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Review

Global eradication of measles: A highly contagious and vaccine preventable disease -what went wrong in Africa?

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This review study reports on global eradication of measles: a highly contagious and vaccine preventable disease-what went wrong in its eradication in Africa. Measles is one of the most contagious human diseases which have continued to cause large outbreaks all over the world even in countries that have achieved high vaccination coverage with a single dose strategy. The disease can also lead to lifelong disabilities including brain damage, blindness, and deafness. These serious complications are rare in developed countries where measles vaccine is widely available, the highest mortality is however found in poor nations. The disease has remained the fifth leading cause of deaths among children less than five years of age, worldwide. It accounts for 44% of total deaths due to vaccine preventable diseases (VPD), among children less than 15 years, the highest mortality occurring in poor communities with malnutrition, overcrowding and low vaccination coverage. Indeed, measles transmission has been interrupted in several countries, reinforcing the view that measles eradication is technically feasible using existing vaccines and intervention strategies. However, measles still accounts for 10% of global mortality from all causes among children aged <5 years (that is, approximately 1 million deaths annually). Progress toward measles control varies substantially among countries and regions. In Nigeria where there is perennial, low routine vaccination coverage and where the quality of the mass immunization campaign is not high enough, large and persistent measles outbreaks continue to occur with high morbidity and mortality. Today, despite the availability of a safe, effective and relatively inexpensive vaccine for more than 40 years, measles still kills more than any other vaccines preventable disease among children. There is therefore, the urgent need to revisit the measles immunization and vaccination programme in Africa and in our country Nigeria with the sole aim of introducing a two-dose schedule to halt the endemic transmission. This is believed to bring about the successful eradication of measles in Africa. Intensified efforts will be necessary to implement appropriate control and elimination strategies, including supplementary vaccination campaigns, expansion of routine vaccination services, and surveillance. These strategies and estimates of the resources will also be required to implement them will require adjustment based on accumulating experience. Programmatic and financial obstacles must be overcome if the final goal of measles eradication is to be achieved.

Key words: Epidemiology, highly contagious disease, immunization, immunosuppression public health, vaccination, vaccine preventable disease, measles, measles virus, measles vaccine.

INTRODUCTION

Measles is one of the most contagious human diseases which have continued to cause large outbreaks all over the world even in countries that have achieved high vaccination coverage with a single dose strategy (Puvimansinghe et al., 2002 reviewed in Adu, 2008). Measles remains a leading cause of death among young children, despite the availability of a safe and effective vaccine for the past 40 years. An estimated 345 000 people, the majority of them children, died from measles in 2005 (the latest year for which figures are available) (WHO, 2007a) . The name measles is derived from the latin, misellus, meaning miserable (WHO, 2007b). It is one of the most contagious diseases known to man and often occurs in explosive epidemics characterized by high fever of 38^{O}C or more; plus the appearance of maculopapular rash of about 3 days or more; with one or a combination of coryza, cough, conjunctivitis and Koplik spots in the oral mucosa of measles' victims (Palevsky, 2002). Measles produces significant illness, death, and disability (Pan American Health Organization, 2005); and infects approximately 40 million people resulting in nearly 1 million deaths annually in developing countries (Oldstone, 1998). It has been reported as a major cause of childhood morbidity and mortality in Nigeria; 212,183 and 168,107 cases were recorded in 2000 and 2001 respectively (WHO, 2001). For instance in 2005, Adamawa State, Nigeria experienced 3,974 cases and 238 measles-deaths (Dubray et al., 2005). WHO/AFRO (2004) reported measles as one of the top five causes of death in children less than five years of age in many African countries. Measles disease is usually characterized by fever of 38^{O}C or more; maculopapular rash of about 3 days or more; with one or a combination of coryza, cough, conjunctivitis and Koplik spots in the oral mucosa of measles' victims (Palevsky, 2002). It is spread through respiration (contact with fluids from an infected person's nose and mouth, either directly or through aerosol transmission), and is highly contagious, 90% of people without immunity sharing a house with an infected person will catch it.

Also, measles is one of the vaccine-preventable diseases (Washington State Department of Health, 2006) hence one of the Expanded Programme on Immunization (EPI) – target diseases for eradication (WHO, 1999). The MV is monotypic and essentially without animal reservoir (Norrby et al., 1995), as a result measles control and eradication should be within reach of aggressive vaccination campaign. Moreover the virus is antigenically stable making the vaccine derived from the 1954 Edmonston isolate provide protection against all MVs (Rota et al. 1994) ; and interrupt its transmission from infected to immune individuals. The industrialized nations of the world (e.g. the US) have used the live attenuated MV vaccine to eradicate transmission of indigenous measles strains (Benenson, 1990). Before the introduction of measles vaccines in the 1960s, almost everyone contacted measles usually during childhood with an estimated 2.5 million death [mainly children] out of about 130 million cases every year (Clements et al., 1992). Today, despite the availability of safe, effective and relatively inexpensive vaccines for more than 40 years, measles still kills more than any other vaccines preventable disease among children (WHO/AFRO, 2004; WHO 2006; Rima et al., 1997). Mortality rates can exceed 10% in certain areas and severe sequelae of measles infections include giant cell pneumonia, inclusion body encephalitis and sub acute sclerosing pan encephalitis [SSPE] (Wen-Bo et al., 1998).

The disease has remained the fifth leading cause of deaths among children less than five years of age, worldwide (Stroebel et al., 2003 reviewed in Adu, 2008). It accounts for 44% of total deaths due to vaccine preventable diseases (VPD), among children less than 15 years, the highest mortality occurring in poor communities with malnutrition, overcrowding and low vaccination coverage (WHO, 2002: Adu, 2008). Vaccination has had a major impact on measles deaths. From 2000 to 2005, more than 360 million children globally received measles vaccine through supplementary immunization activities. Moreover, improvements have been made in routine immunization over this period. These accelerated activities have resulted in a significant reduction in estimated global measles deaths. Overall, global measles mortality decreased by 60% between 1999 and 2005. The largest gains occurred in Africa where measles cases and deaths decreased by nearly 75% (WHO, 2007a).

Furthermore, measles is one of the typical viral diseases of childhood. However, unlike other common viral diseases that is, VZV, rubella, mumps, and parvovirus infections, measles often leads to severe complications that may be fatal. In the third world, there may be up to 900,000 measles related deaths per year. Therefore, there is a lot of pressure on health in different countries in controlling the disease through vaccination. Indeed, measles is targeted by the WHO in its expanded program of immunization (EPI). This review is therefore reports on the global eradication of measles: a highly contagious and vaccine preventable disease and what went wrong in its eradication in Africa using Nigeria as a case study, so that we all can put our hands on desk in order to bring this vaccine preventable disease under control in Africa and in our country, Nigeria.

HISTORICAL BACKGORUND OF MEASLES

Most people regard measles as a mild illness, often no worse than flu. Parents may welcome it as something in-

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evitable, while for many children it means nothing more than an enforced holiday (Axton, 1979). It is a disease of which most of us have personal experience and therefore, is of interest. Many of us possibly retain vivid memories of our own attack, and the way in which it was treated (Axton, 1979). The history, and natural history, of measles can be used to illustrate the major changes in our way of thinking about diseases, and their causes, over the past two thousand years. Similarly, a study of measles helps to emphasize the two inseparable disciplines or philosophies which underly the care of children today — Paediatrics and Child Health (Axton, 1979).

The earliest description of measles is attributed to Rhazes, who went some way in separating the diseases clinically but thought they proceeded from the same cause (Talbot, 1970). The prevailing theory was that the red rash associated with measles represented the mother's menstrual blood, dammed up during the child's sojourn in the womb. Measles was therefore welcomed, as this was the only way the child could rid himself of the so-called 'poison'. For many years children were deliberately exposed to measles for this reason, much as we used to hold german measles parties, before the development of the rubella vaccine (Axton, 1979) . Thomas Phaer, in the chapter of his 'The Booke of Children' entitled 'Small pockes and Measels' wrote: 'This disease is common. It is of two kinds: — varioli, ye measils; morbilli, called of us ye smal pocks. They be but of one nature and proceed of one cause.' However, after listing three humoral causes for the disease, he observed that it can 'commence by the way of contagious, when a sick person infected another' (Axton, 1979).

Measles is a relatively new disease of man. Accounts of ancient Greek disease records as contained in the writings of Hippocrates (470-337BC) does not include records of Measles. Fraser et al. (1974 reviewed in Ogundiji, 2008) described measles as a highly contagious acute infectious disease that result in life long immunity and has animal reservoir and that a human population of several hundred thousand is required to provide new susceptible that will sustain the continued presence of the virus. Populations of this size erupted among humans in the later end of the third millennium BC during the development of ancient Egyptian and Samatrian cities and Measles must have arisen as a result of adaptation of a closely related virus like Rinderpest virus occupying the same genus Morbillivirus with Measles to human population (Good et al., 1977; Ogundiji, 2008).

With the growth of villages and towns, and increased travel between them, a pool of non-immune children is always available and being added to by new births. Measles then becomes endemic — that is, it is always present within the community, moving along established lines of communication (Axton, 1979). In this situation, we find a fairly classical two-year cycle; an epidemic year, when most susceptible children over the age of six months suffer from the disease, followed by a year when there are not enough susceptible children to sustain the epidemic. There is, however, a sufficient number who escape infection for the disease to remain endemic (Axton, 1979). Smallpox, also with no natural animal reservoir, probably in the past followed a similar pattern, and it is interesting that for many years the two illnesses were not separated, but thought of as different manifestations of the same disease (Axton, 1979).

The modern history of measles

The modern history of measles begins in 1670, with Thomas Sydenham's description of his son's attack (Dewhurst, 1966). He was the first clearly to separate measles from smallpox, and he recognized complications such as cancrum oris and encephalitis. At about the same time Mauriceau rejected the mother's blood theory and the infectious or contagious theory became generally accepted (Debus, 1970). Mauriceau also decried the use of red curtains in the sufferer's bedroom. He suggested green would be more appropriate, though probably more on aesthetic than on scientific grounds. Towards the end of the next century, Francis Home tried to transmit measles using blood from an infected child. In eight out of ten children he succeeded, unwittingly demonstrating the presence of an infective principle in the blood stream, a hundred years before the virus was first seen (Talbot, 1970).

The remarkable observations of Peter Panum, a young Danish physician who assisted during an epidemic in Farve Island in 1846 revolutionized measles research. He confirmed that measles was contagious and that it takes a 14-days incubation period between exposure and appearance of rash. In 1954, Enders and Pebbles reported the isolation of measles virus in roller-tube culture of human and rhesus monkey and described the characteristic cytopathic effects that accompany measles virus replication. Adaptation of measles virus to growth in a variety of cell cultures permitted the detailed analysis of virus structure, replication, virus-cell interaction and vaccine development (Enders, 1963).

The next advance came through the astute observa-tions of Peter Ludwig Panum (Talbot, 1970). Panum was a Danish doctor, sent by his Government to investigate an epidemic of measles in the Faeroe Isles in 1846. The geographical situation of the Faeroes was ideal for an epidemiological study: seventeen isolated islands, where the arrival of a boat was noted in the local calendar and provided an excuse for the gathering of the whole population (Axton, 1979) . Visits from the Danish mainland were rare, but the dates were well documented. The epi-demic originated in a single seaman from Copenhagen, who presumably left the city with no signs of measles. The sea journey to the Faeroes was sufficiently long for him to have become infectious on arrival, but not long enough for him to have recovered completely and have ceased excreting the virus (Axton, 1979). By following the

course of the epidemic from village to village, and island to island, using the known movement of people and boats, Panum was able to establish four important facts (Axton, 1979):

1. The measles rash appears twelve to fourteen days after contact.
2. Its greatest infectivity is during the late prodrome — three to four days before the rash appears.
3. The disease is contagious, probably spread by droplets, and not miasmic in origin.
4. The protection from an attack is life-long. The last epidemic of measles in the Faeroes had been in 1781, and Panum found that the only inhabitants immune were those over 64 years old, who had suffered from the disease as children during the earlier epidemic.

Recent history of measles

The more recent history of measles includes the identification of the virus by Hektoen in 1910, the growth and subsequent attenuation of the virus by Enders in 1963 to produce an effective vaccine (Enders, 1963), and the discovery of the relationship between measles virus and a strange and rare degenerative disease of the nervous system of children, called sub-acute sclerosing pan-encephalitis by Payne in 1969 (Payne et al., 1969; Axton, 1979). Until recently measles was perhaps the best known of all the common childhood diseases. The characteristic maculopapular rash, with coryza and conjunctivitis was familiar to every mother. However, as a consequence of the development of an effective live vaccine and vigorous implementation of a policy of immunization of every child, the United States and a few other countries have reduced the incidence of this disease so dramatically that many young doctors have never seen a case. The objective now must be to match this performance in the rest of the world, including the developing countries, where the mortality from measles in malnourished infants makes it one of the leading causes of death in children (White and Fenner, 1994).

THE PRESENT STATE OF THE DISEASE

Our present knowledge of measles is fairly complete although, there remain several very interesting questions unanswered. The classical course of measles in a susceptible child is shown in Figure 1. Eight to nine days after contact with the virus the prodromal illness starts with symptoms of a common cold. After three to five days the illness becomes recognizable as measles with the appearance of a rash starting behind the ears and spreading to the face and trunk within twenty-four hours. After two to three days, rapid improvement occurs, with a fall in temperature, and fading of the rash. Within five days of the appearance of the rash most children are up and about, and have been non-infectious since the third day of the rash Axton, 1979). Currently, measles which was once a common, highly infectious disease of young children is now uncommon in the United Kingdom (Baker et al., 2001).

Disease and mortality burden

We believe that measles deserves our attention because it is one of the major problems in modern Africa, which causes a large number of deaths and leaves many survivors with life-long disabilities (Axton, 1979). The origin of measles is unknown, although similar viruses cause distemper in dogs and rinderpest in cattle. Plague, typhus and other diseases which have changed the course of history, have a natural reservoir in animals (Axton, 1979). Measles, on the other hand, has no host except man, and so the persistence of measles in a community depends on its continual passage from infected to susceptible humans. Thousands of years ago, man probably lived in small family groups, well isolated from his neighbours, and it would be difficult to see how the infection could persist among such groups for any length of time. We know that in isolated islands, epidemics of measles among the non-immune population spread rapidly, but came to an end equally rapidly, after which no new cases of measles occurred for many years, and only then if the virus was introduced from outside (Axton, 1979). While measles is now rare in many industrialized countries, it remains a common illness in many developing countries. More than 20 million people are affected each year by measles. In 2005, it was estimated that there were 345 000 measles deaths globally: this translates to about 945 deaths every day; 39 people die every hour from measles (Table 1).

The overwhelming majority (> 95%) of measles deaths occur in countries with per capita Gross National Income of less than US $1000. The primary reason for continuing high childhood measles morbidity and mortality is the failure to deliver at least one dose of measles vaccine to all infants. In countries where measles has been largely eliminated, cases imported from other countries remain an important source of infection (WHO, 2007a).

EPIDEMIOLOGY OF MEASLES

Molecular epidemiology of measles

In 1998, WHO published guidelines for a uniform nomenclature for designating wild type measles viruses and describing genotypes thereby providing guidelines for laboratory methods used for genetic characterization (WHO, 2007b). In 2001, 2003 and 2005, World Health Organization (WHO) recommendations were updated to take into account the identification of new genotypes resulting from expanded virological surveillance (WHO, 1998, 199a, 2001, 2003, 2005, 2007b). Molecular epidemiology of MVs is an important component of measles

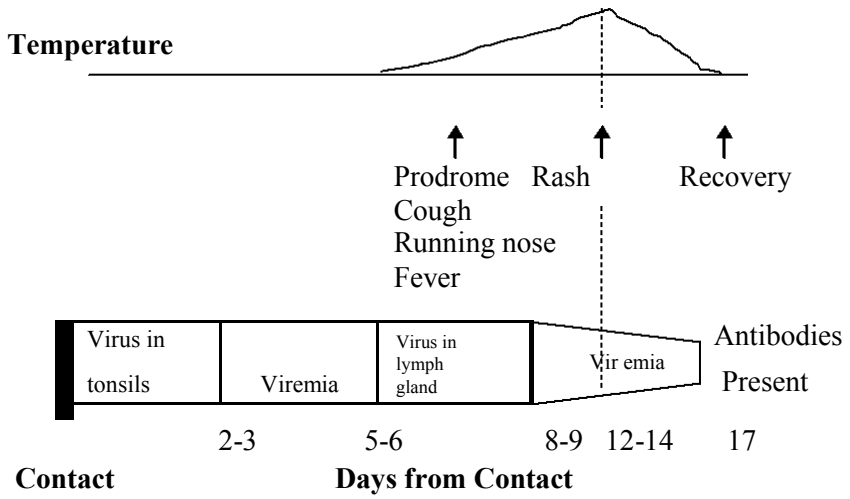

Figure 1. The Clinical Course of Natural Measles Infection (Axton, 1979)

Table 1. Estimated measles deaths, with uncertainty bounds*

Regions	Deaths	uncertainty bounds*
Africa	126 000	[93 000 - 164 000]
Americas	<1 000	[-]
Eastern Mediterranean	39 000	[26 000 - 53 000]
European	<1 000	[-]
South-East Asia	174 000	[126 000 – 233 000]
Western Pacific	5000	[3000 - 8000]
Total	345 000	[247 000 – 458 000]

Source: World Health Organization (WHO) region, 2005
*Based on Monte Carlo simulations that account for uncertainty in key input variables (that is vaccination coverage and case-fatality ratios)

surveillance as it provides a method for identifying the geographical origin and tracing transmission pathways of a virus (WHO, 2007b) . Two measles strain banks, the MV section of the Center for Disease Control and Prevention (CDC) USA, and the Health Protection Agency (HPA) UK, have been designated by WHO to acquire, analyze, store and dispense representative strains (WHO, 2007b). The terms Clade and genotype are used to describe ge-netic characteristics of wild type MVs and for molecular epidemiological purposes, the genotype designations are the operational taxonomic unit while Clades are used to indicate genetic relationship between the various genotypes. Altogether, eight Clades are recognized designated A-H, within the Clades 23 genotypes are recognized. With the exception of genotype F, all of the genotypes have a corresponding references strain (WHO, 2007b).

Molecular epidemiology of MV entails genetic characterization of the wild-type (wt) virus; and it is an important component of measles surveillance (WHO, 2003). Measles surveillance and epidemiological investigation is able to identify the source and transmission pathways of the virus. This is most beneficial when the change in viral genotypes over time in a particular region can be observed, because the information from the genetic analyses can document the interruption of transmission of endemic measles. Consequently, molecular characterization of wt MVs has become a valuable tool for the evaluation of the effectiveness of measles control and elimination programmes. WHO therefore recommended that viral surveillance be conducted during all phases of measles control and that virological activities be expanded to provide an accurate description of the global distribution of measles genotypes. However, recent molecular epidemiologic studies have demonstrated interruption of circulation of genotype D6 viruses that were responsible for the large measles outbreak in Sa˜o Paulo in 1997 and subsequent outbreaks in Rio de Janeiro, Argentina, Chile, Bolivia, Haiti, and the Dominican Republic (Canepa et al., 2000; Oliveira et al., 2002). The record low number of cases and the identification of genotypes other than D6 in association with measles

Table 2. Current knowledge of the global distribution of wild type measles viruses (Rota and Bellini, 2003).

Genotype	Countries with endemic measles or frequent outbreaks or countries identified as the source of imported cases: 1995-2001
B3	Nigeria, Ghana, Kenya, Sudan, Congo, Democratic Republic of Congo, The Gambia, Cameroon
C2	Morocco, Czech Republic, Germany, Denmark, Luxembourg, Spain
D2	South Africa, Zambia
D3	Japan, Taiwan, Philippines[a]
D4	India, Pakistan, Iran, Kenya, Zimbabwe, Namibia, South Africa, Russia, Ethiopia
D5	Japan, Thailand
D6	Russia, Brazil, Argentina, Bolivia, Italy[a], Turkey, Germany, Poland, Dominican Republic, Luxembourg, Spain
D7	Germany, Spain
D8	Ethiopia, Nepal, India
d9[b]	Indonesia, Venezuela
G2	Indonesia, Malaysia
g3[b]	East Timor, Indonesia
H1	China, Korea
H2	Vietnam

Key: a = Identified as source of imported virus only
b = Proposed new genotype, pending isolation of reference strain

cases imported into South and Central America are consistent with regional elimination (PAHO, 2001; Hersh et al., 2000; CDC, 2000).

Distribution of measles genotypes in measles-endemic areas

Recent advances in genomic sequencing technology have lent its support to the monitoring and evaluation of vaccination programmes. Phylogenetic trees are invaluable tools for monitoring the progress of immunization activities. Viruses of the same genetic lineages cluster geographically together in a phylogenetic tree (Adu, 2008). In a study by Adu, Nigerian measles isolates has been classified into Cluster I and II of a newly discovered B3 genotype of Clade B (Hanses et al., 1999). Before 1999, no field isolate of the measles virus from Nigeria had ever been studied and that study put Ibadan and Nigeria in the measles epidemiological map of the world for the first time. According to Adu (2008), various studies by Ibadan Polio lab under his leadership and in collaboration with Center for Disease Control and Prevention in Atlanta and the National Institute for Communicable Disease (NICD) in Johannesburg, South Africa, have used various molecular approaches to:

1. Determine the source of imported viruses
2. Follow the pathway of virus circulation
3. Monitor the progress or lack of progress of the vaccination programme
4. Identify reservoirs sustaining virus circulation
5. Detect gaps in surveillance; and
6. Show geographical distribution of the virus

These efforts are with ultimate aim of detecting the viruses and the un- immunized children and of reaching every Nigerian child with the vaccine in order to stop the unnecessary suffering and untimely death resulting from these vaccine preventable diseases (Adu, 2008).

Table 2 shows the current knowledge of the global distribution of wild type measles viruses. Also listed in Table 2 are countries that have endemic or widespread measles and have been identified as the source of importation of a particular genotype into other countries. In these latter cases, the circulation of a genotype has not been verified by virologists surveillance in the source country but was inferred on the basis of a consistent pattern of importations (Rota and Bellini, 2003). In each of these cases, standard case investigation confirmed that the individuals were traveling in the Philippines during the incubation period. The most frequently isolated measles genotypes in Europe have been C2 and D6 (Santibanez et al., 1999; Rima et al., 1995; Hanses et al., 2000), and genotype D7 (Santibanez et al., 2002) viruses have been shown to circulate widely in the western part of Germany (Rota and Bellini, 2003).

Several measles genotypes have been identified in Africa

Clade B viruses are endemic in the central and western parts of sub-Saharan Africa, and recent analysis of a large number of recent measles isolates from Nigeria, Ghana, The Gambia, Cameroon, and Sudan supports the division of clade B into 3 genotypes, B1, B2, and B3 (Hanses et al., 1999; El Mubarak et al., 2002). Genotype B3 has been divided into two clusters. Genotype B3 cluster 1 viruses have been isolated from Cameroon, Ghana,

and Nigeria and from as far east as Sudan, suggesting that clade B viruses are widely distributed in sub-Saharan Africa. The circulation of genotype B3 cluster 2 viruses appears to be more limited to western Africa (Kouomou et al., 2002). In contrast, genotypes D2 and D4 have been the most frequently detected genotypes in the southern and eastern parts of the African continent. Virus isolates from only one northern African country, Morocco, have been characterized (Rota and Bellini, 2003). The Moroccan viruses were all in genotype C2, suggesting that the pattern of measles genotypes in northern Africa may be more related to the European pattern than to the pattern seen in other parts of Africa (Alla et al., 2002). Measles is endemic on the Indian subcontinent. Genotype D4 and D8 viruses have been isolated in India and Nepal, and genotype D4 was detected in Pakistan (Truong et al., 1999; WHO, 2001). Genotype D4 viruses have also been detected in measles cases imported into the United States from both Pakistan and India (Rota et al., 1998; 2002).

Global experience with measles eradication and control

The efforts of individual countries and global efforts through the EPI have substantially reduced measles morbidity and mortality throughout the world. Worldwide, for 1996, global coverage of the population of children aged 1 year with one dose of measles vaccine is estimated at 81% (CDC, 1997b). However, progress in controlling measles varies substantially among WHO regions. An estimated 36.5 million cases and 1 million deaths caused by measles still occur each year. About half of these deaths occur in Africa. Sixteen of 19 countries in which fewer than 50% of children aged 1 year have received at least one dose of measles vaccine are in Africa. Despite poor measles surveillance, Africa also has the highest reported incidence of measles.

Western hemisphere

In September 1994, the member nations of PAHO established the goal of eliminating measles from the Western Hemisphere by 2000 (CDC, 1998). The strategy adopted included three complementary approaches to immunization:

1. “Catch-up”: a one-time-only mass campaign to vaccinate all children aged 9 months to 14 years, without regard to disease or vaccination history;
2. “Keep-up”: routine vaccination with measles, measles-rubella (MR), or measles mumps- rubella (MMR) vaccine at age 12 months; and
3. “Follow-up”: periodic campaigns conducted approximately every 4 years to vaccinate all children aged 1–4 years, without regard to disease or vaccination history.

According to CDC (1998), application of this strategy has substantially reduced measles transmission in the Americas. Several countries including Chile, Cuba, and the nations of the English-speaking Caribbean have reported no cases of measles for 3 years. In other countries of the region, measles transmission is now occurring only sporadically. Most countries in the region reported sporadic cases or no cases of measles (CDC, 1998).

Western pacific region

The Western Pacific Region of WHO includes the most populous as well as some of the smallest countries of the world. Most countries in the region are now free of polio and are devoting more attention to measles. Approximately 100,000 cases of measles are reported in the region each year, despite measles vaccine coverage exceeding 90% (CDC, 1998). Many of the Pacific island nations have been free of measles for some time, although periodic outbreaks caused by measles importations continue to occur. The number and size of these outbreaks have decreased steadily since the introduction of measles vaccination in the mid-1970s.

Other countries such as Australia, New Zealand, and the Philippines, have already begun measles elimination initiatives or are considering them. China, which implemented a two-dose measles vaccination schedule in 1985, experienced substantial reductions in measles morbidity and mortality beginning in 1987. Fewer than 75,000 cases were reported in 1996, and only 108 deaths were reported in 1995 compared with more than 1 million cases and 4,200 deaths in 1981 (CDC, 1998).

Eastern mediterranean region

According to CDC reports (1998), enhanced control measures of measles were recommended to be undertaken with the aim of eliminating measles from this region. Eight of the 23 countries in the region use a one-dose measles vaccination strategy; in the 15 that use a two-dose strategy, the age at which the second dose is administered and the vaccine of choice (measles vaccine or combination vaccines [MR or MMR]) vary. The Gulf Council countries which include Kuwait, Oman, Bahrain, Qatar, Saudi Arabia, and United Arab Emirates aimed for measles elimination by 2000. Coverage with measles vaccine in Sudan is now approximately >80%. As a result of special efforts to immunize war-displaced children, substantially fewer outbreaks of measles have occurred in refugee camps (CDC, 2008a, b).

European region

There was a strategic plan for elimination of measles from this Region by 2007. Twenty-one countries in the region had reported 90% coverage with at least one dose

of measles (CDC, 2008a, b). The regional strategy to eliminate measles includes: establishing political commitment to measles elimination, developing measles elimination plans based on local epidemiologic data, achieving and maintaining high vaccination coverage, and strengthening surveillance.

Eradication of measles in Africa- what went wrong?

Measles is a major cause of child mortality in developing countries (Cutts et al., 1991). Case fatality ratios of up to 20% have been found in community studies in West Africa (Aaby et al., 1984). Measles has also been reported to increase morbidity (Bhaskaram et al., 1984; Reddy et al., 1986) and mortality (Hull et al., 1983; Aaby et al., 1990) and to worsen nutritional status (Bhaskaram et al., 1984; Koster et al., 1981) for several months after the acute episode (Dollimore et al., 1997). Vitamin A treatment of measles reduces acute case fatality (Dollimore et al., 1997). Otten et al. (2005) reported a striking reduction in measles burden in 19 sub-Saharan African countries after wide-age-range mass measles campaigns. For nine countries (including Cameroon), Otten and colleagues reported a surveillance data for only 1 year after the mass campaigns. Cameroon has sustained the low measles transmission status for 3-4 years since the mass campaigns. The mean annual number of measles cases has dropped from 13260 in 1996-20011 to 340 (34% of 989 measles-like illnesses) in 2003-05. In the past 3-4 years, some of these areas have not seen a single case of measles (Wiysonge et al., 2006).

In South Africa, measles vaccine was added to the National Immunization Days (NIDs) for polio eradication in 1996. During 1997, efforts were made to ensure that all children aged 1–14 years had received measles vaccine during catch-up vaccination campaigns in 1996 or 1997.

Analysis of South Africa's experience during the 1996 NIDs revealed several issues to be addressed in future NIDs in which multiple vaccines are administered (that is, training personnel to administer injections, disposing appropriately of used needles and syringes, and dealing with different target age groups for the two vaccines). The combined 1996 and 1997 campaigns achieved 91% coverage of the eligible age cohort, although coverage varied substantially among provinces and within provinces. According to CDC (1998), South Africa is moving to eliminate measles, but accomplishing the goal will require strengthening surveillance, improving routine vaccination services, and conducting follow-up campaigns.

Several other countries in southern Africa that have made substantial progress in polio eradication, and which have strong basic EPI programs (that is, Namibia, Botswana, Zimbabwe, and Swaziland), also have launched or are planning catch-up measles vaccination campaigns. These countries have not yet established laboratory-based surveillance (CDC, 1998).

Nigeria as a case study

Measles is endemic in Nigeria (Adu et al., 1996) hence Nigerian children are expected to be born with a high level of maternally acquired antibodies which declines rapidly at age 6 months till the child begins to develop its own antibody at age 9 months (Babaniyi et al., 1995). Minimum protective antibody titres vary from one part of the world to the other due to differences in measles epidemiologic pattern in different regions. However, in an endemic area like Nigeria, the required minimum protective antibody titre is 1: 40 (Anon, 1995). The Expanded Programme on Immunization (EPI) was approved by the World Health Assembly in 1977 (WHA, 1998). The efficacy of vaccination and immunization in reducing the incidences of several diseases is clearly shown by the success story of measles control in developed countries of the world (Cutts and Markowitz, 1994). Unfortunately, twenty years after, this level of success has not been matched in Nigeria. In this country, measles has continued to cause high morbidity and mortality among children and children have continued to be paralyzed by these vaccine preventable diseases (CDC, 2008a, b). For example Borno State in the past few years have become the butt of attack of various diseases, with unimaginable human causalities. The recent outbreak of the dreaded measles is just one of them. In recent years, Borno State has hung the "inglorious" gold medal as the most affected state in the country by funning enough preventable diseases, which is non-existent in most parts of the world as a result of years of vaccination; the diseases on the prowl include cholera, cerebra spinal meningitis and measles. Last years, it was cholera that brought the "laurel" to the state killing tens of young and old ones alike in parts of the state. This year the state has started raking the points once again to make sure its ascension to the podium to collect the gold medal back to back is not denied (Olugbode, 2007). Measles, though in the past it has recorded little devastation, but on the strength of current, the report in 2007 has it that about eighty persons are dead and over hundred of children hospitalized. The disease was first noticed in lowly Njimtilo in Konduga local government area where it was reported to have killed about 25 persons and 120 children hospitalized. It soon spread to all parts of the local government and after dealing a major blow there; it was soon on its expedition to other parts of the state with an initial call on Jere, Damboa, Bama and Maiduguri Metropolitan Council (MMC) where it reportedly dispatched an average of 20 children to death (Olugbode, 2007).

In Nigeria, child mortality that is probability of a child dying under the age of five years, per 1000 is 198 for males and 195 for females. Infant mortality rate is 114 per 1000. These figures are exceedingly high and Nigeria is ranked as the 15th highest in the world- among coun-tries with high under-five mortality (UNICEF, 2001). This is unacceptable, especially at such a time when the first modern vaccines had been produced some 70 years ago

and when, with modern technology, it is possible to produce a vaccine or any prophylactic product against virtually any infectious disease once the causative agent has been isolated, but of course, with a few exceptions that have continued to evade detection (Adu, 2008). Measles produces significant illness, death, and disability (Pan American Health Organization, 2005); and infects approximately 40 million people resulting in nearly 1 million deaths annually in developing countries (Oldstone, 1998). It has been reported as a major cause of childhood morbidity and mortality in Nigeria; 212,183 and 168,107 cases were recorded in 2000 and 2001 respectively (WHO, 2001). For instance in 2005, Adamawa State, Nigeria experienced 3,974 cases and 238 measles-deaths (Dubray et al., 2005). WHO/AFRO (2004) reported measles as one of the top five causes of death in children less than five years of age in many African countries.

While many developed countries have successfully controlled measles, and are currently in measles elimination phase (CDC, 2005); Nigeria, in tune with global goal, is on measles control goal (that is, morbidity and mortality reduction). As a result, it recently concluded a nationwide accelerated measles vaccination campaign in June /July, 2006. As one of the leading cause of childhood morbidity and mortality, the need to effectively control and even-tually eradicate measles cannot be overemphasized.

Factors affecting eradication of vaccine preventable diseases such as measles in Africa

Although debate on the possible negative effect of mass vaccination campaigns on routine health services has gone on for decades (Mills, 2005), Wiysonge et al. (2006) reports points to an overall positive effect. High-quality mass campaigns usually achieve high vaccination coverage because of high-level political commitment and adequate planning and monitoring of vaccination activities (Wiysonge et al., 2006).

The high infectiousness of measles

Measles is highly infectious and has a very high attack rate and thus it would be extremely difficult to eradicate the virus altogether through vaccination.

Limited number of related vaccine strains

Protection against measles could be incomplete as a result of limited number of related vaccine strains. This may subject the measles virus to considerable immunological pressure (Tamin et al., 1994).

Low vaccination age

Low vaccination age is known to adversely affect measles vaccine efficacy, mainly due to the presence of maternal antibodies, and this is regarded as primary vaccine failure (Markowitz et al, 1990; Hamkar et al., 2006).

Low vaccination coverage (by increasing non-immune population), including factors contributing to low coverage

Protection against measles could also be incomplete as a result of low vaccinations rates may subject the measles virus to considerable immunological pressure (Tamin et al., 1994). Low vaccine coverage resulting into low levels of population immunity favored the selection, transmission and emergence of wild measles and vaccine derived variants with biological properties indistinguishable from those of wild measles in countries such as Nigeria. Routine immunization coverage is far too low in Nigeria while the quality of the mass immunization is not high enough to wipe out the wild viruses. Measles has continued to circulate and affect Nigerian children because a substantial number of the children are not immunized or are under-immunized (Adu, 2008). Most research activities in Nigeria have focused more on quality control of vaccines and vaccination programmes, vaccination monitoring and evaluations, and molecular epidemiology of measles and polio viruses. Because of the relatively low vaccination coverage rates in many countries, measles continues to circulate in Western Europe (Rota and Bellini, 2003).

Obstacles to measles elimination in the Americas include increasing numbers of infants and children who are susceptible to measles, the circulation of measles virus in other parts of the world, and importation of cases of measles and subsequent spread of measles virus. The number of infants and children susceptible to measles in a population tends to increase over time even when high routine vaccination coverage with a highly effective vaccine is maintained. For example, in a population with an annual birth cohort of 100,000 children, 90% routine vaccination coverage, and 90% vaccine efficacy, approximately 19,000 children are added each year to the population that is susceptible to measles (CDC, 1998; 2008a, b).

Use of low potency measles vaccines

Protection against measles could also be incomplete as a result of vaccine failure (Mathias et al., 1989) . A study by Adu et al. in 1992 and in 1996a identified use of low potency measles vaccines as the major cause of primary vaccine failures among vaccinated children in Nigeria. Also, in a similar study by Onoja et al. in 1992 identified improper vaccine handling and break in the cold chain were found to be the major causes of low or non-sero conversions among vaccinated children in Nigeria.

Lack of potent measles antigen

A readily available measles HA antigen is lacking in most

laboratory in Nigeria. A readily available measles HA antigen will be a very valuable and useful tool for monitoring the progress of measles sero conversion following immunization in Nigeria. Up till now, this measles antigen is still being imported at very expensive amount into Nigeria. Also to import the foreign brands of this measles antigen into Nigeria takes s very long time and often a time, they arrive having lost their potency or very close to their expiry date.

Fast rate of waning

Secondary vaccine failures, however, are largely attributed to the waning of primary antibody response over time (Aaby et al., 1986; Markowitz et al, 1990; Paunio et al., 2000; Pannuti et al, 2004) . According to Adu (2008), it is evident that the Nigerian child is born with solid anti-measles antibody obtained from the mother. However two biological factors adversely affect these antibodies. The rate of waning of these maternal antibodies is so fast that a large proportion of these children are left unpro-tected before the age of the first dose (Adu, 2008). Also, in a study by Oyedele et al. (2004 reviewed in Adu, 2008), 58% of Nigerian children will loose their protective measles maternal antibodies by the age of 4 months while only 3 % are protected between the ages of 6 and 9 months. According to Klingele et al. (2000) and Adu (2008), 30% of Nigerian mothers will pass maternal antibodies that are unable to neutralize the circulating wild type measles virus to their children. These two factors had undoubtedly contributed to the pre- vaccination measles morbidity and mortality commonly reported among Nigerian infants. In a study conducted by Adu et al. (1996b, c), 20% of the children affected by measles in four selected hospitals in Ibadan were the ages of 6 and 8 months (Adu et al., 1997; Adu, 2008). Until recently (Paunio et al., 2000), there has been a lack of convincing evidence for waning immunity after measles vaccination without the boosting effect of natural infection (Paunio et al., 2000; Pannuti et al., 2004). If immunity is waning, we would expect to see a higher occurrence of a high-avidity response with increasing time since vaccination. This was the case in our study, where measles reinfection due to secondary vaccine failure significantly increased with increasing age. Almost all cases of measles reinfection (99%) were seen in the > 10 years age group, indicating that vaccine-induced immunity could wane after about 10 years and for achieving good performance in measles virus elimination a further dose of vaccine for 10-year-old children should be recommended.

Population densities and malnutrition

Increasing worldwide population density and urbanization (particularly in developing countries) do not favour measles eradication. Low rates of vaccine coverage coupled with overcrowding is said to be one of the main risks factors for reemergence of wild and emergence of vaccine associated measles. There is a good deal of evidence to show that measles can precipitate malnutrition. From many parts of the world, epidemics of kwashiorkor have been reported in the wake of epidemics of measles (Gans, 1961; Murphy and La, 1966). The time-lag is usually about two months. During epidemic years, 30% of children admitted to Harare Hospital with malnutrition have suffered from measles during the previous few months. Their admission diagnosis is recorded as malnutrition, and the preceding measles infection is missed unless specific enquiry is made (Axton, 1979).

Taken together, these factors explain how measles may initiate a vicious circle of malnutrition and infection, shown in Figure 2. Starting with a well child, following the right-hand pathway, a child may become undernourished through suffering from any acute infectious illness, including measles. In this undernourished state, the child is more susceptible to other infections, and to suffer from them more severely than normal. It is then only a few steps to the grave. Malnutrition depresses the body's defence mechanisms, so predisposing to severe measles infection. There have been reports that measles itself will depress the immunological system for as long as six to eight weeks. This emphasizes still further the importance of measles as one initiator of the vicious circle (Axton, 1979). In discussing the inter-relationship between malnutrition and infection, this is the heart of the most important problem facing children in every developing country. The answer to malnutrition is not simply the provision of food; it involves preventing infection. Conversely, the prevention of infection, and more specifically the amelioration of its effects in terms of mortality and morbidity, depends on improving the nutritional state of children (Axton, 1979).

Human attitudes and error

Human attitudes toward vaccination for example, false rumors in 2003, that the polio vaccine was unsafe leading to the shut down vaccination campaigns in northern Nigeria, this likely contributed to the outbreak of vaccine preventable diseases such as circulating vaccine-derived poliovirus (cVDPV). There were allegations that the polio vaccine can spread HIV (Kapp, 2004), which further strengthened the boycott and weakened the public's confidence in the vaccine (Agbeyegbe, 2007). Also, it is a well-known and established fact that no vaccine is entirely safe, and even then, there exists the possibility of human error during administration of vaccine (Clements et al., 1999). However, despite questions of safety, vaccines have continually contributed to disease prevention and control (Plotkin and Plotkin, 1999) . Strained relations between the West and Muslims in Northern Nigeria, some of whom identified positively with acts of terrorism (Nigeria World, 2001) provided an enabling environment for advocating boycott of vaccination (Agbeyegbe, 2007).

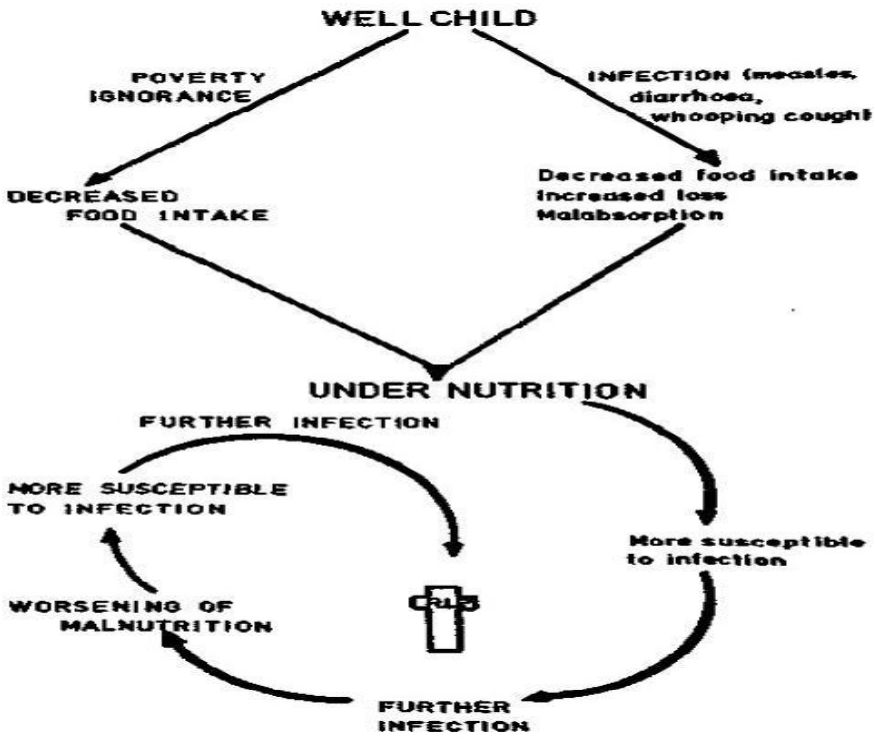

Figure 2. The Vicious Circle: Malnutrition and Infection (Axton, 1979).

Furthermore, deaths from a Pfizer drug trial had created lingering uncertainty in northern Nigeria about the safety of Western health initiative (BBC, 2004).

Political instability

In several countries particularly Afganistan and Somalia, part of Parkistan, Sierra Leone, Sudan, Liberia, Congo, and Ethiopia political instability or armed conflicts make vaccination logistically difficult and unpredictable. In addition to this internal politics in the 2003 immunization boycott, were ramifications from the international political arena. Anti-western sentiments have increased among Northern Muslims fundamentalist following the September 11, 2001 attacks and America's war on terrorism. Given the distrust and growing antagonism towards America, the involvement of the West in a program that benefits Muslims was viewed with suspicion (Agbeyegbe, 2007).

Cultural and religious objections

Many Nigerians are blaming the outbreak on vaccination efforts; an attitude experts fear may ruin previous gains in eradicating vaccine preventable disease in the country. Most of the anti-immunization campaigns in Nigeria have been predominantly Muslim north of Nigeria, and a number of Muslim clerics have been quoted in the Nigerian media as claiming that vaccines are dangerous and cause sterility or illness (Adeija, 2007). Cultural and religious objections under vaccinations efforts, resulting in persistently low immunity in the population and consequently, a high incidence of emerging vaccine-derived viruses and re-emergence of wild viruses. Agbeyegbe (2007) examined the role of religion in the boycott of immunization of vaccine preventable diseases such as polio, as reflected in the questioning of the authenticity and the safety of vaccines by the Supreme Council of Sharia in Nigeria (SCSN). The influential Islamic preachers by raising questions on immunization and the safety of the vaccines laid foundation for the boycott of the northern states of Nigeria from the national immunization programme (Gamii, 2004; Agbeyegbe, 2007) while some predominantly Muslim states in northern, Nigeria implemented the boycott (Agbeyegbe, 2007). Due to the intensity of the religious divide, Muslims dismissed earlier efforts by the Federal Government to assure northern Muslims of the safety of the vaccines as not being credible since Muslims leaders had called vaccination unsafe (Csmonitor, 2004). Religion was however, a proximal factor in the 2003 boycott since principal advocates, SCSN, Jama'atu Nasril Islam (JNI) are Islamic organizations, and their primary concern was for Muslims in Northern Nigeria to boycott the immunization exercise (Agbeyegbe, 2007). Increasingly, some Muslims in the north are resisting compliance with some UNICEF and UN conventions being questioned for their incompatibility

with the application of Sharia. Whereas the undercurrents between Muslims and Christians in Nigeria as well as Western donors may have been sufficient to begin the controversy on the vaccines e.g. polio vaccine, other factors helped to sustain it (Agbeyegbe, 2007).

Apart from the religious belief which has led to apathy against immunization as many believe that the Christian dominated Western World through immunization is out to reduce the population of the Muslims by poisoning their babies, poor ventilation of most houses in the state which is noted for its very hot climatic condition is another cause. There is also the belief that everything in life is from God, which many times make the people to refuse medical treatment. Although, some state government in the northern Nigeria is making effort to stop the apathy to medical treatment, with sensitization programmes during the National Immunization Days (NIDs) and even with the support of religious and traditional rulers called out on their subjects to take immunization for their children, much success is yet to be achieved. There is the need for the people to look in the direction of medical science which has eradicated these diseases in the advanced and developing countries, rather than seek divine intervention (Olugbode, 2007).

Ignorance

In the last measles outbreak in Borno state, Nigeria, the people are presently appeasing their gods, the citizens mostly Muslims are calling on Allah to look down on them with little mercy and send away the demon from hell, which is masquerading as measles to visit their sin on them. It is surprising that most of them are looking unto God to save them from this disease rather than a solution in the sphere of medical science. But to someone who understands their beliefs and philosophies, it would not be a surprise, because it is culturally believed that it is an attack from the gods as a result of infidelity on the part of the parents, especially mothers. But does this cultural belief have any basis in science, Dr. Samuel Ville, a consultant pediatrician at the State Specialist Hospital, Maiduguri said no, "there is no scientific proof or foundation to support this claim, measles is a viral attack" (Olugbode, 2007). One may perhaps want to know the cause of the otherwise preventable diseases in the state? Medical experts believe that the state is afflicted by religious belief above the diseases which has laid siege on it in recent times.

Government negligence

The inability of the Nigerian government to acknowledge the risk involved in vaccination however negligible raises doubt about the sincerity of the government, and positions the boycotts of polio vaccination proponents as a more reliable source of information. The government does not appear to have positioned itself as a credible authority to implement immunization programs. No vaccine is fully safe, a perfectly potent and without risk of administering error (Clements et al., 1999). In 1991, WHO recommended post-immunization surveillance for any nations that implement national immunization programs (WHO, 1991). Beyond monitoring for adverse effects, some countries have established compensation schemes for injuries that result from vaccination (BBC, 2004). Such efforts by government do not necessarily raise suspicion about immunization programs but may rather raise the credibility of government with the public.

Lack of risk communication

Lack of risk communication is one of the factors affecting polio eradication especially in Nigeria. Although, the boycott of immunization is no longer in effect, low participation during vaccination may persist reflecting a failure to implement risk communication (Agbeyegbe, 2007). The silence of the government over the alleged report by JNI and widely in the media that the government acknowledged the use of contaminated vaccines but claimed that the contaminated batch had been completely used, could be interpreted as indicative of the accurateness of the report. To address such situations, risk communication is increasingly becoming important in public health (Rudd et al., 2003). Risk communication offers a two-way communication process that presents the expert opinions based on scientific facts to the public, and acknowledges the fears and concerns of the public, seeking to rectify knowledge gaps that foster misrepresentation of risk (Leiss, 2004; Aakko, 2004; Agbeyegbe, 2007). For example, the biologic effects of vitamin A supplementation on the subsequent clinical manifestations and severity of measles need further elucidation (Dollimore et al., 1997). The information delivered to the public over the immunization boycott period was capable of affecting their risk perception. Public perception of risk shaped by variables such as bias, values, beliefs and experience may disregard facts and rational reasoning, and be entirely subjective. Individuals perceive risks which they are familiar with (polio cases) and have control over (refuse to submit to vaccination) as more acceptable than unfamiliar risk situations (infertility) over which they have no control over which the individual can exercise no control (compulsory vaccination) (Renn, 2004; Aakko, 2004; Ropeik, 2004; Agbeyegbe, 2007).

Lack of good road network

Of the targeted 29 million children, 4 million reside in impoverished and hard-to-reach settlements across the Niger Delta Region **(**Njoku, 2006**)**.

Conflict-Threat of armed militias and forced migration

Another pertinent issue raised by Otten and colleagues is

the effect of migration on measles transmission in sub-Saharan Africa. Epidemiological investigations linked measles outbreaks in Burkina Faso and Cameroon to movement of unvaccinated children from neighbouring countries that had not conducted mass measles vaccination campaigns (Otten et al., 2005). Other challenges facing vaccination teams included the threat of armed militias that roam the area in search of opportunities to seize control over the local oil resources **(**Njoku, 2006**)**.

Increasing international travel

Because of the frequency of travel to and from Europe, measles genotypes C2, D6, and D7 are often associated with measles cases imported from Europe to other parts of the world (PAHO, 2001; Rota et al., 1998; 2002; Rota and Bellini, 2003).

Absence of a follow-up vaccination campaign

The absence of a follow-up vaccination campaign, in addition to low routine vaccination coverage, may have contributed to the outbreak of measles in the state of São Paulo, Brazil in 1997. However, factors not directly related to implementation of the measles control strategy (e.g., in-migration of susceptible young adults from rural areas, high population density, and independent adult transmission) may also have influenced the course of the outbreak. Analysis of the São Paulo experience supports the idea that elimination strategies are unlikely to succeed if they are not implemented completely throughout a country or region (CDC, 1998).

Poor attitude of vaccination record keeping

There is a poor attitude of record keeping among Nigerians as it was practically impossible to obtain the vaccination records of the youths and students screened in a study by Ogundiji (2008). Finally, measles infection is also an urban problem and control efforts will continually be faced with difficulties as long as there is overcrowding in our cities and illiteracy among our people. Vaccines should be educated in all immunization programs to keep their vaccination cards for future reference. Virology Laboratories also should be equipped with adequate test facilities to monitor post vaccination sero conversion among subjects.

Other factors that do not favor eradication

include (CDC, 1998):

1. Logistics questions, including the use of needles and syringes
2. The potential competition for resources with other ongoing eradication efforts (that is, efforts to eradicate polio and Guinea worm)

Current dimensions in eradication of measles in Africa

The measles disease has been eliminated in countries that have maintained high vaccine coverage rates and 4 out of 6 WHO regions now have measles elimination goals (WHO, 2005). Forty-eight percent (48%) reduction in measles death was recorded within 1994-2004. More than 47% of measles death continues to occur in the African Region of WHO (WHO, 2006, 2007a). Since 1962 when the use of live attenuated measles vaccine was introduced in Africa which was derived from the 1954 Edmonson isolate (Rota et al., 1994a), measles is still endemic in African countries like Nigeria and infections in west Africa still results in mortality among children and young adults, many of which develop disease before they can be vaccinated at the age of 9 months all because of lower vaccinations rates and low level of sero conversion after vaccination when compared with developed countries (Sabin 1991).

Immunization programs world wide now prevent greater than 1.5 million deaths from measles in developing countries. Yet approximately 1 million children continue to die each year from measles- a preventable and potentially eradicable disease (Tamin et al., 1994). Clinical diagnosis of measles infection in children is straight forward and often times easy and the laboratory is often not consulted before a definitive diagnosis is made. However, this is often confused with manifestation of other exanthematous diseases like dengue fever, varicella and rubella which shows similar clinical manifestations. As such if therefore necessary to do a differential laboratory diagnosis particularly in measles endemic countries such as Nigeria. Laboratory diagnosis however, is confirmatory and this can be done using direct virus isolation in cell culture using acute phase PBMC of infected patients inoculated into SLAM Vero or B958/B95[a] cell lines. Characteristic cytopathic effect (CPE) can be visualized after about 6 to 8 days of virus culture (Ono et al., 2001).

Currently, there are no antiviral drugs against Measles although there are drugs available for the bacterial super infections that accompany the disease control activities towards measles worldwide are done through vaccination campaigns. In March 2001, WHO and UNICEF jointly released their measles mortality reduction and regional eliminations tagged strategic plan 2001-2005 (WHO, 2003) with the aim of reducing global measles death by the end of 2005. The strategies included:

1. Sustaining high vaccinations coverage.
2. Provision of supplementary immunization activities.
3. Enhancing measles surveillance by integrating epidemiological and laboratory information.
4. Improving clinical management of measles.

Regional measles elimination goals have now been

adopted by 4 WHO Regions with African and South East Asia regions focusing on measles mortality reduction (WHO, 2007a). Although, global routine measles vaccination coverage showed moderate increase between 1997 (71%) and 2004 (76%), coverage varied significantly by geographical region (WHO, 2006). There has also been an increase in the proportion of countries offering supplementary immunization activities (SIAS) to children, from 2000-2004, more than 215 million children aged from 9 months to 14 years received measles vaccine through SIAS in 36 WHO/UNICEF priority countries out of which 28 (78%) were done nationwide and 24 (67%) were in Sub-Saharan Africa (WHO, 2007a).

The relatively recent discovery of genetic variation within wild type measles viruses has led to the suggestion that these viruses have antigenic characteristics that allow them to circulate more efficiently in the presence of vaccine-induced immunity. Although antigenic differences between measles viruses from the various genotypes have been detected by using monoclonal antibodies and polyvalent antiserum (Tamin et al., 1994), the wild type viruses that have the most sequence variation compared with the vaccine are neutralized by antiserum to the vaccine virus (Xu et al., 1998). More important, measles vaccination programs, when properly administered, have been exceptionally successful in all parts of the world irrespective of the endemic genotype of wild type virus. Studies are in progress to explore the potential for biologic differences between measles viruses from different lineages (CDC, 2001; Biellik et al., 2002).

Recent international efforts to control measles infections through aggressive vaccination programs have had a great deal of success. In particular, the Pan American Health Organization (PAHO) reported record low numbers of measles cases in the Americas during 2000–2001, reflecting the overall success of measles control pro-grams in the Western Hemisphere (CDC, 2001). Indige-nous transmission of measles virus has been eliminated in the United States, the most populous country in the region of the Americas, and only 3 of 41 countries in the region reported indigenous measles transmission during 2001 (CDC, 2000, 2001). The success of mass vaccine-tion campaigns in southern Africa has suggested that measles elimination is possible even in developing coun-tries with a high incidence of human immunodeficiency virus infection (Biellik et al., 2002). However, despite these successes, measles remains an endemic disease in many areas of the world, and among children, it is still the most common cause of death from a vaccine-preventable disease (Rota and Bellini, 2003).

In countries where they have been fully implemented, the strategies adopted to eliminate measles (that is, catch-up, keep-up, and follow-up) in the Western Hemisphere have substantially reduced or eliminated measles. Maintenance of high routine vaccination coverage and community-based surveillance (that is, case identification, reporting, and investigation) require adequately trained and equipped primary health-care personnel. Strengthening the primary health-care system and EPI in developing countries, although perhaps not essential for interruption of measles virus transmission, greatly facilitates achieving and maintaining measles elimination in a country or region. In some countries (particularly in the Americas and the United Kingdom), most measles cases are now caused by international importations. Consequently, eliminating measles from these countries requires improvements in measles control in other parts of the world. In the United States, most virus importations originate from Europe and Japan, indicating that developed countries, as well as developing nations, need to improve measles control. Countries can help improve international communication about areas where measles virus is circulating by notifying their respective WHO regional offices about measles importations. Such communication can help national health authorities strengthen surveillance and undertake appropriate remedial actions (CDC, 1998).

Prevention: A cost-effective, safe measles vaccine

Suffering, complications and death caused by measles can be easily prevented through immunization. The measles vaccine is safe, effective and inexpensive. It costs less than one US dollar (consisting of vaccine, injection equipment and operational costs) to immunize a child against measles, making measles vaccination one of the most cost-effective public health interventions available for preventing deaths. Measles immunization carries the highest health return for the money spent saving more lives per unit cost. The vaccine, which has been available for more than 40 years, costs about US $0.33 per bundled dose (vaccine plus safe injection equipment) if procured through the United Nations Children's Fund (UNICEF). In many countries where the public health burden of rubella and/or mumps is considered to be important, measles vaccine is often incorporated with rubella and/or mumps vaccine as a combined, live, attenuated (weakened) Measles-Rubella (MR) or Measles-Mumps -Rubella (MMR) vaccine. Measles vaccine is equally effective whether in the monovalent or in the combined form. Immunization coverage rates for measles vaccination vary significantly by region. WHO and UNICEF estimate that the global average for routine measles immunization coverage between 1999 and 2005 increased from 71 to 77% (WHO, 2007a).

Successes and failures in global eradication of measles

With no animal reservoir, it must be possible to eradicate the virus through a controlled vaccination campaign. In the USA, where vaccination of all children is required before commencing school, case reports have fallen by over 99% but eradication has not been achieved. The vaccination programme has been most effective in the

USA, where measles immunization is compulsory. The incidence rate has also declined dramatically in the UK but without the rigorously pursued vaccination as practiced in the US, it is not likely to be as effective as that in North America. In the third world, malnutrition aggravates measles infection and there are 900,000 measles related deaths per year. Vaccination in these areas has failed to yield dramatic results. The problem is that the vaccine is usually given at 12 months of age (it should not be given in younger individuals because the presence of maternal antibodies may lead to a poor response.) but infection in these areas often occurs earlier in life. Vaccination should therefore be performed on younger children than in the developed world. However, this must be balanced with the fact that the success rate is lower in younger children (50-75% in 6-month-old-children as opposed to 95% for 12-month-old children).

Participants of the Second Meeting on Advances in Measles Control and Elimination (CDC, 1997), agreed that measles eradication is technically feasible with available vaccines and recommended adoption of the goal of global eradication with a target date during 2005–2010, with the provision that measles eradication efforts should not interfere with polio eradication but should build on the successes of the global Poliomyelitis Eradication Initiative (CDC, 1998). The Expanded Programme on Immunization (EPI) of the World Health Organization has a global target of reducing measles incidence by 90% and mortality by 95% from pre-EPI levels by 1995. Both developed and developing countries that have given priority to measles control have substantially reduced measles morbidity and mortality, and some have come close to eliminating measles. A variety of vaccination schedules and strategies have been used, which reflect the differing program goals, health services infrastructure, and availability of resources in different countries. Failure to control measles has usually been due to a failure to implement planned strategies adequately. The highest priority in measles control is to assist countries, especially the lowest-income countries, to implement vaccination programs more effectively (Cutts and Markowitz, 1994).

Cases of measles have been seen in partially immunized children, in babies with residual antibodies, and in people who have been given serum immune globulin for protection. Occasionally, infections have also been seen in the course of live vaccine failure. However, the symptomatology is very much reduced. Exposure to the measles virus is steadily decreasing worldwide due to mass vaccination, and millions of people are protected solely by immunity induced by attenuated vaccines (de Quadros et al., 1996). However, there are doubts about the quality and duration of vaccine-induced immunity (Markowitz et al, 1990; USPSTF, 1996). Two kinds of failures, primary failure and secondary failure, are attributed to measles vaccine (Hamkar et al., 2006). Primary failure indicates that the vaccine has not taken and does not induce any immunological response, while secondary failure indicates that vaccine-induced immunity against measles has waned in the years after vaccination (Paunio et al., 2000; Pannuti et al, 2004).

Low vaccination age is known to adversely affect measles vaccine efficacy, mainly due to the presence of maternal antibodies, and this is regarded as primary vaccine failure (Markowitz et al, 1990; Hamkar et al., 2006). Secondary vaccine failures, however, are largely attributed to the waning of primary antibody response over time (Aaby et al., 1986; Markowitz et al, 1990; Paunio et al., 2000, 2004; Hamkar et al., 2006).

In October 2006, Nigeria has launched a massive immunization campaign to protect 29 million children against measles, a highly contagious virus that kills more Nigerian children than any other vaccine-preventable disease. On 3-9 October, more than 100,000 health workers were mobilized and sent to 17 southern states. Health workers travel by boat to reach children in the Niger Delta Region of Nigeria with measles vaccine. Some 18,000 community health posts were set up to provide children with measles and polio vaccines, as well as vitamin A supplements to boost their immunity. Though, this measles immunization campaign targets 29 million Nigerian children **(**Njoku, 2006**),** the disease continued to roam every nook and crannies of Borno state for souls it could send to early grave, calling on Dikwa and Mafa and arresting few more souls. The disease is still not through with the people of the state as it was reported to have made in-road into the other twenty local government areas (Olugbode, 2007).

UNICEF working with the Government of Nigeria and the Measles Initiative – a global public- health partnership –provided crucial logistical support to ensure that vaccines were transported in a timely, safe manner. To reach every child, health workers often traveled several hours by speedboat, then paddled in wooden canoes or trekked through marshy waters in order to go house to house (Njoku, 2006). All the equipment used in the immunization campaign– solar freezers, deep freezers and refrigerators – is provided by UNICEF (Njoku, 2006) “UNICEF has also supplied medical equipment and drugs to help us carry out the health campaign in Nigeria.” In December 2005, children in Nigeria’s northern states were immunized against measles during the first round of the campaign. The latest round could bring the total number of immunized children to 56 million, making this campaign one of the largest ever against measles in any country. “What we see today, we did not see before”. “We lost so many children to measles because we did not have campaigns like this. “Now we have the campaign and it is saving children’s lives”. Parents should let their children be immunized; it is the right thing to do (Njoku, 2006).

As the serological status preceding measles is usually unknown, it is difficult by conventional means to establish the occurrence of secondary vaccine failures (waning and /or incomplete immunity) and related factors Markowitz et

al., 1990). In a study of vaccinated students who donated blood just before infection, low antibody levels increased the risk of measles (Chen et al., 1990).

There is a report of 4 health care workers who contracted measles despite prior successful vaccination (Ammari et al., 1993). Other case reports of secondary vaccine failure have been published, including one of a Chinese patient who seroconverted after vaccination at 8 months (Markowitz et al, 1990). In a 10-year follow-up study of children in Canada inoculated at 12 months of age, 6–9% developed clinical measles (Mathias et al., 1989). In a study in 1996–97 in the Islamic Republic of Iran 9% of measles cases were among previously vaccinated patients (Mokhtari-Azad et al., 1998).

Understanding the reasons for primary and secondary vaccine failures is important for the evaluation of measles control programmes in developing countries. A high proportion of primary vaccine failures in vaccinated patients with measles can indicate, for instance, problems with improper vaccine handling. However, the introduction of enhanced diagnostic tests for IgM detection such as IgM-capture EIA, with results which may be positive for patients with measles reinfection due to secondary vaccine failure, has highlighted the difficulty in differentiating between primary infection or reinfection due to primary and secondary vaccine failure (Erdman et al., 1993; Paunio et al., 2000; Pannuti et al., 2004). Measles reinfection due to secondary vaccine failure is probably more common than suggested by studies relying on specific IgM (Paunio et al., 2000), because measles-specific IgM is also inducible by reinfection (Erdman et al., 1993). The estimation of IgG antibody avidity is useful for identifying primary and secondary immune responses, but there have been few reports of its use during measles outbreaks (Pannuti et al., 2004). The results of the study by Hamkar et al. (2006), which showed that 18.4% of 365 measles cases confirmed by a positive IgM test mounted a secondary immune response, provide further evidence that the presence of IgM cannot be used as a reliable indicator of a primary immune response (Pannuti et al., 2004).

The avidity (functional affinity) of immunoglobulin IgG antibodies has long been known to distinguish primary from secondary immune responses against many antigens. Virus-specific high-avidity antibodies are generally associated with pre-existing B-cell memory, whereas low-avidity IgG is an indication of the primary immune response (Paunio et al., 2000). Thus, avidity measurement can be used to assess the success of measles vaccination (De Souza VA et al., 1997) and offers a way of assessing the type of vaccine failure without knowledge of prior antibody status (Narita et al., 1996). In a study by Hamkar et al. (2006) in the Islamic Republic of Iran, conducted in 2003, IgG avidity assay was used to analyse sera from laboratory-confirmed measles patients, in order to determine how many were cases of reinfection (that is high- avidity antibodies) and how many were cases of primary infection (that is low- avidity antibodies). A secondary immune response was seen in 18.4% of patients. All unvaccinated patients (16.7%) showed a primary immune response. Of 244 patients with documented vaccination, 75.8% showed a primary immune response and 24.2% showed a secondary immune response, thereby indicating a secondary vaccine failure. Almost all measles reinfections (99%) were seen in patients >10 years old, indicating that vaccination for 10-year-old children is recommended (Hamkar et al., 2006).

GLOBAL MEASLES MORTALITY REDUCTION

GOALS UNICEF Urban measles control initiative

UNICEF, in collaboration with WHO, is supporting an initiative to reduce deaths among young children (that is, those aged <5 years) through urban measles control. The initiative is intended to catalyze improvements in child health activities in underserved urban areas. In such areas, where a substantial percentage of children is susceptible to the disease, measles circulates easily, affects infants, and is often exported to surrounding rural areas. The UNICEF/WHO strategy is to develop local partnerships to improve routine immunization services in poor urban areas, plan and carry out measles campaigns in high-risk areas, develop community-based measles surveillance, and promote child health and development. The proposed target age group is children aged 9–59 months, although the age group may vary on the basis of local epidemiologic findings. In addition to measles vaccination, campaigns undertaken as part of the initiative will include vitamin A supplementation. Vaccine will be administered with autodestruct syringes, and safety boxes will be provided for disposal of used injection equipment. Development of measles surveillance to evaluate the impact of immunization activities will be an integral part of the initiative (CDC, 1998).

Comprehensive strategy for sustainable measles mortality reduction

In May 2003, the 56th World Health Assembly unanimously adopted a resolution to reduce measles deaths by 50% by the end of 2005 compared to 1999 levels. This goal was established a year earlier by the United Nations General Assembly Special Session on Children "World Fit for Children". This goal has been exceeded: activities began in 2000, and led to a 60% decrease in measles deaths worldwide. In May 2005, the 58th World Health Assembly adopted the WHO/UNICEF Global Immunization Vision and Strategy (GIVS). GIVS calls on countries to reduce global measles deaths by 90% by 2010 compared to 2000 estimates. The United Nations Millennium Declaration also set a child survival target: to reduce the under-five child mortality rate by two-thirds by the year 2015 compared with 1990 levels. Routine measles vaccination coverage is an indicator for this target. WHO and UNICEF have developed a comprehensive strategy to

sustainably reduce measles deaths which was endorsed by the World Health Assembly in 2003. The four components of the strategy are as follows:

Strong routine immunization

The delivery and monitoring of other child survival interventions (e.g., vitamin A supplementation, malaria control, and integrated management of childhood diseases) are now being included in childhood immunization programmes, which are often viewed as surrogate measures of the overall strength of the health-care delivery system. Therefore, mass vaccination campaigns can be used to improve routine primary healthcare services in general (Wiysonge et al., 2006). The first dose of measles vaccine is given to children at the age of nine months or shortly thereafter through routine immunization services. This is the foundation of the sustainable measles mor-tality reduction strategy. At least 90% of children should be reached by routine immunization services every year, in every district (WHO, 2007a).

Second opportunity

A 'second opportunity' for measles immunization is provided to all children aged nine months to 15 years. This assures measles immunity in children who failed to receive a previous dose of measles vaccine, as well as in those who were vaccinated but failed to develop immunity following vaccination (approximately 15% of those children vaccinated at nine months of age). The second opportunity prevents the accumulation of susceptible children to dangerous levels, since many older children have missed measles vaccination and have not been infected, so they are not immune. The second opportunity for measles immunization is given either through routine immunization services (if high coverage can be achieved and maintained over time) or through periodic supplementary immunization activities (SIAs). SIAs target large populations (entire nations or large regions) and aim to vaccinate all children regardless of prior vaccination history (WHO, 2007a).

Surveillance

Standard measles surveillance guidelines have been developed and implemented. These include collection of a blood specimen from suspected cases and testing in an accredited laboratory to either confirm or rule out measles infection. Prompt recognition and investigation of measles outbreaks provide important information about programme impact and assure the implementation of appropriate outbreak response activities (WHO, 2007a).

Clinical management of measles cases

Improved clinical management of measles cases including vitamin A supplementation and adequate treatment of complications, if needed with antibiotics (WHO, 2007a).

Immunization strategies

Immunization strategies designed specifically to improve measles control and reduce measles deaths in densely populated urban areas of low-income countries should be developed and supported by national governments, WHO, and UNICEF. These strategies should be directed to vaccinating populations not covered by routine vaccination services or previous catch-up vaccination campaigns. When supplementary vaccination campaigns are conducted in such high-risk urban areas, all children in the target age range should be vaccinated regardless of measles vaccination status or history of previous measles disease. Disease surveillance is essential to monitor the impact of supplementary vaccination activities and should be developed as part of these strategies (CDC, 1998). Combining measles vaccination campaigns with other public health interventions (that is, administration of oral poliovirus vaccine or non-vaccine interventions such as vitamin A supplementation) should be encouraged. However, no single combination of interventions is appropriate in all circumstances; the combination of interventions must be specific to the needs and capacities of countries where they are implemented. For example, countries that can afford combination vaccines should consider using MR vaccine or MMR vaccine. Simultaneous administration of yellow fever vaccine could also be considered in countries at risk for yellow fever (CDC, 1998).

Future dimensions for global measles eradication and in Africa

Several lessons have been learned from previous efforts to eradicate communicable diseases (Hinman and Hopkins, 1998). To eradicate a disease, medical scientists must have a thorough understanding of its natural history. To achieve consensus concerning the appropriate approach to eradication and sustained political commitment of resources, proponents of eradication should consult widely before embarking on the effort. National and international surveillance should be implemented early in the disease eradication program, and surveillance information should be used to guide program strategy. Implementation of the eradication strategy should emphasize flexibility and adaptation to the social, political, and public health circumstances of each country. A specific target date for eradication should be set to focus global efforts and maintain commitment to the goal of eradication (CDC, 1998). In addition to these general considerations, factors to be considered in implementing measles eradication include the high short- term costs of the endeavor, the risk of failure (that is, the probability of failure and the potential consequences of failure), and the

need to strengthen comprehensive health services to achieve eradication (CDC, 1998). Among the factors that favor measles eradication are:

1. The perceived importance of the disease in less developed countries.
2. The availability of highly effective vaccines and vaccination strategies.
3. The likely favorable benefit: cost ratio.
4. Rapid communications developed over the last two decades.
5. The capabilities and know-how that are the legacy of smallpox and polio eradication efforts.
6. Unless field personnel are well trained and supervised and provided with the correct equipment, improper administration of injectable vaccines during mass vaccination campaigns can cause bacterial infections (e.g., abscesses, toxic shock syndrome, or septicemia) and transmit blood borne diseases (e.g., hepatitis B, hepatitis C, HIV, syphilis, and malaria).
7. Proper disposal of needles and syringes is an important component of routine immunization programs and mass measles vaccination campaigns.
8. Training health-care workers in safe injection practices should be part of the planning and implementation of mass vaccination campaigns. Supervisors and senior managers should stress safe injection practices during the vaccination campaign. Evaluation of vaccination campaigns should include measures of observance of safe injection practices and disposal of used equipment.
9. The development of safe and cost-effective alternative technologies suitable for administration of vaccines in mass immunization campaigns (e.g., a new generation of jet injectors) should be encouraged.
10. Surveillance for adverse events after vaccination is important both for routine immunization programs and for mass immunization campaigns. Planning for campaigns should include establishing a mechanism to investigate and respond to reports of adverse events associated with administration of vaccines. At a minimum, the surveillance mechanism should be able to detect deaths and severe adverse events. Community-based surveillance systems can be used to detect adverse events that occur after vaccination as well as cases of measles.

Since it is likely that the 2005 goal will be met on time, more new ambitious goals for measles mortality reduction has been proposed in the Global Immunization Vision and Strategy (GIVS) (WHO/UNICEF, 2005) . The new goal is of 90% reduction measles mortality by 2010 compared with the 2000 level. To achieve this new goal of 2010 measles mortality reduction goal of 90% from 2000 levels, the following challenges must be overcome:

1. Measles mortality reduction activities need to be implemented in several large countries with high measles burden like Nigeria and India.
2. Enhanced efforts are needed to improve immunization systems such that at least 90% of infants are vaccinated before clocking 1 year of age.
3. Priority countries need to carry out SIAS as a follow up every 3-4 years
4. Disease surveillance at all levels should be strengthened.
5. Remaining large countries with high measles deaths such as India, Indonesia, and Pakistan should implement measles mortality reduction activities.
6. To sustain the gains achieved in the 47 priority countries, enhanced efforts are needed to ensure that more than 90% of infants are vaccinated against measles before their first birthday.
7. Priority countries must continue conducting follow-up vaccination campaigns every three to four years targeting children nine months to five years of age until their routine immunization systems are capable of providing all children with two opportunities for measles vaccination.
8. Field surveillance with laboratory confirmation of suspected measles outbreaks will need to be extended to all priority countries to allow effective monitoring.
9. The most effective measles control strategies for these countries, which also contribute to strengthening their health-care systems, should be undertaken early in the process of eradication; the goal should be to demonstrate that measles transmission can be interrupted despite the substantial barriers to success that exist in Africa. Although perhaps not essential for interruption of measles virus transmission, effective routine immunization services facilitate achieving and maintaining measles elimination in a country or region (CDC, 1998).
10. A renewed commitment to the goal of polio eradication is imperative, because much remains to be done to eradicate polio, particularly in the Indian subcontinent and Africa. Success in polio eradication will facilitate progress in measles elimination. Properly implemented, polio eradication and measles elimination activities can be mutually reinforcing and represent a natural joining of efforts. However, conjoining the efforts must not divert attention or resources from progress toward polio eradication. From a global perspective, measles eradication appropriately follows and builds on polio eradication activities. Nonetheless, planning for regional control, elimination, and ultimate eradication of measles should commence before polio eradication has been completed (CDC, 1998).
11. Emphasis is to be put on intense supportive supervision, regular meetings to discuss data, use of data for programmatic action, and regular feedback. The result of these actions has been an increase in routine vaccination coverage from 47% in 2001 to 73% in 2004 as in the case of Cameroon. Cameroon was thus able to complete high quality mass vaccination campaigns and increase routine vaccination coverage (Wiysonge et al., 2006).
12. Research on measles and measles immunization in immunocompromised persons should be conducted to clarify the potential for persistent carriage of measles

virus. Measles virus infection is an important model for immunosuppression in the human host. Research concerning the pathogenesis of measles and immune responses of immunocompromised and immunologically normal persons to wild measles virus and vaccine viruses should continue.

13. Aerosol administration of measles vaccine to school-aged children may be useful for catch-up campaigns but is less likely to be useful for routine vaccination of young children. Additional research is necessary to determine its feasibility in field operations. Further research on alternative routes of vaccine administration should be encouraged. However, because introduction of new vaccines requires extensive testing and regulatory review, and because the safety and efficacy of presently licensed vaccines are well established, the introduction of new vaccines is unlikely to affect the feasibility of measles elimination or eradication.

The future dimensions for measles control and elimination activities include design of a global strategy, preparing an operational plan and budget, obtaining political support, developing a partner/donor coalition, and implementing the strategy. Each step requires action at national, regional, and global levels. In addition, a consensus must be developed concerning the timing of measles elimination in relation to polio eradication. Specifically, should measles elimination be undertaken simultaneously with efforts to eradicate polio? Or should the efforts be undertaken sequentially? It is therefore suggested that measles elimination should not be undertaken at the national level before poliovirus transmission is interrupted. At the global level, in contrast, activities aimed at achieving measles eradication should begin before polio eradication is achieved. Polio eradication must remain the first priority (CDC, 1998).

Funding of measles eradication should also be considered. Projects that attract donor support have been successful (or have a high probability of success) in the past, and are both politically and socially popular, it provide visibility and recognition for donors, and have a specific goal and target date for completion. To attract support from potential partners and donors among governments, nongovernmental organizations, and the private sector, advocates of measles eradication should develop consensus concerning their objectives and strategies and communicate these objectives simply and directly. To succeed, advocates of eradication must reach consensus concerning the global disease burden of measles, likely cost savings from eradicating the disease, and resources required from external sources to accomplish the goal. The advocacy strategy should include identifying the key messages concerning measles eradication, forming coalitions of partners (including those in the private sector), and identifying advocates for fundraising. Consistency in messages about each aspect of measles eradication is essential to the success of the advocacy strategy (CDC, 1998).

Summary

The World Health Organization (WHO) estimates that 45 million cases of measles, with nearly 800,000 fatalities, continue to occur annually (EPI, 1992; de Quadros et al., 1996). Measles outbreaks still occur in both developed and undeveloped countries that have not maintained adequate immunization levels (Rota and Bellini, 2003). It been pointed out that the more rapidly measles elimination activities proceed at the national and regional levels, the more easily measles eradication will be accomplished. Conversely, the more slowly elimination activities proceed, the more difficult eradication will be. Once measles transmission is interrupted in a population, risks for virus importation and reestablishment of transmission increase over time. Conducting repeated follow-up vaccination campaigns is operationally difficult and expensive. Because routine vaccination and follow-up campaigns rarely succeed in vaccinating all susceptible persons in a population, and because the vaccine is not 100% effective, the prevalence of measles susceptibility in the population tends to increase over time. Thus, the more protracted the global measles eradication campaign, the greater the risk for reestablishment of measles in countries where transmission of the virus has been interrupted (CDC, 1998).

In Nigeria, the measles virus immunization is at the age of 9 months. This is a one dose, one time programme and the children are expected to be protected through life. In a country like Nigeria where the MV is endemic and all the risk factors for measles outbreak are abundant, a one dose, one time vaccination programme may not be able to protect the child for life. Antibody elicited as a result of measles vaccination has been demonstra-ted to wane with time (Kremer et al., 2006a, b) hence in a country like Nigeria with measles endemicity and a poor record of supplementary immunization activities (WHO, 2007a), a high antibody level has been noticed in children and young adults in most of the recent studies, this way may be due to a high rate of sub-clinical infections to which youths are exposed to after childhood vaccination. High levels of maternal antibody in pregnant women translates to protection against measles in babies born to them, sub-clinical infections from infants to young female adults may also lead to a higher antibody titre in females since they help mother in babysitting their infant siblings which expose them to measles (an infant disease) more than their male counterparts. There is therefore, the urgent need to revisit the measles immunization and vaccination programme in Africa and in our country Nigeria with the sole aim of introducing a two- dose schedule to halt the endemic transmission. This is believed to bring about the successful eradication of measles in Africa.

Only the short-term solution for the individual child can be provided by doctors or nurses (Axton, 1979). The long-term answer lies in overall change and improvement in the environment, which can only be brought about by integrated development on many fronts. Here, the doctor

takes his correct place in a team, the other members of which will be agriculturalists, politicians and hydrologists, to name a few. It is statutory to remember that the greater part of the decrease in infant mortality in Britain and Europe took place through social revolution, which improved nutrition, housing, and child care, before the discovery of vaccines and antibiotics (Axton, 1979) . We should also recognize that falling child mortality in Europe was followed, after an interval of fifteen to twenty years, by a fall in fertility. The finding of this review study is an indication that the substantial progress made towards measles elimination in sub-Saharan Africa will only be sustained if mass measles vaccination campaigns are synchronized over large geographical areas covering several contiguous countries. A possible scenario would be for the Measles Initiative and national governments to synchronize catch-up mass measles campaigns in the remaining countries with the follow-up campaigns in countries that have already conducted catch-up campaigns (Wiysonge et al., 2006).

In conclusion, immunization and vaccination remains one of the most cost effective strategies to prevent infectious diseases. The most effective and efficient way to protect the health of children is by immunization-before the risk of disease arises. Vaccination has succeeded in eradicating small pox in the world (Fenner et al., 1988). The Expanded Programme on Immunization (EPI) was approved by the World Health Assembly in 1977 (WHA, 1998). The efficacy of vaccination and immunization in reducing the incidences of several diseases is clearly shown by the success story of measles control in developed countries of the world (Cutts and Markowitz, 1994). The success of any immunization programme is dependent, to a large extent, on the quality and level of vaccination coverage. If Nigerian children are not to die unnecessarily from vaccine preventable diseases, the mechanism to improve the quality and raise the level of routine immunization coverage must be put in place (Adu, 2008).

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