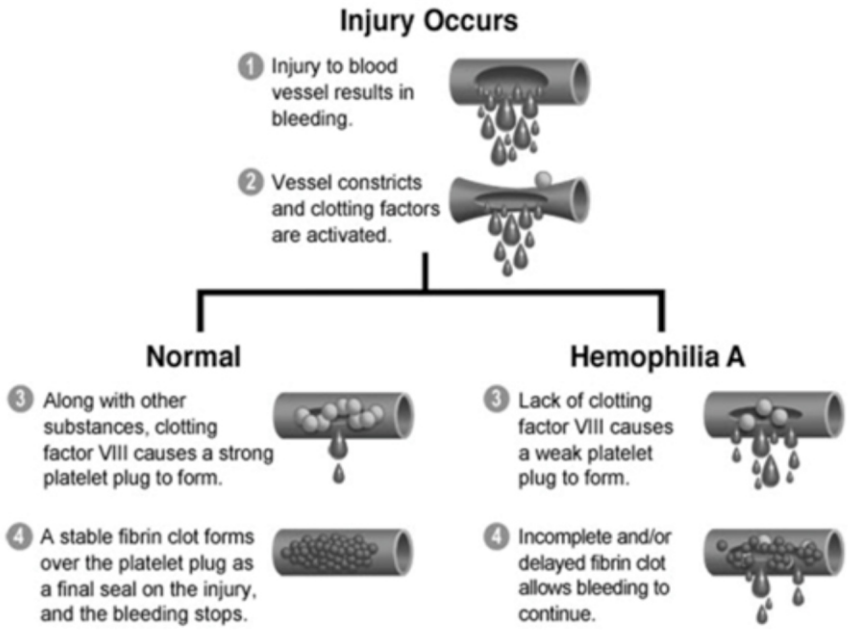
1. *Vascular factor:* Immediate constriction of an injured arteriole or a small artery mediated by sympathetics and catecholamines.

2. *Platelet factor*: Exposure of sub-endothelial matrix encourages adherence of platelets These become activated releasing serotonin, adenosine diphosphate (ADP), von Willibrand factor (vWF) resulting in formation of loose plug of aggregated platelets. (Primary haemostasis)

3. *Coagulation factor*: Fibrin formation via coagulation cascade adding to the loose platelet plug. (Secondary / Definitive haemostasis)

The first two factors are commonly seen in every body including the haemophiliacs but they are not enough to completely stop bleeding except the secondary/definitive haemostasis occurs. However, in haemophiliacs, it is this definitive haemostasis that is defective because of deficiency of coagulation factors that are involved.





TYPES OF HAEMOPHILIA

• *Haemophilia A*: This is the second commonest inherited bleeding disorder occurring in 1:5000 male births due to deficiency of factor VIII. It accounts for 85% of haemophilias and is inherited as an x-linked recessive trait. Some cases arise as a result of spontaneous mutation.

• *Haemophilia B:* It is the third commonest inherited bleeding disorder after von Willibrand Disease and haemophilia A. It is due to deficiency of factor IX. Accounts for 10-15% of haemophilias and inherited as an x-linked recessive disorder.

The most obvious feature of haemophilia is bleeding/ haemorrhage. Severity is correlated with the plasma levels of active factor VIII and IX. The plasma levels for different levels of severity are as in the table below.

Severity	Clotting factor level
Severe	< 1 IU/dl (< 0.01 IU/ml) or < 1 % of normal
Moderate	1-5 IU/dl (0.01-0.05 IU/ml) or 1-5% of normal
Mild	5-40 IU/dl (0.05-0.40 IU/ml) or 5-<40% of normal

SEVERITY OF HAEMOPHILIA AND AGE OF ONSET

• *Severe haemophilia:* Onset is usually in the neonatal period or early infancy.

• *Moderate haemophilia*: Onset period is often 1-2 years.

• *Mild haemophilia:* Age of onset is 2years to adulthood.

SITES OF BLEEDING:

Bleeding can occur in different parts of the body depending on severity. The table below represents this as well as the percentage of occurrence at different sites.

HAEMOPHILIC EMERGENCIES

These are life-threatening bleeding episodes in haemophilia which require immediate treatment. They usually occur in severe and moderate haemophilia and rarely in mild haemophilia.

• In emergencies, treatment with factor should be initiated immediately, even before diagnostic assessment is completed.

Occurence in life-threatening episodes are:
CNS Haemorrhages which include Intracranial haemorrhages and Spinal haematoma

Other emergencies:

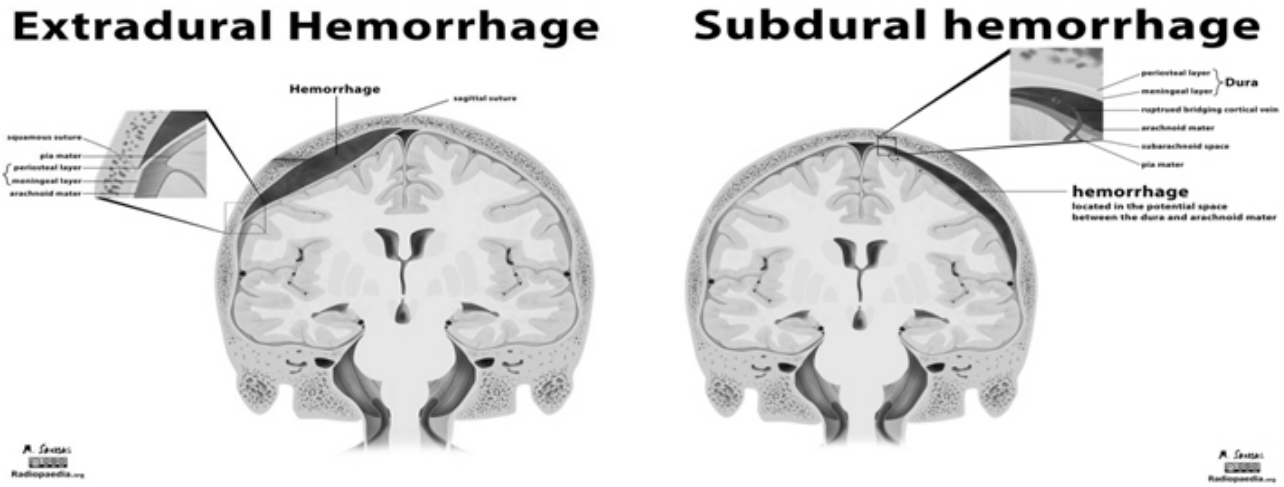
* Tracheal haemorrhages (neck and throat)
* Gastrointestinal haemorrhages
* Compartment syndrome & nerve compression
* Ophthalmic emergencies
* Pseudotumour rupture
* Rare (anaemic heart failure)

CNS haemorrhages

This is the most frequent emergency haemorrhagic event in haemophilia management and major cause of death in children. Sites involve Intracranial or spinal canal. The usual causes Trauma (recent or previous). In the neonates, it could be precipitated by traumatic or instrumental delivery. Trauma was the cause in 57% of a study in Germany (57% Klinge et al) and in 67.2% of another in France (Stieltjes et al). CNS haemorrhage can also occur spontaneously from a previous injured site or where there was an anatomic lesion (e.g. aneurysm, AV malformation).Risk factors for CNS haemorrhages include – HIV, inhibitors, age <5 years, thrombocytopaenia, hypertension.

Intracranial haemorrhages (ICH)

Prevalence in paediatric haemophilia population is 12% (including 'silent' cases [Nelson et al]); 4% in newborns (Ljung 2007). ICH can be subdural, epidural or intra-parenchyma. They all can cause rapidly deteriorating CNS function, oedema, herniation and sudden death. The degree of injury in ICH is volume & duration of bleeding-dependent. Intraparenchymal type can induce permanent structural and/or neurologic sequela



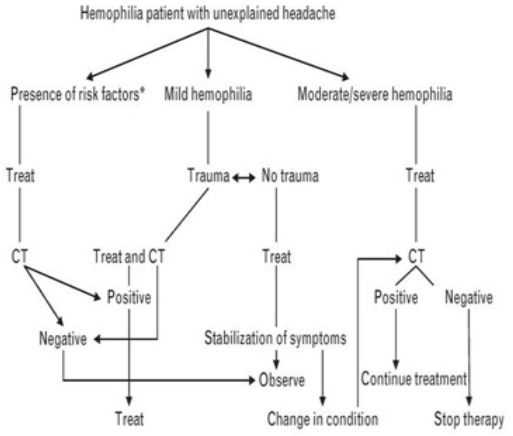
Clinical features of ICH

In the neonates – Features can be vague and simulate features of other neonatal conditions. Commonly seen features include- anaemia, lethargy, hypotension, and shock. Neurologic manifestations may also be seen including seizures and bulging fontanelle. Short or long-term sequelae may manifest relative to the severity of haemorrhage. Neonates pose a diagnostic challenge- As a third of newborns with ICH are new cases, these features may be wrongly interpreted unless the clinician has a high index of suspicion. For other children, They may be asymptomatic especially in subdural bleed. They usually manifest with headache, somnolence, vomiting and localizing signs. Appearance of localizing signs such as seizures, papilloedema, and visual disturbance are usually suggestive of an extensive bleed.

Investigations in ICH

- New mutations (new cases) with ICH -activated Partial Thromboplastin Time (aPTT),-factor VIII & Factor IX assay
- In suspected ICH –transfontanelle ultrasound
- Babies of carrier mothers – Non contrast CT
- Child with features of ICH – CT or MRI
- Child with head trauma or persistent headache – CT or MRI

In children 3-18 years with persistent or unexplained headache, the algorithm below shows steps in the evaluation.



Suggested algorithm for children (≥3–18 years of age). *Risk factors: presence of HIV, hepatitis C or inhibitors, age below 3 years, hypertension, decreased platelets. MRI is recommended as the ideal radiological investigation, if easily accessible.

Treatment of ICH

In intracranial haemorrhage, treat before evaluating. Treatment is done using clotting factor concentrate (VIII or IX). The treatment is based on 3 principles viz

a) Infuse enough factor concentrate to ensure a normal physiologiclevel initially (at least 100% within the normalrange).

b) Infuse frequently enough to ensure that the FVIII or FIX level never falls to a non-physiologic level (i.e., a minimum of 50%).

c) Monitor FVIII or FIX levels as frequently as feasibleto ensure that these physiologic levels are beingachieved.

Intracranial haemorrhage may be an indication for prolonged secondary prophylaxis (three to six months), especially where a relatively high risk of recurrence has been observed.

- surgically approachable sites (in particular subdural hematomas) should be evacuated through neurosurgical intervention. In which, there will be need for pre- and post- surgical factor concentrate infusion.

Spinal haematoma

Spinal haematoma following serious bleed may compress the spinal cord. Early recognition is important for admission and early

replacement with factor concentrate. Also, early intervention is important because it prevents the need for surgery and later spinal deformities in children. Without early intervention, most of them may require spinal decompression. After immediate replacement with concentrate, confirmation with imaging studies will later follow.

Treatment

The factor concentrate level of infusion in emergencies are same though over different durations depending on site as shown in the table below.

	Desired level (IU/dl)	Duration (days)
CNS		
•initial	80-100	1-7
•maintenance	30-60	8-21
Head and Neck		
•initial	80-100	1-7
•maintenance	30-60	8-14
Gastrointestinal		
•initial	80-100	1-7
•maintenance	30-60	8-14

Factors VIII & IX inhibitors

Inhibitors to factors VIII or IX usually develop in ICH and other life-threatening haemorrhages following prolonged infusion of these factors. These inhibitors are immunoglobins of IgG class and they neutralize the coagulant action of factor VIII or IX. The patient then responds suboptimally to the dose that used to produce coagulation effect. Any of these could be done in such situation:

• Use higher doses of factors
• Use bypass agents: rhFVIIa or activated prothrombin complex concentrate (aPCC)
• Increase FVIII level: achieved using desamino-D-arginine vasopressin (DDAVP) (desmopressin)

Neck and Throat haemorrhage

This is a medical emergency which can lead to airway obstruction. Haematoma formation in neck and throat trauma occurs in a cephalocaudal manner. As in other haemophilic emergencies, treat first before evaluation. Hospitalization & evaluation by specialist is important. Immediately raise the factor level & maintain the level until symptoms resolve.

Once the compression is sufficient to cause difficulty breathing, the window for infusion to stop the bleeding may be very narrow. As a result, early intervention is quite necessary. Tracheotomy may be needed terminally.

Gastrointestinal haemorrhage

Common sources include Duodenal ulcer (22%), gastritis (14%).Mallory-Weiss syndrome has also been implicated. Acute GI haemorrhage may present as haematemesis, haematochezia or melaena. Once these symptoms cause acute drop in haemoglobin concentration, the clinician has an emergency in his hand.

Routine factor concentrate replacement regimen is the rule in this situation. Appropriate diagnostic work-up is later instituted(typically endoscopy or colonoscopy) if the bleeding recurs after replacement therapy is withdrawn. For lower GI bleeding, ruptured AV malformation or aberrant vessels may be involved. In possible surgery, pre- and post- surgery factor replacement is required.

Acute abdominal haemorrhage

An acute abdominal (including retroperitoneal) haemorrhage in haemophiliacs can present with abdominal pain and distension. It may also present as paralytic ileus. Immediate factor concentrate should be given until aetiology is defined using appropriate radiologic studies. Appropriate consultation may be needful. Bleeding may be severe enough to require laparotomy and removal of injured abdominal organ.

Ophthalmologic haemorrhage

Usually, this follows trauma to the eye in a haemophiliac. Anterior or posterior chamber of the eye may be involved resulting in hyphaema, vitreous haemorrhage, haemorrhagic glaucoma, retinal detachment etc.It is an ophthalmologic emergency. Immediate infusion of factor concentrate to 100% activity is

necessary followed by emergency assessment by an ophthalmologist.

Conclusion

Emergent bleeding events, while uncommon among people with haemophilia, require recognition and immediate intervention with high-dose coagulation factor concentrate infusion. Other care, such as surgery, may need to be undertaken urgently. However, replacement with FVIII or FIX must occur first or in parallel with any intervention in a patient with haemophilia who is critically ill.

Only removal of an acutely injurious agent or cardiopulmonary resuscitation supersedes factor replacement in a critically ill patient with haemophilia. Not only must enough coagulation factor concentrate be infused initially to reduce or stop bleeding, it must be given as often as necessary to permit healing from the injury. Ideally measurement of the in vivo factor level on a frequent and ongoing basis is performed to ensure that the desired circulating plasma levels are maintained. Importantly, special management considerations from experts in the respective medical field should be considered.

Guidelines for acute management of severe haemorrhage in haemophilia A and B

1. Assure adequate airway, breathing, and circulation by assessing respiration, pulse, and blood pressure (basic cardiopulmonary resuscitation guidelines).
2. Attain venous access as quickly as possible.
3. Infuse appropriate FVIII (haemophilia A) or FIX (haemophilia B) at a dose to achieve physiologic levels immediately (50 IU/kg body weight FVIII or 100-120 IU/kg high purity FIX respectively; 70-80 IU/kg of prothrombin complex concentrate if high purity FIX is unavailable).
4. Obtain CT scan, ultrasound, or other imaging studies as indicated to ascertain bleeding site/source.
5. Request consultation from appropriate physician consultant for bleeding site (e.g., ophthalmologist for bleeding in/around the eye).
6. Hospitalize.
7. Monitor FVIII/FIX levels respectively on a frequent basis to maintain level in the mid physiologic range.
8. Continue with frequent bolus or continuous clotting factor infusions adjusted according to measured FVIII or FIX plasma levels until the acute bleeding event has resolved. Dosing may be adjusted downward as the risk for further bleeding is substantially reduced.
9. Examine the patient following hospitalization to ensure any sequelae receive appropriate long-term care.

Challenge to the management of haemophilic emergencies in Nigeria.

- All the treatment of haemophilic emergencies involves immediate intervention using coagulation factor concentrate.These factors are not readily available in our environment and when they are, they are very costly and not easily affordable, therefore, here, in Nigeria, fresh frozen plasma is commonly used but again, they are not available in large enough quantity to manage these emergencies.

Usually, in the treatment of these conditions, use is made of whole blood while waiting for the availability of the factor concentrates. The outcome in the management of these emergencies with whole blood as against the concentrates is predictable.

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CURRENT TRENDS IN THE MANAGEMENT OF DIABETIC PERIPHERAL NEUROPATHY

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ABSTRACT
Diabetic peripheral neuropathy is a common chronic complication of diabetes occurring in both type 1 diabetes and type 2. Painful diabetic neuropathy is associated with poor quality of life and is difficult to treat. It occurs in over half of patients with diabetes. It presents in a 'glove and stocking' pattern. The pathophysiology of diabetic neuropathy centers on chronic hyperglycaemia which results in advanced glycation end products formation, increased sorbitol through increased glucose metabolism via the polyol pathway with resultant oxidative stress and various vascular and metabolic mechanisms. These ultimately result in endoneurial damage, nerve hypoxia and subsequently abnormal nerve conduction following axonal degeneration. Risk factors for neuropathy include smoking, older age, poor glycaemic control and the presence of other cardiovascular risk factors such as hypertension and dyslipidaemia. Clinical diagnosis involves a detailed history to detect positive and negative symptoms such as tingling, pain, numbness, oedema etc. A thorough neurological examination including tests for fine touch, pain, temperature, vibration perception (with 128Hz tuning fork or biothesiometer), joint position sense and reflexes is important. A Semmes-Weinstein 10g monofilament can predict the risk of ulceration. Treatment involves a multi-disciplinary approach with counseling, ensuring adequate foot care and strict glycaemic and blood pressure control. Drugs used in management include tricyclic antidepressants, Serotonin noradrenalin re-uptake inhibitors and anticonvulsants such as gabapentin and pregabalin. Newer agents include aldose reductase inhibitors etc. These drugs should be used judiciously to minimize side effects and also with caution in the elderly and those with cardiovascular disease. Pain reduction is achieved in about 30-50% of patients. Diabetic neuropathy should be screened for annually in every patient with diabetes

1. INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple etiologies, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Diabetes results in chronic complications leading to increased morbidity and mortality. Morbidity and mortality arising from diabetes mellitus is as a consequence of chronic hyperglycaemia which acts through various molecular mechanisms to lead to cell damage and oxidant stress. Hence the central initiating factor is chronic hyperglycaemia of which the duration and magnitude of the exposure of the cells to hyperglycaemia are both contributory. Abnormalities such as abnormal vascular permeability and blood flow occur which are especially evident in the retina, glomerulus and peripheral vasa nervorum. Intracellular hyperglycaemia is also implicated e.g in the vascular endothelial cells.

2. CHRONIC COMPLICATIONS OF DIABETES

The chronic complications of diabetes are loosely classified into Microvascular and Macrovascular complications as shown in Table 1 below

Table 1: Chronic complications of diabetes mellitus

MICROVASCULAR	MACROVASCULAR
Nephropathy	Stroke
Retinopathy	Ischaemic heart disease
Neuropathy	Peripheral vascular disease
Foot disease	Foot disease

Table 2: Mechanisms of damage by hyperglycaemia

MECHANISM	EFFECTS
Increased polyol pathway flux of glucose and excess activity of Aldose reductase	Increased sorbitol with osmotic cell damage
Increased intracellular advanced glycation end products (AGEs)	Altered intracellular protein function Altered gene expression
Activation of Protein Kinase C	Abnormal extracellular matrix components Abnormal blood flow, vascular permeability, angiogenesis, vascular occlusion, pro-inflammatory gene expression
Increased hexosamine pathway flux	Changes in gene expression, matrix proteins

3. DIABETIC NEUROPATHY

Diabetic neuropathy is a descriptive term meaning a demonstrable disorder, either clinically evident or sub-clinical, that occurs in the setting of diabetes mellitus WITHOUT other causes of peripheral neuropathy. Diabetic neuropathy includes manifestations in the somatic and/or autonomic nervous system. Diabetic neuropathy is among the most common long-term complications of diabetes and is a significant cause of morbidity and mortality in patients. It contributes significantly to the risk of lower extremity amputation in diabetic patients.

The set of clinical syndromes that describes diabetic neuropathy affects distinct regions of the nervous system, singly or combined. Progression may be slow and the syndrome may remain clinically silent.
It occurs in up to 50% of DM patients and is a major cause of increased morbidity and mortality3. It results in poor quality of life. Neuropathy can also occur in persons with impaired glucose tolerance and metabolic syndrome,. Diabetic neuropathy increases the risk of amputation 1.7 fold and 12 fold if there is associated deformity.
In Nigeria diabetic peripheral neuropathy was reported in as much as 59.2% of diabetic patients in the DIABCARE multi-center study.

3.1 *Pathophysiology of diabetic neuropathy*

Increased nerve glucose from hyperglycaemia leads to increased formation of advanced glycation end products (AGEs) and increased free radical formation. The subsequent reduction in nitrous oxide (NO) formation will lead to vasoconstriction and occlusion of endoneurial capillaries. These result in nerve hypoxia and structural nerve damage leading to a reduction in nerve conduction velocity.

Microvascular defects in the endoneurial vessels, such as gross basement membrane thickening, endothelial cell proliferation and hypertrophy as well as reduced oxygen tension have been noted. There is a decrease in sensory and motor amplitudes, which is suggestive of axonal destruction. The loss of axons leads to a reduction in amplitudes and not conduction velocities. The longest nerve fibres are usually affected first, though there is some evidence of early small fibre involvement 6.

3.2 *Classification of Diabetic Neuropathy*

RAPIDLY REVERSIBLE
Hyperglycemic neuropathy

GENERALIZED SYMMETRICAL POLYNEUROPATHY

Acute sensory neuropathy
Chronic sensorimotor neuropathy (diabetic polyneuropathy)
Small-fiber neuropathy
Large-fiber neuropathy

Autonomic neuropathy

FOCAL AND MULTIFOCAL NEUROPATHIES

Focal-limb neuropathy—includes mononeuropathy and entrapment syndromes Cranial neuropathy Proximal-motor neuropathy (amyotrophy Truncal radiculoneuropathy Coexisting chronic inflammatory demyelinating neuropathy (CIDP)

3.3 Chronic sensorimotor neuropathy (diabetic polyneuropathy)

It is a symmetrical, length-dependent, sensorimotor polyneuropathy attributable to metabolic and microvessel alterations. Proton Magnetic resonance (MR) spectroscopy investigation of the thalamus suggests thalamic neuronal dysfunction in diabetic polyneuropathy (DPN). Painful DPN is accompanied by increased thalamic vascularity, whereas painless DPN is associated with greater thalamic microvascular impairment.

3.3 *Risk factors for diabetic peripheral neuropathy*

The risk factors associated with diabetic peripheral neuropathy include; older age, tall height, poor glycaemic control, increased duration of diabetes, increased triglycerides, smoking, hypertension and obesity. In the EURODIAB prospective complications study, the risk of incident diabetic neuropathy was 1.5 fold in patients with concomitant hypertension.

3.4 *Clinical features*

The onset is usually insidious; though it may be acute in which case it runs a rapid, self-limiting course. The common positive symptoms include tingling, pain, prickling, paraesthesiae etc. Reported 'negative' symptoms include; numbness, limb 'asleep' etc.

Acute sensory DPN has a relatively rapid onset, with severe burning pain, aching, weight loss, and marked symptom. Other DM complications are unusual. They have mild sensory signs and minor electrophysiological abnormalities. Complete recovery usually occurs within 12 months[12].

The sensory abnormalities occur and progress in a 'glove and stocking' pattern, starting in the feet and progressing symmetrically upwards.

Neuropathic oedema may occur and muscle wasting if severe. Pain is a dreaded feature of peripheral neuropathy. It is typically worse at night, interferes with sleep and may be associated with severe depression. Hyperalgesia may occur. The pain may be described as burning sensation, knife like, electrical sensation, knife like, squeezing, hurting, constricting etc[12].

Foot deformities such as high arch, flat foot, callus, claw/hammer toes may be seen in long-standing cases. Neurological examination yields a symmetrical loss of fine touch, pin prick, pain and temperature, loss of vibration perception, joint position sense and loss of reflexes; ankle jerk and/or knee jerk.

Large fibre damage is manifest as weakness, wasting, loss of vibration, position sense and reflexes. Small fibre disease manifests as pain, autonomic symptoms, normal strength and reflexes and is electrophysiologically silent6.

The sequelae of DPN include Charcot's joints, muscle wasting, foot deformities such as high arch, clawed toes, callus, abnormal foot pressures and Diabetic foot ulcer.

3.5 *Diagnosis of distal peripheral polyneuropathy*

A diagnosis may be made upon routine screening in an asymptomatic or in a symptomatic patient. Clinical screening tools include the use of screening instruments such as the Michigan Neuropathy screening instrument and the Nerve impairment score of the lower limbs These scoring systems are a sum of various modalities such as vibration, temperature and pin-prick sensations. The Michigan neuropathy score has 15 items.

Clinical examination of a patient involves a symmetrical neurological examination of the limbs to assess sensations such as fine touch, pain, temperature, joint position sense, vibration and reflexes (ankle and /or knee jerk).

A Semmes-Weinsten 10g monofilament assesses pressure perception when gentle pressure is applied sufficient to buckle the nylon filament. The monofilament is applied to four sites of the foot; namely the plantar surfaces of the hallux and the first, third and fifth metatarsal heads. An abnormal test predicts foot ulceration. A 1.0g monofilament is said to have higher degree of sensitivity than the 10g monofilament.

Vibration sense is tested with a 128Hz tuning fork. A Biothesiometer is also used to assess vibration sense in a semi-quantitative manner. It has also been shown to be a useful predictor of foot ulcer risk.

3.6 *Investigations*
The diagnosis is mainly clinical; however the following may be useful;
1. Nerve conduction studies which show reduced nerve conduction velocity.
2. Nerve biopsy; this is not done routinely but may be useful to exclude other causes of neuropathy.
3. Investigations to exclude other causes of neuropathy will be done such as Vitamin B12 deficiency; (may be Metformin induced), Full Blood Count and Erythrocyte sedimentation rate (ESR), Electro;ytes, urea and creatinine levels, urinalysis will be carried out.

3.7 *Management*
Non-diabetes related causes must be excluded e.g paraneoplastic syndromes, alcohol, Human immune deficiency virus infection, Chronic inflammatory demyelinating polyneuropathy (CIDP), use of medications such as Isoniazid, chemotherapy. DPN is not diagnosed on basis of one feature alone; at least 2 features i.e. signs, symptoms or tests need to be present. Other measures include the assessment of blood glucose control and profiles, optimal management of hypertension and dyslipidaemia according to guidelines. The patient has to be advised to quit smoking and adequate support provided to help him/her.
The overall aim of supportive management is to achieve optimal stable glycaemic control and avoidance of excess glycaemic surges.

The patient's usual footwear and foot practices should be reviewed and the patient should be counseled appropriately by a trained diabetes educator and if available have proper podiatrist review.

3.7.1 *Pharmacological agents:*
Several classes of drugs are useful in the management of diabetic peripheral neuropathy. Patient's response is however variable and the condition remains difficult to treat. In persons with painful neuropathy, pain reduction is usually of the magnitude of 30-50%.
a. Tricyclic anti-depressants: these are useful and include Amitriptyline 25–75 mg/day, Imipramine 25–75 mg/day.
They are balanced serotonin and noradrenaline reuptake inhibitors. They also block α-adrenegic, H1-histamine, muscarinic cholinergic and N-methyl-D-aspartate receptors. They are effective with pain relief of about 50% in up to 30% of patients. They have anti-cholinergic side effects such as dry mouth, urinary retention etc. They are relatively contra-indicated in persons with cardiovascular disease especially ischemia and should also be used with caution in orthostatic hypotension which they tend to worsen. They also cause sedation.
b. Serotonin noradrenalin re-uptake inhibitors; these include Duloxetine 60–120 mg/day (indicated for painful diabeticperipheral neuropathy by US Food and Drug Administration and European Medicines Agency) and Venlafaxine 150–225 mg/day.
c. Anti-convulsant drugs such as Gabapentin 900–3600 mg/day, Pregabalin 300–600 mg/day (indicated for painful diabetic peripheral neuropathy FDA approved), Carbamazepine 200–800 mg/day, Topiramate 25–100 mg/day.
Gabapentin acts peripherally to decrease pain perception and common side effects include sedation and dizziness.
Pregabalin acts peripherally at the GABA receptor to block pain perception. It causes less sedation than Gabapentin but may cause weight gain and peripheral oedema and thus should be used with caution in patients with heart failure.
Carbamazepine acts mainy by blocking sodium channels on the Aδ nerve fibers.
d. Opiates are indicated for the treatment of painful diabetic neuropathy and include; Tramadol 200–400 mg/day, Oxycodone 20–80 mg/day, Morphine sulfate sustained-release 20–80 mg/day.
e. Topical Capsaicin cream (0.075%) is also useful in the management of painful DPN and is applied sparingly three to four times daily. It is an alkaloid derived from chilies and acts peripherally by depleting the neurotransmitter substance P from sensory nerves. Side effects include local burning, tingling and sneezing or coughing during application.
f. Other medications include Vitamin B12 and folate supplementation and the use of simple analgesics such as paracetamol and NSAIDs.

3.7.2 *Other pharmacologic agents*
These include Aldose reductase inhibitors, Gamma Linoleic Acid, Vasodilators-ACE?, AGE inhibitors, Antioxidants, nerve growth factors (NGFs) etc which are being tried for efficacy4.
a. Aldose reductase inhibitors:

these act by reducing the flux of glucose through the polyol pathway. They have been shown to improve nerve fibre density. Examples include Tolrestat and zenarestat. They have however been withdrawn due to adverse effects.

b. Protein kinase C-β inhibition; these drugs normalize hyperglycaemia-induced decreases in endoneural blood flow. These drugs are undergoing clinical trials.

c. ϒ-linolenic acid; this is an essential fatty acid which is a component of neuronal membrane phospholipids3. 4.0 Conclusion Diabetic neuropathy is a common chronic complication of diabetes mellitus resulting in increased morbidity, mortality and poor quality of life. It may be asymptomatic, hence the need for regular screening of patients. Diagnosis is mainly clinical, though investigations may be necessary to exclude other diagnoses. Symptomatic treatment is useful, especially in painful neuropathy, however pain reduction may be minimal.

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MANAGEMENT OF HAEMOPHILIA
CHALLENGES AND FRUSTRATIONS IN A RESOURCE-POOR SETTING.

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INTRODUCTION

My first exposure to haemophilia was as a third year student of medicine. I remembered being in awe of the historical perspective of the disease, diagnosis, clinical presentation and management a feeling which was quickly dismissed as one of those 'diseases of the textbook' which rarely afflicted our people and if I am lucky will see one or may be two in my practice. Now as a haematologist, a coagulation specialist how wrong I was in that assessment. Unfortunately this same assessment is still ingrained in the thoughts of many clinicians some specialists, as well as other health workers. The last Novo Nordisk powered health personnel training of 2013 organized by the Haemophilia Foundation of Nigeria exposed the paucity of awareness among doctors and other health workers alike with comments like " I am yet to make a diagnosis of haemophilia in more than 20 years of practice", "Do we have haemophiliacs in our environment", Oh! It's only a disease of the textbooks. This almost non-existence awareness among health care personnel is in my thoughts the most important challenge experienced in the management of haemophilia. If the primary care physicians, clinicians, specialists, have low index of clinical suspicion, this would mean being imprisoned in the era of doubt about the prevalence of haemophilia in our environment, new diagnosis are not made, undocumented increase in mortality and morbidity rates and most importantly, the government persistent categorization of haemophilia as lowest of the low in their list of high priority public health conditions.

This short review is aimed at drawing the attention of medical students, resident doctors specialists and other health care professionals to existence of these condition among Nigerians, the imminent threat it has on the quality of life, psyche, with increase undocumented morbidity and mortality rates of males afflicted with these disorder

HISTORICAL BACKGROUND

The word "haemophilia" is coined from two Greek words: haima, meaning blood, and philia, meaning affection1. There are documented evidence in history of these condition has long existed in man long before its affliction of Queen Victoria lineage prompting the name 'Royal disease'. The Talmud, a collection of Jewish rabbinical writings on laws and traditions, as far back as 2nd century AD, stated clearly that circumcision should be avoided in the index male if there was a record death of two of his brothers previously, or if a brother from the same mother but different fathers also died from the procedure2. This actually was without doubt the first evidence of maternal transmission of the disease. Abulcasis, or Abu Khasim, a 10th century Arabian physician, also documented families whose male relatives died from uncontrolled bleeding after trauma2.

Other remarkable landmarks in the history of haemophilia are
* John Conrad OTTO in 1803 published the first article describing a condition known today as haemophilia
* Friedrich Hopff, a student at the University of Zurich, and his professor Dr Schonlein, in 1828 first coined the term "haemorrhaphilia" for this disease condition, which was later shorted to "haemophilia."
* Eric Von Willebrand brought the world attention to another disease condition which he term "pseudohaemophilia".
* Dr Alfredo Pavlovsky, in 1947 distinguished two types of haemophilia in his lab—A and B.
* Prof Etim Essien in 1969 diagnosed the first Nigerian with haemophilia (See table 1 for other important time-lines in the history of haemophilia)

WHAT IS HAEMOPHILIA?

Haemophilia is an inherited condition characterized by qualitative or quantitative deficiency of blood clotting proteins. Persons living with haemophilia are unable to achieve a blood clot, they do not necessarily bleed faster than people without haemophilia but they bleed longer.

Haemophilia is a rare disease. The common type of haemophilia is the classical haemophilia or haemophilia A, which results from the lack of or presence of defective factor VIII. Another type of haemophilia is haemophilia B or Christmas disease named after Stephan Christmas who was first diagnosed of this disease in 1952. This results from deficiency of factor IX. Another rare type of haemophilia is Haemophilia C which results from deficiency of factor XI It's estimated that (1: 5000 males for haemophilia A, 1:30,000 males for haemophilia B) [1] In Nigeria it's projected that we have 9,000 to 12000 males with Haemophilia. Of this figure, according to Haemophilia Foundation of Nigeria (HFN) only 180 persons have being identified and diagnosed with haemophilia. This clearly indicates that quite a number of persons with haemophilia in our country are still undiagnosed. The implication of these is quite daunting as this could lead to undocumented increased morbidity, mortality rates as well as poor quality of life resulting
from debilitating and disabling outcomes of this condition.

MODE OF INHERITANCE

In contrast to earlier beliefs common to our people, Haemophilia A and B can affect people of any race and colour. The most severe cases of haemophilia occur almost exclusively in males. For women to be affected by a severe case, they must receive the gene from both mother and father(a carrier mother and a father living with haemophilia) which is extremely rare, have random inactivation of one X chromosome a process known as lyonization, or possess only one X chromosome as you would have in Turner females.

The mode of inheritance for haemophilia A and B is X linked recessive. In the case haemophilia C, this is different. The defective gene can both be transmitted by both mother and father and hence it's mode of inheritance is autosomal recessive and its commonly seen amongst the Ashkenazi Jews of Eastern Europe where it is estimated that approximately

TABLE 1: SOME IMPORTANT HISTORICAL EVENTS [2]

1828	Term "haemorrhaphilia" first used. Later shortened to "haemophilia."
1926	- Erik von Willebrand identifies a bleeding disorder, later called von Willebrand disease (VWD)
1940s	1940s -whole blood transfusions given at hospital
1955	First infusions of factor VIII in plasma form
1952	Researchers describe what is now called factor IX clotting protein
1957	Researchers in Sweden identify von Willebrand factor as the cause of VWD
1969	**Professor Etim Essien diagnosed first Nigerian with haemophilia**
1958	First use of prophylaxis for haemophilia A
1964	Dr Judith Graham Pool discovers cryoprecipitate
1968	First FVIII concentrate available
1970s	Primary prophylaxis therapy experiments begin
1970s	Freeze-dried plasma-derived factor concentrates available
1977	Desmopressin identified to treat mild haemophilia and von Willebrand disease
1980s	1980s - Factor VIII, FIX and von Willebrand factor genes cloned
1982	CDC reports first AIDS cases among people with haemophilia
1985	First inactivated factor concentrates available
1992	FDA approves first recombinant FVIII products
1995	Prophylaxis becomes standard of treatment in US
1997	FDA approves first recombinant FIX product
1998	First human gene therapy trials begin
2000s	2000s - FDA approves first recombinant factor products made without human or animal plasma derivatives
2013	Gene therapy trials underway at three sites in the US

FDA; Food and Drug Administration

8% of the population carry the defective gene[3].
In about 30% of cases, there is absence of a family history of haemophilia and this has been attributed to spontaneous mutation of haemophilia gene. The well documented "flip tip" inversion mutation involving intron 22 of the factor VIII gene is an example of such spontaneous mutation. [3] By this no family is spared by this condition and hence the absence of family history of bleeding disorder **does not rule out the diagnosis of haemophilia**

SYMPTOMS OF HAEMOPHILIA
Some cultural and religious practices like infant circumcision may herald the first episodes of bleeding in a suspected case of haemophilia. Notably there are other differential diagnoses to post circumcision bleeds ranging from poor technique, prematurity, neonatal thrombocytopenia, congenital disease of bilirubin metabolism, sepsis etc. With low index of clinical suspicion among health care professionals in our environment, haemophilia most time is not considered until the procedure has been done and the child starts bleeding. There are many undocumented death from post circumcision bleeds especially those done in rural setup with primary health care centres equipped with poor and sometimes non-existent blood bank services to handle such bleeding episodes. Bleeding episodesmay also occur during crawling, teeth eruption, bruises from falls, and bleeding into the joints, soft tissues and muscles, which are seen more frequently after the age of two. Persons living with haemophilia can bleed into any muscle or soft tissue with some sites more common than others. Common symptoms of haemophilia are:
* bleeding into joints (knees, elbows, ankles, shoulders, hips, wrists in descending order of frequency)
* bleeding into soft tissues and muscles (the ileopsoas muscle around the hip may lead to nerve compartment syndromes, calf, forearm, upper arm, Achilles tendon, buttocks facial neck)
* bleeding in the mouth from a cut, bitten tongue or loss of a tooth (especially in children)
* blood in the urine (haematuria),
* ecchymosis.

Uncommon sites
* bleeding into the ear
* bleeding into the eyes
* bleeding into muscles of palm

Emergency /life threatening bleeding
* Intracranial bleed
* Retropharyngeal bleeding
Intracranial bleeding is the leading cause of death from bleeding in haemophilia. The importance of increasing awareness as well as index of clinical suspicion cannot be over emphasized. Early recognition of these symptoms is therefore important to improve chances of survival.
Some of the symptoms of intracranial bleeding are
* Persistent or increasing headache
* Repeated projectile vomiting
* Sleepiness or a change in normal behaviour
* Sudden paresis of an arm or leg
* Neck stiffnessor complaints of pain with neck movement
* Double vision
* Nystagmus
* Poor coordination
* Convulsions or seizures

DIAGNOSIS
The nonspecific tests for coagulation; activated partial thromboplastin time (APTT) is prolonged while the prothrombin time, thrombin time, fibrinogen assay and platelet time are essentially within reference range. The activated partial thromboplastin time tests for the intrinsic pathway of coagulation.
The most common error is for most clinician to base their clinical decision just on the results of activated partial thromboplastin time. There are other conditions aside from deficiency of intrinsic pathway clotting factors of coagulation which can lead to prolongation of APTT viz are heparin therapy, presence of inhibitors and presence of lupus anticoagulant.
Next on the line of investigation are the mixing experiments. Here equal volumes of pooled normal plasma are mixed with the test plasma. If the APTT corrects by more than 50% of the difference between the clotting times of the normal and test plasma, a factor deficiency is indicated. Poor correction would suggest an inhibitor possibly to one of the clotting factors in the system or the non-specific such as lupus anticoagulant.[4]

Using modification of normal pooled plasma like aged plasma adsorbed plasma, plasma FVIII plasma and FIX deficient an help improve the specificity of the mixing experiments. See table below.

Pattern of mixing text results in the presence of individual factor deficiency[4]

Defect in test plasma	APTT	Aged or FVIII deficient plasma	Adsorbed or FIX deficient	Normal plasma
FVIII	abn	no corr	corr	Corr
FIX	abn	corr	no corr	Corr
FXI/FXII	abn	corr	corr	Corr
Inhibitor	abn	no corr	no corr	No corr

Based on the mixing experiment results, the confirmatory factor assay of the suspected factor deficiency will be done. Factor VIII assayfor Factor VIII deficiency and FIX assay for FIX deficiency. The reference ranges for FVIII and FIX plasma levels should be derived by local laboratories but the reference range for FVIII and FIX are 50-150% 5and 70-120% 6 respectively. Sadly more than 5 decade after the first Nigerian was diagnosed, we are still yet to boast of reference diagnostic laboratory in most of our teaching hospitals for diagnosis of haemophilia and other bleeding diseases. Reasons from lack of requests from clinicians due to low index of clinical suspicion, paucity of reference laboratory with good laboratory practice in haemostasis, non-availability of reagents, to lack of laboratory personnel expertise.

Clinical classification of Haemophilia

Severity	F VIII activity	Clinical manifestations
Severe	<1%	Spontaneous hemorrhage from early infancy Frequent spontaneous bleeding and haemarthrosis
Moderate	2-5%	Hemorrhage secondary to trauma or surgery Occasional spontaneous and haemarthrosis
Mild	>5%	Hemorrhage sec to trauma or surgery Rare spontaneous bleeding

TREATMENT

"Medical care for haemophilia is specialized. A person with haemophilia must receive care from healthcare workers who have expert knowledge of the bleeding disorder. The wide-ranging needs of people with haemophilia and their families are best met through Haemophilia Treatment Centres (HTC) rather than by individual doctors."7

The treatment of haemophilia may involve prophylaxis, management of bleeding episodes, treatment of factor VIII (FVIII) inhibitors, and treatment and rehabilitation of haemophilianaturopathy. Use of factor replacement products, use of blood component transfusion in the absence of factor replacement therapy and other medications, including pain medications, is typically required.9

The best advocated standard management care model for haemophilia is comprehensive care, which is defined as a "systematic, multidisciplinary team approach that provides services in a coordinated, proactive manner to improve the health and quality of life for people with bleeding disorders. Such care includes specialized diagnostics, evaluation, treatment, rehabilitation, and education".8

Factor Replacement Therapy

This is the standard treatment protocol with the objective of replacing the deficient factor.

Various factor concentrates are available to treat haemophilia A and B. Fresh frozen plasma and cryoprecipitate are no longer used in haemophilia treatment in developed countries (because of the lack of safe viral elimination and concerns regarding volume overload)9. Though still a concern in our environment, unfortunately it is still the major treatment protocol in our environment due to non-availability and accessibility of factor concentrates in our environment.

Factor concentrates can either be plasma derived or recombinant which has the advantage of elimination of viral contamination.

Continuous infusion of anti-haemophilic factors prevents the fluctuations in plasma levels in factor concentrations that occur with intermittent infusion; this benefit is particularly important when treatment is required for prolonged periods. In addition to improved haemostasis, it also reduces the amount of factor used, which is very cost effective approach especially in our environment where there is scarcity of factor concentrates. The indications would include intracranial haemorrhage, iliopsoas bleeding, and preparation for surgery. In most minor-to-moderate bleeding episodes, intermittent boluses are adequate.

For example in Haemophilia A which is the commonest type of haemophilia in our environment Doses of FVIII concentrate are calculated according to the severity and location of bleeding. A known treatment rule is FVIII 1 U/kg increases FVIII plasma levels by 2%. The reaction half-time is 8-12 hours. Some guidelines to target levels to be achieved based on severity of bleeding are as follows:

* Mild haemorrhages (i.e., early haemarthrosis, epistaxis, gingival bleeding): Maintain an FVIII level of 30%
* Major haemorrhages (i.e., haemarthrosis or muscle bleeds with pain and swelling, prophylaxis after head trauma with negative findings on examination): Maintain an FVIII level of 50%
* Life-threatening bleeding episodes (i.e., major trauma or surgery, advanced or recurrent haemarthrosis): Maintain a FVIII level of 80-90%; after stabilization, maintain levels above 40-50% for a minimum of 7-10 days9

Other treatment protocols which may be beneficial in mild haemophilia A are Vasopressin and fibrinolytic agents like epsilon amino caporic acid and traxenemic acid.

THE FUTURE

Gene therapy offers the possibility of cure for most genetic disease and haemophilia is not excluded. With very promising ongoing research inconcept of gene therapy in haemophilia, the future holds the possibility of cure for haemophilia.

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EPIDEMIOLOGY OF LEUKAMIAS IN AFRICA

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INTRODUCTION

The study of epidemiology of leukemia's in Africa has been held back by the lack of accurate population CENSUS figures, the shortage of haematologists and the under development of laboratories. Therapy is almost always grossly inadequate because of limited supplies of pharmaceuticals, the absence of radiotherapy except in few areas and the liability or unwillingness of patients to continue treatment regimens for long periods of time. Despite these handicaps, a large corpus of knowledge has been acquired. This is of global interest, especially in the questions it raised as to epidemiology and possible etiologies.

ACUTE LEUKAEMIAS

The acute leukemias of multipotential primitive/progenitor cells divided mainly into: Acute lymphocytic leukemia's (ALL) and Acute myelogenous leukemia's have been reported to be less common (28.9%) than chronic leukemia (71.1%) in a study in Nigeria and other parts of Africa. They are not common neoplastic disease in Nigeria (and indeed in Africa).In a study carried out to determine the burden, prevalence and general outcome of acute leukemia seenbetween April 2003 and July 2008 in the University college hospital, Ibadan, showed that the population of AML (56%) slightly exceeds that of ALL. Male: female ratio was 2:1 in each subtype, AML cases were older (mean age= 21.4 years, age range = 4-60years) compared to ALL with a mean age of 20.4 years. L2 -sub-type of ALL was most commonly diagnosed. In Ilorin, Nigeria of Ilorin teaching hospital on the current pattern of hematological malignancies between January 1996 to December 2005, the distribution of the various leukemias were ALL 8 (4.9%), AML 18(4.9%), CLL 20(5.4%) and CML42 (11.4%)

Moreover, of 535 consecutive cases of acute leukemia diagnosed in Cape Province of South Africa. Between 1978 and 1985, demographic data are incomplete in 75 black patients and they had to be excluded from the spatial analysis of the remaining 460 cases, 223 (48.5%) occurred in white patients and 237 (31.5%) in those of mixed ancestry, classified as coloreds according to the population registration Act. The average incidence was 2.12, 1.37 and 0.58/100,000 for whites, colored's and blacks respectively. There was no temporal trend in the incidence of acute leukemia between the three race groups.

In sub-Sahara Africa the epidemiology of acute lymphoblastic leukemia is represented in the table below

EPIDEMIOLOGICAL PATTERNS OF ACUTE LYMPHOBLASTIC LEUKAEMIA

PATTERN	SOCIOECONOMIC STATUS	INCIDENCE 10 5/YEAR	EXAMPLES
I	LOW	< 0.1	Much of TROPICAL AFRICA
II	INTERMIDIATE	< I*	Nigeria,Kenya,south African blacks, North Africa, Gaza Arabs US BLACKS
III	HIGH	2-3 **	South African Whites

KEY: * peak incidence 5-14 years 5-14 years, predominantly. T-ALL *peak incidence 2-15 years, predominantly C-ALL

There has been a perceptible increase in the frequency of diagnosis of c-ALL in black children during the past five years in Nigeria, South Africa and Zimbabwe with an emerging peak at 3 to 4 years of age, although there is a tendency for relatively more black than white children to present between 5 and 10 years of age (8-10). In Johannesburg, South Africa, it has been shown that black males with c-ALL, had the lowest CD10 antigen density, as well as having the worst prognosis. While females had the highest CDD 10 antigen density and the best prognosis, while the black females and white males occupied intermediate positions. It was hypothesized that the low density CD10 pattern in males and blacks could be a genetic marker of poor prognosis, regrettably. It may be said that patients with ALL in tropical Africa have benefited little or not at all from the great advances which have been made in management during the past decades.

Acute myeloid leukemia is diagnosed at equal frequency as ALL in childhood in sub-Sahara Africa, in contrast to the western world where childhood ALL is seen about four times as often as

AML. The difference in relative rates is due in part to low incidence of c-ALL in African children, but also it seems that there is high incidence AML. The male to female ratio can approach 4:1 and AML is especially common in boys' age 5 to 14 years. AML is seen at any age amongst adults and at about equal gender incidence. There appears to be a dual distribution of AML in Africa: one pattern affects children of low socio economic status. Exposure to chemicals, toxic waste and radioactivity at work and in the environment is increasing and is largely uncontrolled in sub-Saharan African. Cigarette smoke is probably the main source of individual exposure to benzene and represents the commonest identifiable cause of AML, certainly in males, and may account for over 20% of the diseases in some populations. Prognosis for patients with AML in sub-Saharan Africa treated with correctional cytotoxic therapy remains uniformly poor with median survival about 9 months.

CHRONIC LEUKAEMIAS

The chronic leukemia's arise from the lymphocytic (chronic lymphocytic leukemia, cii) or myeloid(chronic myelogenous leukemia'saml) prelusion cells with their various subtypes. Chronic leukemia's (71.1%) has been reported to be more common that acute leukemia's (28.9%) in a study in Nigeria and other parts of Africa. They are not uncommon neoplastic diseases in Nigeria (and indeed Africa) and there is no doubt that adult leukemia in Africa occurs as often as it does in the Caucasian.

Despite challenges of a resource-limited environment, the outcome of chronic myeloid leukemia (CML) patients in South Africa is similar to that in developed countries, thanks to access to tyrosine kinase inhibitors through patient assistance programmes and clinical trials. The annual incidence of AML is around 1 per 10 throughout the world. The male to female ratio is about 1:5:1, with a slight higher rate amongst black males (2a).The peak of frequency of diagnosis is Africa in the fifth decade, as it is in the western world, but more patients are young than 40years than older, reflecting the age distribution of the population. The disease is not uncommon even in childhood, about 10% of patients in Nigeria and 19% in Sudan being below 15 years of age (1, 2). African patients respond as expected to cytotoxic therapy. Chronic lymphatic leukemia epidemiology both the gender and age distributions of CLL in tropical Africa differ greatly from those in the western world. In West Africa, the male to female ratio is 1:1, as compared to 2:1 in the western world. CLL is common under the age of 40years and may occur as early as the teens in Africa, whereas it is rare in young western adults. There is arising frequency in women up to the end of their reproductive period of life, and CLL is seen twice as commonly in women than in men below the age of 45 years, the male to female ratio is the same as in the western world. Similar pattern is seen in east Africa, but it is not so pronounced. All the younger patients with CLL are of low socioeconomic status or come from rural areas. It is postulated that the unique pattern of CLL in tropical Africa is the result of recurrent malaria and other infections, leading to both a depression of T-cell control of B-cell proliferation and direct antigenic and mutagenic stimuli to B-cell proliferation. Factors like endemic malaria, transmission of other infections which could include antigenicviruses; numerous pregnancies favour the proliferation of a large pool of B-cells in which there is a relatively high chance of somatic mutations leading to a monoclonal proliferation of B-cell. The chances of developing CLL should be in theory greater in patients with HMS than in the general population and it has been demonstrated recently that chlorallymph proliferation can complicate HMS, and could lead to the evolution of CLL or splenic lymphoma with villous lymphocytes.

In conclusion, the study of epidemiology of leukemia's in Africa has been held back by the lack of accurate population census figures, shortage of hematologists and the under development for laboratories. Therapy is almost always grossly inadequate because of limited supplies of pharmaceuticals, the absence of radiotherapy except in a few centers, and the inability or unwillingness of patients to continue treatment regimes for long periods of time.

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A Risk Assessment of Arsenic in Rice - 1:

Current Evidence and Policy Implications in the US.

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Background

Arsenic is a naturally occurring, widely distributed metalloid, although it is frequently classified as a metal. It exists in elemental form, but more commonly in combination with carbon and hydrogen as organic arsenic or with other elements such as oxygen, chlorine or sulfur as inorganic arsenic (ATSDR, 2007). Inorganic arsenic is more toxic to humans, more readily absorbed and excreted at a slower rate compared to organic arsenic (Hughes, 2011). Human exposure to arsenic can be via ingestion of contaminated soil, food, or water, dermal contact or inhalation and the ubiquitous nature of arsenic makes exposure more likely.

Water had been regarded by some researchers as the main source of human exposure to inorganic arsenic (Bhattacharya et al, 2012). However, current evidence suggests that the majority of arsenic exposure is via food, mostly seafood, rice, mushrooms and poultry. In addition, diet is the main exposure source for people with limited exposure via drinking water (EFSA, 2009).

Health effects of arsenic are multisystemic and include characteristic skin changes, viz., hyperkeratinization and hyperpigmentation. Skin cancer may also be a potential consequence of chronic exposure. Indeed, inorganic arsenic is classified as a known human carcinogen by the EPA, International Agency for Research on Cancer (IARC), and the Department of Health and Human Services (DHHS). Other health effects include peripheral neuropathy, adverse effects on enzymes involved in heme synthesis and degradation, including inhibition of coproporphyrinogen and heme synthetase, and activation of heme oxygenase (ATSDR, 2007). In addition, irritation of the respiratory tract, gastrointestinal irritation, and neurological symptoms are other well-known health effects of arsenic.

Growing Concerns in Food and Food Products.

There have been growing concerns as regards the level of both total and inorganic arsenic in food in the recent past. The realization of the health effects of arsenic, including its potential for carcinogenesis, and the lack of regulatory standards for arsenic in food products had piqued the public interest in this area. Major contributors to inorganic arsenic in food include cereals and cereal-based products (approximately 50% of total exposure), bottled water, coffee, rice, beer, fish and vegetables (De Calle, 2012; Meacher et al, 2002).

Arsenic in Rice.

A lot of the interest in arsenic exposure in food has been focused on rice and rice products. Arsenic exposure via rice and rice products has gained more prominence as a major concern due to the fact that rice is a staple food product for more than half of the global population (USDA, 2012). Assimilation of arsenic from the soil in rice has been found to be faster than in other cereals, and the growing patterns coupled with mounting environmental pollution helps to concentrate arsenic in rice (Williams et al, 2007; Signes-Pastor, 2009).

About 56% of U. S. domestic rice utilization is consumed directly as food, 16 percent for processed foods and beer, and 10 percent used in pet food (USDA, 2013).

Rice cultivated in the U.S. contains higher total arsenic and lower inorganic arsenic levels compared to other countries (Mehrag et al, 2009). Mean total arsenic levels and inorganic arsenic levels in rice in the U.S. have been estimated as 0.25 mg/kg and 0.1mg/kg, respectively (Mehrag et al, 2009). Consumption of rice is on the rise while the use of processed rice products such as flour, and syrups is widespread. Average consumption is about 1 cup of cooked rice per day. In addition, rice-based products including rice cereals were often the first solid foods introduced to infants during weaning (Jackson et al, 2012). Many people believe that rice-based cereals are the least allergenic to children (AAP, 2012).

Consumption of rice has been associated with increased urinary excretion of arsenic compounds (Pearson et al, 2007). Mehrag and colleagues (2008) indicated that inorganic arsenic exposure to babies, 4-12 months of age, from rice-based baby food products could be higher than the maximum exposures from drinking water to adults, and can have deleterious health effects. Davis et al (2012) found that rice is a source of arsenic exposure in U. S. children and showed that total urinary arsenic among children increased 14.2% with each ¼ cup increase in cooked rice consumption. Gilbert-Diamond et al (2011) also showed a statistically significant association between elevated urine arsenic levels in pregnant women attending antenatal visits in the U. S. Dietary exposure to inorganic arsenic in children under 3 years of age is about 3 times that of adults (EFSA, 2009).

Different methods have been devised for measuring total and inorganic arsenic suggesting that the variability in testing protocols may affect estimation of arsenic levels in food. The European Union Reference lab for Heavy Metals in Feed and Food (EU-RL-HM) carried out a proficiency test for determining the total and inorganic arsenic in rice and concluded that inorganic arsenic levels in rice were independent of analytical method applied (De Calle, 2011). They suggested that considerations should be made to introduce possible maximum levels for inorganic arsenic in rice (De Calle, 2011)

Current Standards

The United States Environmental Protection Agency (EPA) maximum contaminant level for arsenic in water is 10ppb. The US Food and Drug Administration (FDA) proposed an action level of 10ppb for inorganic arsenic level in fruit juice (Taylor, 2013). Apparently, China has set the minimum risk levels for inorganic arsenic levels in rice to 0.15microgram/gram (USDA FAS, 2006). However, there are no WHO, U.S., or European Union standards for total and inorganic arsenic in food including rice and rice products (Pearson et al, 2007).

Recent FDA Efforts

The FDA started studying arsenic in food products in 1991through its total diet study program (FDA, 2013a). In response to the growing concerns with arsenic, especially inorganic arsenic, the FDA increased its surveillance activities specifically in rice and rice products in 2011. These activities were further expanded a year later culminating in a study of arsenic in 200 samples of rice and rice products. In 2013, the FDA even went a step further to study an additional 1,300 samples of rice and rice products (FDA, 2013b). The samples analyzed include various types of rice grains and rice products including pasta, infant and toddler cereals, snacks such as rice cakes, cookies, and pastries, and beverages such as beer, rice wine and rice water. Specific brands, however, were not analyzed. The results were released in September 2013.

The average levels of inorganic arsenic in rice ranged from 2.6 to 7.2 micrograms per serving. The average inorganic arsenic levels in rice products ranged from 0.1 to 6.6 micrograms per serving. It is noteworthy that the levels in infant formula were among the lower categories. In the concluding statement, the FDA submits that these amounts are not high enough to cause any immediate or short term deleterious health effects to humans (FDA, 2013b).

Policy Implications,

Recommendations and Future directions

Based on current literature and the results of the FDA studies, it is recommended that consumers vary the grain content in their diet. Consuming rice products in moderation is also encouraged. Parents of infants and toddlers are also advised to apply moderation in the quantity of rice products on serving. The American Academy of Pediatrics indicates that there is no evidence that rice cereal has any advantage over other grains as the first solid food fed to infants (AAP, 2012). Hence, parents are encouraged to diversify the grain content of their infants' first solid meals. Dehusking and cooking may also reduce arsenic compounds in rice (Signes et al, 2008; Carbonell-Barrachina et al,

2009).

There is no evidence in peer-reviewed literature of chemical risk assessment for arsenic in rice (FDA, 2013b). The FDA has proposed to carry out a study to that effect. It would also be helpful to have research in this area from other researchers. Long-term effects of inorganic arsenic in rice should be researched as well. There is also a need to look at specific products in terms of inorganic arsenic levels to ensure that results are not over-generalized. Meanwhile, all stakeholders including the rice industry, consumer groups and regulatory agencies should endeavor to collaborate on ensuring that rice production is optimized with public health in mind.

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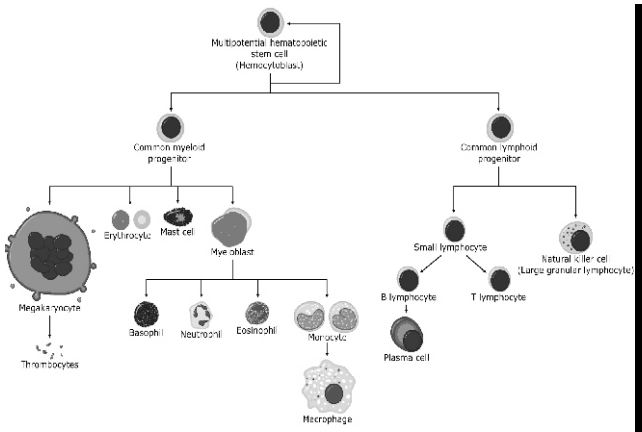

THE DYNAMIC TERRITORY OF THE HAEMATOPOETIC STEM CELLS MICROENVIRONMENT DURING DEVELOPMENT

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Abstract

The haematopoetic sysetm has become the best understood stem cell- derived system because it has been intensity studied for many decades. While a lot of progress has recently been made in describing the bone marrow components that maintain and control blood stem cell function in the adult, very little is currently known about the regulatory micro environment in which the first adult-repopulating hematopoietic stem cells are formed during development.

This review summarizes the recent advances that have been made in defining the cellular components as well as the souble and physical factors, that are part of the niche involves in regulating hematopioetic stem cell generation in the embryo.

Introduction

The hematopoietic system is a highly dynamic system that is maintained at a rapid rate of turnover, producing millions of new cells every second to maintain homeostasis and respondto immunological challenges such as infection, and also respond to respiratory stress, or bleeding. This critical balance is maintained and supplied by a hierarchy of progenitors, stemming from a relatively small population of self-renewing, multi-potent, largely quiescent cells, known as hematopoietic stem cells (HSCs). [1] Definite HSCs arising in the embryo can provide a wealth of information to further our understanding of the production, maintenance, and cell fate decisions of HSCs.

HEMATOPOIESIS IN DEVELOPMENT

Hematopoiesis occurs in two waves during development. The first, known as primitive hematopoiesis is transient and supplies the needs of the early embryo, including tissue oxygenation during rapid growth. The second wave is known as definite hematopoiesis and culminates in the production of definitive HSCs, which are capable of long-term multilineages repopulation of irradiated adults following injection into the blood stream.[2] In the mouse embryo, the first definitive HSCs appear autonomously in the aorta-gonad-mesonephros region (AGM) region at embryonic day 10-11 [3,4], HSCs are also found in the yolk sac [3], placenta [2] and fetal liver [4], although the AGM remain the only region of the wild-type embryo that can expand HSCs in organ culture [3,]. While the AGM is capable of expanding HSCs at embryonic day II [2] It's primary role in vivo is to promote denovo HSC generation. The placenta, however have mitotically active hematopoietic cells [II]. It is also capable of denovo generation of hematopoietic stem /progenitor cells in addition to receiving HSCs generated elsewhere.The yolk sac is the origin of the primitive hematopoietic wave and also of some transient definitive hematopoietic cells.

DEFINITIVE OF HSCS HAVE DISTINCT PROPERTIES IN THE ADULT AND THE EMBRYO

The earliest definitive HSCs expand at a faster rate to give rise to the full complement of adult HSCs and so are highly proliferative. In contrast, adult Bone marrow(BM) HSCs divide rarely. HSCs isolated from embryo fetal liverat day 14-15 expand at a fast rate when compared with adult HSCs [18]. These fetal characteristics persist around 3 weeks after birth, but by 4 weeks, HSCs are similar to adult HSCs. The HSCs found in the AGM have a number of distinct properties that suggest that they may constitute a third, functionally and phenotypically discrete population of HSCs.

ENVIRONMENTAL REGULATION OF HSCs

Stem cell regulation is achieved through the integration of intrinsic and extrinsic factors. The concept of a stem cell 'niche" was first put forward in the field of hematopoiesis in 1978 [4]. The presence of this local tissue

microenvironment where stem cells reside is now thought to be an important factor in regulatory stem cells behavior in a diverse range of cell systems.

The niche is the convergence of metabolic, humoral, paracrine, neural, structural, and physical signals that act to regulate stem cells [3]. For HSCs, it is predominantly comprised of stromal cells, which provide cell-cell contact for HSC anchorage, signaling, and trafficking; and an extracellular matrix, which contains soluble factors is secreted by these cells.These factors can either act directly on HSCs or indirectly via the microenvironment. Other cells types in the vicinity may also provide signals that affect HSC behavior.

Given the innate ability of HSCs to behave differently according to physiological need, and the known role of the niche in influencing HSC activity, it is unsurprising that while the HSC niches in the embryo and adults share a number of characteristics, they must be custom made to support the features of stem cells activity that predominate at the time.

This is most obvious in the embryo, where HSC niches in different anatomical locations support different functions. Meanwhile the adult BM must both support highly quiescent HSCS and also manage their differentiation and mobilization into the blood in seemingly different compartments. Understanding specific environmental cues that affect HSC birth and behavior is critical for recreating culture conditions conducive to generating and expanding HSCs form both hematopoietic tissue and pluripotent stem cells in vivo.

SOLUBLE FACTORS

Soluble factors can affect various facets of hematopoiesis and interestingly many behave differently in adult and embryonic microenvironments, suggesting the presence of different downstream target in either the HSCs or their niches.Identifying sources of soluble factors that influences hematopoiesis also provides clues as to which cell types make up the hematopoietic microenvironment.

NICHE CELL TYPES

Cells in the HSC niche can use physical and chemical signals to influence hematopoiesis. These signals can originate not only form the stromal or endothelial cells immediately surrounding them, but also other nearby cells. Gene expression profiling of the AGM around the time of HSC emergence has revealed that unregulated genes are not limited to those of the developing hematopoietic system, but also include the developing vascular, muscular, skeletal and nervous system [5]. Given the short distance between the developing organs in the AGM, it is likely that signals from one organ system affect cells in another, while the vascularity and nerve supply of the BM likewise expose it to alternative extrinsic signals. Some of the main cell types and signals emanating from them in the AGM are:

(1) Osteogenic cells
(2) Mesenchymal stem (stomach cells)
(3) Sympathetic nervous system
(4) Signals from cells in the gut
(5) DLK1 – expressing cells.

Osteogenic cells

In the adult BM HSC niche, as early as 1975, a supportive role for osteogenic cells was inferred by the finding that progenitors and transplanted HSCs are concentrated in the endosteal region of the BM [2]. Increasing the frequency of osteoblasts in the BM results in a parallel increase in HSCs, which supports a specific role for osteoblasts as niche cells?

Endothelial cells

There is now a substantial amount of evidence to suggest that AGM HSCs are derived from specialized endothelial cells known as hemogenic endothelial cells, which can produce blood cells via a process termed endothelial hematopoietic transition. This is thought to result in the appearance of intra-aortic clusters of cells that express endothelial as well as hematopoietic marker. These cluster are particularly abundant in the middle region of the dorsal aorta around the junction with the vitelline artery, which is also the region where HSCs are concentrated [3] and they are absent in embryos deficient in HSC production [4]. Whether endothelial cells and cells within the intra-aortic clusters also acts as mini niches that support emerging HSC is currently unknown.

Mesenchymal stem/stromal cells

Stromal cells are derived from mesenchymal/stomach cells (MSCs);Mulitpotent cells that can differentiate along connective tissue linage pathways [6]. During development mesenchymal stem/progenitor cells have been identified in hematopoietic organs and circulating blood at times when they harbor HSC activity [5]. Although clonality has not been examined, only the AGM region is able to give rise to osteogenic, chondrogenic, and adipogenic cells at EII of hematopoietic region development, the same property is found in E12 -14 circulating blood, E 14 fetal liver, neonates and adult BM but not E12 yolk sac[5]. MSC have also been isolated form human placental [2]

Sympathetic nervous system

Investigation of the role of the transcription factor Gata 3 has

revealed that signals from the sympathetic nervous system regulate HSC emergence in the embryo.

In the adult HSC niche, the sympathetic nervous system has also been shown to play a role in HSC regulation. Pharmacological or genetic ablation of catecholamine signaling causes osteoblast suppression, CXCL 12 down regulation and inhibited HSPC mobilization following administration of granulocyte colony stimulating factor [6]. In addition, denervation to remove Schwann cells around BM nerves com promise HSC quiescence [6] while the mechanism proposed was via activation of Transforming growth factor Beta, the effect of removing the nerve cells cannot be discounted especially since a direct effect of catecholamineon HSC proliferation has also been reported.

Hematopoietic activity has been associated with ventral structures in several organisms. The ventral domain of the dorsal aorta contains most of the HSC activity at EII.5 and it is the only domain that is able to initiate HSCs in E 10.5 explant cultures and expand HSCs in EII.5 explant cultures . This suggests that the ventral region of the dorsal aorta contains excusive signals that are capable of inducing and expanding definitive HSCs
DLK1 – expressing cells
DIK1 is a paternally expressed imprinted gene encoding an atypical notch ligand, DIKI which exists in both soluble and membrane bound forms.The gene is regulated in the HSC –rich middle third of the dorsal aorta compared with the nostril and caudal thirds, it has also been shown to promote the hematopoiesis [5] and examination of the AGM at EII shows that it is expressed in sympatho-adrenal cells, were it is downstream of gata3, as well as the smooth muscles layer of the dorsal aorta and the ventral mesenchyme, where it is downstream of run Xi.

Physical factors
There is evidence that the circulation in the embryo stimulates AGM hematopoiesis. Nitric-oxide production form endothelial cells is triggered by the sheer stress induced by pulsatile flow that occurs as a consequence of the heart beating.

Progenitor numbers from para-aortic splanchno-pleura-derived cells (the precursors tissue of the AGM) from NCXI embryos, which lack a heart beat, can be increase by exposure to shear stress that is equivalent to the hemodynamic shear stress experience by the embryonic aorta at E10.5[44].Reduction of nitric oxide synthase activity,and therefore nitric oxide results in reduced progenitors compared with type E10.5AGMs and reduced phenotypic and functional HSCs from E11.5 AGMs. The positive effect of shear stress in HSCs may explain why HSCs emerge in the middle third of the dorsal Aorta, in particular at its junction with the vitelline artery interestingly, nitric oxide synthesis 1(NOS1) production by stromal cells in the fetal liver is associated with negative regulation of hematopoiesis, revealing another difference between the AGM and fetal liver niches.

Conclusions
Hematopoiesis occurs sequentially at multiple sites in the developing embryo. Each site harbours a different balance of HSC emergence, maintenance, proliferation, differentiation, and death and must therefore comprise a niche that functions accordingly. It is important to understand the AGM in hematopoiesis because it is a conserved location of HSC emergence from zebra fist to humans, presumably due to an evolutionary advantage for HSCs to arise in the aorta. Some of the regulatory signals, such as hedgehog, BMP, nitric oxide, prostaglandins, and metabolic factors, are also conserved. Niches factors can be soluble or membrane bound, and be under physical temporal or spatial regulation. Moreover, as exemplified by DIK1 and nitric oxide, the same signal may have opposing effects in different tissue, further highlighting the importance of the micro-environment.

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Applications of Molecular Biology In Medicine

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Introduction

Variety is the spice of life. It is variation in the genome that underlies the differences between living things in general; from animal and plant kingdoms through the phyla, classes, genera and species, to single individuals. Most of molecular biology is actually molecular genetics and has to do with these differences in the genome. In applying molecular biology to medicine, these genomic differences are exploited in advancing the understanding, diagnosis and treatment of disease.

This article includes discussion of the applications of molecular biology in:

* Understanding the aetiology and mechanisms of disease
* Diagnosis
* Treatment
* The biomedical /pharmaceutical industry and pharmacogenomics
* Forensic medicine or medico-legal practice
* Pre-implantation genetic testing (diagnosis) in embryos
* Population genetics.

Understanding the Aetiology and Mechanisms of Disease

Molecular biology has facilitated the understanding of the aetiology and pathophysiology of many diseases, such as neoplasia. Genes are of cardinal importance in the development of neoplastic diseases. This is because neoplasia are essentially, disorders in which there is uncontrolled cell division and genes are crucial in the control of cell division. Molecular biology has revealed that malignant disorders of cell proliferation (cancers) arise in many cases when there is an abnormality of a gene that codes for a protein or micro-RNA which plays a role in cell division. The cardinal importance of genes in development of neoplasia is illustrated by the fact that a cell which does not have a nucleus (and therefore has no genes) does not become neoplastic. The mature red blood cell and the blood platelet are very good examples. There is no known disease arising from the neoplastic transformation of the mature erythrocyte or blood platelet. These cells do not undergo neoplastic transformation because they contain no genes. By contrast, the immature cell of the erythroid lineage in the bone marrow which has a nucleus and genes – the erythroblast – is known to undergo neoplastic transformation which leads to the disease called erythroleukaemia (Di Gugliemo's Disease). Similarly, the nucleated cell in the bone marrow which gives rise to the blood platelet – the megakaryocyte – does undergo neoplastic transformation; leading to acute megakaryoblastic leukaemia. The genes found to be abnormal (mutated) in various neoplasia code for substances which have a function in the process of cell division. An example is C-MYC which codes for a transcription factor and is found to be abnormal in Burkitt's lymphoma. Other examples are JAK2 and ABL that code for enzymes that attach phosphate groups and so activate proteins that transmit the signal for cell division in cells. The genes that are abnormal in breast cancer – BRCA1 and BRCA2- code for DNA repair enzymes. If a cell cannot repair its DNA or genes when damaged; it will accumulate genetic abnormalities and is at high risk of becoming neoplastic.

If the product of a gene has a role

in the control of cell division, the normal function of the product may either have the effect of stimulating or suppressing cell proliferation. The abnormality (mutation) that occurs in such a gene may lead to gain of function of the gene. An example is the abnormal ABL which, joined to nucleotides in the BCR gene, has a product with greater enzyme activity than the normal ABL. The more active abnormal enzyme activates the proteins that transmit signals for cell division far more than the normal cell enzyme. So, the effect of the genetic abnormality that leads to the neoplastic disease called chronic myeloid leukaemia is a gain of function of the gene product. When such a gain of function leads to a neoplasm, the gene is called an oncogene. On the other hand, if the effect of the gene abnormality that leads to neoplasm is a loss of function of the gene product, the gene is a tumour suppressor gene. Examples are BRCA1 and BRCA2genes that, when mutated, the product loses its function as a DNA repair enzyme.

In the light of the above, many neoplasia are indeed genetic disorders. These genetic disorders are usually acquired after birth and affect somatic cells such as the pluripotent haemopoietic stem cell in chronic myeloid leukaemia, or breast epithelial cell in breast cancer. Since the haemopoietic stem cell is not involved in reproduction, the genetic abnormality that causes chronic myeloid leukaemia is not transmitted from a parent to the offspring. This situation is different from sickle cell disease or haemophilia in which the genetic abnormality is present in the germ cells (sperm or ova) involved in reproduction; as a result of which the offspring are born with the genetic disorder; that is, the abnormal gene is inherited and the disease is congenital, not acquired as in chronic myeloid leukaemia. Molecular biology has led to the understanding that many neoplastic diseases are acquired genetic disorders of somatic cells. It is for this reason that abnormality of DNA or gene is associated many conditions/factors that predispose to neoplasia: ionizing radiation, chemical carcinogens such as benzene and alkylating agents, Down's and Fanconi' syndromes, paroxysmal nocturnal haemoglobinuria and myelodysplasia.

More recently, it has come to light that another group of genes (distinct from conventional oncogenes and tumour-suppressor genes) also contribute to the neoplastic process.MicroRNA genes, unlike other genes involved in cancer, do not encode proteins. Instead, the products of these genes consist of a single RNA strand of about 21 to 23 nucleotides. With a length of 21-23 nucleotides, they are very small or 'micro' compared with the much longer messenger RNAs which contain hundreds or thousands of nucleotides. The function of miRNAs is to regulate gene expression. A microRNA molecule can anneal to a messenger RNA (mRNA) containing a nucleotide sequence that complementsthe sequence of the microRNA. This way, the microRNA blocks translation of the messenger RNA (protein synthesis) and /or causes degradation of the mRNA, i.e regulates expression of the gene from which the messenger RNA was made.
With this background information about microRNA genes, let us consider how they contribute to the development of neoplasia.

RNA quantitation studies of various neoplastic cells show that they may over-express, or under-express, specific microRNA genes. For example, miR-15a and miR-16-1 are deleted or down-regulated in most indolent cases of chronic lymphocytic leukaemia; and miR155 gene is over expressed in aggressive CLL, diffuse large B-cell lymphoma, carcinoma of the breast and colon. Since a microRNA inhibits gene expression, if its own gene is up-regulated in a neoplasm, one can infer that it inhibits a tumour-suppressor gene; in other words, its effect is similar to that of an oncogene. On the other hand, if a miRNA gene is down-regulated in cancers, its effect is like that of a tumour-suppressor gene; because its normal function is probably to inhibit an oncogene. The function of microRNA genes depends on their targets in a specific tissue. A miRNA gene acts as a tumour suppressor in a given tissue if its miRNA inhibits an oncogene; it can act as an oncogene in another tissue if its miRNA inhibits the messenger RNA of a tumour-suppressor gene. Many microRNA genes occur in parts of chromosomes that are rearranged, deleted, or amplified in neoplastic cells. Parts of the genome consistently involved in chromosomal rearrangements in cancers but do not code for 'oncogenes' or 'tumor-suppressor genes' appear to contain microRNA genes.

Diagnosis of Disease
Diagnosis of disease has largely gone molecular. It is expected that, as more and more diseases are characterised at the molecular level, the trend towards molecular diagnosis will continue; eventually becoming the norm. Specific diagnosis of haemoglobinopathies and various malignancies is currently based on

demonstrating the genetic abnormality unique to those conditions. Specific diagnosis of sickle cell anaemia, for example, depends on demonstrating that the A=>T mutation is present in the two beta-globin genes in the individual. Such molecular diagnosis is preferred because it is more exact or specific, and allows a more accurate description of the relationship between genotype and phenotype. Various malignancies are currently diagnosed by demonstrating the genetic abnormality unique to each condition. Examples are:
acute myeloid leukaemia
translocation from chrom 8=>21
t(8;21)
acutepromyelocytic leukaemia
t(15;17)
acutemonoblastic leukaemia
inversion/del 16 erythroleukaemia
trisomy 8
Burkitt's type ALL
t(8;14) t(2;8) t(8;22)
breast cancer
mutations of BRCA1 /BRCA2

Therapeutics and the Pharmaceutical / Biomedical Industry

The prototype of targeted molecular therapy developed by the pharmaceutical industry is treatment of chronic myeloid leukaemia with imatinib – an inhibitor of the overactive bcr-abl tyrosine kinase that drives cell proliferation in this neoplasm. Imatinib works by occupying the grove in the abl part of bcr-abl where ATP normally binds, and prevents ATP from donating a phosphate to tyrosine residues in the substrate signal transduction proteins within the cell. By preventing the activation (phosphorylation) of molecules that transmit the stimulus (signal) for cell division, tyrosine kinase inhibitors such as imatinib, nilotinib and ponatinib, reduce neoplastic cell proliferation and confer clinical benefit in chronic myeloid leukaemia.

With the success story of tyrosine kinase inhibitors in treatment of CML, targeted molecular therapy for myeloproliferative neoplasia has been tried using inhibitors of the mutant JAK2; but the clinical benefits have not matched that of TKIs in CML.

Considering the role of micro RNAs in development of neoplasia, inhibiting micro RNAs might be beneficial in the treatment of neoplastic diseases. For example, targeted inhibition of micro RNA-191has potential for therapy of ALL or AML with 11q23 translocation and those solid tumours in which this miRNA is overexpressed.

Forensic Medicine

Molecular biology is applied in the identification of individuals in forensic medicine or medico-legal practice. For example, DNA analysis to demonstrate the presence of specific genes that are expected to be inherited by a child from a parent, or the absence of such genes that are expected to be inherited, is used to help a court of law determine the probability that an individual is a parent, sibling, or other types of blood relative of another person.

In addition, matching of specific genes in DNA extracted from the biological sample (such as buccal mucosal swab, saliva or blood) taken from a suspect with the same genes in DNA from a forensic specimen (such as semen, hair or blood) could help in identifying the culprit during the investigation of a crime.

Population Genetics

The prevalence of specific genes in different human populations could be used to assess if there is any ancestral relationship between them. Such population genetics data can help historians and archeologists trace the migration of peoples from one geographical region to another, over the past centuries.

Pre-implantation Genetic Diagnosis

After in-vitro fertilization (test tube baby) DNA is extracted from a single cell taken from the embryo at about the16-cell stage (embryo biopsy) and analysed to determine if the embryo has or does not have a specific desirable gene, or an abnormal or disease-causing gene. The embryo that has the desired gene or does not have the abnormal gene is then implanted in the uterus for further development. This process of pre-implantation genetic diagnosis could be used to produce 'designer babies' that are:
(a) potential donors of organs or haemopoietic stem cells for transplant to particular individuals (e.g, siblings) because they have the same HLA genes.
(b) babies who do not have the gene for specific diseases, such as sickle cell anaemia or haemophilia.
(c) babies of preferred gender; either because being a female means that the child is unlikely to have haemophilia A for example, or the parents desire a male or female child.

Developments in molecular biology make it imperative that current and future generations of doctors will practice medicine at a far more molecular level than their predecessors. It is necessary that medical students and practising doctors are equipped with the knowledge and skills required for molecular medicine.

BLOOD TRANSFUSION REACTIONS

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INTRODUCTION:
Blood transfusion reactions are abnormal changes in physiology occurring in the recipient following transfusion of whole blood or blood products. Blood transfusion has been of great importance in the history of medical practice. It is used in conditions of severe anemia, excessive hemorrhage, hemolytic disease of the newborn, Sickle Cell Disease, etc. However, for some reasons, there have been occasions of adverse reactions arising from the transfusion.

CLASSIFICATION: Can be classified based on: Time of onset or Mechanism of the reaction
Based on time of onset
* Acute/Early onset/Immediate Blood Transfusion Reactions
* Delayed Blood transfusion Reactions
Early onset transfusion reactions are usually acute reactions that occur during transfusion or anytime within 24 hours following transfusion of the blood or blood components, while late or delayed reactions occur from 24 hours to 2 weeks following the transfusion.

1. Acute/Immediate e.g.
* Allergic reactions
* Acute hemolytic reactions
* Febrile non-hemolytic reactions (FNHR)
* Transfusion related acute lung injury (TRALI)

2. Delayed e.g.
* Delayed hemolytic Reactions
* Transfusion-associated graft versus host disease (GVHD)
* Post-transfusion purpura.
* Based on mechanism of action
* Immune-mediated the examples above for acute and delayed
* Non immune mediated iron overload, circulatory overload, transfusion associated sepsis, etc.

AETIOPATHOGENESIS & CLINICAL FEATURES:
Approximately 400 antigens have been identified on red blood cells. A single person cannot have all these antigens. Individuals who lack particular blood group antigen may produce antibodies against it, leading to blood transfusion reactions when given blood containing the antigen.

Acute/Immediate
* Allergic reactions:
Recipient's antibodies vs donor plasma proteins. Hypersensitivity and acute inflammation, giving rise to urticarial rash, abdominal pain, hypotension etc.
* Acute hemolytic transfusion reactions
This is the most dangerous type of transfusion reaction. Usually results from transfusion of ABO incompatible unit. Mostly caused by clerical error. Anti-A and Anti-B are naturally occurring, thus prior sensitization not needed. Antibodies bind to RBC antigens leading to compliment mediated hemolysis. Clinical Features occur in phases: Haemolytic shock phase; This may occur after only few milliliters of blood have been transfused. Clinical features include; Flushing, headache, precordial pain, pyrexia ,chills, shortness of breath, vomiting, rigors and hypotension, haemolysis and haemoglobinuria, jaundice and disseminated intravascular coagulation(DIC) may occur. The oliguric phase; Occur in some patients with a haemolytic reaction, in which there is renal tubular necrosis with acute renal failure. Diuretic phase; fluid and electrolyte imbalance occur during the recovery from acute renal failure.

* Febrile non-hemolytic reactions:
Recipient's antibodies vs. donor WBC or platelet specific antigens. The antibodies are stimulated by previous transfusion or pregnancy. This is the most frequent type of acute transfusion reaction. Normally occurs about 30minutes after the onset of transfusion. Clinical features include Fever (>1' c above baseline) and rigors may develop during red cell transfusion. Typically, only fever is present. However some recipients may experience severe rigors, chills, hypotension and vomiting.

* Anaphylactic Reactions:
Occurs when an individual has previously been sensitized to an allergen present in blood. Common cause is anti-IgA in patients with IgA deficiency. Signs may include; dyspnoea, wheezing, anxiety, hypotension, bronchospasm, erythema, flushing, urticaria, pruritus.

* Transfusion Related Acute Lung Injury (TRALI)
Antibodies against WBC contained in donor's plasma reacts with recipient's WBC. Antibody-bound WBC infiltrate the lungs, activating granulocytes in pulmonary vasculature giving rise to increased vascular permeability and pulmonary oedema. Symptoms and Signs include rapid onset of dypsnoea, hypoxemia, rales, without cardiogenic edema and fever.

Delayed reactions (after 24hrs)
* Delayed Haemolytic Reactions
Rhesus and Kidd antigens are the

common causes. Prior exposure is needed from previous transfusion or pregnancy. The previously formed antibodies bind to the antigens leading to extra-vascular hemolysis in the reticulo-endothelial systems.

* Transfusion associated Graft Versus Host Disease (GVHD) Transfused white cells reacts with recipient's antigens . Observed in immunocompromised patients or 1st/2nd degree relations, who share HLA antigens and so do not recognize the lymphocytes as non-self.

Non-immune mediated reactions

* Transfusion associated sepsis: Bacterial contamination of a blood component is rare but severe and sometimes fatal cause of transfusion reactions. The transfusion of bacteria-contaminated blood leads to septicaemia, after which sepsis will lead to circulatory failure.

* Bacterial Contamination Bacterial contamination of a blood component is rare but severe and is sometimes, a fatal cause of transfusion reactions. Signs include; high fever, shock, tachycardia and weak pulse, without a clear focus of infection

* Viral infections: hepatitis, HIV, CMV, etc. Other infections: toxoplasmosis, malaria, syphilis.
* Circulatory overload: when large volume of blood is transfused within short period of time. Pulmonary edema and acute respiratory failure. Shortness of breath, hypoxemia, and rales, with orthopnoea, Tachycardia, distended jugular veins.

* Iron overload: repeated red cell transfusion over many times

* Hypothermia: when cold blood is transfused

EPIDEMIOLOGY: Blood transfusion Reactions (BTR) occur worldwide and among every group, however the prevalence varies, occurring more in developing countries. In the United States, it occurs more in black populations (SCA). Also multiparous women have been noted to have higher incidence of BTR. The reactions also occur more in group O neg. recipients and in directed donations (relations).

Reported incidences of acute transfusion reaction (ATR) differ significantly. While incidence of 0.2%2 and 0.34%3 are reported in Europe and South America, respectively, the incidence of acute immune-mediated transfusion reactions is reported to be 11.8% in North East Nigeria, out of which 0.01% was due to Acute hemolytic transfusion reaction (AHTR), 9.8% due to febrile non-hemolytic transfusion reaction (FNHTR) and 2% attributed to allergic transfusion reactions.4 Similarly, at the Obafemi Awolowo University Teaching Hospital, the overall incidence of transfusion reactions is 8.7% (40 cases), with febrile non-haemolytic transfusion reactions (FNHTR) constituting 65% of these.5

A study at the Aminu Kano Teaching Hospital, on the pattern of acute blood transfusion reactions among adults in North-Western Nigeria showed that the incidence of acute transfusion reaction (ATRs) was 3.6%, out of which 3.3% were febrile non-hemolytic transfusion reaction (FNHTR) and 0.3% were acute allergic reactions (AAR).6
In North Eastern part of Nigeria by Umaru Nasira Ibrahim in Department of Obs & Gyna, Federal Medical Centre, Azare ,Nigeria in June 2013 showed that 1602 pregnant women received blood which gives a rate of 10.5% of total number of pregnant women. Acute reactions were found in 26.3%, Non haemolytic febrile reaction in 47.7%and Allergic reaction in 24.5%.

OBSERVATIONS DURING BLOOD TRANSFUSION

* Transfusions should only be given when the patient can be observed
* Blood pressure, pulse and temperature should be monitored before and 15 minutes after starting each pack
* In conscious patients, further observations are only needed if the patient has symptoms or signs of a reaction
* In unconscious patients, check pulse and temperature at intervals during transfusion
* Signs of abnormal bleeding during the transfusion could be due to disseminated intravascular coagulation resulting from an acute haemolytic reaction.

ACTIONS TO BE TAKEN IF BLOOD TRANSFUSION REACTIONS OCCUR

* STOP the transfusion. Call for assistance.
* Assess patient clinically for above signs /symptoms.
* Measure temp, pulse rate, BP, respiratory rate, O2 sat.
* Check if identity of recipient corresponds to detail on unit transfused and document from blood bank
* To provide supportive care to the patient. More specific treatments depend on the nature and presumed cause of the transfusion reaction.
* Most hospitals and medical centers have transfusion reaction protocols.

MANAGEMAENT OF ACUTE TRANSFUSION REACTIONS

* **Mild allergic reaction:** Give chlorpheniramine or diphenhydramine 10 mg slowly i.v and restart the transfusion at a slower rate and observe more frequently Febrile non-haemolytic transfusion reaction: If temperature rises ≤ 1.5°C, observations are stable and patient is otherwise well, Give paracetamol, Then restart infusion at a slower rate. Observe more frequently.

* **Acute hemolytic transfusion reaction:** Mortality rate is high (up to 40%). Stop the transfusion; maintain renal output with intravenous fluids and diuretics (furosemide or mannitol);

Maintain urine output at > 100 mL/hr. Treat DIC with heparin; Inform blood bank of transfusion reaction. Return the unit together with patient's anticoagulated blood sample.

*** Severe allergic reaction:** Discontinue transfusion and give chlorpheniramine 10 mg slowly i.v. Commence O2. Give salbutamol nebulizer. If severe hypotension or bronchospasm, give adrenaline (epinephrine) 0.5 mg i.m. Send clotted blood sample to transfusion laboratory. Take down unit and giving set, and return intact to blood bank with all other used/unused units Bacterial infection of unit: Take down unit and giving set/return intact to blood bank with all other used/unused units. Make aggressive attempts to identify organism. Take blood cultures, repeat blood group/cross-match/FBC, coagulation screen, biochemistry, and urinalysis. Monitor urine output and Commence broad-spectrum antibiotics if suspected bacterial infection.

*** Transfusion-related acute lung injury (TRALI):** Discontinue transfusion, Give 100% oxygen. Treat as acute respiratory distress syndrome (ARDS). Ventilate if severely hypoxaemic. May consider younger products: packed red blood cells 2 weeks, platelets 3 days, washing components to prevent syndrome. Fluid overload: Give oxygen and furosemide 40–80 mg i.v.
Iron overload: Chronic administration of iron chelator such as deferoxamine

*** Delayed Haemolytic Transfusion Reaction:** Repeat compatibility tests to identify causative antibody and avoid blood with corresponding antigen in future.

*** Post Transfusion Purpura:** Rare, Give Intravenous immunoglobulin 1g/kg/day x 2 days, plasma (exchange) transfusion.
Transfusion Associated Graft Versus Host Disease. Prevention: irradiate all blood components for recipients with severe immune compromise. Avoid transfusing blood from 1st/2nd degree relatives.

PREVENTION OF BLOOD TRANSFUSION REACTIONS:
The patient's safety depends on adherence to standard procedures for taking samples for compatibility testing, administering blood, record-keeping and observations. When taking blood for pre-transfusion testing, positively identify the patient at the bedsideand label the sample tube and complete the request form clearly and accurately after identifying the patient.
* Ensure that the identification of each blood pack matches the patient's identification
* Check that the ABO and RhD groups of each pack are compatible with the patient's
* Check each pack for evidence of damage
* If in doubt, do not use and return to the blood bank
* Complete the forms that document the transfusion of each pack
* Ensure recipients receive units of blood or components correctly labeled with their names

CONCLUSION
Blood Transfusion Reactions are preventable. To reduce risk of occurrence: The type of blood component transfused should be appropriate to the clinical situation and whole blood therapy should be avoided or restricted to specific situations. Also, patients with previous history of transfusion should be monitored closely as they have a higher risk of developing transfusion reaction and also transfusion of blood stored for more than 3 days should as much as possible be avoided, especially in patients that have a potential risk of transfusion reaction. Bedside blood filters that have been shown to decrease the incidence of FNHTR should be provided in order to achieve meaningful reduction in the rate of blood transfusion reactions. Establishing a haemovigilance system of monitoring, collating, and analyzing data on adverse effects of blood transfusion both locally and nationally will help in reducing the incidence of Blood Transfusion Reactions especially acute transfusion reactions.6This system of haemovigilance if incorporated into the blood transfusion service will promote effective monitoring of blood transfusion and reduce wastage of scarce blood/blood products.7

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DEVELOPING TREATMENT FOR MALARIA

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According to the latest estimates released in December 2013, there were about 207 million cases of malaria in 2012 (with an uncertainty range of 135 million to 287 million) and an estimated 627000 deaths (with an uncertainty range of 473000 to 789000). Malaria mortality rates have fallen by 42% globally since 2000 and by 49% in the WHO African Region.

Most deaths occur among children living in Africa where a child dies every minute from malaria. Malaria mortality rates among children in Africa have been reduced by an estimated 54% since 2000.

This is good news!! Thanks to the unremitting efforts made by passionate researchers to find out the most effective methods of eradicating this life threatening disease.

Notwithstanding, new frontiers of research are still open for procuring a lasting solution to malaria burden worldwide especially in Sub Saharan Africa.

These recent advances in the treatment of malaria include;
1. Reinforcement of combination chemotherapy.
2. Development of analogs of preexisting drugs.
3. Use of natural products.
4. Use of non-conventional drugs with antimalarial properties.
5. Drug resistance reversers and chemosensitizing agents.
6. Compounds active against new targets.
7. Malaria vaccine.

1.COMBINATION CHEMOTHERAPY

Current practice in treating cases of malaria is based on the concept of combination therapy since this offers several advantages including reduced risk of treatment failure, reduced risk of developing resistance, enhanced convenience and reduced side effects. Prompt parasitological

confirmation by microscopy or alternatively by rapid diagnostic test is recommended in all patients suspected of malaria before treatment is started. Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible. Artemisinin-based combination therapy (ACT) is now the currently recommended treatment of uncomplicated malaria worldwide. This is due to its rapid clinical and parasitological cure rate,low relapse rate,absence of resistance and good tolerability profile.

2. DRUG ANALOGS

These substances are derived from preexisting conventional antimalarial medications with comparable pharmacokinetic and pharmacodynamic properties. Examples include pyronaridine (related to chloroquine), tafenoquine (a more active slowly metabolized analog of primaquine), and bulaquine (also a congener of primaquine). Bulaquine has comparable anti relapse activity when used for 5 days, is partly metabolized to primaquine and is better tolerated in G6PD deficient patients.

3. PLANT PRODUCTS

Extracts from diverse families and species of plants are being used for the treatment of malaria in some communities. Examples include the plant family Accacia whose bark extract when mixed with quinine stops the remittent fever of malaria and the leaf of the well-known plant Carica papaya (pawpaw) when boiled in water has some degree of antimalarial activity. However, much is still left to be desired in extracting the full antimalarial potentials in these products.

4. NONCONVENTIONAL DRUGS WITH ANTIMALARIAL PROPERTIES

Compounds active against other diseases such as folate antagonists, tetracyclines and iron chelators have been found to be effective against malaria parasites when used singly or synergistically with other conventional anti malarial medications. Doxycycline, for example, has been used as a single agent in treatment of malaria.

5. DRUG RESISTANCE REVERSERS AND CHEMOSENSITIZERS

Combining previously effective drugs with compounds that reverse parasite resistance such as the calcium channel blocker verapamil, the tricyclic antidepressants desipramine, the phenothiazine trifluoperazine, and the antihistamine chlorpheniramine, has been shown to raise the efficacy by many folds.

New chemosensitizing agents such as the tricyclic acridone molecules with a short alkylamine chain attached to the central nitrogen atom could make chloroquine-resistant parasites susceptible to the drug again!! This action is attributed to blocking the PfCRT pump protein, meaning that the chloroquine can reach its target site. This new class of antimalarial drug have dual role in that it can reverse the malarial parasite resistance to existing drugs and also have antimalarial action.

6. NEW TARGETS

Certain agents have been designed to target novel sites on the malarial parasite such as the cytosol, parasite membrane, food vacuole, mitochondria, chloroplast-like organelles and ribosomes. These agents are still under experimental trials.

7. MALARIA VACCINE (RTS,S/ASO1 Vaccine)

A vaccine has been constructed for malarial! It is a hybrid construct of the hepatitis B surface antigen fused with a recombinant antigen derived from part of circum sporozoite protein. It is primarily designed for infants and young children in Sub Saharan Africa. The WHO has already taken the unusual step of indicating that it would recommend this first malaria vaccine for use in some African countries as early as 2015.

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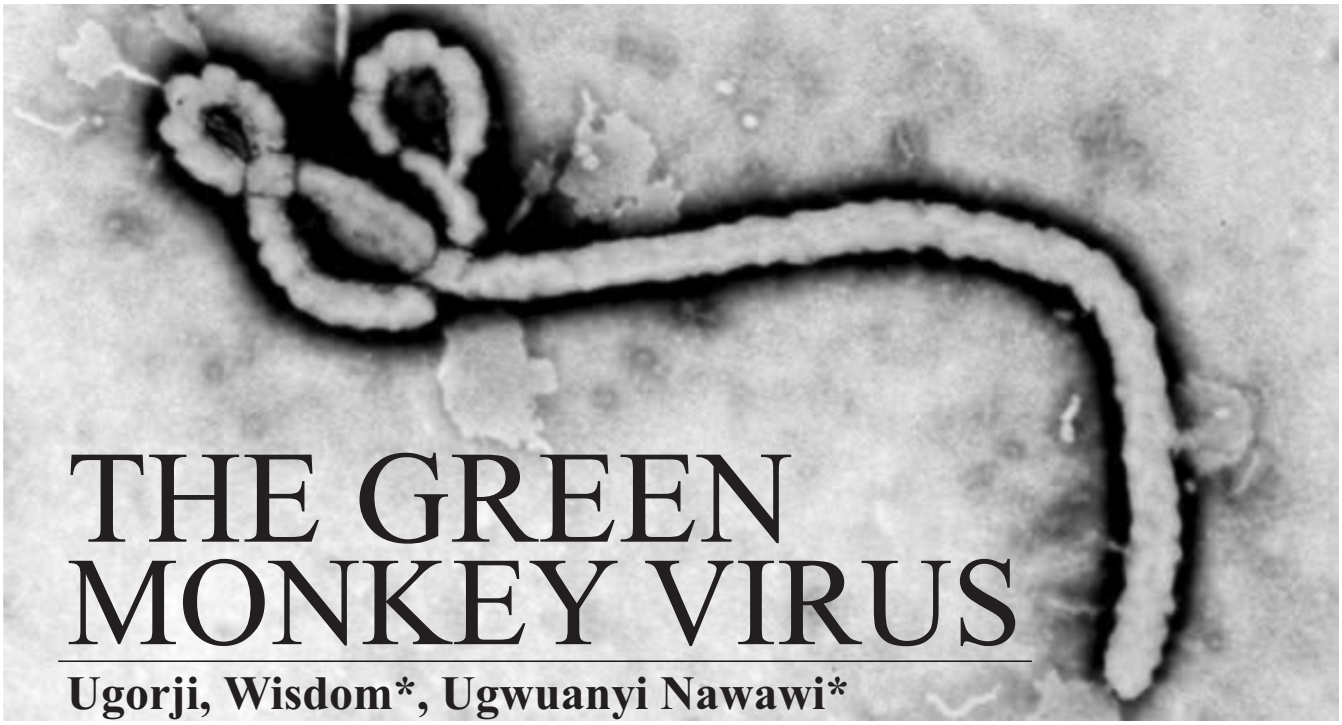

THE GREEN MONKEY VIRUS

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Introduction

The Green – Monkey virus is more-popularly recognized as the Ebola virus and in our day is a horrid harbinger of death. Ebola virus, the cause of the Ebola Haemorrhagic Fever (EHF) or Green – Monkey Fever has been taxonomically grouped under the order Mononegavirales the family Filoviridae, genus Ebola virus. The genus is further divided into five species, the deadliest of which is Zaire Ebola virus. The Reston Ebola virus is the least virulent of the species and though airborne, it has only been shown since 1989 to cause disease in monkeys, not humans. The specie names have been derived from their locality of discovery and so far, four of the five have led to seven major human outbreaks of Ebola Haemorrhagic Fever(number of deaths above hundred) with fatality rates of 50-90% between 1976 and 2014. It is true that this disease is currently without cure yet progress towards definitive treatment is no loss cause and this exposition aims at exploring various prospects for prevention and treatment. Attention would be given briefly to aetiology, symptomology, transmission and diagnosis of Ebola Haemorrhagic Fever.

Brief Historical Background

In Yambuku, Zaire (currently DR Congo), on 26 August,1976 came the first fatal outbreak of Ebola. This date should not replace the year of first sighting-albeit non-fatal-which is 1972 in Tandala, Zaire. Scientists have also argued that between 425BC and 430BC, Ebola virus could have been the cause of three hundred thousand deaths in Athens during the Peloponnesian War. Ebola virus derived its name from the Ebola River near Yambuku.

Aetiology

Ebola Haemorrhagic Fever in humans is caused by all known Ebola virus species excluding Reston ebola virus. These are Zaire ebola virus, Sudan ebola virus, Ta'i Forest ebola virus, and Bundibugyo ebola virus.

General Structure

The viruses are pleomorphic but basically follow a long and filamentous bacilli form. They could also take on a 'U' shape and are between 800-1400nm long. The viral particles contain a unique single-stranded molecule of negative-sense RNA surrounded by an envelope derived from the host cell membrane that is covered with 7nm spikes placed 10nm apart on the virion's surface. The viruses are composed of 7 polypeptides, a glycoprotein, a nucleoprotein, a polymerase and 4 other proteins.

Entry and Pathophysiology

Endothelial cells, polymorphonuclear phagocytes

and hepatocytes seem to be main target cells for Ebola viruses but before entry into these cells can occur, the cholesterol transporter protein, Niemann-Pick CI (NPCI) is required. This is so because NPCI mediates direct binding of the viral envelope glycoprotein before encountering the phagocytes. On encountering the cells, Ebola virus binds to specific host receptors with concomitant fusion of its envelope with the cell from where it begins processes of its replication. After the virus has replicated and multiplied, it takes over synthetic machinery of the infected cell and begins creating the Ebola virus glycoprotein which does two things majorly: (I) It initiates the binding of the virus to endothelial cells after it has been released from the infected phagocytes and (ii) It suppress early steps of neutrophil activation. In course of the infection, cytokines (TNF, IL-6, IL-8)are released and they mediate induction of fever and inflammation which are chief manifestations of the first phase of Ebola disease.

Signs and Symptoms

Symptoms of Ebola Haemorrhagic Fever develop 4-16 days after initial infection and from this time victims are expected to either die or show improvements in 5-10 days. The incubation period of between 2-21 days is usually dependent on how the virus was contracted. Symptomology is divided under two phases namely:

* Influenza-like phase characterized by malaise, chills, fever, lethargy, joint pain, sore throat, severe headache, muscle pain, chest pain, cough, hiccups,
* Haemorrhagic phase characterized by uninhibited bleeding from all body orifices as eyes, mouth, ears, nose, anus and vagina. There is also multiple organ dysfunction, disseminated intravascular coagulation, hypotension and focal tissue necrosis. Petechiae, purpura, ecchymosis, hematomas, seizures and coma are not uncommon sightings in this phase.

Contrary to common belief, it is not the bleeding that brings about death but multiple organ dysfunctions due to fluid redistribution.

Transmission

Ebola virus is transmitted via the following ways:

1. Person – Person Spread

* From an infected personto a non-infected person through direct contact and contact with the blood, faeces, vomitus, urine, semen of the infected person. Also sharing needles and sharp objects with an infected person.
* By touching, washing or kissing dead bodies as well as washing hands in the same container as those who have touched the dead bodies.
* Males that survived Ebola infections have been shown to transmit the virus for periods up to 7 weeks after clinical recovery via sexual intercourse.

2. **Animal – Man Spread**

* Direct contact with infected Monkeys, Gorillas, Chimpanzees and Bats as well as carcass or meat of these animals. Fruit bats have been discovered to be natural reservoirs for the Ebola virus since they show no clinical signs of disease despite harbouring large numbers of the virus. They were also implicated in the 1976 and 1979 outbreaks having resided near the cotton factory where index cases were reported.

After the bats pick and eat fruits they drop leftovers to the ground. The non-human primates become infected after they finish off these scraps smeared with the bat's saliva into which Ebola virus has been shed. Human contact with all such infected primates facilitates transmission of the virus (hence, the name-Green Monkey).

Ebola Haemorrhagic Fever is a very contagious disease needless to say. However in much-affected Africa very little is being done to alleviate poor social standards that necessitate rapid spread of the disease. There are risk factors peculiar to Africa that predispose one to infection as well as factors that hamper transmission.

Factors influencing spread of Ebola Haemorrhagic Fever in Africa

PREDISPOSING FACTORS	FACTORS DISCOURAGING SPREAD
Unhygienic and non-precautionary medical practices such as reuse of syringe needles	High fatality rates of the disease
Poorly educated caregivers and medical staff	Remote areas where infections occur
Consumption of bush meat	Rapidity of demise of patients truncate person to person transmission
Unwholesome burial traditions encouraging contact with bodies of dead persons	Newly developed vaccines for non-human primates
Poor enlightenment concerning the disease	Inadequacy of existing roads hinder easy migration of victims
Habitation near forests and wildlife	
Primitive occupations such as hunting	

Diagnosis
A major method of diagnosing Ebola Haemorrhagic Fever is proper medical history taking covering especially, travel and occupational history and exposure to wildlife. Laboratory diagnosis involves isolating ebolaviruses from or detection of ebolavirus antigen in patient blood or serum. Prospects for treatment of Ebola Haemorrhagic Fever.

Prevention of this disease revolves around abstaining from direct exposure to the Ebola virus (as treated under Transmission) and administration of a vaccine. No vaccine and no definitive treatment is currently available to address this disease. However, immense work is undergoing to produce a cure for Ebola Haemorrhagic Fever. Current research in this regard exploits many components of the pathophysiology of Ebola.
The cholesterol transporter Niemann-Pick CI is necessary for Ebola infection and as such individuals with mutated NPCI have been discovered to be immune to Ebola virus.This indicates that genetic mutations in the gene coding for NPCI could render humans resistant to the virus. This is one path-blazing discovery that many scientists are exploiting currently.
Researchers from the U.S. Army Medical Research Institute of Infectious Diseases have found out that clomiphene and toremifene-both, oestrogen receptor drugs-have inhibited progress of Ebola virus in mice. The authors of the research are convinced that if orally administered these drugs could be used in treating infections on their own or together with antiviral drugs.

Hyperimmune equine
Immunoglobulin had once been used to treat a lab worker who had come down with the disease in Russia. The endeavor was however, unsuccessful yet more probes are still ongoing in improving this form of treatment. One other area of promise is the recombinant post- exposure vaccine used to treat a German researcher who accidentally pricked herself with an ebola virus contaminated needle. The treatment was successful because the woman survived, though Ebola virus infection in her case had not been conclusive. This vaccine is known as recombinant Vesicular Stomatitis Indiana Virus and has been used successfully as post-exposure prophylaxis in nonhuman primates. This vaccine presents hope in reducing Ebola virus transmission from animal to man.

As of today, treatment of Ebola Haemorrhagic Fever is basically supportive and involves rehydration therapy, administration of anticoagulants and pain management. Also, it was recorded in 1995 that seven out of eight patients who had received blood from previous survivors recovered from the infection.

All hope is not lost then in combating this new scourge of the human race and so the popular comment '...pray you fall into the surviving 10%' might soon become a figment of storytelling.

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HIV/AIDS
IN THE 21ST CENTURY

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INTRODUCTION

Acquired Immunodeficiency Syndrome (AIDS) is a human viral disease that ravages the immune system, undermining the body's ability to defend itself from infection and disease. Caused by the human immunodeficiency virus (HIV), AIDS leaves an infected person vulnerable to opportunistic infections infection by microbes that take advantage of a weakened immune system. Such infections are usually harmless in healthy people but can prove life-threatening to people with AIDS. Although there is no cure for AIDS, new drugs are available that can prolong the life spans and improve the quality of life of infected people.

AIDS is one of the deadliest epidemics in human history. It was first identified in 1981 among homosexual men and intravenous drug users in New York and California. Shortly after its detection in the United States, evidence of AIDS epidemics grew among heterosexual men, women, and children in sub-Saharan Africa. AIDS quickly developed into a worldwide epidemic, affecting virtually every nation.

The United Nations Program on HIV/AIDS (UNAIDS) estimates that the worldwide number of new cases of HIV infection peaked in the late 1990s with more than 3 million people newly infected each year. However, some regions of the world, especially Vietnam, Indonesia, and other countries in South East Asia, continued to see an increase in the early 2000s. In addition, the number of people living with HIV or AIDS has continued to rise as the result of new drug treatments that lengthen life.

This write-up will focus on the causes of HIV/AIDS, its prevalence/epidemology in Africa (West Africa and Nigeria), the pathophysiology, management, treatment and most importantly the prevention.

EPIDEMIOLOGY OF HIV/AIDS IN AFRICA

While cases of AIDS have been reported in every nation of the world, the disease affects some countries more than others. About 90 percent of all HIV-infected people live in the developing world (in the third world countries: Africa). AIDS has struck Sub-Saharan Africa particularly hard. Two-thirds of all people living with HIV infection reside in African countries south of the Sahara, where AIDS is the leading cause of death. The African countries south of the Sahara have some of the best HIV surveillance systems in the world.

They provide solid evidence that the HIV infection rate has stabilized at a relatively low level in Senegal and that the extremely high rates in Uganda have been reduced. However, in most sub-Saharan countries adults and children are acquiring HIV at a higher rate than ever before: the number of new infections in the region during 1999 was 4.0 million. This acceleration effect is yet another challenge posed by long-standing epidemics. As the rate of HIV infection in the general population rises, the same patterns of sexual risk result in more new infections simply because the chances of encountering an infected partner become higher.

PATHOPHYSIOLOGY

The pathophysiology of AIDS is complex. Ultimately, HIV causes AIDS by depleting CD4+ T helper lymphocytes. This weakens the immune system and allows opportunistic infections. T lymphocytes are essential to the immune response and without them; the body cannot fight infections or kill cancerous cells. The mechanism of CD4+T cell depletion differs in the acute and chronic phases. After the virus enters the body there is a period of rapid viral replication, leading to an abundance of virus in the peripheral blood. During primary infection, the level of HIV may reach several million virus particles per milliliter of blood.

This response is accompanied by a marked drop in the number of circulating CD4+ T cells. This acute viremia occurs in virtually all people with the activation of CD8+ T cells, which kill HIV-infected cells, with consequent antibody production, or seroconversion. The CD8+ T cell response is thought to be important in controlling virus levels, which peak and then decline, as the CD4+ T cell counts rebound. A good CD8+ T cell response has been linked to slower disease progression and a better prognosis, though it does not eliminate the virus. During the acute phase, HIV-induced cell lysis and killing of infected cells by cytotoxic T-cells accounts for CD4+ T cell depletion, although apoptosis may also be a factor. During the chronic phase, the consequences of generalized immune activation coupled with the gradual loss of the ability of the immune system to generate new T cells appear to account for the slow decline in CD4+ T cell numbers.

Although the symptoms of immune deficiency characteristic of AIDS do not appear for years after a person is infected, the bulk of CD4+ T cell loss occurs during the first weeks of infection, especially in the intestinal mucosa, which harbors the majority of the lymphocytes found in the body. The reason for the preferential loss of mucosal CD4+ T cells is that a majority of mucosal CD4+ T cells express the CCR5 co-receptor, whereas a small fraction of CD4+ T cells in the bloodstream do so.
HIV seeks out and destroys CCR5 expressing CD4+ cells during acute infection. A vigorous immune response eventually controls the infection and initiates the clinically latent phase. However, CD4+ T cells in mucosal tissues remain depleted throughout the infection, although enough remain to initially ward off life-threatening infections. With continuous destruction of the CD4 cells, the immune system weakens and paves way for opportunistic infections and then to AIDS.

TRANSMISSION OF HIV/AIDS

This deadly killer can be transmitted in several ways. The three major ways are:

* **Sex with infected person:** This is the leading mode of HIV transmission among youths. HIV transmission occurs most commonly during intimate sexual contact with an infected person, including genital, anal, and oral sex. The virus is present in the infected person's semen or vaginal fluids. During sexual intercourse, the virus gains access to the bloodstream of the uninfected person by passing through openings in the mucous membrane—the protective tissue layer that lines the mouth, vagina, and rectum—and through breaks in the skin of the penis.
* **Mother to child transmission:** HIV can be transmitted from an infected mother to her baby while the baby is still in the woman's uterus or, more commonly, during childbirth. The virus can also be transmitted through the mother's breast milk during breast-feeding. Mother-to-child transmission accounts for 90 percent of all cases of AIDS in children. It is particularly prevalent in Africa.
* **Blood transfusion:** Transmission through this means is mostly caused by carelessness of some hospital agencies/doctors/health workers. Because of this, all hospitals are enjoined to take extra medical care in screening blood for transfusions.

In some cases, direct contact with HIV-infected blood is also a means of transmission. This can be by sharing of contaminated needles, contaminated clippers, razors etc. Less frequently, HIV infection results when health professionals accidentally stick themselves with needles

containing HIV-infected blood or expose an open cut to contaminated blood.

MANAGEMENT/ TREATMENT

While no medical treatment cures AIDS, in the relatively short time since the disease was first recognized, new methods to treat the disease have developed rapidly. Health-care professionals focus on three areas of therapy for people living with HIV infection or AIDS:

1. Antiretroviral therapy using drugs that suppress HIV replication;
2. Medications and other treatments that fight the opportunistic infections and cancers that commonly accompany HIV infection; and
3. Support mechanisms that help people deal with the emotional repercussions as well as the practical considerations of living with a disabling, potentially fatal disease.

In addition to antiretroviral therapy to combat HIV infection, effective drug treatments are available to fight many of the medical complications that result from HIV infection. Doctors try to prevent infections before they begin to avoid tasking a patient's weakened immune system unnecessarily. A doctor instructs an HIV-infected person on ways to avoid exposure to infectious agents that produce opportunistic infections common in people with a weakened immune system. Doctors usually prescribe more than one drug to forestall infections.

DETECTION/MONITORING OF HIV INFECTION.

Since HIV was first identified as the cause of AIDS in 1983, a variety of tests have been developed that help diagnose HIV infection as well as determine how far the infection has progressed. The standard test to detect HIV antibodies in the blood is the enzyme-linked immunosorbent assay (ELISA). In this test, a blood sample is mixed with proteins from HIV. If the blood contains HIV antibodies, they attach to the HIV proteins, producing a telltale color change in the mixture. This test is highly reliable when performed two to three months after infection with HIV. The test is less reliable when used in the very early stage of HIV infection, before detectable levels of antibodies have had a chance to form. Doctors routinely confirm a positive result from an ELISA test by using the Western Blot test, which can detect lower levels of HIV antibodies. In this test a blood sample is applied to a paper strip containing HIV proteins. If HIV antibodies are present in the blood, they bind to the HIV proteins, producing a color change on the paper. The combination of the ELISA and the Western Blot test is more than 99.9 percent accurate in detecting HIV.

Other tests can be used to screen donated blood, blood products, and body organs for the presence of HIV.

PREVENTION OF HIV/AIDS INFECTION

A saying goes that “prevention is better than cure”. This saying applies mostly to the transmission through sexual means. Abstinence from promiscuity is the best way to protect oneself from this killer disease. Some deceive themselves in thinking that by the use of condoms, the infection can be prevented. But sincerely speaking, use of condom (ironically protected sex) does nothing in preventing HIV transmission. There are many holes in condom through which the retrovirus causing this infection can pass through.

Also transmission through contact with HIV-infected blood can be prevented by sterilization of all hypodermic needles used during surgical operations, sterilization of clippers and most importantly not sharing ones personal belongings that can easily be exposed to blood, e.gs, clippers, finger cutters, razors, e.t.c. For mother to child transmission, prevention primarily involves the use of a combination of antivirals during pregnancy and after birth in the infant but also potentially include bottle feeding rather than breastfeeding. If replacement feeding is acceptable, feasible, affordable, sustainable and safe mothers should avoid breast-feeding their infants however exclusive breast-feeding is recommended during the first months of life if this is not the case. If exclusive breast feeding is carried out the provision of extended antiretroviral prophylaxis to the infant decreases the risk of transmission.

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PUFFING OUT LIFE

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At the time of writing, the author was a 1st year pre-clinical student of the College of Medicine, UNN.

As I watched him "puff out life", I felt like moving nearer to him and shouting, 'drop that stick'. He looked handsome, young and misled. That stick, the cigarette, popularly known as 'cigar'. Cigarettes were invented in Brazil by rolling tobacco leaves in paper. People used to believe that tobacco had medicinal values. In earlier times tobacco was called 'herba panacea' meaning cure-all herb. Some people even believed that smoking cleaned the lungs. In 1959, a French ambassador named Jean Nicot brought tobacco plants to Portugal, telling friends it was used in treating wounds, asthma and cancer. The word nicotine and nicotiana were formed from Jean Nicot's last name.

In the sixties, several countries outlawed tobacco use but in America and Spain, it was a major crop and source of income. In 1859, the first report linking smoking with certain diseases was published, but after World War 1, a group of tobacco companies joined forces and denied that tobacco causes any harmful effect.

INGREDIENTS THAT ARE FOUND IN CIGARETTE

Tobacco is not the only ingredient in the cigarette. There are so many other ingredients such as:

- Ammonia: by adding ammonia to cigarettes, nicotine in its vapour form can be absorbed through the lungs more quickly. This in turn makes the brain get a higher dose of nicotine with each puff decreasing the number of years of the smoker more.

- Angelical root extract: known to cause cancer in animals.
- Arsenic: Used in rat poisons.
- Benzene: Used in making dyes synthetic rubber.
- Butane: As gas used in lighter fluid.
- Carbon Monoxide: Poisonous gas.
- Cadmium: Used in batteries.
- Cyanide: A deadly poison.
- DDT: a banned insecticide
- Ethyl Furoate: causes liver damage in animals
- Lead: Poisonous in high doses
- Formaldehyde: used to preserve dead specimens
- Methoprene: An insecticide
- Megastimatrienone: A chemical naturally found in grape fruit juice
- Maltitol: Sweetener for diabetics
- Naphthalene: Ingredient in moth balls
- Methyl isocyanate: Its accidental release killed 2000 people in Bhopal, India in 1984.
- Polonium: Cancer-causing radioactive element
- Tar: Used in road construction.

With the above stated ingredients does one need any prophet to stop smoking, remember 'to be forewarned is to be forearmed'.

WHAT HAPPENS IN THE BODY OF A CIGAR SMOKER

- The heart speeds up, from 10 to 20 beats per minute
- The blood vessels constrict, or tighten, so that blood pressure goes up by 5 to 10 points.
- The temperature of the skin drops by 6°F (that's because the blood is rushing to the heart, where it would be needed in real crisis)
- The level of blood sugar, the body's store of energy, falls, because the blood sugar is being burned up in a stressed out reaction.
- The hypothalamus, which

regulates hunger, gets a "speed-up" message, so the appetite falls too.

At an average rate of ten puffs per cigarette, a one to three pack-a-day smoker inhales 70,000 to 200,000 individual doses of mainstream smoke during a single year. According to chemists at R.J. Reynolds Tobacco Company, cigarette smoke is 10, 000 times more concentrated than the automobile pollution at rush hour on a freeway. The lungs of smokers puffing a daily ration of 20 to 60 low to high tar cigarette, collect an annual deposit of one quarter to one and one –half pounds of gooey black material amounting to a total of 50 to 90 million pounds of carcinogen-packed tar for the aggregate of current American smokers.

WHAT MAKES A CIGARETTE SO IRRESISTIBLE

A Persian proverb says, "for every pound of learning a person has, he needs ten pounds of common sense to know how to use it. One might still know all the consequences and continue to smoke because cigarette smoking is a true addiction! According to K.H. Ginzel, one simply needs to consider that no drug is self-administered with the persistence, regularity and frequency of cigarette. Recent research has proven that it is for the nicotine in tobacco that the smokers smoke, the chewer chews and the dipper dips. The earlier one recognizes that smoking doesn't solve problems, it doesn't alleviate pain, and it doesn't make you high. The aggressive promotion and advertisement feature alluring role models from theatre, film and sports smoking, has given cigarette an enticing imagery. It would be necessary to mention that as there is more addiction in cigarette, there is also death.

HOW TO STOP SMOKING

John Quincy Adams, when he decided to quit smoking it took him three months. He wrote a letter to Reverend Samuel Cox. He wrote:

"I have often wished every individual afflicted with this artificial passion could force it upon himself to try but for three months the experiment which I made, am sure that it would turn every acre of tobacco land into a wheat field, and five years to the average of human life".

The best way to "drop the stick " is to get busy and always remind oneself when the temptation comes the many effects of smoking and also the benefits of stopping. Some of these benefits of quitting smoking are:

- After twenty minutes the blood pressure drops to normal.
- After eight hours,carbon monoxide level in blood drops to normal.
- After forty-eight hours, a nerve ending starts growing and the senses of smell and taste are enhanced.
- In one to nine months, coughing, sinus congestion, fatigue, and shortness of breath decrease and cilia, (tiny, hair like cells that move continually to cleanair that is breathed in) regrow in the lungs.
- After five years, the chance of dying from lung cancer decrease by almost half.

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REKINDLING THE SPIRIT OF EXCELLENCE AMONG MEDICAL STUDENTS

Mbachi, Chimezie (MBBS Nig.)

Recently we have seen the revamping of open heart surgery in University of Nigeria Teaching Hospital (UNTH) after about 20yrs of dormancy. Who would have believed that the supporting elite team from diaspora was headed by Dr. Onyekwere, Nzewi, who trained in UNTH before his sojourn abroad? In addition to this, the visiting guest speaker at the just concluded conference for the Society for Gastroenterology and Hepatology in Nigeria (SOGHIN), Dr. Okolo, who is the Chief Endoscopist in John Hopkins hospital USA, was a product of this great institution.

There is no doubt that we are in an ever changing world. About 20yrs ago, the Nigerian student could buy his books with about N5 but today, N50, 000 will barely be enough to buy all your textbooks. At that time, students leave their rooms open and go for lectures and during their period of absence, the porters arrange their beds. Today you dare not leave your room open even if it is for 20minutes. Back in the days, you walk about 100m from your hostel to the wards but today we travel about 40km from our hostel to the wards and have very limited clinical experience. Also about 20yrs ago, there was considerable level of interest in foreign medical licensing exams and our students excelled very well but today despite the worsening state of our nation compared to the 50's, a considerable lower number of students attempt and very few get good scores.

Even if none of the above can be reversed to its status quo I believe strongly that the last can. The question in our minds will be why the trend? Are Nigerians becoming less intelligent with time?

The reasons for this downward trend are that the average Nigerian medical student's mentality of today is that of mediocrity with an aim of 50% and nothing more. They hardly want to understand basic concepts of the topics and always try to divide what they read into relevant(features they can see) and irrelevant(molecular and genetic) aspects. The relevant things are vital for getting the 50% pass mark; after all 50% and 69% will have same 'PASS'.They tend to leave pathophysiology for another day preferring to cram what they wrote down in their notes. They don't seem to be interested in investigations especially laboratory and radiological, not done in their environment no matter how basic they seem to be, e.g. blood gas analysis, MRI, CT scan etc.

Excellence is no more celebrated as the average Nigerian medical student doesn't see the need to study hard. Whether he or she studies or not, N150, 000 will afford a house-man ship slot while the distinction students will stay at home.

One would ask: 'Can this trend be reversed'?The answer is YES. It has been proven that intelligence quotient is 70% genetic and 30% environmental. Here are some tips to help us achieve this goal:

- Aim to know as much as you can. Don't say some things are irrelevant because it is those things we take as irrelevant that the foreigners are interested in. The world is going molecular.
- Try to understand the concepts by reading your textbooks from preface to index. The world is now a global village and technology can be used to our advantage. Instead of chatting online for hours, we can join groups on Facebook where we can be challenged by the questions posted by members of the group and discussions that follow. There are also similar groups online that give you information about foreign medical licensing exams.
- Attend conferences and drug shows; they expose you to new concepts in management of case.
- Try to go for short postings overseas. Some are sponsored.
- Try to be part of a research group while in school. All these improve your Curriculum vitae.

Some people will ask, “Are we trying to encourage brain drain”? The answer is 'NO'. We need to equip ourselves with the necessary tools to compete favourably internationally so that just the same way some Nigerians who have mastered the art of open heart surgery come back to help the locals, we too will not be left behind in this moving global train of mastery in different aspects of the medicine. There won't be anything wrong if Nigerian medical students strive to get the world class training and come back in the nearest future to impact the locals.

MEDIKKA QUIZZES?

Compiled by the Editorial board

1. Ahmed is a 2-year-old boy who presents to the paediatric referral clinic with easy bruising. His mother states that over the last 2 days bruises have been appearing on his body spontaneously or with minimal trauma and that he also had two short nose bleeds the previous day. He is otherwise well but his mother says that he had a cold about 2 weeks ago. He has had no previous illnesses but had a circumcision at 2 months of age for religious reasons with no excessive bleeding. He is on no medication. There is no family history of bleeding disorders. On examination, He is well, playing and apyrexial. There is no pallor. He has widespread purpura and bruising over the flexor and extensor surfaces of all four limbs, trunk and face. There is some blood crusted around his nose. Investigations: Haemoglobin 10.2 g/dL,White cell count 9.6 x 109/L, Neutrophils 4.2 x 109/L, Platelets 6 x 109/L.
What is the diagnosis?

2. Ihuoma is a 14-year-old girl who presents to the Accident and Emergency department complaining of pain in her chest and back. Her pain started this morning and has been worsening throughout the day, despite taking paracetamol, ibuprofen and codeine phosphate. She is finding it difficult to breathe deeply and the pain is worse on inspiration. She has HbSS sickle cell disease and has been admitted to hospital three times in the last month with painful crises.

Examination: Her temperature is 38.8_C, her heart rate is 120 beats/min, blood pressure of 135/85 mmHg, respiratory rate 40 breaths/min, and oxygen saturation 91 per cent in air. She is in pain and unable to take a deep breath. There are bronchial breath sounds at both lung bases. Heart sounds are normal. Her abdomen is soft and non-tender and her ears and throat are unremarkable.
What is the most likely cause of the Ihuoma's chest pain?

3.A 36-year-old nulliparous woman presents to the gynaecology outpatient clinic with heavy, regular periods. Her menstrual cycle is 28 days. The periods last for 5 days, with clots during the first 2 days. Up to 40 sanitary towels are required for each period. The patient has no significant dysmenorrhoea and there is no intermenstrual bleeding. She complains of feeling 'run down' and lacking in energy. Her recent smear was negative and she is not using any contraception.
What are possible differential diagnoses?

4. A 54-year-old woman has been amenorrhoeic for the past 18 months, and recently started to have some vaginal bleeding. Her last cervical smear, taken 2 years ago, was normal. She is not on hormone replacement therapy (HRT).
What are the likely differential diagnoses?

5. A 60-year-old asymptomatic man is found to have a leukocytosis when a routine CBC is obtained. Physical exam shows no abnormalities. The spleen is of normal size.
Lab data include:Hgb: 9 g/dL (normal 14 to 18), Leukocytes: 40,000/μL (normal 4,300 to 10,800)
Peripheral blood smear shows a differential that includes 97% small lymphocytes.
The most likely diagnosis is…?

6. A 38-year-old female presents with recurrent sore throats. She is on no medications, does not use ethanol, and has no history of

renal disease.
Physical exam is normal. A CBC shows Hgb of 9.0 g/dL, MCV is 85 fL (normal), white blood cell count is 2,000/µL, and platelet count is 30,000/µL.
The best approach to diagnosis is…?

7. An elderly homeless male is evaluated for anemia. On exam, he has purpura and ecchymoses of the legs. Perifollicular papules and perifollicular hemorrhages are also noted. There is swelling and bleeding of gums around the patient's teeth as well as tenderness around a hematoma of the calf.
The most likely diagnosis is…?

8. A victim of blunt abdominal trauma requires a partial hepatectomy. He is rapidly transfused with 8 units of appropriately crossmatched packed red blood cells from the blood bank. He is noted in the recovery room to be bleeding from intravenous puncture sites and the surgical incision. His coagulopathy is likely due to thrombocytopenia and deficiencies of **which clotting factors?**

9. The surgeon should be particularly concerned about which coagulation function in patients receiving anti-inflammatory or analgesic medications?
a. APTT
b. PT
c. Reptilase time
d. Bleeding time
e. Thrombin time

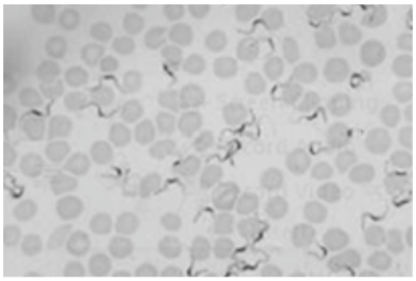
10. A 72-year-old man presents to the office for routine follow-up. He is under treatment for hypertension and congestive heart failure with enalapril and a diuretic. His blood pressure is under acceptable control and he has no symptoms of heart failure at present. He does complain that he has been coughing frequently in the past few months. History and examination reveal no other cause of a chronic cough, so you decide to discontinue his enalapril and start him on losartan.
a. What is the mechanism of action of enalapril?
b. What is the likely cause of the cough?
c. What is the mechanism of action of losartan?

11. A 23-year-old male trips while playing basketball and suffers trauma to the right wrist. The wrist is slightly swollen, tender, but not deformed. However, deep palpation of the anatomical snuff box elicits extreme tenderness.
What is the most likely diagnosis and the most likely anatomical defect.

12. 42-year-old obese diabetic woman complains of soreness of the left leg. She had gallbladder surgery 2 weeks previously. Her left calf is tender but without erythema. She is afebrile. **Most likely diagnosis and which vessels are likely affected?**

13. A 22-year-old male has had a 30-minute bilateral epistaxis with drainage of blood to the nasopharynx and choking. He denies trauma, bleeding disorders, or use of anticoagulant medications. Anterior nasal pinching did not help. **What is the most likely anatomical explanation for this condition?**

14. Two days after receiving the antimalarial drug primaquine, a 27-yearold Igbo man develops sudden intravascular hemolysis resulting in a decreased hematocrit, hemoglobinemia, and hemoglobinuria. Examination of the peripheral blood reveals erythrocytes with a membrane defect forming “bite” cells; when crystal violet stain is applied, many Heinz bodies are seen.
The most likely diagnosis is…?
15.



A 22-year-old man develops a rubbery, red, 1-cm chancre on his right forearm. Three months later, he develops splenomegaly and lymphadenopathy. Two months later, he dies as a result of progressive wasting with cachexia and decreased mentation. At the time of his death, a peripheral blood smear had the appearance shown in the figure above.
What is the most likely cause of death?

16. A 9-year-old boy living in Accra, Ghana has had increasing pain and swelling on the right side of his face over the past 8 months. On physical examination, there is a large, nontender mass involving the mandible, which deforms the right side of his face. There is no lymphadenopathy and no splenomegaly, and he is afebrile.
What is the likely diagnosis and which virus is likely involved?

ANSWERS

1. The diagnosis is idiopathic thrombocytopenia purpura (ITP). This condition is caused by antibodies to platelets. The history of a viral infection 2 weeks prior to the onset of the ITP is typical, as is the isolated, very low platelet count in an otherwise well child.

2. Rebekah has acute sickle chest syndrome. Thrombosis, infection and fat embolism to the lung produce a syndrome of pleuritic chest pain, shortness of breath and fever. The pathology often evolves from the lung bases and produces consolidation, which may be clinically apparent before radiographic changes appear. hypoxia and acidosis, so these factors need to be corrected with hyperhydration and supplemental oxygen.
3. Dysfunctional Uterine Bleeding, Uterine leiomyoma (fibroids), Uterine endometriosis (adenomyosis).
4. Atrophic vaginitis, endometrial polyp, hyperplasia and carcinoma, cervical polyp and cancer.
5. Chronic lymphocytic leukemia is the most common of all leukemias, with incidence increasing with age. Patients are usually asymptomatic, but may complain of weakness, fatigue, or enlarged lymph nodes. The diagnosis is made by peripheral blood smear, as mature small lymphocytes constitute almost all the white blood cells seen. No other process produces a lymphocytosis of this morphology and magnitude.
6. Bone marrow biopsy. This patient has an unexplained pancytopenia. If all three elements (red blood cells, white blood cells, and platelets) are affected, the cause is usually in the bone marrow (although peripheral destruction from hypersplenism can occasionally cause pancytopenia). In this patient without a history of liver disease or palpable splenomegaly on physical examination, a bone marrow production problem is the most likely culprit
7. The signs and symptoms described are most consistent with scurvy (vitamin C deficiency). This syndrome can occur in older patients who are poorly nourished. Perifollicular papules develop when hairs become fragmented and buried in the follicle. Capillary fragility occurs, and bleeding into soft tissue is common.
8. The answer is factors V and VIII. When large amounts of banked blood are transfused, the recipient becomes deficient in (the "labile" factors) and an acquired coagulopathy ensues. Since banked blood is also deficient in platelets, thrombocytopenia may also develop.
9. The answer is **d**. Platelet dysfunction, measured by bleeding time, has been associated with a long list of drugs. Among nonsteroidal anti-inflammatory and analgesic medications, aspirin, indomethacin, phenylbutazone, acetominophen, and phenacetin have been implicated, along with aminopyrine and codeine.
10. Adrenoceptor selectively antagonized by metoprolol: β1. The effect of b-adrenoceptor antagonists on the cardiovascular system: Reduction of sympathetic stimulated increases in heart rate, contractility, and cardiac output; lower blood pressure as a result of effects on the heart, renin-angiotensin system, and CNS; increased atrioventricular (AV) conduction time and refractoriness.
a) Mechanism of action of enalapril: Inhibits the conversion of angiotensin I to angiotensin II, this also inhibits the angiotensin II-stimulated release of aldosterone. Angiotensin-converting enzyme (ACE) inhibitors also impair the inactivation of bradykinin.
b) Mechanism of ACE inhibitor-induced cough: Secondary to the increased bradykinin levels, whichis caused by reduction in the inactivation of bradykinin.
c) Mechanism of action of angiotensin receptor blockers (ARBs): Antagonists of angiotensin-1 (AT 1) receptors which mediate the pressor effects of angiotensin II.
11. Most likely diagnosis: Wrist fracture. Most likely anatomical defect: Fracture of the narrow middle portion of the scaphoid carpal bone
12. Most likely diagnosis: Deep venous thrombosis (DVT). Vessels likey affected: Anterior and posterior tibial veins and fibular Veins
13. Most likely anatomical explanation: Posterior epistaxis
14.Glucose-6-phosphate dehydrogenase (G6PD) Deficiency
Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme of the hexose monophosphate shunt pathway that maintains glutathione in a reduced (active) form. Glutathione normally protects hemoglobin from oxidative injury. If the erythrocytes are deficient in G6PD, as occurs in G6PD deficiency, exposure to oxidant drugs, such as the antimalarial drug primaquine, denatures hemoglobin, which then precipitates with erythrocytes as Heinz bodies. Macrophages within the spleen remove these bodies, producing characteristic "bite" cells. These red cells then become less deformable and are trapped and destroyed within the spleen (extravascular hemolysis).
15. The findings are consistent with African trypanosomiasis, or sleeping sickness.
16. This patient has the endemic African variety of Burkitt lymphoma, a B-cell lymphoma that typically appears in the maxilla or mandible of the jaw. This particular neoplasm is related to Epstein-Barr virus infection.

THE AFRICAN SCOURGE CALLED EBOLA

AKUBUILO UGOCHUKWU
Director General, Public Health Programmes Committee,
University of Nigeria Medical Students Association.

INTRODUCTION
Ebola Virus Disease is a severe, often fatal illness in humans. Outbreaks that occur primarily in remote villages in Central and West Africa, near tropical rainforests, have a case fatality rate of up to 90 percent. Ebola causes Ebola virus disease in humans, with case fatality rate ranging between 60-90 percent. Hunting for "bush meat" in forest and pre-forest areas and eating of bats have been associated with this outbreak.

LATEST OUTBREAK
As of July 24, 2014 1,093 infections and 660 deaths had reported in Guinea, Sierra Leone, and Liberia. Sierra Leone is the hardest-hit country with 454 cases, but with most deaths at 314. Liberia reported 224 infections, along with deaths. Others include Democratic Republic of Congo, Uganda, Sudan, and Gabon.

NATURAL HOST
In Africa, the fruit bats, particularly species considered possible natural hosts for Ebola virus. Some of these bats are found in Nigeria.

TRANSMISSION
Originally known as "Zaire fever", Ebola virus disease is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals. Infection has been documented through the handling of infected chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.

SIGNS AND SYMPTOMS
EVD is a serve acute vital illness often characterized by the sudden onset of fever, intense weakness, muscle pain, headache and sore throat, followed by vomiting, diarrhea, rash, impaired kidney and liver function, and in some cases, both internal and external bleeding. The time interval from infection with the virus to onset of symptoms is 2 to 21 days.

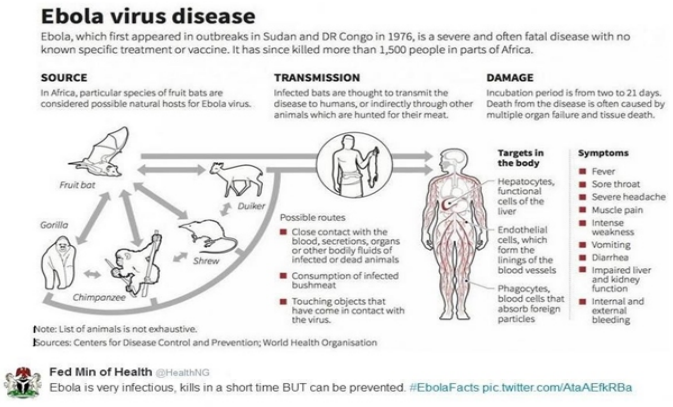
DIAGNOSIS
Definite diagnosis of Ebola virus infections is only attainable in a laboratory through several types of tests ranging from antibody-capture enzyme-linked immunosorbent assay, ELISA, to virus isolation by cell culture. Hospital records show that samples from patients are an extreme biohazard risk, hence testing is recommended to be conducted under maximum biological containment conditions.

TREATMENT
Currently, there are no clinically available licensed vaccines for EVD. Severely ill patients require intensive supportive care.
It is not always possible to identify patients with EVD early because initial symptoms may be non-specific so health care workers should apply standard precautions consistently that include: basic hand hygiene, respiratory hygiene, and the use of personal protective equipment, safe injection practice and safe burial practice.

HAZARDOUS PRACTICES
* Burial ceremonies in which mourners have direct contact with the body of the deceased person can also play a role in the transmission of Ebola.
Don't handle remains of people that died of the disease because they are still contagious.
Specially organized and trained teams should bury the remains, using appropriate safety equipment.

* Sexual Intercourse: Infected men who have recovered from the disease can still transmit the virus through their semen for up to seven weeks after recovery. People are infectious as long as their blood and secretion contain the virus.

PREVENTION
* *Wash your hand frequently:*
As with other infectious diseases, one of the most important preventive measures for Ebola virus is frequent hand-washing. Use sanitizer, soap and water, or use alcohol based land rubs containing at least 60 percent alcohol when soap and water aren't available.
* *Avoid bush meat:* Avoid buying or eating wild animals, including nonhuman primates sold in local markets. Avoid bat meats and bat products. Avoid buying or eating wild animals or keeping as pets.
* *Avoid undue contact:* Avoid contact with anyone who may have been exposed to the Ebola virus. In particular, avoid contact with the person's body fluids and tissues, including blood, semen, vaginal secretions and saliva. People with Ebola are most contagious in the later stages of the disease.
* *Watch out for people with flu like symptoms and sudden fever.* Gloves and other appropriate protective clothing should be worn when handling sick animals or their tissues.
* *Follow infection-control procedures:* If you're a health care worker, wear protective clothing and carefully disinfect and dispose of needles and other instruments. Injection needles and syringes should not be reused.



REFRENCE: Centers for Disease Control and Prevention, World Health Organization.

MEET THE MEDIKKA FOUNDING FATHER

PROFESSOR JONATHAN CHUKWUEMEKA AZUBUIKE
MD, FAAP, FMCPaed., FWACP, OFR.

Chairman, Medical and Dental Council of Nigeria(MDCN)

Professor J C Azubuike, from Nkwerre, Nkwerre Local Government Area, Imo State, was born in Aba, where he had his education in Township School, Aba, and then went to Government College, Umuahia.

He passed the entrance examinations to the University College, Ibadan, to study Chemical Engineering, and after passing the intermediate B.Sc. of London University (as was the practice then), succumbed to family pressure to change to Medicine. He left Nigeria for Bonn, West Germany, to study Medicine at the University of Bonn, the then West Germany capital from where he graduated MD in November 1964.

After his internship in Germany, he passed the United States Examination for Foreign Medical Graduates (ECFMG) and then went on to undertake post-graduate studies in Paediatrics, doing the Residency programmes at St Raphael's Hospital (Yale University Medical Center-affiliated), New Haven, Connecticut, New York University Hospital, New York City, and the Children's Hospital Medical Center (Harvard University Medical School) Boston, Massachusetts. He took a Fellowship in Ambulatory Paediatrics/Paediatric Endocrinology at the Children's Hospital Medical Center, and passed the American Board of Paediatrics examination in 1970.

After a Fellowship in Neonatology at the University of Bonn Teaching Hospital, in Bonn, Germany, he joined the Department of Paediatrics of the University Of Nigeria Teaching Hospital, Enugu, in 1974 as a Lecturer in Paediatrics. He became the Foundation Professor of Paediatrics, University of Nigeria in 1980.

He was HOD, Paediatrics, 1979-1982 and 1997-2000, Foundation Deputy-Provost, College of Medicine, University of Nigeria, Enugu Campus, Enugu; 1982-1986, Senate Member of the University of Nigeria Governing Council, 1986-1989 and Deputy-Vice Chancellor, UNEC, Enugu, 1989-1993. He retired in 2004.

He has published widely in local and international journals and examined in many medical schools, as well as at the West African and the Nigerian National Postgraduate Medical College examinations.

He is a Foundation Fellow of both the West African College of Physicians and the National Postgraduate medical College of Nigeria. He was Chairman, Faculty of Paediatrics, National Postgraduate medical College of Nigeria 1999-2002, Vice-President 2002-2004 and President 2004-2005. He was elected Fellow, Royal College of Physicians of Edinburgh in July 2006.

He was Vice-Chair, 2000-2002 and Chair 2002-2004, NARCH (Nigeria Applied Research for Child Health), a USAID/Boston University-sponsored project to help improve child mortality in Nigeria as well as facilitate capacity-building among young Nigerian academics. He is also the Director, School Health Consultancy Services Nigeria. He is the initiator, Coordinator and Chief Editor of the standard textbook in Paediatrics both within and outside Nigeria, with the title “Paediatrics and Child Health in a Tropical region” which first appeared in 1999. The second edition appeared in 2007 and work is on- going on the third edition.

He has also participated in academic and professional activities outside Nigeria. He was Consultant Paediatrician to Saudi-Arabian Oil Company (ARAMCO) and the Tabuk Military Hospital on Saudi Arabia, 1987 and 1988. He was also Professor of Paediatrics, Sultan Quaboos University Medical School, Muscat, Oman, 1993-1995.

He is past President, Rotary Club of Enugu, 1999/2000 and 2006/2007 and a Paul Harris Fellow of Rotary International. He speaks fluent German.
Socially, he is an intensely private person and still loves to play lawn tennis till today. He is married to Dr Adije Bassey Azubuike, a general physician. They have three grown-up children.

He received the national award, Order of the Federal Republic of Nigeria (OFR) in 2008.

Presently, he is, since November 2013, the Chairman, Medical and Dental Council of Nigeria (MDCN), the body responsible for the accreditation of all Medical Schools in Nigeria as well as the practice of Medicine and Dentistry in the country.

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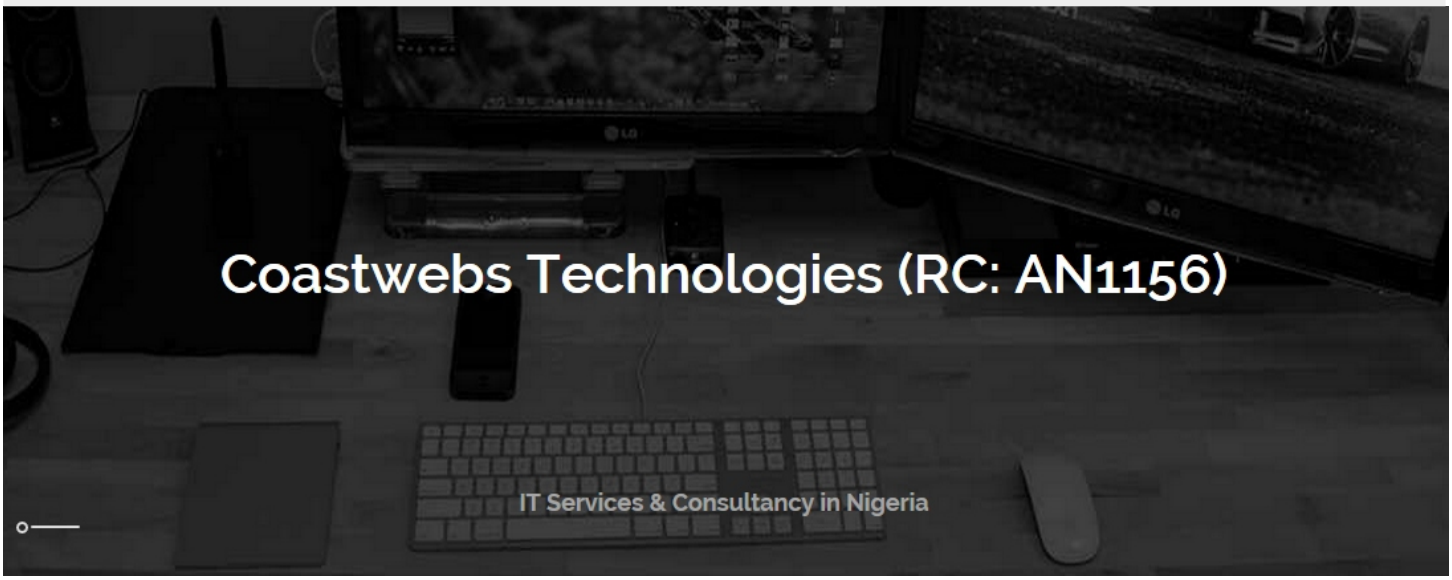

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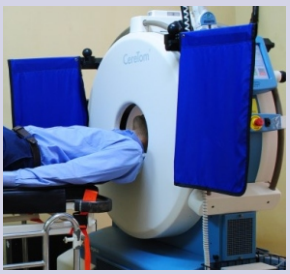


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