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LIST OF CONTRIBUTORS

Amina Ismail (Ministry of Health, Disease Surveillance and Response Unit)
Ann Barasa (University of Nairobi, Department of Pathology - Immunology)
Boniface Osano (University of Nairobi, Department of Paediatrics & Child Health)
Domic M. Mutie (Ministry of Health, Unit of Immunization & Vaccines)
David E. Simiyu (University of Nairobi, Department of Paediatrics & Child Health)
Douglas Makewa (Kenyatta National Hospital)
Elizabeth Maleche Obimbo (University of Nairobi, Department of Paediatrics & Child Health)
Ernest K. Some (Ministry of Health, Unit of Immunization & Vaccines)
Evans Amukoye (KEMRI)
Evans Mokaya (USAID-MCHIP)
Ezekiel M Wafula (University of Nairobi, Department of Paediatrics & Child Health)
Fabian Esamai (Moi University)
Fred N Were (University of Nairobi, Department of Paediatrics & Child Health)
Isaac Mugoya (USAID-MCHIP)
John Ogange (World Health Organization, Kenya)
Lora Shimp (MCHIP Headquarters)
Lucy W. Muchiri (University of Nairobi, Department of Pathology)
Pamela Ochieng (Ministry of Health, Unit of Immunization & Vaccines)
R. K. A. Sang (Ministry of Health, Unit of Immunization & Vaccines)
Rose Kamenwa (Aga Khan University Hospital)
Tatu Kamau (Ministry of Health, Unit of Immunization & Vaccines)
Walter Jaoko (University of Nairobi, Department of Microbiology)
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We would also wish to thank all those who were involved in the writing of the first edition of the manual of April 1982.

Special thanks go to USAID/MCHIP WHO, a n d N E S I for their continued technical support and funding of various activities and teams that sat to review the manual.

Dr. Ephantus Maree,

HEAD of UNIT OF VACCINES AND IMMUNIZATION SERVICES
DEDICATION

This manual is dedicated to:

The late Prof. Nimrod Bwibo, a founder faculty member of the Department of Paediatrics and Child Health at the University of Nairobi. Prof Bwibo dedicated his professional life to the training and development of Paediatrics in Kenya and was tirelessly committed to Child survival and Immunization.

And,

The late Prof. Julius Meme, who worked conscientiously in training child health and enhancing child survival while serving in different positions at the University of Nairobi, Department of Paediatrics and Child Health and in Government.
FOREWORD

The Expanded Program of Immunization (EPI) manual has been extensively revised and updated in this second edition with the inclusion of new chapters, and updating of existing chapters and broadening of the scope of material covered. A wide range of topics are covered in three broad sections; the first section deals with the principles and practice of immunization, and familiarises readers with the philosophy behind and targets of the EPI programme. The second section covers the practical aspects of immunization including vaccine handling, transport and storage. The third and largest section covers individual vaccine preventable diseases and vaccines specific to each disease.

There has been much growth in the field of childhood vaccines and immunization over the two decades that have lapsed between the first and second editions of the EPI manual. After the major achievement of eradication of smallpox through vaccination, the EPI is currently working towards the eradication of polio and elimination of measles. In addition to the original 6 EPI antigens against tuberculosis, polio, diphtheria, pertussis, tetanus and measles, new antigens such as hepatitis B virus, yellow fever, Haemophilus influenza type B, and pneumococcal vaccines are now routinely provided. Additional effective vaccines are under consideration for routine inclusion in EPI programs (some of which are already provided routinely in private paid health care settings) such as rotavirus, measles/mumps/rubella, meningococcal, influenza virus, hepatitis A virus, human papilloma virus and varicella zoster virus vaccines. These new antigens are covered in detail in this manual. Other vaccines are under development such as vaccines against HIV and malaria and insight into progress is provided. Similarly, rapid development of innovations and new technologies for delivery of vaccine antigens such as jet injectors, vaccine patches, vaccine nasal sprays and aerosols have been discussed.

This manual is intended for use by medical students and clinicians; however it may be useful to other health workers, to enable them develop a firm foundation of core knowledge and skills on childhood vaccines and immunization, as well as the principles and structure of the EPI. We envision that this shall be introduced largely during pre-service medical training, and utilised alongside practical sessions at various points (central storage up to child immunization clinics) in the EPI thus strengthen undergraduate training. For working health professional, continued practical exposure will consolidate their understanding, during which time the manual may continue to serve as a valuable resource. Ultimately it is our hope that this manual shall contribute to the improvement and strengthening our child immunization services at all levels.
This edition is a collaborative effort between the Department of Paediatrics & Child Health of the University of Nairobi, the Unit of Vaccines and Immunization of the Kenya Ministry of Health (MOH), with contributions by paediatricians from the Unit of Child Health of the MOH, Moi University Department of Child Health, Kenya Medical Research Institute, and support from UNICEF, WHO and Maternal and Child Health Integrated Program (MCHIP). It is our sincere belief that all who use this manual will find it a valuable resource, and that it shall be put to good use.

Prof Elizabeth Maleche Obimbo,
CHAIRPERSON, DEPARTMENT OF PAEDIATRICS & CHILD HEALTH
SCHOOL OF MEDICINE, UNIVERSITY OF NAIROBI.
Learning Objectives
This chapter deals with concepts and principals of Vaccinology; at the end of this chapter, the student should:

• Define the terms used in basic immunology and vaccination
• Describe the various forms of immunity
• Describe the various types of vaccines
• Outline the properties of ideal vaccines
• Describe new technology and ideas contributing to future vaccines development and delivery

1.1 Introduction
Immunity is the ability of the body to resist harmful disease organisms that can cause infectious diseases whereas immunology is study of the origin, structure and function of the immune system. Vaccines are one of the success stories in the history of public health that have greatly reduced morbidity and mortality worldwide. Vaccinology began with the success of Jenner’s and Pasteur’s vaccines against smallpox, anthrax and rabies. Subsequently there has been tremendous development in the vaccine field with new antigens and technologies. Healthcare providers (HCPs) need to be well acquainted with current vaccination knowledge and be equipped with strategies for implementing vaccine recommendations in their clinical setting. Therefore, it is important to understand the immune mechanism that delivers protection which will then guide the design of more effective vaccines.
1.2 **Milestones in Vaccine Development**

1885: First use of live attenuated viral vaccine (rabies) in humans

1909: First live attenuated bacterial vaccine (Bacillus Calmette-Guerin, or BCG) created for use against tuberculosis

1921: Diphtheria toxoid developed

1924: Tetanus toxoid produced

1930s: Pertussis vaccine developed

1932: Yellow fever vaccine developed

1940s: Diphtheria-tetanus-pertussis (DTP) combination introduced

1955: Inactivated polio vaccine introduced

1963: Live attenuated oral polio vaccine introduced

1963: Measles vaccine introduced

1986: First recombinant vaccine (hepatitis B) introduced

1990: First polysaccharide conjugate vaccine (Haemophilus influenzae type b) introduced

This was followed by faster introduction of Meningococcal conjugate (MCV4), Pneumococcal Conjugate vaccine, Rotavirus Vaccine and Human papillomavirus (HPV) whereas Malaria and HIV Vaccines are under development.

1.3 **Natural history of diseases**

Entry and multiplication of infectious agents in the body (at the onset) with typical signs and symptoms apparition occurring later may result in complete recovery or, if severe, may result in disability (e.g. paralysis in polio or blindness in measles) and even death depending on body immunity.

It is therefore important to understand the immune mechanism that delivers protection against the infectious agent. This understanding will guide the design of more effective vaccines. With the goal of **generating and sustaining** the number of antigen **specific B & T cells** against a particular pathogen / antigen sufficient to provide **protection**.
1.4 **Terms used in immunology**

**Antigen:** Any substance, usually a protein that is capable of eliciting an immune response. The antigens that can cause a disease are called pathogens.

**Antibody:** A protein produced by plasma cells in response to an antigen

**Immunity:** Protection against infectious disease

**Immunogenicity:** The inherent ability of an antigen to induce an immune response.

**Seroconversion:** When an individual following a disease or vaccination generates antigen-specific antibodies.

**Vaccination:** The process of administering a vaccine or manipulation of the immune system to induce protective immunity.

**Vaccine adjuvant:** Substance that is added to a vaccine to enhance immunogenicity without having any specific antigenic effect in itself. These may include mineral salts (aluminium and calcium phosphate), organic adjuvants, particulate adjuvants, virosomes, microbial derivatives, oil emulsions and surfactant based formulations.

**Incubation period:** The interval between exposure to an infectious agent and onset of clinical symptoms. The incubation period varies for different diseases from a few hours to several months or even longer for some diseases, e.g. leprosy.

1.5 **Types of immunity**

1. Natural immunity:

2. Herd immunity: This develops when a high proportion of the target population in the community has been immunized with live vaccines, usually 80% and more in order to prevent the spread of infectious diseases.

3. Passive immunity: Immunity that results from transfer of antibodies from one person/animal to another and this offers antibodies that can protect a person temporarily for example when maternal antibodies are passed to the fetus during pregnancy.

4. Artificial immunity (vaccination) or active immunity: when a person’s own immune system develops protection after exposure to a disease or from vaccination. It usually lasts for many years.
The human body may acquire immunity:

a. Naturally, as a consequence of stimulation of immunity by deliberate exposure to an antigen or by an infection or

b. Artificially through immunization

c. Passively from the maternally for newborns

The cells of the Immune system are classified as:

- Antigen Presenting Cells: Monocytes, macrophages, dendritic cells and B cells
- Polymorphonuclear (PMN) Granulocytes: Neutrophils, Eosinophils, Basophils
- Lymphocytes: T Cells, B Cells and Plasma Cells, Natural Killer (NK) Cells

There are broadly two lines of defence that protect a person from pathogens:

1. *Non-specific (or innate) immunity*, which is the first-line protection against a vast number of harmful pathogens. These may be physical such as the skin and mucus membranes, chemicals such as enzymes and acids in the body, complement system or cells such as phagocytes.

2. *Specific (or adaptive) immunity*, which is an antigen specific response developed after encounter with a pathogen or after vaccination. A key feature of adaptive immunity is that following the initial contact with antigen (*immunologic priming*), subsequent antigen exposure leads to more rapid and vigorous immune responses (*immunologic memory*). The adaptive immune system consists of dual limbs of cellular and humoral immunity.

   i. The cellular system
      
      - T-cells that mature in the thymus. They have receptors for antigens.
      - Cytotoxic T-cells destroy pathogen infected cells, cancer cells, and foreign cells.
      - Helper T-cells regulate both the cellular and humoral immune systems.

   ii. Humoral: the principal effectors of humoral immunity are B lymphocytes through production of antibodies after natural exposure to pathogens

An ideal antigen should induce both cellular and humoral immune responses. Some organisms require pre-existing antibodies in the body for appropriate body immune response such as poliomyelitis, tetanus and diphtheria. Vaccination is aimed at achieving production of such antibodies. To develop a vaccine we must first consider what happens in a natural infection to produce
protective immunity - these are called “the correlates of protection” An effective vaccine against intracellular pathogens should only induce effector mechanisms ultimately leading to the destruction of the parasites. The vaccine should not trigger components of the immune response favoring the survival of the pathogen.

1.6 Types of vaccines

Scientists take many approaches to designing vaccines against a microbe. These choices are typically based on fundamental information about the microbe;

- how it infects cells,
- how the immune system responds to it,
- practical considerations, such as regions of the world where the vaccine would be used in view of transportation.

Researchers may make vaccines as:

- Live, attenuated vaccines
- Inactivated vaccines
  - Whole
  - Fractional
    - Protein based
    - Polysaccharide based
- Conjugate vaccines
- DNA vaccines
- Recombinant vector vaccines

Live, attenuated vaccine is the closest thing to a natural infection; these vaccines are good “teachers” of the immune system. They consist of live pathogens that have been altered to a non-pathogenic form. They elicit strong cellular and antibody responses and often confer lifelong immunity with only one or two doses. However, not everyone can safely receive live, attenuated vaccines such as HIV patients and those on chemotherapy.

Sub-unit vaccines contain part of the microbe and include:

- Toxoids (inactivated toxins) such as Tetanus toxoid (TT),
• Acellular vaccines containing antigens purified from wild pathogens (acellular pertussis vaccine), Hepatitis B vaccine, HPV, Haemophilus influenza type b vaccine (Hib) and Pneumococcal vaccine

Polysaccharide (non-conjugate) vaccine: composed of purified bacterial capsule carbohydrate fragments (polysaccharides only). These vaccines elicit poor T cell memory immune response in children <2 years of age, compared to conjugated counterpart vaccines. Bacterium possesses an outer coating of sugar molecules called polysaccharides. Polysaccharide coatings disguise a bacterium’s antigens so that the immature immune systems of infants and younger children cannot recognize or respond to them. Researchers can make a conjugate vaccine for the polysaccharide to get around this problem

Conjugate Vaccines are a type of subunit vaccine where an antigen or toxoid from a microbe that an infant’s immune system can recognize is linked to the polysaccharides such as Haemophilus influenzae type B (Hib) vaccine. Conjugate vaccines contain polysaccharides bound to various proteins (tetanus toxoid, CRM, D protein of non-typeable Hib) to improve their immunogenicity (e.g. conjugated PRP-T polysaccharide of Hib or conjugated meningococcal or pneumococcal or pneumo-OM vaccines).

Unlike polysaccharides vaccines, conjugated vaccines can trigger strong immune response and immune memory for lasting protection in infants.

DNA vaccines are under development and they show great promise. Several types are being tested in humans using newer technology in immunization. DNA vaccines dispense with both the whole microbe/organism and its parts. The body’s own cells become vaccine-making factories, creating the antigens necessary to stimulate the immune system

DNA vaccine against a microbe would evoke a strong antibody response to the free-floating antigen secreted by cells, and the vaccine also would stimulate a strong cellular response against the microbial antigens displayed on cell surfaces. Naked DNA vaccines consist of DNA that is administered directly into the body DNA. The vaccine cannot cause the disease because it wouldn’t contain the microbe. Examples include influenza and herpes.

Recombinant Vector Vaccines are still experimental vaccines similar to DNA vaccines, but they use an attenuated virus or bacterium to introduce microbial DNA to cells of the body. “Vector” refers to the virus or bacterium used as the carrier. Researchers are working on both bacterial and viral-based recombinant vector vaccines for HIV, rabies, and measles

Monovalent vaccines contain single purified antigen(s) or single strain / type / serotype of inactivated or attenuated pathogen such as BCG, rotavirus and measles.
Multivalent (or polyvalent) vaccines contain multiple strains, types, serotypes or serogroups of the same pathogen such as DTP and MMR.

1.6.1 Vaccine constituents

Active material(s): Antigens or molecules that react with specific receptors on T and B cells and activate these cells to induce antigen-specific T and B immune responses.

Inactive materials

- Adjuvants (aluminium salts, mono-phosphoryl lipid A or MPL, etc) enhance immune responses of vaccine antigens
- Preservatives (phenoxyethanol, formaldehyde, thiomersal / thimerosal, or antibiotics) prevent bacterial growth especially in multi-dose vaccines
- Stabilizers (proteins or other organic compounds) extend the shelf-life of the vaccine
- Salts and acidic solutions (sodium hydroxide, sodium chloride, sodium borate and acetic acid) maintain pH
- Solvents such as calcium carbonate, xanthan gum and sterile water
- Diluents for reconstituting lyophilised or freeze-dried vaccines

1.6.2 Characteristics of an ideal vaccine

1. Immunogenic, provoking a good immune response; but not pathogenic.
2. Providing long-lasting immunity;
3. Safe, with no or very rare adverse event following immunization (AEFIs); Vaccination is only of benefit if it provides a significant degree of protection against a disease with minimum side effects
4. Stable in field conditions and can be stored reasonably long without or with minimum cold chain requirements (heat stable);
5. Combined with several antigens producing immunity against a number of diseases;
6. Effective after a single dose hence requires few immunisations to induce protection
7. Administered preferably by non-injectable routes (oral or through inhalation);
8. With affordable cost and accessible to all;
9. Suitable for administration early and late in life (Effective in the old & very young)

10. Give life-long immunity

11. Broadly protective against all variants of organism

12. Prevent disease transmission

13. Rapidly induce immunity

14. Transmit maternal protection to the baby

1.6.3 **Challenges in vaccine development**

a. Adaptation of microbial agents to host immunity

b. Development of escape strategies by microbes:
   
   i. emergence of new antigenic variants (e.g. Pneumo, Flu, MenB, malaria, HIV, TB…)

   ii. complex interaction with host immune system (e.g. immunomodulation)

1.6.4 **Future vaccine development**

A number of new vaccines with major potential for controlling infectious diseases are at advanced stages of development (Malaria, TB, Dengue, schistomiasis,…)

Move to universal immunization including use of HPV, Rotavirus, Pneumococcal and under-utilized vaccines (Haemophilus influenza type b, hepatitis B and yellow fever vaccines).

Improved vaccines for optimizing immunogenicity & safety

- New adjuvants used to optimize B cell responses (level, quality, duration, memory) and generate appropriate T cell responses (help, effector, memory)

- Immune system targeting formulations

- New live vaccine vectors (non-replicating)

1.7 **Vaccines Used in National Immunization Programmes**

Each vaccine is selected based on safety, effectiveness, reasonable price and the ability to combat childhood disease of significant public health importance.
### Characteristics of Selected EPI Vaccines

<table>
<thead>
<tr>
<th>Vaccines (number of doses in primary series)</th>
<th>Type of Vaccines</th>
<th>Form</th>
<th>Vaccine Efficacy</th>
<th>Duration of Immunity (after primary series)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG (1) Attenuated Mycobacterium bovis</td>
<td>Freeze-dried</td>
<td>75-86%</td>
<td>Unknown Immunity wanes in time</td>
<td>Prevents TB meningitis and miliary TB Reconstituted before use</td>
<td></td>
</tr>
<tr>
<td>Diphtheria (3) Toxoid</td>
<td>Liquid</td>
<td>&gt;87%</td>
<td>Around 5 years</td>
<td>Prevents all forms of diphtheria</td>
<td></td>
</tr>
<tr>
<td>Tetanus toxoid (3) Toxoid</td>
<td>Liquid</td>
<td>&gt;95%</td>
<td>5 years</td>
<td>Prevents neonatal and tetanus in adults</td>
<td></td>
</tr>
<tr>
<td>Pertussis (3) Killed whole-cell bacterium</td>
<td>Liquid</td>
<td>80%</td>
<td>Unknown. Immunity vanes in time</td>
<td>Efficacy is higher against severe disease</td>
<td></td>
</tr>
<tr>
<td>Polio (3) Attenuated live virus of 3 types: 1,2,3</td>
<td>Liquid</td>
<td>72-98%</td>
<td>Lifelong</td>
<td>There is no “cross” immunity between vaccine types</td>
<td></td>
</tr>
<tr>
<td>Measles (2) Attenuated live virus</td>
<td>Freeze-dried</td>
<td>&gt;85% at 9 months</td>
<td>Lifelong</td>
<td>Duration is longer when boosted by wild virus. Reconstituted before use</td>
<td></td>
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<tr>
<td>Hepatitis B (3) Surface antigen of the HB virus</td>
<td>Liquid</td>
<td>75-95%</td>
<td>&gt;15 years</td>
<td>Efficacy is against chronic infection</td>
<td></td>
</tr>
<tr>
<td>Hib (3) Polysaccharide linked to protein</td>
<td>Liquid</td>
<td>&gt;95%</td>
<td>At least 3 years</td>
<td>Prevents Hib meningitis and pneumonia</td>
<td></td>
</tr>
<tr>
<td>Yellow fever (1) Attenuated live virus</td>
<td>Freeze-dried</td>
<td>90-98%</td>
<td>For several decades, possibly for life</td>
<td>Reconstituted before use</td>
<td></td>
</tr>
<tr>
<td>Men Afrivac (1) Attenuated</td>
<td>Freeze-dried</td>
<td>Unknown</td>
<td>Protect birth cohorts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus (2 &amp;3) Live attenuated</td>
<td>Liquid</td>
<td>Unknown</td>
<td>Prevents diarrhoeal diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pnemococcal vaccine (3) Conjugated</td>
<td>Liquid</td>
<td>Unknown</td>
<td>Prevents pneumonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV (3) Subunit vaccine</td>
<td>Liquid</td>
<td>Unknown</td>
<td>Adoscent-Cervical cancer Genital warts (quadrivalent)</td>
<td></td>
<td></td>
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</table>

*Adapted from WHO/V&B/02.28 "Core Information for the Development of Immunization"*
REFERENCES:


Warrington et al. An introduction to immunology and immunopathology. Allergy, Asthma & Clinical Immunology. 2011,7:S1
Learning Objectives

At the end of this chapter, the student should be:

- Familiar with the origins and aims of vaccination as a tool for disease control, prevention and elimination.
- Able to discuss the origins and concept of the Expanded Programmes on Immunization (EPI).
- Able to state the aims and objectives of EPI Programmes including the Universal Child Immunization (UCI) target.
- Conversant with and able to describe a short historical background and implementation of the Kenya EPI Programme.

‘Whatever can be done to ensure the health and well-being of children, helps to lay the foundation of health in adult life, and of the health of those children’s children’.


2.1 INTRODUCTION

Variolation (the deliberate inoculation of a person with small pox material in order to prevent the disease) was practiced for centuries in Africa, China and India. In 1721, Lady Mary Wortley Montangu, the wife of the English ambassador to Turkey introduced it into Europe (1). Approximately at the same time, the Rev. Cotton Mather in America learnt it from his African slaves and introduced it in Boston (1). Seventy five years later, a student, Edward Jenner, had noted that milk-maids who had suffered and recovered from cow-pox, were protected from small pox. On 14 May 1796 he demonstrated and practiced his first inoculation on an 8 year old boy, with cow-pox materials and showed that the boy became immune to small pox. The word vaccination (from latin word for cow: vacca) then replaced variolation when Jenner announced his findings.
By 1801, Dr. Jenner’s document on vaccination had been translated into 5 languages, more than 100,000 persons had been vaccinated in England and Jenner predicted the eventual annihilation of small pox.

Louis Pasteur later developed, by mere chance, the means of reducing the virulence (i.e the capability of a germ to cause disease) of microbes without changing their ability to induce immune responses. This was the process of **attenuation** and has been used to develop some of the most successful vaccines. By 1988, it was estimated that about fifty human vaccines were approved or under trial. In 1977, the World Health Assembly (WHA) set the year 1990 as the target date for **Universal Child Immunization** (UCI), aiming to immunize all the children of the World against the six childhood diseases, namely, tuberculosis, poliomyelitis, measles, whooping cough, tetanus and diphtheria. It was the same year that the World’s last-ever endemic case of small pox was diagnosed in the Somali port of Merka. The victim, was a young Somali hospital cook, Ali Maow Maalin, who recovered fully from the disease.

Small pox had been eradicated, continent by continent, and now in Africa “**small pox target zero**” had been reached, 181 years since Jenner’s discovery in 1796. Indeed in 1980, the 33rd WHA officially declared the complete eradication of small pox from the face of our planet. This was after 13 years (1967-1979) of a sustained effort in the systematic fight against this disease: **surveillance** and containment by means of **immunization** were the epidemiological methods used to achieve this success.

## 2.2 Origin of Expanded Programmes on Immunization (EPI)

Immunization is a proven cost-effective weapon in the **control**, **prevention** and even **elimination** of diseases. Child Survival and Development (CSD) especially in developing countries, had been negatively affected by the six vaccine preventable diseases of Childhood. Since the 1950’s, industrialized countries have recorded great successes in the improvement of child health by, among other ways, reducing childhood vaccine-preventable diseases, which used to cause significant morbidity, mortality and disability during the pre-immunization era. Immunization does, in part, break the cycle: infection- diarrhea-malnutrition-infection, thus extending its impact beyond the prevention and control of individual diseases.

During the 1950’s and 1960’s most developing countries already had elements of immunization services. These were, however, available on a small scale or offered sporadically. The vaccines used were not always potent and most children did not complete their immunization schedules. Thus maximum benefit was not derived from these services. This was reflected in the continuing incidence, mortality and disabilities from these vaccine-preventable diseases. By 1977, it was estimated that 5 million children died each year in developing countries as a result of these diseases.
while many more (perhaps an equal number) became disabled through: brain damage, paralysis, stunted growth, chronic lung diseases, deafness and blindness.

It was in this light that the World Health Organization (WHO) reviewed the existing immunization services and came up with the following six weaknesses:

- low immunization coverage, ranging from 5-20% in most developing countries.
- frequent use of non-potent vaccines.
- inadequate managerial skills in the health workers offering immunization services.
- shortage of human and material resources invested in immunization activities.
- limited community participation in the programmes.
- lack of regular monitoring, periodic evaluations and little attempt to make appropriate adaptations.

These shortcomings indirectly mapped out the line of action which countries, in collaboration with WHO, UNICEF and other agencies, could take in order to strengthen, improve and expand their existing immunization services. There was the felt need to strengthen, improve and expand those existing immunization services. This then was, and still is, the basis for the WHO Global EPI Programme.

2.3 AIM AND OBJECTIVES OF EPI PROGRAMMES

The main aim was to make immunization complementary to other Primary Health Care (PHC) services, in a bid to reduce morbidity, mortality and disability, initially from the 6-vaccine preventable diseases of childhood: tuberculosis, poliomyelitis, measles, whooping cough, tetanus and diphtheria. Countries had the option of taking on other diseases of public health concern and prioritize them such as yellow fever in West-Africa and Hepatitis B most countries in sub-Saharan Africa and South East Asia. All these diseases addressed by EPI Programmes have been termed “EPI - target diseases”.

The objectives of EPI Programmes were:

- to provide immunization against the EPI-target diseases to all children of the world (and Tetanus toxoid for pregnant women or women of child-bearing age) by the end of the year 1990.
- to promote countries’ self-reliance in immunization programmes, including vaccine production and quality control.
- to implement the programme activities, not as immunization campaigns, but in a deliberate intensified and sustainable manner within the framework of the existing Maternal and Child Health Services.
2.4 EPI PROGRAMME ACCELERATION

1977 was the onset of the implementation of the EPI programmes. In 1982, the EPI programmes’ progress towards the goal of Universal Child Immunization by 1990 was noted to be slow. It was estimated that of the 15 million African children born annually, one million died from the EPI-target diseases and additionally 400,000 become disabled. Using the first DPT vaccine as an indicator of access to immunization and 3rd DPT as an indicator of completion of immunization, only 31% of the children had access to immunization and 20% completed their immunization (2). To improve this bleak picture the EPI Programme Acceleration was recommended using a 5 point approach:

- the promotion of EPI within the context of PHC, as without the development of all aspects of health, children who had been immunized would still continue to die from other diseases like malnutrition, diarrhoeal diseases and malaria.
- the investment of adequate human resources in EPI. This personnel should be sufficient in numbers, and conversant with appropriate managerial skills, as poor programme management appeared to be a severe constraint in health workers charged with looking after these programmes.
- The investment of adequate financial resources in EPI, two thirds of which, if possible, should be generated within the implementing countries.
- efforts to be made to ensure that EPI programmes were continuously monitored, periodically evaluated and appropriately adapted.
- the pursuit of research efforts, especially operational research, the results of which would assist in better programme management, should be an in-built component of any EPI programme.

During the mid-decade evaluation in 1985, significant progress in EPI programmes was noted. However immunization coverage levels for the six target diseases still remained below the 50% mark. To further promote the progress of the EPI Programme Acceleration, WHO and UNICEF issued the Joint Statement for ‘Planning Principles for Accelerated Immunization Activities’, in which it precisely recommended:

- an intensive mobilization of political will within countries
- the application of new techniques of communication and social mobilization
- sustained application of the management support required to transform that mobilization into effective programmes (3).
The Joint Statement further crystallized four areas suggested to enhance the increase in immunization coverage by accelerating and strengthening the existing services. These included:

- the provision of immunization and information about immunization at every health contact
- the reduction of drop-out rates between the first and last immunizations
- priority to be given to the control of measles, poliomyelitis and neonatal tetanus
- improvement of immunization services to the disadvantaged urban populations.

To promote the EPI Programme Acceleration in the African region, 1986 was declared African Immunization year. A consensus was also reached that by the end of 1990 at least 75% of all eligible African children and pregnant women would be fully immunized.

All these efforts, globally and in the African Region, started to gradually bear fruit as in August 1987, the information available to the WHO, showed that immunization coverage with three doses of DPT or polio vaccines had for the first time surpassed the 50% level in both developing and developed countries (4). As a result, in developing countries 1 million deaths from measles, pertussis, and neonatal tetanus were being prevented and over 175,000 cases of poliomyelitis prevented. This level of immunization, however, still permitted over 3 million deaths from EPI-target diseases and 250,000 cases of poliomyelitis to occur.

In 1989, just a year before the due date for UCI, the EPI Global Advisory Group in reviewing the overall Global EPI Status, found 60% of the children had received BCG and the third doses of DPT and Polio by their first birthday. Measles coverage stood at 50%. Thus an estimated 1.9 million deaths from measles, whooping cough and neonatal tetanus were being prevented in developing countries in addition to 240,000 cases of poliomyelitis. However, there was no room for complacency, since at such immunization coverage levels, 3 million children would still die annually, 200,000 would be paralysed and same 150,000 blinded from these diseases (5).

2.5 KENYA EXPANDED PROGRAMME ON IMMUNIZATION (KEPI)

2.5.1 History of KEPI

In June 1980 Kenya adopted and became committed to EPI and KEPI was launched with the assistance of the Danish International Development Agency DANIDA. It’s aim was encompassed in: ‘The Childhood Immunization Statement Policy’ for Kenya, to immunize, free of charge, all Kenyan children aged 0-5 years (this was revised in 1985 to focus on children of 0-11 months of age) and all pregnant women, with the available recommended EPI vaccines, so as to reduce the morbidity, mortality and disability from the 6 common childhood infectious diseases (tuberculosis, poliomyelitis, tetanus, whooping cough, measles and diphtheria). The immunization was to
be offered in government and in non-government health facilities. The uptake of immunization services was to be based on individual motivation rather than through coercion. Motivation rather than coercion is the preferred approach.

Prior to the launch of KEPI (1950 – 1980) childhood immunizations were given in ad-hoc mechanisms through primary schools.

2.5.2 Objectives

The objectives contained in the 5-year “KEPI’s Plan of Operation” proposal, prepared in 1980, were as follows:

Immunization Coverage

Immunization Coverage of 75% for single-dose antigens (BCG and measles) and 60% for multiple dose ones (D.P.T., Polio and Tetanus Toxoid) was proposed during the first 3 years of KEPI’s operation in a given district. Thereafter, the aim was to attain a minimum of 80% FOR ALL THE ANTIGENS. A joint Ministry of Health /DANIDA mission reviewed this objective and found it realistic. (6

Cold Chain System

The Cold Chain System was to be re-enforced in terms of better vaccine storage and handling so as to ensure that the increased immunization coverage was with potent vaccines. One Central Vaccine Store (CVS) in Nairobi and two Regional Vaccine Stores (RVS) in Mombassa and Kisumu, respectively, were to be set up.

Cold Chain Equipment such as freezers, refrigerators, and cold boxes were to be supplied to all hospitals, all health centres and 50% of the total of the then available 1234 dispensaries.

Training

Training was to be of three types: at Senior, Supervisory and Operational levels. A target of 400 supervisors and 3,000 vaccinators was set. This meant that approximately 10 supervisors per district and a minimum of 2 vaccinators per immunization centre would be trained. This objective aimed at improving the managerial skills of Health Workers.

Integration

Integration of KEPI with Maternal and Child Health services was done from the outset as the former was not to run as a vertical programme especially at the peripheral level.
Public Motivation

Public Motivation was to be effected in any district where cold chain equipment was being installed and Health Worker training going on.

Monitoring and Evaluation

Programme monitoring and evaluation was to be achieved by strengthening the Routine Immunization Reporting System, the use of “Check Lists” during supervisory visits to immunization centres and a biennial evaluation by an external team.

Research

Operational Research for better programme management was the final objective of KEPI.

2.6 IMPLEMENTATION

The implementation of KEPI was planned in 3 stages namely:

- The preparatory stage
- the demonstration and pre-testing stage
- the operational stage

2.6.1 Preparatory Stage: Mid 1980 - mid 1981

During this stage a KEPI Management Unit was set up with a core staff of 8-10 personnel headed by the KEPI Manager. A plan of operation previously written was reviewed and up-dated.

The Plan of Action covered the following areas:

- equipment
- transport, procurement and distribution
- training schedules
  - identification of trainers
  - number of staff cadres to be trained
- training materials
  - data collection
  - public mobilization activities
2.6.2 Demonstration or pre-testing stage: Mid 1981-mid 1982
During a 9-12 month period EPI field operations were tried in Kirinyaga, one of Kenya’s then 41 districts. An evaluation carried out at this stage was encouraging.

2.6.3 Operational Stage: Mid 1982 – 1986
The KEPI programme was introduced step by step in Coast, Nyanza and Western Provinces of Kenya. The dry North and North Eastern districts which are sparsely populated were initially not included.

For KEPI to be “operational” in a district implied that:

• the health staff had been re-trained.
• the cold-chain needs had been identified and the equipment procured and installed.
• transport had been provided.
• public mobilization had been done.

Except for the public mobilization which lagged behind, the operational stage was completed in June 1986, six months ahead of schedule.

Some of the successes recorded during this operational stage are noted below:

• by 1984, the proportion of children aged one year who were fully immunized, had risen to 43%.
• no vaccine shortages were experienced by the program.
• a pool of Trainers in both Supervisory Skills, Operational level and Cold Chain Maintenance skills was created so that no external technical assistance was needed.
• a Kenyan-designed and written Operational Level Training Manual was produced.
• a total of 950 immunization centres were set up and provided with cold chain equipment.
• KEPI was evaluated twice (1984 and 1986) by an external mission and met with their approval.

2.6.4 Consolidation stage: 1987 – 1990 and beyond
The main thrust of this final stage was to:

• offer better quality immunization services putting into routine practice skills learned during KEPI training courses
• increase and sustain the immunization coverage by 11 months with a target coverage by 1990 of 90% for BCG, 80% for DPT3, OPV3 and measles and 75% for tetanus toxoid.

• reduce the EPI target diseases as follows:
  • reduction of neonatal tetanus from 10 per 1,000 live births in 1985 to 5 per 1,000 live births
  • to interrupt the transmission of poliomyelitis by 1993 and possibly eliminate it altogether by 1995
  • to shift age specific incidence of measles from age group 1-2 years to age group 4-6 years by 1993
  • to incorporate one new antigen namely Hepatitis B (initially as a pilot project in one of the districts), with effect from mid 1990.

During this stage, and based on cost effectiveness and sustainability considerations, KEPI was guided by the following principles to help it achieve its target:

• the use of “fixed”/static health facilities for immunization
• the integration of the KEPI programme within Maternal and Child Health services
• the provision of cold chain equipment to all hospitals, all health centres and 50% of dispensaries
• training of personnel in all areas of operation
• biennial evaluations of district programmes by external teams
• regular feedback to staff.

NB Sentinel Station Reporting for measles, poliomyelitis, and neonatal tetanus was planned to start from 1990.

2.7 PROGRAMME MONITORING

Immunization returns were to KEPI through the Routine Health Information System (H.I.S) of the Ministry of Health. By 1984, pre-KEPI Surveys carried out in 31 of the then 41 districts in Kenya, showed an average immunization coverage of 43% by 23 completed months. However, these surveys were costly and not all districts could be covered. In March, 1987, the first well organized National Immunization Coverage survey was done and it revealed that 51 % of Kenyan children had been fully immunized (9,10). It was encouraging to note that 75% of the children had completed DPT and Polio immunization. However, only 60% had received measles immunization. The National Demographic Survey of 1989, showed that 71% of the children with cards were fully immunized (11).
KEPI was reviewed by External Evaluation Teams every two years from 1984. Their reports initially showed a positive trend in KEPI’s performance.

A quarterly KEPI Newsletter was used to give feedback to staff at the periphery. In addition, every 6 months a 2-day seminar for District KEPI Coordinators was held. In 1989, two more seminars: one for District Health Education Officers and the other for Provincial Medical Officers, were added to these regular events.

2.8 FROM KEPI TO UVI
Recognizing that vaccination has been one of the most successful and cost-effective public health intervention in history, eradicating smallpox, significantly lowering the prevalence of poliomyelitis and dramatically reducing the morbidity and mortality of several other illnesses, the Ministry of Health in 2007, consolidated all vaccination services under a single unit called the Division of Vaccines and Immunization (DVI) and developed a policy to integrate all current vaccination practices. The aim was to standardize practices and opportunities for vaccination services. This unit is now called Unit of Vaccines & Immunization (UVI) replaced the DVI after restructuring of the Ministry of Health in line with devolution as per The Constitution of Kenya (2010).

2.8.1 Unit of Vaccines and Immunization
The Unit of Vaccines & Immunization (UVI) replaced the Division of Vaccines & Immunization after restructuring of the Ministry of Health in line with devolution as per The Constitution of Kenya (2010). The Division of Vaccines & Immunization (DVI) became effective from 1st July 2007, and represents the Ministry of Health’s new direction in the coordination of immunization services for the general public. UVIS has an extended scope to consolidate all vaccination services previously coordinated by other divisions within the Ministry of Health.

Vision: Efficient and high quality immunization services that are accessible, equitable, and affordable to every Kenyan.

Mission: To promote and guide in the provision of high quality immunization services to all Kenyans

2.8.2 Mandate
• To coordinate vaccination services for all vaccine preventable diseases through the provision of guidelines and selected priority vaccines and related biological (sera, immunoglobulins)
• Advice on immunization schedules for all age cohorts in line with the Kenya Essential Package for Health (Ref. NHSSP-II 2005-2010).
2.8.3 The portfolio of UVI includes:
1. EPI infant vaccines
2. Tetanus for pregnant women
3. Tetanus toxoid for trauma
4. Vaccinations for special groups
   • TT for special occupational risk groups
   • Hepatitis B vaccine for health workers and other persons at risk e.g prisoners
   • Typhoid vaccine for food handlers and special categories of health workers
   • Vaccination for foreign travelers (e.g yellow fever, meningitis).
5. Routine emergency vaccinations
   • For animal (dog) bites
   • For snake bites
6. Special emergency (outbreak response). Vaccinations including the following
   • Poliomyelitis
   • Measles
   • Meningitis
   • Emerging infections – influenzas
7. Specialized products
   • Immune sera – e.g. rabies immunoglobulins
   • Anti-D sera for rhesus O-negative pregnant women

2.8.4 Core functions of the unit of vaccines & immunization:
1. Policy regulation and oversight
2. Commodity security & quality assurance
3. Monitoring and evaluation
4. Advocacy and Resource Mobilization
5. Capacity strengthening
1. Policy regulation and oversight
   i. Coordinating periodic reviews of the National Immunization Policy
   ii. Developing and updating training guidelines and materials for immunization service delivery
   iii. Facilitating the training of national and regional trainers

2. Commodity security & quality assurance
   i. To ensure continuous availability of adequate stocks of all Ministry of Public Health & Sanitation procured vaccines, related immunologicals and support logistics at all levels of service delivery.
   ii. To ensure that all vaccines, anti-sera and vaccination devices used for human health within the country meet defined minimum quality standards

3. Monitoring and evaluation
   i. Develop multi-year and annual operational plans
   ii. To set multi-year and annual performance targets
   iii. To monitor national immunization coverage trends and provide periodic reports on the same.
   iv. To monitor respective disease burden trends and correlate the same against immunization coverages

4. Advocacy and Resource Mobilization
   i. Annually review country wide vaccination social mobilization/advocacy needs.
   ii. Develop and periodically revise social mobilization guidelines & strategies in line with vaccination performance trends in the country
   iii. Determine multiyear and annual funding needs for universal immunization activities and develop comprehensive resource mobilization plans.
   iv. Develop and periodically review resource mobilization guidelines & strategies in line with immunization funding needs.
5. Capacity strengthening

i. Develop and periodically review guidelines and training materials/teaching aids on vaccine preventable diseases

ii. Spearhead the revision of curricula of medical institutions in relation to
   • current information on vaccine preventable diseases
   • updates required by different cadres of health workers

REFERENCE


Learning Objectives

At the end of this chapter the student should be:

• Familiar with the National Immunization schedule currently in practise
• Capable of calculating the yearly, quarterly and monthly immunization coverage targets
• Familiar with the preparatory and implementation tasks at MCH immunization site
• Capable of making calculations for adequate vaccine needs of a vaccination post
• Capable of monitoring immunization performance

3.1 INTRODUCTION

The main objective of immunization activities is to reduce morbidity and mortality caused by immunizable diseases. It is the responsibility of the Health Facility In-Charge to schedule immunization sessions so that they meet the community’s needs and expectations in terms of convenient hours of operation, socio-cultural acceptable standards of quality service and individual comfort.

This chapter will address only those tasks that are related to conducting immunization sessions, even though health workers have many other responsibilities to perform in addition to vaccination.

Health workers in the MCH/FP clinics see sick children, and give them appropriate treatment or advice. They make decisions as to whether the children should be vaccinated or not depending on known contraindications to vaccination. EPI in this sense is integrated into the management of sick and well-children and generally all maternal and child survival activities.

3.2 POLICY OF IMMUNIZATION

Each country has an immunization policy which usually follows WHO’s general guidelines. Immunization policies enable a country to standardize immunization procedures/practices. The policy in Kenya is to:
• All vaccines for human use in Kenya must meet quality requirements as determined by the Pharmacy and Poisons Board and must be duly approved for use within the country by the Pharmacy and Poisons Board.

• All vaccines for human use must be qualified as safe under normal circumstances of use. All known and unknown adverse effects of specific brands should be well articulated.

• Where the safety profile of a particular vaccine or immunological cannot be guaranteed but the risk of the disease is serious, then the vaccine/immunological should be administered after obtaining consent from the client.

• All vaccines intended for simultaneous use with other antigens must have proven immunological efficacy in the presence of the other vaccine and must not significantly interfere with the immune response to the other vaccine.

• Administration of vaccines outside the National Immunization Schedules should be guided by the known disease burden/risk of the area/region or specific individual/community risk of exposure to the targeted disease or a specific medical indication of the client.

• All vaccines for human use must be stored in specialized medical refrigerators as prescribed by the World Health Organization. The specifications for these refrigerators can be obtained from the Division of Vaccines and Immunization or from the WHO official website.

• All injectable vaccines must be administered only by duly registered clinicians.

• All injectable vaccines are to be administered using non-reuseable injection devices.

• Reconstitution of all lyophilized (freeze dried) vaccines must only be done with their matching diluents as provided by the specific manufacturer.

• All reconstituted multi-dose vial vaccines must be discarded after the manufacturer’s prescribed maximum duration of use (usually between 4-6 hours).

• All unused doses of a liquid multi-dose vial vaccine without a preservative must be discarded 6 hours after opening of the vial - e.g. multi-dose vials of liquid Pneumococcal Conjugate Vaccines.

• Routine screening for immune status of individuals (including infants) prior to vaccination is not advocated. However, where special circumstances dictate this should be overseen by a qualified clinician.

• Routine screening for HIV status prior to vaccination is also not advocated except in special circumstances as determined by a consultant clinician.

• A fully immunized child is one who has received all the prescribed antigens and Vitamin A doses under the national immunization schedule before the first birthday.

• A fully immunized person – (other than an infant) refers to an individual who has
• received all the prescribed doses for a particular antigen or,
• is beyond the ‘window period of efficacy’ of an antigen - where only one dose is required (e.g. yellow fever vaccine)

• Some Vaccine Preventable Diseases (VPDs) are notifiable and information on all suspected cases of these diseases must be fully documented and reports forwarded immediately to the Division of Disease Surveillance and Response (DDSR) of the Ministry of Public Health & Sanitation.

• ALL notifiable VPDs must be investigated as per the prescribed guidelines from the Division of Disease Surveillance and Response.

• All efforts must be made by health workers to prevent drop-outs from all immunization schedules through careful counseling of clients regarding
  • the importance of vaccines,
  • possible side effects and how to manage them,
  • the consequences of not completing the schedule.

• All efforts must be made by health workers to identify and respond to missed opportunities for vaccinations by
  • Screening all children aged below five years presenting at health facilities and outreach sites for their vaccination status
  • Screening all women of child bearing age at health facilities and outreach sites for their vaccination status (esp. for tetanus toxoid)
  • Screening all special target groups for vaccination status whenever possible (e.g. food handlers etc.)

• All health workers must advocate for comprehensive utilization of immunization services to their community leaders and members.

• All immunizing facilities must ensure that vaccinators are updated annually on the principles and practice of immunization service delivery through attendance of Continuous Medical Education sessions (CMEs) or updates to be conducted by District Health Management Teams, either through seminars or during supervisory visits.

There are very few absolute contraindications to immunization. In general, health workers should immunize all eligible children whether they are sick or not.

• In case a child requires admission in the ward, the decision whether or not to immunize is left to the admitting doctors. They should follow the principle “no child above 9 months of age should enter a ward without being immunized against measles and no child should
be discharged from the hospital without having its immunization status checked and vaccines due administered accordingly”.

### 3.3 National Immunization Schedule

#### 3.3.1 National Infant Immunization Schedule

The current schedule in use in Kenya (Fig 1) was developed in 1986 and revised in 1989, 2001 and 2011. This was necessitated by the need to introduce polio birth dose, (1989), the introduction of the pentavalent vaccine (DPT-HepB-Hib) and the introduction of the 10 valent pneumococcal vaccine in 1989, 2001, and 2011 respectively.

**NB:** A second dose of measles is now included in the schedule at 18 months of age or at first contact after 18 months for all children. The first dose between 9 and 12 months of age and the second dose between 18 and 24 months of age. If a child has missed the first or the second, both doses should be administered up to five years of age maintaining the interval of at least 4 weeks between the doses.

**Table 2: Summary of the Immunization Schedule, vaccine dosage and route of administration**

<table>
<thead>
<tr>
<th>Contact</th>
<th>Vaccine dose</th>
<th>Age of child</th>
<th>Dosage</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BCG</td>
<td>At birth or at first contact</td>
<td>• 0.05 ml</td>
<td>• Intradermal</td>
</tr>
<tr>
<td></td>
<td>OPV birth dose (trivalent)</td>
<td>At birth or at first contact (within the first two weeks of life)</td>
<td>• 2 drops</td>
<td>• Oral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>OPV I</td>
<td>At six weeks of life or at first contact</td>
<td>• 2 drops</td>
<td>• Oral</td>
</tr>
<tr>
<td></td>
<td>DPT-HepB-Hib 1</td>
<td></td>
<td>• 0.5 ml</td>
<td>• Intramuscular into the upper outer aspect of the left thigh</td>
</tr>
<tr>
<td></td>
<td>PCV10 - 1</td>
<td></td>
<td>• 0.5 ml</td>
<td>• Intramuscular into the upper outer aspect of the right thigh</td>
</tr>
<tr>
<td></td>
<td>Rota - 1</td>
<td></td>
<td>• 1.5 ml</td>
<td>• Oral</td>
</tr>
<tr>
<td>3</td>
<td>OPV II</td>
<td>At 10 weeks or 4 weeks after OPV I and DPT-HepB-Hib 1</td>
<td>• 2 drops</td>
<td>• Oral</td>
</tr>
<tr>
<td></td>
<td>DPT-HepB-Hib 2</td>
<td></td>
<td>• 0.5 ml</td>
<td>• Intramuscular into the upper outer aspect of the left thigh</td>
</tr>
<tr>
<td></td>
<td>PCV10 - 2</td>
<td></td>
<td>• 0.5 ml</td>
<td>• Intramuscular into the upper outer aspect of the right thigh</td>
</tr>
<tr>
<td></td>
<td>Rota - 2</td>
<td></td>
<td>• 1.5 ml</td>
<td>• Oral</td>
</tr>
<tr>
<td>Vaccine dose</td>
<td>Age of child</td>
<td>Dosage</td>
<td>Route</td>
<td></td>
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<tr>
<td>--------------</td>
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<td>--------</td>
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<td></td>
</tr>
<tr>
<td>4</td>
<td>OPV III DPT-HepB+Hib 3 PCV10 - 3</td>
<td>At 14 weeks or 4 weeks after OPV II and DPT-HepB-Hib 2</td>
<td>• 2 drops • 0.5 ml • 0.5ml</td>
<td>• Oral • Intramuscular into the upper outer aspect of the left thigh • Intramuscular into the upper outer aspect of the right thigh</td>
</tr>
<tr>
<td>5</td>
<td>Vitamin A 100,000IU</td>
<td>At 6 months of age</td>
<td>One capsule</td>
<td>Orally</td>
</tr>
<tr>
<td>6</td>
<td>Measles 1st dose</td>
<td>At 9 months or first contact after 9 months</td>
<td>0.5 ml</td>
<td>Subcutaneous into the right upper arm (deltoid muscle)</td>
</tr>
<tr>
<td>7</td>
<td>Yellow fever</td>
<td>At 9 months or first contact after 9 months – in four special districts</td>
<td>0.5 ml</td>
<td>Subcutaneous into the left upper arm (deltoid muscle)</td>
</tr>
<tr>
<td>8</td>
<td>Vitamin A 200,000IU</td>
<td>At 12 months of age</td>
<td>One capsule</td>
<td>Orally</td>
</tr>
<tr>
<td>9</td>
<td>Measles 2nd dose</td>
<td>At 18 months or first contact after 18 months</td>
<td>0.5 ml</td>
<td>Subcutaneous into the right upper arm (deltoid muscle)</td>
</tr>
<tr>
<td>10</td>
<td>Vitamin A 200,000IU</td>
<td>At 18 months of age</td>
<td>One capsule</td>
<td>Orally</td>
</tr>
</tbody>
</table>

**NB:** Yellow fever vaccination is still currently only given routinely to children in Baringo and Marakwet districts.

Vitamin A, though not a vaccine is given during growth monitoring and/or vaccination sessions every 6 months till 5 years.

The following are important points to remember while using the immunization schedule:

- Most vaccine-preventable diseases of childhood occur very early in life. If this schedule is followed according to specification, children will complete their primary vaccinations before the age of one year, and will therefore be unlikely to suffer from these diseases. **Every effort should therefore be made to complete the primary vaccination series on schedule.**

- There are few contraindications to immunization. Health workers should immunize all eligible children whether they are sick or not.

- In case a child requires admission to hospital the decision whether to immunize or not is left to the receiving doctors. They should follow the principle that no child should be discharged from hospital without having their immunization status checked.
• Antibodies present in breast milk do not interfere with the take of oral polio vaccines; therefore mothers should be encouraged to continue breast feeding.

• If polio birth dose, for some reason was not administered within the first two weeks of life, it should not be administered. One should then wait until the child is six weeks old and then give OPV 1 together with DPT-HepB+Hib1 and PCV as per the schedule.

• Regardless of the interval between the two doses of DPT-HepB-Hib, PCV and polio vaccines, the doses already given should not be repeated.

• All vaccines can be given at the same session if needed, but they must be given in separate syringes and sites. This means that every time a health worker gets into contact with a child, the immunization record of the child should be checked and missing immunizations for which the child is eligible administered. For instance, if a child is seen for the first time when ten months old, one should give BCG, DPT-HepB+Hib 1, PCV, OPV 1 and measles and ask the mother to come back four weeks later for DPT-HepB+Hib 2, PCV 2 and OPV 2.

• Booster doses after primary immunizations are not included in the routine schedule. However, these immunizations are provided in the private health sector.

• Currently, Kenya provides a second opportunity for measles vaccination through supplemental immunization activities (SIAs). However, in 2013 Kenya will introduce a second dose of measles vaccination into the routine immunization schedule in accordance with WHO guidelines.

3.3.2 Tetanus vaccination for pregnant women

The current EPI recommendation regarding tetanus vaccination for pregnant women is a “5-T.T. Schedule” administered as follows:

• a pregnant woman in her 1st pregnancy should receive two 0.5ml tetanus toxoid (TT) injections spaced at least four weeks apart between the fourth and eighth months of gestation.

• She should receive a single additional dose of T. T. as early as possible in her second trimester in subsequent pregnancies, up to a maximum of three additional doses. A total of 5 doses of Tetanus Toxoid vaccine given across four pregnancies will protect herself and all subsequent newborns from tetanus for 20 years.
**Tetanus Toxoid Schedule for Pregnant Women**

<table>
<thead>
<tr>
<th>GRAVIDA</th>
<th>Tetanus toxoid vaccination schedule</th>
<th>Expected maternal outcome</th>
<th>Expected outcome for neonate</th>
</tr>
</thead>
</table>
| First pregnancy | **1<sup>st</sup> TT dose** *(given from the fourth to sixth month i.e. 2<sup>nd</sup> trimester)*  
|               | **2<sup>nd</sup> TT dose** given one month after the 1<sup>st</sup> dose *(between the fifth & eighth month)* | Works as an immunological primer **but does not confer protection against maternal tetanus at delivery.**  
|               |                                                                                                   | Confers protection from maternal tetanus at delivery & for about 1 – 3 years from tetanus in general **however approx. 10% may respond poorly to 2<sup>nd</sup> dose** | **No protection from tetanus at birth!**  
|               |                                                                                                   |                                                                                         | Confers protection at birth (PAB) for ≈90% of neonates due to adequate titres of maternal antibodies |
| Second pregnancy | **3<sup>rd</sup> TT dose** *(given anytime between the forth & eighth months)*                      | Immunity boosted for 5 years                                                            | PAB ≈100% from neonatal tetanus                                  |
| Third Pregnancy | **4<sup>th</sup> TT dose** *(given anytime between the fourth & eighth month)*                    | Immunity boosted for 10 years                                                           | PAB for the neonate                                              |
| Fourth pregnancy | **5<sup>th</sup> TT & last dose** *(given anytime between the fourth & eighth month)*            | Immunity boosted for 20 years                                                           | PAB for the neonate                                              |
| Subsequent pregnancies | **No more TT doses required**                                                                   | Immunity adequate for rest of parous life                                                | Adequate PAB for the neonate                                      |

**NB:** **AFTER A FULL COURSE OF FIVE DOSES OF TETANUS TOXOID SPREAD OVER FOUR PREGNANCIES, A WOMAN WILL BE ADEQUATELY PROTECTED DURING ALL HER SUBSEQUENT PREGNANCIES AND THEREFORE DOES NOT NEED TO RECEIVE ANY FURTHER DOSES.** However should a woman conceive again 20 years after her 5<sup>th</sup> dose of T.T. she will require an additional dose of the vaccine.

It is also important to note that a woman who has received any number of doses of tetanus toxoid during pregnancy is also protected against the risk of tetanus arising from trauma, for the specified duration equivalent to the number of doses that she has received. That is, if a woman has received three doses of tetanus toxoid over two pregnancies, she has in effect acquired protection against the disease for a period of 5 years and therefore if she sustains a contaminated injury during this time she will not need another dose.

The purpose of T.T. vaccination of pregnant women is not only to protect the mother against tetanus, but especially to protect the newborn against neonatal tetanus which has a high case fatality rate close to 90%. This is referred to as providing “PROTECTION AT BIRTH (PAB)” from tetanus for the neonate, and allows for the child to survive the first month of life.
3.3.3 WHO proposed TT immunization schedule

As part of the strategy towards the elimination of neonatal tetanus by 1995, WHO proposed a *broadened* tetanus toxoid schedule including all women of child bearing age (15-45 years), and administered outside pregnancy. This schedule aimed at providing life long protection for women against tetanus and hence also indirectly protecting their future newborns through passive immunity.

**Definition of CBAW:** Generally refers to females from menarche to menopause but is usually described in terms of specific years *i.e. females 15 years to 49 years.*

However the age range may be altered in relation to local conception and childbearing dynamics/experiences.

The schedule for CBAW aims to provide:

- A blanket protection against future maternal tetanus for girls/women of child bearing age irrespective of their reproductive health goals
- Ensured protection at birth (*PAB*) from tetanus for all future neonates and therefore reduce the risk of the baby dying from a preventable disease before the first month of life

(It is assumed that the majority of CBAW (in Kenya) will be or are exposed to the risk of tetanus during deliveries, or during spontaneous/induced abortions due to limited access to quality delivery services.)

**T.T. immunization schedule for women of child bearing age (CBAW) in Kenya**

<table>
<thead>
<tr>
<th>Dosing schedule</th>
<th>Administration schedule</th>
<th>Duration of immunity conferred</th>
<th>Benefits for</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; TT dose</td>
<td>At first contact</td>
<td>Nil</td>
<td>Primes woman’s system</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; TT dose</td>
<td>One month after 1&lt;sup&gt;st&lt;/sup&gt; TT</td>
<td>1-3 years</td>
<td>CBAW + PAB for future neonate</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; TT dose</td>
<td>Six months after 2&lt;sup&gt;nd&lt;/sup&gt; TT</td>
<td>5 years</td>
<td>CBAW + PAB for future neonate</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; TT dose</td>
<td>One year after 3&lt;sup&gt;rd&lt;/sup&gt; TT</td>
<td>10 years</td>
<td>CBAW + PAB for future neonate</td>
</tr>
<tr>
<td>5&lt;sup&gt;th&lt;/sup&gt; TT dose</td>
<td>One year after 4&lt;sup&gt;th&lt;/sup&gt; TT</td>
<td>20 years</td>
<td>CBAW + PAB for future neonate</td>
</tr>
</tbody>
</table>

3.4 ESTABLISHING THE TARGET POPULATION

In order to accurately plan for the logistics required nationally for vaccinating all eligible children in Kenya it is important to define the target population for EPI services. It is also used to estimate immunization coverage.
Currently the operational target population for the nine main vaccines given (excluding tetanus toxoid) is children aged 0-12 months.

However this age group is further sub-divided into two specific target groups as follows

1. **Live births** – this is the expected number of children to be born in a given year based on population projections from the Central Bureau of Statistics, Ministry of Planning. This target group is used for determining the number of BCG doses that will be required. It is also used as a *proxy target* for the number of doses of tetanus toxoid for pregnant women – *assuming that all pregnancies will result in live births*.

2. **Surviving infants** – this is the number of children expected to survive up to the first year of life. Again it is determined by subtracting the known proportion of children who die before their first year of life (infant mortality). This target is used to calculate the doses required for all the other antigens.

**Demographic Data**

Immunization targets set at national, province and district level are based on the latest national census or Central Bureau of Statistics and updates.

**FORMULA**

Surviving Infants = (Total population x (CBR) x (1-IMR))

Live births = \(\frac{(\text{Surviving Infants} \times 1000)}{(1000 - \text{IMR})}\)

- Pregnant women = No. of live births

**Example**: To calculate the target population for Busia district for the year 2006 at the district hospital.

**Steps**

Total population for district A (2006) = 453,463

Crude birth rate (CBR) = 4.5%

Infant mortality rate (IMR) = 125.9

K is constant (1000) = 1000

Target for surviving infants = total population x CBR x IMR
\[
= 452,463 \times 4.5\% \times 125.9\% = 25,634
\]

Target population for Live birth (BCG) = \textbf{Surviving Infants x1000} \\
\( \frac{1000 - \text{IMR}}{1000} \)

\[
= 25,634 \times 1000 = 29,326
\]

\[
= (1000 - 125.9\%) = 874.1
\]

Hence target population = 452,463 x 24\% = 108,592

The number of children aged less than one year in a catchment area is the ‘target’ population for immunization services. To be able to know this target population one needs to know the number of children born each year in the catchment area, as these are the new children that will require immunization. For ease of calculation in Kenya, one can assume that the number of children born in any catchment area is approximately 5\% of the total population. Therefore to calculate the target population one needs to know the total population of the area.

\section*{3.5 CONDUCTING VACCINATION SESSIONS}

\subsection*{3.5.1 Vaccination sessions}

In Kenya, the Government Policy is to immunize on a daily basis during normal working hours so as to increase opportunities of access to immunization services. Ideally, vaccination sessions should be scheduled so that all children in an area served by a health facility can receive their first set of immunizations conveniently enough before the age of one year.

In planning immunization sessions one may consider the number of children immunized by a health facility daily. If there are at least ten or less children immunized daily then immunization sessions should be scheduled for a given period of each day e.g. in the morning or during the afternoon. This must be agreed upon with the local community and is aimed at minimising wastage of vaccines, many of which cannot continue to be used more than six hours after reconstitution.

Fewer sessions per week may be planned where less than ten children are immunized daily, to avoid wastage of vaccines and time. Local leaders \textbf{must} be consulted when determining the best days and times to conduct vaccination sessions.

Daily immunization sessions are convenient as parents do not have to worry about remembering the scheduled days and times.

During vaccination sessions staff should be friendly to encourage parents and their children. The immunization status of each child should be checked by asking the parents about their child’s immunizations and confirmed by examining the child health card. Additionally BCG scars should
be checked.

Immunizations should be administered to all children even if they are sick unless they require hospitalization. Sick children with pending immunizations should be referred for immunization during discharge from hospital.

Special contraindications for vaccination include:

- Children with overt immuno-suppression (AIDS, malignancies etc.)
- Children with known history of reaction to a particular antigen

All these cases should be referred to a paediatrician for further advice.

The time interval between doses of immunizations should be checked. Second or third doses of polio, OPV DPT-HepB-Hib and PCV should not be given if the time interval is less than a month from the previous dose. On the other hand, even if the time limit is long past the minimum interval of 4 weeks, the next doses should be given. DO NOT START THE SCHEDULE AGAIN.

Before the administration of any vaccine, parents/guardians should be informed of:

- The name of the vaccine/s that will be given
- The diseases that the vaccine is protecting against
- Whether there will be any immediate side effect

After immunization parents should again be informed about

- the vaccines the child has received
- any possible reactions from the immunization and what to do about it
- what are the pending vaccines and when the child should be returned to the health facility

In case of vaccination sessions that occur during field outreaches parents should still be reminded about the dates and location of the next outreach.

Tally sheets should be filled accordingly after each vaccine has been administered. The date of vaccination should be duly noted on the Mother and Child booklet next to the corresponding vaccine. The mother and child permanent registers must also be filled in properly. The vaccinator should explain clearly to parents when to return the child for the next immunization. It should be emphasized to them that even sick children should be returned for immunization according to schedule.
Six hours after reconstitution all partially used **reconstituted vaccines** must be discarded. This includes the following vaccines

- BCG vials,
- DPT-HepB-Hib vials (Reconstituted pentavalent vaccine)
- Measles vials
- Yellow fever vials
- PCV (Liquid- No preservative)

**Non-lyophilised vaccines** such as Oral Polio Vaccine, Tetanus Toxoid vaccine and liquid Pentavalent vaccines can be returned to the vaccine refrigerator for subsequent use (up to a maximum of 4 weeks), on condition that they:

- Have not expired
- Have not been contaminated
- Have not been exposed to excessive cold or heat
- Have not been immersed in water
- Have not been disturbed or precipitated
- the VVM, if attached, has not reached the discard point

At the end of the immunization session/day the number of doses of each antigen used, and those returned to the refrigerator must be documented in the vaccine stock ledger. The tally sheet must also be summarised and the sum total for the day entered in the monthly summary sheet.

### 3.5.2 Immunization safety

Immunization activities are integrated with Maternal and Child Health services which include:

- health education
- growth monitoring (weighing & dietary counselling)
- review and management of any illness
- vaccination
- antenatal care
- postnatal care
- family planning
- screening for communicable diseases
In selecting an immunization site a large enough room/area should be chosen. Whether the site is outside or inside a building the rules for organizing the patients’ flow still remain as follows:

- Two doors are required, one for letting clients in and the other for exit.
- When a room does not have two doors, the staff will have to decide how best they can improvise.
- There should be a designated waiting area outside the room/away from the actual vaccinating area.
- The expected number of vaccine doses to be used must be collected in a vaccine carrier with conditioned ice-packs at the beginning of every day from the main vaccine refrigerator. This is to minimise repeated opening of the main vaccine refrigerator.
- Clients must be guided into a single queue when entering the MCH room/area to avoid confusion.
- A sturdy table should be available with adequate space to place the vaccine carrier, syringes and documentation tools.
- There should be two chairs/stools, one for the patient/client and the other one for the health worker at the vaccinating table.
- As far as possible allow only one patient/client at a time into the MCH room/area, to provide privacy.
- Triage for sick children should be conducted periodically during each session and these children attended to first.
- All pregnant and post natal women should be screened for tetanus toxoid vaccination status by card and history and vaccinated where necessary.

The arrangement of space in your facility will affect how you perform your work and how quickly parent/guardian finishes the immunization process. The space that you set up for immunizations should be:

- In a clean area not directly exposed to the sunlight, rain or drought.
- Convenient for Health Worker who is preparing vaccines and immunizing.
- Easily accessible to parent/guardian, but arranged in such away that it is not crowding around the immunization station.
- Quiet enough for health workers to be able to explain what he or she is doing and give advice.
- Sick children should be identified and attended to first.
- Ask if the child has any symptoms or if the mother has any other complaints.
• Ask her about the feeding habits of the child.
• Examine the child physically.
• Check for BCG scar on the second visit after the injection and during her subsequent visits. *(If BCG scar is not visible six weeks after injection, repeat once).*
• Look at the child’s growth monitoring chart and interpret it
• Look at the child’s immunization status and vaccinate as appropriate
• Provide vitamin A supplementation as appropriate

AS FAR AS POSSIBLE ALL CLIENTS PRESENTING FOR VACCINATION SERVICES MUST BE SERVED AS SOON AS POSSIBLE AND MUST NOT BE MADE TO WAIT UNTIL A QUORUM DEVELOPS! Unpredictable waiting times are one of the most frustrating prospects for all clients.

**Note:** The person who administers the immunization should arrange equipment and materials at the immunization station and record the data on the immunization registers.

Additionally,
• Other clinicians in admitting health facilities should be reminded to screen and refer children for immunization before discharge.
• All pregnant women must also be encouraged to attend the MCH clinic as early as possible in the pregnancy, and should receive tetanus toxoid immunization between the 4th – 8th month of gestation.
• It is a policy in Kenya to give T.T. to patients with wounds following trauma. Such patients *should be referred to the injection room or another treatment room* for the TT vaccine and follow up advice. Trauma victims should *never be mixed* with MCH clients.

### 3.5.3 Safe injection practices

The Division of Vaccines and Immunizations advocates for the use of Auto-disable syringes for the administration of all injectable vaccines, and for the use of sterile disposable syringes for the reconstitution of lyophilised vaccines.

The use of auto-disable syringes guarantees that the syringe will only be used once and cannot be reused severally for other children. Re-sterilization of injection equipment is no longer recommended for vaccinations.
A safe injection is one that does not harm the recipient, nor expose the health worker and the community to any risk.

An injection is considered safe for:

- The mother or child, when a health worker uses a sterile syringe and a sterile needle and appropriate injection technique;
- The health worker, when he or she avoids needle-stick injuries; and
- Community, when waste created as a result of used injection equipment is disposed off correctly and does not cause harmful levels of pollution and injuries.

In addition to using quality injection equipment, safe injection practices entail the following:

- Reconstitution of each vaccine with its matching diluent
  - Diluents may appear to be simple water, but in fact contain stabilizers to improve heat stability, bactericides to maintain sterility, chemicals to assist in dissolving the vaccine into liquid, and buffers to ensure the correct pH of the mixture. Failure to use the correct diluent could result in a dangerous or impotent vaccine.

- Injection of the vaccine into the right plane i.e. subcutaneous vaccines should not be injected intramuscularly

- Injection of the correct dose

- Safe disposal of the used syringes and needles

Some common injection practices that can cause harm to the recipient:

- Re-using a syringe or needle
- Leaving needle on the vial for withdrawal of additional doses.
- Touching sterile parts of syringe and needle.
- Applying pressure to bleeding injection site with used materials or dirty fingers.
- Keeping freeze-dried vaccines for more than 6 hours after reconstitution.
- Mixing two partial opened vaccines to constitute a dose.
- Storing medications and vaccines in the same fridge.

Practices that can harm Health worker:

- Recapping.
- Placing used needles on surfaces or carrying them from point of use for disposal at a designated area.
- Sorting out mixed health care wastes.
• Using injection equipment for non-injection purposes.

Practices that harm the community
• Leaving used syringes and needle in unprotected areas where they can be easily accessible to children and grazing animals.
• Community can also be at risk when injection equipment is carelessly disposed off and because of its commercial value, it can be retrieved, resold and reused.

3.6 Adverse event following immunization - AEFI

Definition
An adverse event following immunization is a medical incident that takes place after an immunization and is believed to be caused by the immunization.

Immunization and AEFI
The goal of immunization in Kenya is to protect the individual and the public from vaccine preventable diseases. Although modern vaccines are safe, no vaccine is entirely without risk.

3.6.1 Possible Causes of AEFIs
The causes of AEFIs can be categorised as follows:
• Programme errors, i.e. an error in handling, reconstitution or administration of the vaccine.
• Nature of the vaccine (vaccine properties) or individual response to the vaccine itself
• Coincidence, when there is no causal association between the immunization and the medical condition of the child or women. The latter just coincides with immunization.
• AEFI with unproven association with vaccine. Sometimes the cause of AEFI remains uncovered. With increased quality of investigations,
• Most of the unknown causes probably will be classified in one of the above three categories.
Remember, children in the immunization age group may have symptoms unrelated to immunization due to common infections at the same time.

Steps in identifying AEFIs
• Detect and report AEFIs
• Investigate AEFIs
• Analyse reports of AEFIs
• Take appropriate action following reports of AEFIs
• Evaluate the reporting system for AEFIs
Programme Error

A programme or programmatic error is usually person-based rather than vaccine – or technology-based (e.g. injection site abscess). It can generally be prevented through proper staff training and an adequate supply and proper use of safe injection equipment. In addition, regular supervision will greatly contribute to the reduction of this unwanted phenomenon.

Programme errors can be avoided by observing the following basic rules:

• Reconstitute your vaccine only with the diluent supplied by the manufacturer

• Discard reconstituted vaccines at the end of each immunization session and never retain them. (Remember, opened vial policy applies only to liquid formulation of vaccines!)

• Do not keep drugs or other substances in the vaccine refrigerator

• Use sterile needle and sterile syringe for each injection

• Employ safe injection practices

• Full investigation of an AEFI is needed to pinpoint the cause and to correct inappropriate immunization practices

Notifiable AEFIs include the following:

1. All injection site abscesses

2. All cases of BCG lymphadenitis

3. All deaths that are thought by health workers, or the public, to be related to immunization

4. All cases requiring hospitalizations that are thought by health workers, or the public, to be related to immunization

3.7 Immunization waste management

It is important that adequate measures are put in place to ensure safe disposal without causing harm to the children, school environment and the surrounding the community.

The health worker must ensure used syringes and needles are disposed immediately into the safety box. The safety boxes should be ¾ full to prevent accidents and should be destroyed by incineration or burnt and suitably buried.

Other injection wastes such as cotton wool swabs and the syringe liners should also be disposed in a suitable receptacle and similarly destroyed through incineration or burning and burying.
AT ALL TIMES HEALTH WORKERS MUST ENSURE THAT IMMUNIZATION WASTES ARE PROPERLY MANAGED SO AS TO REDUCE RISK OF INJURY TO CLIENTS, THEMSELVES AND THE LARGER COMMUNITY.

3.8 Educating parents about immunization activities

Ideally, the education process should be conducted in three phases:

- **Group talk before vaccinating children**
  
  Parents should be seated and comfortable as they listen and participate in the discussion. It should be kept short and practical. Parents should be encouraged to ask questions.
  
  Here the health worker should give an overview of the benefits to the family, the larger community and even the country of monitoring the growth of children and vaccinating them, by giving illustrative examples of diseases that have been eradicated or nearly eliminated through the extensive use of vaccines. The message should strongly emphasize that reduction of diseases and the promotion of good health in any community is the collective responsibility of all members.

- **Individual advice at the vaccination station/table**
  
  Every effort should be made to ensure that parents understand and can describe important facts about immunization. Health workers should explain the recommended age for each vaccine, the diseases that will be prevented, the number of doses required and possible side effects of each vaccine.
  
  As health workers vaccinate each child, parents should be encouraged to raise any queries they may have. Especially while giving DPT-HepB-Hib and OPV it should be emphasized that a single dose will not be protective enough and the child must complete the remaining two doses. Parents are to be continuously reminded that their children will only be fully immunized when they receive measles vaccine at nine months.
  
  Parents should be requested to encourage other parents within their community to have their children immunized.

- **On exiting the station** (or when leaving for home after immunization).
  
  Health workers should periodically interview parents as they leave the health facility to determine whether
  
  - They understood what was done to their child and why,
  - Whether they are familiar with the diseases being protected (signs & symptoms)
• Whether they were satisfied with the way they were served
• If they are advised on a return date
• If they were advised on any side effects
• Whether they would recommend immunization services to others

3.9 Screening children and recording information obtained

All children presenting at MCH clinics whether sick or well should be screened for their general state of health and developmental maturity for their age. Enquiry should also be made about the child’s immunization status as per the parent’s understanding and through the Child Health Card.

After each vaccination the Child Health Card should be up-dated and the parent advised on the next return date. Parents must also be impressed upon about the importance of retaining the Child Health Card well at home as well as the need to always carry it when taking the child to a health facility for whatever reason.

All children vaccinated in a health facility or outreach site must be duly recorded in a Permanent Register which is then retained at the health facility in line with all other official government documents. The Permanent Register when properly filled will contain key socio-demographic details of each client and will monitor the progress of immunizations until the child is fully immunized. Because this register is retained at the health facility, defaulters can be easily recognised and followed up.

The Permanent Child Register also provides a useful back-up record in case a parent loses the Child Health Card and a new card has to be updated.

How to fill in the Mother and Child Health book

• Fill in the child biographical data.
• Establish the child’s birth date. If the parents do not know their child’s birth dates estimate as accurately as possible to the month.
• Record weight on the “road to health graph”, and interpret the weight gain/loss to the parent.
• Record any diseases reported and reason for follow up and give an explanation to parents.
• Determine vaccine/s due to be administered,
• If the child is too young to receive a particular antigen (e.g. the child has been brought for measles vaccination at 7/months), provide an explanation as to why the child should not be immunized, and give a return date.
• Note: the only children who should not be immunized are those who are critically ill requiring hospitalization.

Monthly Reporting forms

These are the tools used to aggregate the total number of children reached on monthly basis extracted from daily immunization tally sheet (MOH 702).

For monitoring of coverage and drop out for the three target antigens DPT/HepB+HIB-1, DPT/HepB+HIB-3 and Measles, DVI uses the Immunization monitor chart. The data is extracted from the aggregated MOH 710 and entered in the monitor chart. At the district level ensure that all immunizing health facilities reports are per standard – thus maintain 100% timeliness and completeness. The District Health Records and Information Officer (DHRIIO) should then upload the data on monthly basis to the District Health information System (DHIS).

Monthly reporting indicators

In order to know the progress of the immunization indicators of each antigen, every month the following questions should be answered:

• What percentage of the monthly target children received each vaccine this month? To do this the following formula should be used:

  \[
  \% \text{ Vaccinated with DPT-HepB+HIB1} = \frac{\text{No of children who received DPT-HepB+Hib1}}{\text{Monthly target}} \times 100
  \]

• What percentage of children who received DPT-HepB+HIB1 and did not receive DPT-HepB+HIB3vaccine (i.e. the drop out rate)?

  \[
  \text{Drop out rate in } \% = \frac{\text{No. of children who received DPT+HepB-Hib1} - \text{No. of children who received Measles}}{\text{No. of children who received DPT- HepB+Hib 1}} \times 100
  \]

• What percentage of children who received DPT- HepB+HIB1 and did not receive Measles vaccine (i.e. the drop out rate for DPT-HepB+HIB1 - Measles)?

  \[
  \text{Drop out rate in } \% = \frac{\text{No. of children who received DPT+HepB-HIB-1} - \text{No. of children who received Measles}}{\text{No. of children who received DPT-HepB-Hib1}} \times 100
  \]
• What percentage of children who received BCG and did not receive Measles vaccine (i.e. the drop out rate - BCG to Measles)?

Drop out rate in % =

\[
\frac{(No. \ of \ children \ who \ received \ BCG \ - \ No. \ who \ received \ Measles)}{No. \ of \ children \ who \ received \ BCG} \times 100
\]

• How many children or women within the target were not reached?

Number of children not vaccinated = (Target population) minus (Number vaccinated with specific antigen)

Number of ANC/CBAW not immunised = (Target population) minus (Number vaccinated with specific antigen).

3.11 ADMINISTRATION OF VACCINES

• Hands should be washed before and after handling vaccines. All the vaccines and diluents must be kept cold at the correct temperature (+2°C - +8°C) for the duration of the immunization session.

BCG

• Route of administration - Intradermal

• Dose - full dose 0.1 ml - for children over 1 year (12 months) of age half dose 0.05 ml - for children less than one year of age.

• Site: Left fore arm, into the outer aspect of the left fore arm at the junction of the upper and middle thirds.

DPT-HepB+Hib (Pentavalent)

• Route of administration - intramuscular

• Dose - 0.5 ml

• Site - upper outer part of the left thigh

MEASLES

• Route of administration – subcutaneous

• Dose – 0.5 ml

• Site - in the deltoid muscle of the upper arm

TT

• Route of administration - intramuscular
• Dose - 0.5 ml  
• Site - in the deltoid muscle of the upper arm

POLIO
• Route of administration - oral  
• Dose - 2 drops (read manufacturers instructions)

PNEUMOCOCCAL (PCV)
• Route of administration – Intramuscular  
• Dose – 0.5 ml  
• Site - upper outer part of the right thigh

ROTA VIRUS VACCINE
• Route of administration - oral  
• Dose – 1.5 ml

Follow up Activities
• Health workers should make sure that all parents know the current immunization schedule with special emphasis on measles vaccine to be given at 9 months. They should encourage as many children as possible to receive measles vaccine. Measles being the last immunization in the schedule can be used to measure the coverage of the programme.
• Ensure that each child has received all the vaccinations he/she was supposed to receive.
• Ensure that parents can tell the possible reactions and what to do about them.
• ensure that parents are aware of the exact return dates and the importance of second and third doses of DPT-HepB-Hib, Oral Polio Vaccine, and pneumococcal vaccine.
• parents should be given their Mother and Child Health book and encouraged to bring the book with them each time they visit the health facility either for immunization or when ill.

Destruction of Opened and Unused Vaccines
To avoid vaccine wastage health workers should encourage as many members of the community as possible to complete the immunization schedule. At the end of each vaccination session, unused and opened lyophilised vaccines should be dealt with, in one of the following ways:
• Pour vaccines into the pit latrines
• Burn them
• Break the empty vials
3.12 EVALUATION

The purpose of evaluation is to determine whether the set targets are being met. Evaluation should be done quarterly, annually or biannually. During the evaluation of immunization activities the EPI programme uses combination of the Monitor chart and EPI Access and Utilization Algorithm/ (categorization).

The analysis of immunization performances using both monitor chart and algorithm will assist the EPI focal officers to respond to the following questions:

- Were immunization sessions held daily?
- Did you have enough vaccines?
- Did you have enough syringes and needles to provide safe injections?
- Was the cold chain maintained and were all the refrigerator temperatures in the safe range of +2°C to +8°C?
- Did you check the immunization status of children and pregnant women who came to the clinic?
- If yes, did you give the women and children all the vaccine they were due to receive?
- Did you inform them about pending immunizations and the return date?
Tabulation and Response of The Problems

The cause of any identified problems/challenges detected should be based on the knowledge of the areas served by the health facility and the district. The district health management team should identify the cause of the problem facing the health facility using the following criteria:

- Planning and management of human and material resources
- Supportive supervision
- Service delivery (Reaching the target population)
- Linking services with community
- Data collection and management

The facility staffs can then identify the workable solutions facing them by using the existing resources or source for the external resources to tackle the problem through developing the facility micro plan. The district will then factor the micro plan into the district multi year plan budget.
**3.13 CALCULATING REQUIREMENTS**

The following parameters are required in estimation vaccines:

1. Size of the total population
2. Target population to be given vaccines
3. Expected coverage for each antigen
4. Number of doses to be given as per immunization schedule
5. Wastage rate and wastage factor
6. Frequency of supply
7. Reserve stock

**Example:**

Using BCG Vaccine to forecast for annual vaccine requirements

- **Estimate the size of the total population**
  
  Example district A has a population of 452,463 people. The proportion of live births is 6.4814%  

- **Calculate the target group**
  
  The live birth population is used to estimate the target group for BCG vaccine
  
  Target population for Live birth (BCG) = 6.4814% × 452,463 = 29,326

- **Estimate expected coverage**
  
  The expected coverage for BCG vaccine is 80%

  Multiply the target population with 0.80 to get the total number of children to be immunized in the year which is 29,326 children × 0.80 = 23,461 children

- **Calculate the number of doses to be given for BCG vaccine which is one dose per child**

  Therefore we multiply by 1

  = 23,461 x 1 = 23,461 doses of BCG vaccine

- **Estimate wastage rate for BCG vaccine**

  BCG wastage rate is 50% which is equivalent to wastage factor of 2
Formula: To calculate wastage factor

\[
\text{Wastage factor} = \frac{100}{(100 - \text{Wastage rate})}
\]

\[
= \frac{100}{(100-50)} = 2
\]

- Total amount of BCG vaccines required annually

Total target population X 1(dose) X wastage factor

\[
= 23,461 \times 1 \times 2 = 46,922 \text{ doses}
\]

The total annual doses of BCG required is 46,922 doses plus a reserve stock of 25% of the total annual doses

\[
= 0.25 \times 46,922 = 11,731 \text{ doses.}
\]

Therefore the total annual doses will be 46,922 + 11,731 = 58,653 doses

- **Total amount of BCG vaccines required monthly**

To get monthly requirement, take the annual requirement divided by 12 months

\[
= \frac{58,653}{12} = 4888 \text{ doses}
\]

To get the doses in vial divide 4888 doses by 20 because BCG is a 20 dose vial.

\[
= \frac{4888}{20} = 245 \text{ vials}
\]

Vaccines for children and mothers are ordered monthly at health facility level and quarterly at the district level.

In order to cater for vaccine wastage due to inadequate clients to consume all doses in a vial once opened (among other reasons), a wastage factor (corresponding to the degree of wastage of a particular vaccine) will have to be incorporated into the equation as follow:
### Indicative Wastage Factor by Antigen

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Percentage wasted</th>
<th>Wastage factor (multiplier)</th>
<th>Basic annual number of doses required in location ‘B’</th>
<th>True annual number of doses required (Basic doses x wastage multiplier)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>50%</td>
<td>2</td>
<td>1,300</td>
<td>2,600</td>
</tr>
<tr>
<td>DPT-HepB-Hib</td>
<td>30%</td>
<td>1.1</td>
<td>3,900</td>
<td>4,290</td>
</tr>
<tr>
<td>Pcv</td>
<td>30%</td>
<td>1.1</td>
<td>3,900</td>
<td>4,290</td>
</tr>
<tr>
<td>OPV</td>
<td>30%</td>
<td>1.1</td>
<td>5,200</td>
<td>5,720</td>
</tr>
<tr>
<td>Measles</td>
<td>30%</td>
<td>1.1</td>
<td>1,300</td>
<td>1,430</td>
</tr>
</tbody>
</table>

To allow for any delays in receiving the vaccines an additional two weeks stock is ordered at the health centre level. The health facility is therefore issued with a 6 weeks stock.

### 3.14 Supervision

In order to achieve the objective of the programme, supervision should be undertaken using a standardized checklist which can be modified from time to time to conform to emerging programme objectives.

Structured supervision should be conducted periodically (preferably quarterly) from national to county and district levels and also from county to district and district level to health facility level, preferably by a team of two or three officers.

Ad-hoc supervisory visits also play a role during times of urgent problem solving need as when a disease outbreak has occurred in an area. However this type of supervision is not the most suitable for improving the knowledge, attitudes and practices of health workers.

#### 3.14.1 County level supervision of sub-county & health facility immunization services

Although it is proposed that during supervision two to three members of the County Health Management Team (CHMT) may participate in the visits to districts, the specific members selected will be at the discretion of the County Medical Director.

However, **one of the following members** of the CHMT must be present in all of the visits:

a. The County EPI Logistician

b. The County Medical Records Officer or their representative

c. The County Public Health Officer or their representative
3.14.2 EPI Operational aspects to be addressed during every visit

As far as possible sub-Counties should be alerted about the intended visit in good time to ensure that all the core EPI-relevant DHMT members are on hand during the visit.

Objectives: to monitor progress of immunization coverage in each district.

Review of Sub-County plan of action for immunization coverage.

a. Does the DHMT have an operational plan for the current year for improving immunization services?

b. If available, what are the key components of the plan?

c. What percentage of this plan has been achieved so far?

d. What have been the successes and constraints?

e. What strategies have been tried so far to increase immunization coverage?

Financing district immunization services

a. What are the various sources of funds for immunization services? (i.e. GoK/FIIF/ donor; direct and indirect support)

b. What proportion does each source contribute to the total funds?

c. How reliable are the various sources of funding?

d. How are the various funds accounted for?

e. Are there other opportunities for resource mobilization?

f. Are there other major providers of immunization services e.g. NGOs?

Immunization performance monitoring

a. How many immunizing facilities does the district have?

b. How are these facilities distributed in the district relative to population densities?

c. How many of these facilities send reports on time to the DMOH?

d. What are the constraints to timely reporting from the facilities?

e. Discuss performance in the flow of district immunization reports from district to national levels through the DHIS.

f. Has the DHMT ranked its divisions in terms of performance – both coverages & dropout rates?
g. Has a formal SWOT analyses been done for each division (so as to provide guidance on immunization problem solving)?

h. Have district immunization targets been calculated?

i. Have divisional and facility immunization targets been determined?

j. Does the DHMT have a formal health services supervisory schedule for the year/ quarter/month?

k. If supervisory visits to health facilities are not regular, determine the limiting factors.

**Immunization logistics**

a. Determine how the district secures its supplies of vaccines, injection equipment, data collection tools, cold chain equipment etc.

b. Determine how the distributions of EPI logistics are rationalized.

c. What are the gaps in immunization service provision and expansion? Are there any local solutions to these problems?

d. Who is in-charge of the vaccine depot, and is this the same person who issues out vaccines & diluents to facilities?

e. Is the district vaccine store secure?

f. Does the district vaccine depot have adequate storage capacity for vaccines? If inadequate, how is the district coping?

g. Does the district vaccine depot have adequate stocks for three months?

h. Are the refrigerators serviced regularly?

i. Are refrigerator/freezer temperatures recorded twice daily?

j. Is the vaccine stock ledger up to date?

**Data management**

a. Is the DHMT conversant with the various immunization services reporting tools and procedures? 

b. Is the DHMT conversant with the expected flow of information from facility to national levels, including deadlines for reporting to each level?

c. How often are reports written for routine immunization activities in the district? Is it annually/quarterly/ monthly? Ask to see a copy of the most recent report.
d. Are the district routine immunization reports disseminated to stakeholders?

**Disease surveillance activities**

a. Is the district disease surveillance team active? *Ask to see a copy of the minutes of the last meeting.*

a. Are surveillance target indicators for AFP, Measles & MNT acceptable?

**Advocacy for immunization services**

a. Has DMOH solicited for support for immunization services at the District Development Committee

b. Has the DMOH recently organized for a stakeholders meeting for general health service provision and/or immunization services in particular?

c. What are the common forums used by the DHMT to advocate for immunization service utilization?

**3.14.3 Sub-County level supervision of health facility immunization services**

As with the county level supervision, three to four members of the DHMT may participate in the visits to immunizing health facilities, the specific members selected will be at the discretion of the DMOH.

However, *one of the following members* of the DHMT must be present in all of the visits

a. The District Medical Officer of Health

b. The District Public Health Nurse or the Deputy

c. The District Medical Records Officer or their representative

d. The District Public Health Officer or their representative

**3.14.4 EPI Operational aspects to be addressed during every visit**

As far as possible health facilities should be alerted about the intended visit in good time to ensure that all the relevant staff are on hand during the visit. Both the MCH nurse/staff and the Public Health Technician of the locality should be present, as well as a Medical Records Technician if available.

During visits, teams are expected to remain together and must not separate to evaluate different sections of the facility independently as this will confuse and stress the officer/s being supervised.

Therefore the team should guide the health worker *systematically* through each of the EPI aspects being evaluated, before proceeding to the next.
All DHMT teams should ensure that they have carried a kit of extra sets of data-collection tools during every visit to replenish any stock-outs that may be found at facilities.

**Objective:** to provide personalized supportive supervision

**Review of the general organization of the MCH**

a. Does the current arrangement allow for free movement of the HW & clients?

b. Is the room neat and clean?

c. Are there any other *conflicting services* provided in the MCH (e.g. curative services like injections and dressing of wounds)?

d. Can this be avoided?

e. Is the clients’ waiting bay adequate, clean & well ventilated?

**EPI service provision system**

a. Does the MCH operate daily? NB: MoH policy is to provide for daily immunization.

b. What time does the MCH begin and close its activities every day?

c. What is the average number of clients seen per day? Discuss whether this correlates with the catchment population.

d. Is the flow of patients clear and smooth?

e. Are clients served immediately on arrival or made to wait until there is a quorum? NB: if waiting is unavoidable due to lack of staff, DHMT should advise on ways of alleviating the problem, both short term & in the long run.

f. Are immunizations tallied immediately or after the session is over (based on recollection)?

g. Is the Permanent Child Register filled properly or with ticks & strokes?

h. Are clients advised on how to manage any adverse effects of vaccination?

i. Are the Child Welfare Cards duly filled and clients advised on return dates as they leave?

j. Does the HW know the immunization target population for the facility?

k. Is the target population prominently displayed in the MCH?

l. Is the monthly cumulative immunization chart displayed and up to date?

m. Is the drop-out chart displayed and up to date?

n. Does the facility conduct any outreach services? If so, how often?
Cold-chain equipment

a. Is the vaccine refrigerator appropriately situated (i.e. in a well ventilated room & off the floor)? *Note if the top surface is misused as a shelf.*

b. How many people have access to the KEPI fridge?

c. Are the temperatures recorded twice daily?

d. Where and how are the temperature charts stored?

e. Does the fridge have a reliable thermometer?

f. Is the current temperature reading acceptable?

g. When the vaccine refrigerator was last defrosted?

h. Is the fridge tidy?

i. Does the fridge contain packing trays?

j. Are vaccines stored at the correct levels?

k. Are there other foreign materials stored in the KEPI fridge (e.g. lab. reagents; insulin)?

l. How are these foreign items segregated from the vaccines & diluents?

m. Are there any expired/frozen/damaged/unlabelled or reconstituted vaccines in the fridge that need to be discarded?

n. Check the condition of the available vaccine carriers, including the size & fit of their ice packs.

O. Does the health worker *condition* the ice packs before putting them inside the vaccine carrier?

Availability of vaccines and injection supplies

a. Is the vaccine stock ledger well kept and up to date? *Do a physical count of the vaccines in the fridge and those in use to see if they agree with the stock ledger.*

b. Are there any stock-outs currently? *If yes find out why and what action has been taken.*

c. Is vaccine wastage calculated daily? *If not, determine whether the HW knows how monitor wastage?*

d. Are there adequate diluents for the vaccines in stock?

e. If not, how did this come about and how is the HW managing?
f. Is reconstitution of freeze dried vaccines carried out using only the specific diluent provided by the manufacturer for each type of vaccine? *(NB: Diluents may appear to be simple water, but in fact contain stabilizers to improve heat stability, bactericides to maintain sterility, chemicals to assist in dissolving the vaccine into liquid, and buffers to ensure the correct pH of the mixture. Failure to use the correct diluent could result in an impotent vaccine.)*

g. Are AD syringes used for **all** injectable vaccines? *If not, find out why and determine the most feasible immediate solution.*

h. Are there adequate stocks of AD syringes and disposable reconstitution syringes for the vaccines available?

**Management of immunization wastes**

a. Are safety boxes used routinely during immunization sessions? *If not, why?*

b. Where safety boxes are used, check that they are used correctly, (i.e. for syringes & needles only and not being overfilled).

c. Physically check the disposal sites for the filled safety boxes as well as the destruction methods used ( “burning & burying in a pit” or incineration)

d. Check whether other immunization wastes such as swabs an syringe wrappers are collected and destroyed in an appropriate manner.

**Data management**

a. Does the MCH have all the required immunization data collection tools?

b. Are these tools well understood by the health worker?

c. Who actually fills these tools?

d. Where and how are they stored on completion?

e. How are they forwarded to the next level?

f. What are the constraints (if any) in completing the various forms or forwarding them to the next level?

g. Are health workers able to interpret the data collected for local action?

h. Discuss what the current available coverage data means to the health worker.

i. Does the health facility receive feedback on its performance from the district level?
Disease surveillance activities

a. Are all health workers at the facility aware of Integrated Disease Surveillance and Response (IDSR) activities?
b. Can they name the EPI diseases under surveillance?
c. Do they know the case definitions of the EPI diseases under surveillance?
d. Are case definition posters displayed in the MCH?
e. Does the facility have the IDSR reporting forms?
f. Do Health Workers know how to investigate cases under IDSR?
g. Are there any constraints to investigating these cases?

Other health service delivery issues

a. The DHMT must always review any other pressing issues on general health service delivery while at the facility.

Summary of key findings and recommendations to be recorded in the facility’s supervisory book

NB: NEVER SHOULD DHMT SUPPORTIVE SUPERVISORY VISITS TO HEALTH FACILITIES BE HURRIED! THE DHMT MUST BE PREPARED TO SPEND AT LEAST TWO HOURS AT EACH FACILITY. However care must be taken not to interrupt normal service delivery during visits.

Further Reading


7. Immunization in Practice 8 modules WHO training course, Geneva.
Learning objectives:
At the end of the session the health worker will be expected to:

1. Define the cold chain system.
2. List the cold chain equipment used in the country.
3. Demonstrate packing of vaccines in the cold chain equipment.
4. Describe basic principles of refrigeration.
5. Discuss equipment installation procedure.
7. Carry out preventive maintenance activities.
8. Conduct basic fault finding procedure and remedial action.
9. Be able to order spare parts.
10. Be able to take equipment inventory.
11. Know common cold chain emergencies.

4.1 Definition
Cold chain is a process of maintaining vaccines in a potent state from the manufacturer to the recipient (child and woman of child bearing age). Vaccines lose their potency when exposed to high temperature, sunlight or freezing conditions depending on type.
The cold chain system

Figure 5.1 shows how supplies of vaccines travel in cold chain links from the manufacturer to the central vaccine store and eventually to the recipient through the regional and district vaccine depots and finally to the immunizing health facility.

An efficient cold chain system requires trained and skilled staff, reliable equipment and adherence to set standards.

Immunization Vaccine Delivery System

The vaccine delivery system

The supply chain must deliver the right vaccines in the right place, at the right time, in the right quantities, in the right condition, at the right cost.
4.2 COLD CHAIN EQUIPMENT

The equipment used in maintaining cold chain must meet standards set by WHO and UNICEF for safe vaccine storage. They vary depending on the level of use. Below is a list of the equipment currently used in Kenya.

1. Cold rooms and freezer rooms
2. Freezers and Ice-lined refrigerators
3. Gas electric refrigerators
4. Solar Refrigerators
5. Vaccine carriers
6. Cold boxes
7. Icepacks
8. Thermometers

4.2.1 Cold Rooms and Freezer Rooms

These are large rooms, specially constructed for storage of large quantities of vaccines. They have two cooling units; one running while the other is standby, a 24-hour temperature monitoring system with an alarm, a recorder, and a backup generator that will turn on automatically when the regular power is interrupted. Cold rooms are found at the national and regional levels while freezer rooms are only found at the national level.
4.2.2 Freezers / Ice-lined Refrigerators

Freezers and ice-lined refrigerators are used at Central, Regional & District stores

**Freezer**

![Freezer MF314](image)

**Freezer MF314**

Used for large storage of antigens and freezing of icepacks at the central, regional, district and sub district level.

**Ice-lined refrigerator**

![Ice-lined refrigerator TCW3000AC](image)

**Ice-lined refrigerator TCW3000AC**

Used for large storage of antigens at the district and sub district level. It can be converted into either a refrigerator or a freezer based on need.
4.2.3 Gas Electric refrigerators

There are currently three major types of gas electric refrigerators used in the country; these are Sibir 170GE, RCW42EG and RCW50EG.

**Sibir170GE**

Vaccines are placed in shelves in order of sensitivity with the most sensitive to heat (OPV) being on the first shelf below the evaporator. TT and DPT+HepB – HiB being most sensitive to freezing are placed on the second last shelf from the bottom. Vaccines are packed leaving space of about 5cm in between the packets for air circulation. The upper cabinet is used for freezing of icepacks.
This fridge is used at the district vaccine store and at the immunizing facilities with high target population.

**Packed upright refrigerator e.g. (Sibir 170 GE)**

**RCW 42 EG**

The refrigerator is designed for use at the service delivery point. It is operated either on electricity or gas and has top opening door. Trays of different colors are used to store each type of vaccine. The most sensitive to heat being oral polio vaccine is kept in blue tray that is placed at the bottom most part of the fridge while the most sensitive to freezing being DPT+HepB-HiB is kept in the red tray which is the top tray. A sticker is pasted on the front side of the refrigerator to guide on the vaccine arrangement and the arrangement order must be observed at all the times.

The figure below shows a picture of RCW 42 EG while figure 5.8 shows the arrangement of vaccines in the refrigerator.
<table>
<thead>
<tr>
<th>Tray Colour</th>
<th>Position</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purple</td>
<td>Top</td>
<td>Pneumoccocal</td>
</tr>
<tr>
<td>Red</td>
<td>Second</td>
<td>DPT+HepB-Hib</td>
</tr>
<tr>
<td>Orange</td>
<td>Third</td>
<td>Tetanus Toxoid</td>
</tr>
<tr>
<td>Yellow</td>
<td>Fourth</td>
<td>BCG</td>
</tr>
<tr>
<td>Green</td>
<td>Fifth</td>
<td>Measles / Yellow Fever</td>
</tr>
<tr>
<td>Blue</td>
<td>Bottom</td>
<td>Polio</td>
</tr>
</tbody>
</table>

**Arrangement of Vaccines in RCW42EG**

**RCW 50 EG**

This is similar to RCW42EG but has a double vaccine carrying capacity. It is suitable for use at places with higher target population or sub district depots. It also has higher fuel consumption.
Solar refrigerator

This is used in areas with high sun intensity. Sunrays are converted into electric energy, which is then used to supply the refrigerator.

Solar refrigerators are suitable for use at the service delivery points.

Arrangement of vaccines is similar to that of RCW.
Cold Box

Cold boxes are normally used for transportation of vaccines. They can also be used for temporary storage when a refrigerator breaks down. The cold life of a cold box varies depending on the type, the number of openings and the ambient temperature.

Packing ice packs in cold box

Packed Cold Box

Vaccine Carrier

Vaccine carriers are used to transport vaccines from district stores to service delivery points (outreach / mobile) and during immunisation sessions. The cold life in a vaccine carrier is approximately 8 hours.

Types of vaccine carriers

Icepacks

Icepacks are flat rectangular plastic containers filled with water or gel. They are used in vaccine carriers, cold boxes or refrigerators to maintain temperatures. Always have at least an extra set of icepacks as a reserve while one set is in use.

Thermometers

Different types of thermometers are used to monitor cold chain temperature. These are the dial and alcohol thermometers as shown below. They indicate the safe operating ranges of temperature of between +2°C to +8°C for refrigerators and –15°C to –25°C for freezers.
4.3 BASICS PRINCIPLES OF REFRIGERATION

Terminologies

- Refrigeration - The process of removing heat from an insulated space to maintain cold temperature.
- Refrigerator - This is an airtight equipment connected to a power source which can either be gas or electricity to achieve cooling.
- Refrigerant - A fluid with low boiling point which circulates in the refrigeration system to facilitate cooling.

Types of refrigeration systems used in EPI

- Compression system
- Absorption system

4.3.1 Compression type

This type of refrigeration system uses a compressor, which when connected to electricity pumps the refrigerant through the pipes. The pipes connect the inside of the refrigerator to the outside. As the refrigerant circulates, it absorbs heat from inside lowering the temperature inside the refrigerator. The refrigerator hums when in operation. An example of this refrigerator is TCW 1152

4.3.2 Absorption type

This type of refrigerator has a heating unit, which uses either gas or electricity. When the heating unit is supplied with a source of heat the refrigerant boils, evaporates and circulates through the coiled pipes where it looses heat changing into liquid as it enters the pipe inside the refrigerator. Due to the low boiling properties of the refrigerant it evaporates again as it enters the inside pipes.
and this results into cooling. Absorption refrigerator is quiet when in operation. An example of absorption type of refrigerator is RCW 42 EG.

The figures below are showing the parts of absorption type refrigerator.

Refrigerator Parts (front & inside)

Refrigerator Parts (back side)

How to receive and install (gas/electric refrigerator)

Action on receipt

• Check the packaging case for damage. If there is damage, **notify the supplier before unpacking**.
• Unpack the refrigerator carefully.
• Check the refrigerator. If it is damaged, notify the supplier/District.
• Look for the manufacturer’s instruction manual. This should be inside the packaging case or in the refrigerator.
• Read and follow the instructions given in the manual carefully.
• If the instructions are missing, use this book instead
• Check that the flue baffle is hanging inside the flue.

### Checking flue baffle

#### Installation

• Ensure the room is well ventilated.
• Place the refrigerator in the coolest part of the building.
• The refrigerator should be kept off droughts.
• Minimum clearances to wall and roof must be at least 30cm and 40cm respectively as shown in the figure in the next page.
• Upright refrigerators should be placed on wooden blocks (25 to 50mm) thick to avoid dampness.
• Ensure that the refrigerator is leveled well.
Refrigerator showing spacing for installation

<table>
<thead>
<tr>
<th>Refrigerator levelled</th>
<th>Refrigerator not levelled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plumb line will be in line with refrigerator</td>
<td>Plumb line will not be in line with the refrigerator</td>
</tr>
<tr>
<td>No spill from a full saucer of water</td>
<td>A full saucer of water will spill when placed on top</td>
</tr>
</tbody>
</table>

Checking levelling

Lighting the gas refrigerator

Instructions for lighting the gas refrigerator (in absence of the manufacturer's instructions).

- Make sure that there are no draughts from doors or windows. These will make it difficult to light the gas burner.
- Identify the control knobs and other parts for gas operation.
• Connect the gas cylinder to the refrigerator with the gas supply pipe. Check that the connections at each end of the pipe are tight.

• Open the valve on the gas cylinder and check for leaks at all gas connections using foam from soapy water.

• Turn the gas thermostat knob to medium position or position number (4)

• Open the gas valve by pushing the gas valve knob on the flame failure device as far down as possible and keep it pushed in.

• Push the igniter button to light the gas. Look through the sight glass/window to see the flame.

• If the gas does not light, push the igniter button again. Repeat, if necessary until you can see the flame.

• After you see the flame, keep the flame failure device button pushed in for at least 15 seconds, and then release it.

• Check that the flame stays lit. If it goes out, repeat the lighting procedure.

**Note:** When lighting for the first time, or after replacing the gas cylinder, the flame may go out easily. This is because of air in the gas supply tube.

**Adjusting the temperature, ensure a 48hr observation period**

• After checking the inside temperature, the control knob can be turned towards a warmer or colder position if necessary.

• The control knob is usually marked “1” to “7”, MIN”, “MED” and “MAX” or with an arrow indicating how to turn to colder temperature as shown in fig 5.17.

• No. “1” or “MIN” gives the warmest and No. “7” or “MAX” gives the coldest temperature.

**Types of control knobs**
4.4 MONITORING COLD CHAIN TEMPERATURE

How to use the cold chain temperature-monitoring chart

Read and record the refrigerator temperature twice daily, morning and evening including weekends and public holidays. Carefully record these temperature readings on the cold chain-recording sheet:

You must enter:

- Name and type of refrigerator
- Name of the district
- Name of the health institution
- Power Source (Normally operating on)
- The date
- The number of icepacks frozen today
- The number of icepacks used today
- The number of hours of electricity failure
- Shortage of gas (Mark with X)
- Gas cylinder renewed (Mark with X)
- Plot the temperature morning and evening
- Report on faults and problems at the bottom off the chart
- Note that the bold line is for start of the day which is mid night and the broken line mid day. Charting should therefore be done at the centre of the bold and dotted line in the morning, and at the centre of the broken and bold line for the evening charting as shown on figure 5.21.
Charting temperature-monitoring chart for refrigerators

Preventive maintenance activities

Daily activities

- Check temperature twice, in the morning and evening including public holidays and weekends and chart on the temperature-monitoring chart. Ensure the temperature is between +2°C to +8°C.
- Check that the refrigerator is operating and the burner flame is blue for gas refrigerator.
- Make sure that there is enough gas in the cylinder. Health worker should know how long a cylinder takes when running continuously.
- Ensure that vaccines are well arranged in the refrigerator
- DO NOT keep any other item in refrigerator apart from vaccines and diluents.
- Keep a spare gas cylinder available and always replace the gas cylinder before it is completely empty.

Weekly activity

- Check the ice formation on the evaporator. If the ice is thicker than 6mm to 10mm defrost the refrigerator.
- Check that the refrigerator is level.
Monthly activity

- Check that the condenser and cooling unit are clean. Remove any dirt or dust with a soft brush or cloth.
- When necessary, clean inside and outside of the refrigerator with a damp cloth.
- Clean door gasket and powder it with perfume free talcum.
- Check the gas connections for leaks
- In solar refrigerator
  - Gently wash the panels with plenty of water and soft cloth (avoid use of detergents)
  - Check battery acid level and top up with distilled water when necessary.
  - Check battery terminal for tightness and corrosion. Lubricate with battery terminal jelly or petroleum jelly.

Yearly activity – by the medical engineering technician

- Clean the gas burner and gas jet
- Clean the flue and baffle

What to do if the refrigerator is not working properly

The refrigerator is not working properly if any of the following happens:

- The refrigerator is not cooling at all
- The refrigerator is not cold enough above 8 degrees centigrade
- The refrigerator is too cold below 2 degrees centigrade

Follow these instructions when using the fault finding flow chart.

Ensure that Vaccines are transferred into a vaccine carrier or cold box before determining the fault.

- Always start with the first possible fault as shown on the flow diagram.
- Make sure that a fault does not exist before going on to the next one.
- If, after checking all the possible faults, the refrigerator is still not working properly, start at the beginning and check everything again.
- If, after checking all the possible faults twice, the refrigerator is not working properly, refer to the district for further action by a trained technician
Checking the door sealing

Place a thin paper (foolscap) strip in between the door and body of refrigerator

- Close the door.
- Pull the paper strip (Foolscap), if it moves easily or falls by itself, the door gasket is faulty, or the door hinges are loose or broken. Take necessary action and if unable, refer for further action by a skilled technician.

Refrigerator not working at all

Checking gas supply

- Always keep a spare gas supply tube.
- Use soapy water to check for any gas leakage
• If there is a leakage in the gas supply tube, replace it.
• Does not use the refrigerator on gas operation if there is leaking connections, which you cannot repair, refer to the district for further action by a skilled technician.

Checking the gas thermostat
• Remove the capillary tube end from the evaporator.
• Put the capillary tube end into a glass of ice cubes.
• Turn the thermostat control knob to “maximum” position.
• Watch the flame in the sight glass and slowly turn the thermostat control knob towards the “minimum” position. If the flame gets smaller, the thermostat is working. If the flame does not get smaller, the thermostat is faulty. Replace the thermostat.

Checking the thermo-element
• Check that the nut “A” between the thermo-element and the flame failure device is tight.
• Check that the tip “B” of the thermo-element goes into the flame 3 to 4 mm (3/16 inch). If it does not, loosen the fastening “C” and adjust the position of the tip of the thermo-element.
• Check the flame failure device.

Flame failure device

Checking the flame failure device
• Press the flame failure device button as far in as possible.
• Light the burner and wait for 15 to 20 seconds.
• Release the button and check the thermo-element. If the flame is accidentally blown out, the flame failure device must shut off the gas supply within one minute.
• Blow out the flame. Wait for one minute.
• Try to light the burner without pressing the flame failure device button.
• If the burner lights, the flame failure device is faulty. Replace it.

**Defrosting**

It is quite normal for ice and frost to form on the evaporator. A thin layer of frost does not affect the cooling performance but if the frost grows thick approximately (6 to 10m (1/4 –3/8”) or more), it must be removed by defrosting.

**Defrosting Procedure**

• Move the vaccine into another refrigerator or store it in a cold box with icepacks
• Turn off the gas supply (or remove plug from the wall socket if on electric operation).
• Open the door of the refrigerator and leave it open for the ice to melt normally or use warm water with a cloth to thaw the ice
• Do not use knives or other sharp instruments.
• Wipe the freezer compartment dry.
• Clean and dry the refrigerator.
• Light the burner (or plug in three pin top plug into the wall socket if on electric operation).
• Wait until the temperature stabilises between +2°C to +8°C.
• Place the vaccine inside and close the door.

**Cleaning the flue and baffle**

• Turn off the gas supply
• Remove the burner protection plate.
• Cover the burner with a piece of clean cloth, to protect it and to collect the dirt.
• Remove the flue top. Take the flue baffle out of the flue.
Cleaning the flue and baffle

Cleaning the refrigerator

- Always clean the inside of the refrigerator when defrosting.
- Use warm water and soap.
- Never use scouring powder, steel wool or abrasive cleaners on any refrigerator with a metallic surface paint.
- Clean the door gasket and put same talcum on it.
- Wipe all parts dry before starting the refrigerator.
- Clean the outside with a soft brush or a piece of cloth.
- Clean the condenser and cooling unit with soft brush.
- Light the burner (connect the power plug into the wall socket if on electric operation).
- Wait until the temperature stabilizes between +2°C to +8°C to return vaccines.

Cleaning the gas burner and gas jet

There are different types of burner units. You should use the manufacturer’s instructions for your refrigerator. If the instructions are missing, ask the district for a new copy.

- Transfer the vaccines into a vaccine carrier or cold box.
- Turn off the gas supply.
- Remove the cover plate(s) if any, which protect the burner and jet.
- Remove the gas jet. This is located on the gas inlet side of the burner.
- Wash the gas jet carefully in alcohol, kerosene or petrol. Blow through it to dry (Do not use any sharp object to clear the jet.)
• Check that the jet is completely clear by looking through it against the light.
• If the jet is damaged or badly blocked that cannot be cleared, fit a new one.
• Clean the gas burner with a soft brush and blow it free of dust.
• Replace the parts and Check for leaks.
• Light the burner and wait until the temperature inside has come down to +2°C to +8°C before replacing the vaccine.

Replacing the door gasket for RCW 42 EG

1. Check that the size of the replacement gasket is correct.
2. Pull out the old gasket carefully.
3. Clean the groove with a wet cloth or gauze.
4. Press in the replacement gasket into the groove, and ensure that the gasket has not left any gap.

Replacing door gasket

Replacing the gas thermostat

To replace the gas thermostat, the main steps are as follows:

1. Turn off the gas supply.
2. Remove the capillary tube end from the evaporator and carefully pull it out of the rear of the refrigerator cabinet.
3. Disconnect other gas equipment parts from the thermostat. Two different types of connection between the gas thermostat and gas pipe are shown below.
Gas thermostat

4. Connect the new thermostat.

5. Fasten the capillary tube end to the evaporator.

Note: Be very careful not to break the capillary tube. Make sure that the capillary tube makes contact with the evaporator only where it is to be fastened.

6. Check for leaks before lighting the burner.

Replacing the flame failure device (safety valve) and thermo-element

There are different types of flame failure device. You should use the manufacturer’s instructions for your refrigerator.

To replace the flame failure device, the main steps to be followed are:

1. Turn off the gas supply.

2. Unscrew the thermo-element nut and remove the thermo-element from the flame failure device.

3. Disconnect the gas thermostat, gas pipe and any other parts from the flame failure device.
Flame failure device connections

4. If the thermo-element must also be replaced, disconnect the other end of the thermo-element from the gas burner unit. Connect the new thermo-element to the gas burner unit. Adjust the tip correctly.

5. Connect the thermo-element to the flame failure device, and tighten the nut fully.

6. Check for leaks before lighting the burner.

Starting on electric operation

- If the refrigerator has been on gas operation, take the following action:
  - Turn off the gas supply at the gas cylinder.
  - Wait until the burner flame goes out.
  - Disconnect the gas supply regulator from the gas cylinder.
  - Check that the power supply voltage is correct (220V – 240V).
  - Plug in the top plug into the wall socket.
  - Turn the thermometer control knob to medium or position 4, put a thermometer in the fridge and leave the refrigerator running for 3 to 4 hours. If it does not start, ensure that the plug is wired correctly.
  - Read the temperature inside the refrigerator. It must be between +2°C to +8°C.

Adjusting the temperature

After confirming that the refrigerator is working on electricity, it is important to check the temperature because the temperature setting for gas operation may give very low temperature for electric
operation. Monitor the refrigerator and adjust the thermostat control knob accordingly depending on the temperatures inside the refrigerator. The temperature must stabilise between (+2°C to +8°C).

If the refrigerator does not cool, follow the instructions shown in the figure below.

Refrigerator not cooling at all on (electrical operation)

Replacing the three pin top plug

The standard plug is the square three pin 13 Amp. top plug shown below.

Equipment come with different type of plugs when imported, but all plugs that do not correspond to the three pin top plug must be replaced to the ones shown.
Three pin top plug

The correct colour codes must be observed when doing the wiring.

- Red or Brown wires are for LIVE wire
- Black or Blue wires are for NEUTRAL wire
- Yellow/Green or Green wire for EARTH wire

The top plug normally has markings on the pins corresponding to the wires as shown.

- E  for Earth
- N  for Neutral
- L  for Live

When making connections the correct colour code of wires must correspond with the pins. Failure to do so will result into short-circuit.

Ordering spare parts

a. When ordering spare parts, always state:

- Manufacturer and model or type (shown on the data plate on the fridge)
- Voltage and wattage (if electric parts are ordered)
- Serial number (shown on the data plate)
- Spare parts description (use the names given in this manual)

b. Location of a data plate varies from model to model. Usually it is located on the rear, on the lower door or on the walls inside the refrigerator. In some other brands, the data plate may be found behind the bottom drawer.
c. Always keep in stock

- One spare full gas cylinder.
- One spare gas supply pipe.
- One spare heater (for electric operation).
- Spare fuses or fuse wire for electric operation.

**Equipment inventory**

It is important to keep records of equipments. A good equipment inventory will provide the information needed to track the location, maintenance schedule, replacement and evaluation of the adequacy of the equipment. Records for each piece of equipment should include:

- Technical information (brand, model, serial number, date of entry into service and date of final removal from service)
- Specific location
- Current condition (working, in repair, un-repairable)

**Preparing for emergencies**

Emergencies can interrupt immunisation services if not planned for. Some of the common cold chain emergencies include:

- Equipment breakdown.
- Electric power failure.
- Shortage of gas.
- Shortage of spare parts.

There should be a warning system for identifying equipment failure and make arrangements in advance for moving vaccines to the nearest health facility or location that has appropriate substitute equipment.

The district should be notified as soon as possible of such failure.

**Cautions:**

- Use only one power source
- Emergency plan
- Transferred vaccines need to be captured in the ledger books
Learning Objectives

At the end of this chapter, the student should be able to:

• define the role and importance of communication and social mobilization in the EPI Programme
• describe the essentials of planning, implementation, monitoring and evaluation of EPI communication interventions
• identify, analyse and address challenges related to communication and the use of research findings and data to guide immunization communication planning and messages

5.1 INTRODUCTION

Communication is a key component to the overall immunization programme, which also includes cold chain and logistics, training, supervision and monitoring, etc. Advocacy, social mobilization, and communication aim to inform, educate and enable community and target populations to accept, demand, and use immunization services.

Each of these strategies plays a major role in supporting EPI. Advocacy aims at developing supportive policies and guidelines, and raising/increasing resources for and commitment to sustainable financing of vaccine. Social mobilization aims at ensuring that key actors join efforts to ensure wider community participation and ownership to promote immunization among specific population groups. Communication for Social and Behaviour Change aims at providing knowledge and promoting positive attitudes for the adoption of immunization practices at both individual and collective levels, i.e., by transforming the practices into norms to which individuals accept and conform.
5.2 IMPORTANCE OF COMMUNICATION FOR IMMUNIZATION

It is not enough to develop and maintain good physical and material infrastructure for immunization and ensure that services are available and reliable; communities must also be aware of, accept, trust, and utilize these services. The ultimate objective of these services is to raise and sustain immunization coverage for the target groups and reduce the vaccine preventable diseases.

To achieve higher coverage and a significant reduction of drop-out rates, community participation is indispensable. However, KEPI and other KAP studies have shown that even some people who have access to services do not use them because of lack of adequate or correct information or mistrust or lack of confidence in the service. People cannot participate in what they do not know, believe in or accept. Hence, the need to inform families and communities of the potential benefits of immunization, the safety of vaccines, and where and when services can be accessed. Health workers must be knowledgeable and skilled in communicating with service users. At minimum, every adult who leaves a place of immunization should know what immunization(s) the child has just received, the possibility of side effects and what to do if they arise, and when and where the child has to return for the next immunization. In addition, the health worker should encourage the caregivers to make a return visit according to schedule and ensure that the services are available.

It is important to understand potential barriers to immunization to be able to design communication interventions appropriately. Service delivery related barriers were addressed in the previous chapter on Maximizing Opportunities for Immunization. Following are some of the communication and social related barriers:
<table>
<thead>
<tr>
<th>Communication and information related reasons/factors</th>
<th>Family or societal characteristics</th>
<th>Parental attitudes and knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Lack of health educators</td>
<td>• Illiterate caregivers</td>
<td>• Caregivers’ lack of knowledge about immunizations</td>
</tr>
<tr>
<td>• Poor communication from health worker (perceived provider rudeness or a lack of trust in him/her)</td>
<td>• Low education level of caregivers</td>
<td>• Motivation</td>
</tr>
<tr>
<td>• Lack of information on vaccination schedule, when child is due, where to receive vaccinations</td>
<td>• Low socioeconomic status</td>
<td>• No understanding of vaccine importance (Caregivers frequently not aware of the need to vaccinate their child or the threat of disease transmission if their child was not vaccinated).</td>
</tr>
<tr>
<td>• Inadequate media messages</td>
<td>• Living in a large family/having older siblings</td>
<td>• No information on when to vaccinate</td>
</tr>
<tr>
<td>• Dissemination of inadequate or incorrect information by health care worker</td>
<td>• Belonging to minority group</td>
<td>• Misconception of vaccinations (ranging from the impression that vaccinations do not work to the concerns that vaccinations harm the child, or cause disease or other adverse event such as sterility).</td>
</tr>
<tr>
<td>• Lack of media exposure</td>
<td>• Migrants</td>
<td>• Fear of side effects</td>
</tr>
<tr>
<td>• Lack of community involvement</td>
<td>• Blue collar worker/occupation</td>
<td>• Fear of vaccination</td>
</tr>
<tr>
<td>• Gender of health worker</td>
<td>• Marital status - mom unmarried</td>
<td>• Being female child</td>
</tr>
<tr>
<td>• Lack of trust or social connections</td>
<td>• Male headed household</td>
<td>• Religious/cultural/traditional beliefs against vaccines</td>
</tr>
<tr>
<td>• Lack of home visits by health worker</td>
<td>• Mother’s age</td>
<td>• Lack of family discussions on vaccines</td>
</tr>
<tr>
<td></td>
<td>• Other domestic issues (conflict/death)</td>
<td>• Reject vaccinations - no reason</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mother’s autonomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Previous bad experience with clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Social pressure against vacci- nations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Contraindications to vacci- nations incorrectly interpreted; and children for whom vaccinations were otherwise appropriate are not vaccinated.</td>
</tr>
</tbody>
</table>
5.3 RESOURCE MOBILIZATION AND ADVOCACY FOR IMMUNIZATION COMMUNICATION

The first responsibility in the attainment of good health lies with individual families and communities. Through social mobilization, families need to be stimulated to make the intelligent, informed and free choice of demanding and using immunization services. Correspondingly, the health system must meet their needs and expectations. Programme managers therefore need to advocate for, mobilize and ensure resources (human, materials and supplies, operational costs) in order that the services are available as planned and meet and satisfy the demand created. In this connection, therefore, it is necessary to plan and implement social mobilization activities to sensitize and empower a wide variety of stakeholders to gain and sustain their involvement in immunization and not allow this to lapse over time. Various target groups are partners in this effort, as described in section 5.4 below.

5.3.1 Communication skills

Health team managers should keep their own staff and the public informed and improve their communication skills by:

• providing timely technical information and feedback on immunization programme changes, achievements and the status of indicators
• conducting supportive supervision and on-the-job capacity building of health staff through training and learning opportunities and open and encouraging dialogue and discussion
• assisting staff in liaising with and updating the community, particularly through communication with leaders and during meetings
• training and supervising health staff to identify immunization problems and causes and in effective, good quality health worker/client interaction

Communication with mass media

Below are some suggestions on how immunization staff can work with the media to communicate information effectively on the immunization programme and activities:

Some suggestions on using the mass media (e.g., television, radio, newspapers)

• Develop an informed media network for accurate reporting and to be an ally.
• Inform the media in advance about programmed activities, specifying the date, place and participants so that these activities may be given wide media coverage.
• Sponsor the media to observe immunisation activities and events so that they can cover stories and broadcast information.
• Provide the media with human interest and success stories from the programme.
• Prepare and issue regular press releases to the media for their use in broadcasts or articles.
• Organise regular interviews with the media, involving different advocates of the programme (eg leaders, experts, etc.).
• Advocate with the media allies for regular and varied programmes on EPI (such as phone-ins, talk shows, panel discussions).

Face to face communication has been known to be the most effective way of communicating as it allows for interaction and instant feedback. Health workers should therefore be trained and encouraged to practice good interpersonal communication. This is especially crucial at the health facility level between the health worker and the caregivers. In Kenya, the health worker is the most important and credible source of information on immunization for the caregiver and therefore it is crucial that they inform and motivate caregivers to return to complete all immunizations. The experience of the caregiver at the health facility will determine to a large extent whether or not they returns. For instance a rude health worker will put off the mother. Health workers therefore need to be supervised by the DHMT to ensure that they are polite and helpful, make caregivers at ease, listen and encourage caregivers to ask questions, and use teaching aids to help provide information.

Before the parent leaves, the health workers should establish that they know the following information:
• which vaccine(s) was administered
• the disease(s) it protects against
• which side effects to expect and what to do about them
• the date of return
• importance of taking care of the Child Health Card and bringing it at every subsequent visit.

5.4 THE ROLE OF THE HEALTH WORKER IN IMMUNIZATION COMMUNICATION (with special reference to the District Medical Officer)

In Kenya, the success of any public health programme depends on the team-work of the District Health Management Team (DHMT), consisting of the following Section Heads under the leadership of the Medical Officer of Health: Public Health Nurse, Public Health Officer, Health Education Officer, Hospital Secretary/Administrator, Nutritionist and Clinical Officer. The DHMT members would assist in the planning, implementing, monitoring and evaluating Social Mobilization activities. The team also liaises with other partners (e.g. donors, NGOs, policy-makers) to ensure immunization services.
The role and functions of the Medical Officer of Health (MOH) are crucial in that he is able to use his knowledge, position and expertise in a facilitatory manner to assist in the planning, implementing, supervising, and evaluating the Communication for Immunization process at district level. Physicians (and Clinical Officers) generally manage and supervise rather than give immunizations, therefore their most important EPI role is to advocate for and assure quality of services.

5.4.1 Analysis and Planning

EPI staff should maintain a permanent dialogue not only with vaccination and health staff, but also with the community leaders and caregivers, in order to enhance their understanding of the importance of timely completion of the vaccination schedule. Realistic planning requires that a district “Situation Analysis” be done, including use of existing data from the health information reporting system and surveys especially in terms of: current immunization coverage, knowledge attitudes and practices (KAP) of potential and real service users, missed opportunities for immunization, and population profiles as well as the human and material resources at the disposal of the DHMT

Each district must determine the reasons why their population either accept or refuse immunization. Some of the reasons that have been found in Kenyan studies include:

- lack of adequate and correct information on immunization
- bad experiences at the health facility such as rudeness of staff, overcrowding and long waiting periods
- fear of side effects arising from bad experience with previous immunizations
- false contraindications such as failure to immunize children sick with diarrhoea, cough and malnutrition
- failure to immunize children whose mothers claim previous measles infections
- some health facilities do not immunize on a daily basis
- long distances from Health facilities
- cultural beliefs and rumours

The DHMT should investigate and determine the reasons for non-acceptance of immunization through KAP surveys, Focus Group Discussions, interviews and observations. Through this analysis, the DHMT can develop the immunization communication plan within the AOP. The MO should also collaborate and communicate with other government departments, and non-governmental organizations in order to mobilize more resources to make up for any short-falls from the Ministry of Health's budget.
In addition, the Medical Officer should work with communication specialists to:

- Integrate communication into overall AOPs
- Ensure that a communication specialist is a member of the DHMT, participates in meetings, and provides technical advice to the staff that are implementing the communication interventions as defined in the strategic plan and their terms of reference or job description
- Strengthen the capacity of partners who support immunization and communication
- Coordinate and supervise implementation of communication activities
- Ensure that educational materials and other tools are available and equitably distributed
- Monitor the process and the outcomes of communication interventions for corrective action when and where needed
- Hold meetings with civil society, community groups and with the media to communicate progress, constraints, programme developments, and needs
- Provide feedback to staff, communities, partners, and media
- Involve the community at all levels in planning, implementation and monitoring of immunization activities to ensure demand creation and participation
- Planning, mobilizing and managing resources for communication

The communication strategy should be appropriate to the characteristics of the vaccines or technologies and, in the case of new vaccines, should be included in the Introduction Plans as well as the timelines for preparation, launch, implementation, and monitoring (including the pre- and post-introduction evaluations). Appropriate basic messages for the public need to be developed and tested, based on target audience analysis (e.g. through KAP or other studies or assessments) to assure them that the immunization service is now improved because it offers protection against more diseases and that these vaccines are highly effective and have virtually no side effects. Many of the new vaccines are being linked with existing routine immunization schedules to ensure that children receive more protection early in life but also to minimize efforts for health workers and caregivers (i.e. by not increasing the number of visits required and/or to enable coordinated logistics and program management).

With new vaccines like PCV and rotavirus, there is a need to ensure awareness and understanding of which diseases the new vaccines prevent and that they prevent the most severe strains of the diseases (and therefore will greatly reduce morbidity and mortality from those), but not all strains. As well there is a need to ensure caregivers understand the importance of having multiple injections at the same time.
5.4.2 Implementation

In addition to planning, the MO should actively participate in implementation of communication activities, including information dissemination, training, supervision/monitoring, and promoting immunization communication among government, local (civil society and community) and political leaders to assure them of good quality and available immunization services and motivate them to be involved.

The Reaching Every District (RED) approach has been used in Kenya since 2003 to better address the operational components for a functional immunization program.

The table below outlines how communication can be used to support the RED components:

<table>
<thead>
<tr>
<th>Operational components (RED)</th>
<th>Examples of communication support</th>
</tr>
</thead>
</table>
| Planning and management of resources            | • Advocate for resources to support training of health educators to improve their skills in support of immunisation communication  
|                                                 | • Include key activities for communication in overall EPI workplan and as part of EPI programme activities  
|                                                 | • Include communication line-item in EPI budget                                                                 |
| Reaching target populations                     | • Engage community in planning of immunisation outreach  
|                                                 | • Negotiate with and disseminate information on outreach (e.g. dates, times, location) to communities  
|                                                 | • Encourage health worker to inform communities about services  
|                                                 | • Broadcast outreach schedule through local media and use local contacts to inform community on immunisation visit  
|                                                 | • Share reports with decision-makers to show how outreach improves coverage and can reduce disease burden  |
| Supportive supervision                           | • Ensure that health workers are communicating appropriate messages to caregivers  
|                                                 | • Observe that health workers complete child health records correctly during vaccination sessions  
|                                                 | • Include communication questions in supervisory checklists and questionnaires for exit interviews  
|                                                 | • Observe communication between health workers and caregivers during vaccination sessions and provide feedback  
<p>|                                                 | • Discuss key immunization messages and how to improve interaction between the health worker and the community during supervisory visits |</p>
<table>
<thead>
<tr>
<th>Operational components (RED)</th>
<th>Examples of communication support</th>
</tr>
</thead>
</table>
| **Links between community and service** | • Enhance community ownership by ensuring community involvement in planning and utilisation of immunisation services (e.g. conduct planning meetings with community, provide community with status on immunisation targets)  
• Improve interaction of health workers and clients at every point where services are provided to the public  
• Identify and develop links/partnership with community structures (e.g. religious groups, women's groups, NGOs, traditional leaders)  
• Strengthen capacity of health workers/vaccination teams through training, supervision, to communicate effectively with clients and the community |
| **Monitoring for action** | • Ensure that data set includes details on communication and behaviour-related reasons for drop-out and refusals  
• Share immunisation data with health educators and involve them in data analysis, micro-planning, workplan development, and supervision  
• Include communication component in the monitoring plan with activities strengthening links with community  
• Insert key communication indicators as part of the list of district and facility immunization indicators that are being tracked and monitored |

### 5.4.3 Monitoring and Evaluation

Periodic evaluation of immunization communication is important within the AOP. Although collecting monitoring data helps to identify programme strengths and weaknesses, monitoring alone cannot fix a problem. For example, outcome data may show that mothers’ knowledge about immunization is high while impact data show that desired behaviour is low (no change in drop-out rates). Thus, if monitoring has correctly identified a programme weakness, this should signal further inquiry about why the programme objective (lowering drop-out rate) has not been achieved. It may be a communication issue, service delivery, supply, or management issue.

Monitoring of communication process and outcome should be done in conjunction with other EPI monitoring, adding communication indicators to existing immunization monitoring forms / mechanisms at all levels. Effective monitoring helps determine: if all hard-to-reach groups are being reached, if appropriate channels are being utilized (what channels are most effective at reaching the various participant groups), the impact of communication interventions on the
participant groups’ knowledge, attitudes and practices; the need for and nature of actions to undertake/implement for continuous improvement of activities.

The evaluation of the communication component can be carried out within the overall EPI evaluation exercise or separately to have a more comprehensive view of the role of communication for improving coverage and quality of services. The evaluation can be conducted internally by the EPI staff and externally with participation of experts, which ensures the objectivity of the exercise. The EPI Manager should make sure the evaluation team has a communication specialist to make an in-depth analysis of the communication component. Evaluation will compare the actual outputs, outcome and impact of the communication interventions to the planned ones and determine the extent to which and how communication efforts have influenced the quality and quantity of the immunization services.

The MO will assist in the development of the evaluation tools, seeking collaboration with other government ministries in terms of manpower, equipment and transport needs during the exercise. He will participate in the compilation, analysis and interpretation of the data and information collected, as well as its dissemination to interested parties. Finally he will use the evaluation information for his district’s “forward planning”.

1.8 Target Groups

Some of the target groups which have been identified for advocacy and communication include:

<table>
<thead>
<tr>
<th>Group</th>
<th>Relevance in immunization</th>
<th>MO consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caregivers</td>
<td>Primary participants to ensure child is vaccinated</td>
<td>Ensure effective communication to gain their trust. Provide sufficient information on vaccination program, schedule, safety, side effects, protection</td>
</tr>
<tr>
<td>Community and Religious Leaders</td>
<td>Help shape public opinion and can mobilize their communities to support and/ or participate in EPI</td>
<td>Advocate, build trust and partner with these leaders to garner their support and participation</td>
</tr>
<tr>
<td>Community groups</td>
<td>Influence community members and can mobilize caregivers and foster behavior change and support to EPI</td>
<td>Inform and involve them in immunization activities to identify and track eligible children and target populations (to support activities and prevent left-outs and drop-outs)</td>
</tr>
<tr>
<td>Health educators/ mobilizers</td>
<td>Assist in planning, implementing and monitoring communication interventions to support EPI</td>
<td>Ensure that they have basic, factual information on immunization to inform caregivers and communities (See also activity above for Community Groups)</td>
</tr>
<tr>
<td>Group</td>
<td>Relevance in immunization</td>
<td>MO consideration</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Immunization staff</td>
<td>Critical information sources on immunization, with public and during vaccination sessions</td>
<td>Develop and monitor staff interpersonal communication and counseling skills, and ensure that they are motivated, have proper working conditions and materials, and receive formative supervision</td>
</tr>
<tr>
<td>State, district, facility staff</td>
<td>Provide information and implement plans, guidelines, policies, data from national level. Conduct supervision and provide feedback.</td>
<td>Communicate information to them on new policies, technical updates, and program status in a timely manner and ensure supportive supervision and feedback</td>
</tr>
<tr>
<td>Private sector and NGOs</td>
<td>Provide services to marginalized and hard to reach populations, where health structures weak. Give technical advice, implement health programmes, monitor and collect data, conduct operational research. Can also pressure governments to recognize vaccination as a child right and to provide financing</td>
<td>Solicit their assistance with policy and strategy implementation. Provide them with technical updates and coordinate on planning, monitoring, supervision, identification of bottlenecks and corrective measures, and feedback on results.</td>
</tr>
<tr>
<td>Statisticians</td>
<td>Collect and analyze data that are useful for the program and can be shared with communities for feedback and improvements</td>
<td>Verify that all data collected are analyzed, summarized, used in evidence-based measurable planning and presented to the authorities and the public for feedback and action.</td>
</tr>
<tr>
<td>Mass media</td>
<td>Communicate immunization information to the public</td>
<td>Brief them on immunization issues and progress to equip them with factual information to disseminate. Solicit their support to provide technically correct updates to the public.</td>
</tr>
<tr>
<td>Community media</td>
<td>Accessible to often marginalized or underserved populations. Communicate immunization information.</td>
<td>Involve them in immunization information dissemination and liaise with them to plan and implement strategies for reaching underserved.</td>
</tr>
<tr>
<td>Politicians / policy makers</td>
<td>Support policies/strategies, including ensuring financing and other resources. Advocates in planning and disseminate information.</td>
<td>Advocate with them to ensure sufficient funding and support for immunization plans. Inform them of issues and progress and solicit their involvement to positively promote immunization to the public.</td>
</tr>
</tbody>
</table>
1.9 MESSAGES AND COMMUNICATION CHANNELS

The following were identified by KEPI and various studies as priorities for immunization messages:

• importance of immunization; why immunize a child?
• the diseases children are protected against after immunization
• importance of completing the schedule on time and the consequences of not doing so
• side-effects and what to do about them
• the need to immunize even sick children when they are due
• the need to immunize against measles despite history of measles infection
• the importance of the Child Health Card
• community participation for mobilization for immunization

Using this information, the following basic messages were developed by KEPI, and should be complemented by more focused messages with communities and caregivers, based on local situational analysis and pre-testing:

• All children under 12 months need to be vaccinated against these diseases, i.e. TB, whooping cough, diphtheria, tetanus, measles, poliomyelitis, hepatitis B, Hib, pneumonia, rotavirus, yellow fever.
• Children need to get all immunizations at the right time to protect them from these diseases.
• Immunization prevents death and disability from these diseases.
• An immunized child is a protected child.
• Every healthy child must have an up-to-date immunization card.
• Immunizations are free. You can get them at any health facility.
• Immunizing your children saves time and money.
• Investing in immunization is a priority for Kenya.

Every child who is due for immunization must be immunized unless severely ill or hospitalized.

Messages should be targeted to particular issues and groups and pre-tested before disseminating. They should be motivating, persuasive, credible, and action-oriented.

Maximum effort should be made to have free broadcast and press coverage of the improved immunization service. This involves preparing press releases and briefing materials and holding news conferences at the national and sub-national levels. If affordable, TV and radio can be used to
reach health workers and populations. Traditional media can also be used, particularly to reach underserved populations.

The basic strategy for reaching rural populations is to orient local political, social, educational and religious leaders and organizations. Print materials are appropriate for health workers, but managers should carefully consider whether to prepare print materials addressed to the public, given the cost and the public's ability to understand them and take appropriate action based on the information. Remember that the most important source of information for parents is likely to be local health workers, so be certain that health workers understand the basic messages and are capable of responding to questions and concerns. Community fora can also be important channels, such as women's groups, barazas, District Stakeholder Forum, Dialogue Day, Health Center Management Committee

References


Learning Objectives

By the end of the session, the learner should be able to:

1. Understand the background of EPI disease surveillance
2. Define the term disease surveillance
3. Outline the disease surveillance structure
4. Outline types of disease surveillance
5. Describe steps in EPI disease surveillance
6. Describe steps in investigation for the three EPI target diseases
7. Detect, investigate, report and respond to outbreaks of the three EPI target diseases
8. Understand the role of laboratories in disease surveillance
9. Understand the IDSR concept

6.1 BACKGROUND OF EPI DISEASE SURVEILLANCE

As part of efforts to monitor control, elimination and ultimately eradication of Vaccine Preventable Disease, (VPDs), surveillance unit became an essential component of KEPI. This started as sentinel surveillance but eventually became full-fledged unit with focal persons at all levels of the health sector both public and private.

The disease surveillance unit in KEPI was established in 1995. The unit initially was purposefully established to implement the Global Polio Eradication Initiative through AFP surveillance. Building on the AFP surveillance already in place; measles, NNT were brought on board, but emphasis being, without compromising the quality of AFP surveillance. The same structures were to be used to assist role out Integrated Disease Surveillance and Response in Kenya.
Effective disease surveillance is a key strategy in public health interventions.

Surveillance data is used for

1. Public health decision making and action
2. Improve timeliness of information exchange and dissemination
3. Standardize the data collected
4. Ensure adequate surveillance infrastructure
5. Improve local data analysis
6. Enhance teamwork amongst surveillance partners
7. Optimal use of resources
8. Formulate policy

The experience gained in surveillance will position EPI to address the challenges of disease prevention in future.

KEPI MU surveillance unit has grown over the years and through the surveillance system, the focal persons at National, Provincial and District level support roll out of the IDSR surveillance strategy in the country

**6.2 Surveillance structure:**

Disease surveillance for the EPI target diseases (Polio, Measles and NNT) is made possible by some important factors i.e

- Availability of an effective tool (vaccine)
- Mostly one host (Human)
- Effective broad definition
- To satisfy local and global disease control standards

There are also conditions under surveillance to monitor the efficacy/effectiveness of newly introduced vaccines in the EPI programme e.g. hepatitis B and haemophilus influenzae b, the aim being to determine whether there is justification of having the vaccines in the national immunization schedule for the EPI programme. In Addition, surveillance measures whether the disease burden and pattern has changed over the years since the introduction of these new antigens.
This is done in sentinel sites selected based on agreed criteria. An example is the ongoing sentinel surveillance for rota virus in Kenyatta National Hospital with a view to introducing rota virus vaccine in the national EPI programme.

The surveillance for these conditions/diseases will now be discussed in detail.

- **AFP surveillance for polio eradication**
- **Measles**
- **NNT**
- **Hib/PBM (sentinel)**
- **Rota virus (sentinel)**

**What is disease surveillance?**

Disease surveillance is the collection, analysis, and interpretation of data to determine disease trends and patterns. Disease surveillance provides information such as:

- Disease incidence, morbidity, and mortality, and progress in achieving disease control goals
- Changes in patterns of morbidity and mortality among different age groups in different geographical areas and among different economic, social, or cultural groups
- Impact of immunization strategies on disease incidence
- Disease trends and its determinants in order to improve health

It can also be described as the collection and collation of health data for action.

Is the ongoing monitoring and sharing of information about the trends of disease...
Note: Definitions used in surveillance are symptomatic to ensure sensitivity of the surveillance system in picking suspected cases rather than specificity to maximize case detection.

The overriding value of disease surveillance, however, is its use as a tool to identify the presence of infectious diseases and guide actions to prevent them from becoming threats to public health.

This chapter describes the activities required to carry out that function.

6.3 TYPES OF DISEASE SURVEILLANCE

1. Facility-Based Routine Surveillance - health workers are required to report on the number of individuals that come to their facility and are diagnosed with notifiable diseases. The process of detecting and reporting information on diseases that bring patients to the health facility is known as passive surveillance eg MOH 719.

2. Community-Based Surveillance - With proper training, members of the community can expand facility-based surveillance by detecting and reporting cases that may go undetected by the health facility.

3. Sentinel Surveillance - Sentinel surveillance is the collection and analysis of data by designated institutions selected for their geographic location, medical specialty, and ability to accurately diagnose and report high quality data.

Surveillance Activities
Surveillance for communicable diseases involves:

- Detection
- Investigation
- Reporting
- Analysis and interpretation
- Presentation
- Response

Detection
Surveillance begins with case detection. To accurately detect disease, health workers need case definitions that are appropriate for the local context, and they need practice in applying them, especially when they do not see a specific illness very often such as is the case of Polio. Even with appropriate case definitions, clinical diagnoses can be a problem. Many illnesses have similar symptoms, such as fever and rash, and can be differentiated only by laboratory tests that may not be accessible.
Each facility should have a disease surveillance focal person who should co-ordinate through availing the specimen collection tools, carry out Active Case Search and communicate to the District Disease Surveillance Co-ordinator (DDSC).

Investigation and Reporting
Ministry of health through HMIS require that facilities routinely report the total count of cases of each reportable disease that has occurred within a specified time usually monthly in the MOH 719. When no cases have occurred during the period, the report should indicate this fact (Zero report). For EPI target diseases reporting is case based i.e. each case should be reported individually using the IDS Form.

**Surveillance and Data Flow**

**Summary**

- **Health care facility** (Detect, collect specimens, Investigate and respond)
- **District Health Office** (collect specimens, investigate, Analyze, and respond)
- **National Health Office** (Investigate, analyze, and respond)

Analysis and Interpretation
Surveillance data are of little use for local decision-making and planning unless health workers know how to analyze the data and understand their implications. Health workers need to be able to interpret trends and patterns of disease in order to inact prompt control measures and avoid actions that are not appropriate. In order to analyze and interpret surveillance data, health workers need to be aware of the limitations and peculiarities of the data set. Presentations can be done using graphs, tables, maps etc. An example is shown below
Response

Disease surveillance enables managers to respond to existing problems and take steps to prevent anticipated problems. Responses may include verification of reported cases, treatment, search for new cases, or supplemental vaccination activities, but all must be tailored to the disease and the situation.

6.4 THE ROLE OF LABORATORY IN DISEASE SURVEILLANCE

The major role of the laboratory is to provide timely information on the circulation of the causative organism, which will guide appropriate public health intervention.

In view of the non-specific nature of surveillance definitions, which are symptomatic, to ensure sensitivity of the system in picking suspected cases rather than specificity to maximize case detection; laboratory confirmation is an important component of the national disease surveillance system.

Effective diagnostic virology depends upon correct timing and collection of clinical specimens and their proper transport to the laboratory under optimal conditions. This requires close cooperation between virologists, epidemiologists and clinicians.

The collection of specimens will depend on set criteria for each disease. Details of specimen collection will be discussed during discussion of each disease below.

The EPI diseases/conditions targeted for control have designated and WHO accredited laboratories to investigate and confirm the diagnoses. These laboratories form the global network of WHO accredited laboratories.
In Kenya, the WHO accredited laboratories include

- KEMRI Polio Laboratory
- KEMRI Measles laboratory
- KEMRI Yellow Fever laboratory

Other laboratories supported by WHO for sentinel surveillance include

- KNH Microbiology laboratory
- KEMRI ARI (influenza) Laboratory

In case any of the accredited laboratories fails to meet the accreditation standards, routine splitting of specimens with parallel processing in accredited laboratories has to be instituted. This is to ensure stringent quality standards are maintained to meet the global certification requirements. (Refer WHO\ EPI\ Geneva 97.01)

The core functions of a laboratory include

- Vaccine potency
- Monitoring and verifying transmission
- Monitoring susceptibility profile of the population
- Monitoring sensitivity of antibiotics

**Field Exercise**: To identify, record and summarize cases of priority diseases seen in a health facility. This is a practical exercise (field exercise) to ensure that you have acquired appropriate knowledge and skills in detection and reporting of priority diseases. This will be conducted in an out-patient department of the nearest busy health facility that offers integrated health services (for example a health center or district hospital)

**Tasks**

- The **clinical practitioners** in the group should work alongside their colleagues and assist them in making diagnosis by using standard case definitions provided in the **Technical guidelines** (refer pages 23 to 28 and 197 to 206)
- You should go through the outpatient register and **select new cases of priority diseases** that need reporting to the next level
- Identify about **20** such **new cases** and summarize (linelist) them
- Each group should summarize the strengths and weaknesses of the surveillance system in the health facility
Groups should make recommendation on how to improve the surveillance system

Feedback

Each group should present their findings and recommendations in the plenary

6.5 STANDARD CASE DEFINITIONS FOR EPI TARGETED DISEASES

Ministry of Health targets eighteen notifiable diseases. (Refer to IDSR Guideline August 2004). However this chapter will concentrate on EPI diseases only. KEPI currently targets three diseases (Polio (AFP), Measles and Neonatal Tetanus (NNT) with active surveillance activities.

Epidemic-Prone Diseases

- Measles
- Yellow Fever

Diseases Targeted for Eradication

- Acute flaccid paralysis (AFP)/polio

Diseases Targeted for Elimination

- Neonatal tetanus
- Measles

Measles - Any person with fever and maculopapular generalized rash and cough, coryza or conjunctivitis (red eyes) or any person in whom a clinician suspects measles. A measles death is a death occurring within 30 days of onset of the rash.

Acute flaccid paralysis (AFP)/polio - Weakness or flappiness of sudden onset, not due to trauma, in a child less than 15 years of age or in any case in which a clinician suspects polio

Neonatal tetanus - Normal suck & cry for the first 2 days of life+ Onset of illness between 3 & 28 days of age + Inability to suck followed by stiffness and/or convulsions.

Yellow fever - Any person with sudden onset of high fever (>39E rectal or 38E axillary), followed by jaundice within two weeks of onset of first symptoms.

Simplified messages for use in community surveillance

Inform community health workers, traditional healers, birth attendants, health workers who conduct outreach activities in hard-to-reach areas, and community leaders about the priority diseases and conditions under surveillance in your area. Use simplified messages such as the following to help the community to recognize when a person with these signs should be referred to the health facility.
Simplified community messages

**Acute flaccid paralysis** Any acute paralytic disease  
**Measles** Any person with fever and rash  
**Neonatal tetanus** - Any newborn, who is normal at birth, and then after 2 days, becomes unable to suck or feed.

**AFP (POLIO) SURVEILLANCE**
Weakness or floppiness of sudden onset, not due to trauma, in a child less than 15 years of age or in any case in which a clinician suspects polio

**Current Situation**
Polio eradication initiative has been implemented in Kenya since 1996. The last case of confirmed polio was in 1984, and since then intensified surveillance to detect, report and investigate all AFP cases has been on-going. Kenya attained all the required indicators in 2003 and 2004. However these gains are at the national level but we still have districts and provinces who have not attained all the required indicators. This calls for more action from the facility level in terms of stool adequacy and investigation of all AFP cases within 14 days of paralysis onset.

**Acute Flaccid Paralysis (AFP)**

**Acute**: rapid progression of paralysis, <2-3 days (from onset to maximum paralysis)  
**Flaccid**: loss of muscle tone, “floppy” (as opposed to spastic or rigid)  
**Paralysis**: weakness, loss or diminution of motion
Differential Diagnosis for AFP

Acute Flaccid Paralysis

- Transverse myelitis
- Other enteroviruses
- Traumatic neuritis
- Coxsackie virus
- Echovirus
- Guillain-Barre Syndrome
- Poliovirus

Clinical Spectrum of Poliovirus Infection

- Paralytic poliomyelitis: 0.5%
- Clinical illness, no paralysis: 4-8%
- Asymptomatic infection: 90-95%

Why do AFP surveillance?
- Detect circulation of wild polioviruses
- Demonstrate absence of wild polioviruses
- Show that surveillance meets the performance needed for certification
- Guide immunization activities
Global Eradication of Poliomyelitis

Table 1:

<table>
<thead>
<tr>
<th>What makes it possible?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No significant animal reservoir</td>
</tr>
<tr>
<td>• Effective tool (oral polio vaccine)</td>
</tr>
<tr>
<td>• Survives poorly in environment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>What makes it difficult?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic infection</td>
</tr>
<tr>
<td>• Other diseases with similar symptoms</td>
</tr>
</tbody>
</table>

Strategies for Polio Eradication

• Strong routine immunization programme- target coverage of 80% and above
• National Immunization Days (NIDs) or SNIDs
• Acute flaccid paralysis surveillance
• “Mopping-up” immunization

Health facility staff should search and investigate all cases of AFP within their catchment areas

Why do AFP surveillance?

• Detect circulation of wild polioviruses or
• Demonstrate absence of wild polioviruses
• Show that surveillance meets the performance needed for certification
• Guide immunization activities

Key Indicators for Surveillance Performance

• Non-polio AFP rate in children < 15 years of age:
  Objective: >2/100 000 population < 15 years
• 2 adequate stools collected within 24 to 48 hours apart & within < 14 days after onset of paralysis: Objective: > 80%
What is Adequate Stool Specimen?

Adequate stool specimen entails

- Two stool specimens
- Collected at least 24 to 48 hours apart
- Collected ≤ 14 days of paralysis onset
- Each specimen of adequate volume (8-10 g)
- Packed adequately and shipped in a specimen (vaccine) carrier below 8°C (Note: vaccine carriers used to transport the specimen should be designated as specimen carrier and labeled as so.)
- Arriving within 3 days of collection at KEMRI, Nairobi, in good condition

Stool Collection and Packaging

- Collect at least 1 adult “thumb sized” (8 g) amount of stool
- Place in clean plastic container, such as wide mouthed plastic bottle with an external screw-on cap
- Side of container should be labeled with name, identification number of the case, number of specimen (1 or 2), and date of collection using a water-resistant pen
- Place specimen container in sealed plastic bag
- Store separately from vaccines and other clean items

Store in refrigerator or any container that can maintain temperature below 8°C until shipment has been arranged

Transporting Stool Specimens to KEMRI Polio Laboratory, Nairobi

- Place specimen in vaccine (specimen) carrier below 8°C between frozen ice packs
- Complete IDSR form for each case, including the following information:
  - Date collected
  - Case identification data
  - Date of paralysis onset
  - Date of last OPV dose
  - Place IDSR form, white copy, in separate and sealed plastic bag. This same form will be sent to KEPI. The other three copies of the form should be sent accordingly i.e pink to PMO (PDSC), Green to DMOH (DDSC) Yellow for your surveillance file in health facility.
National Polio Expert Committee, National Polio Certification Committee and National Task Force were constituted by Ministry of Health and KEP to classify all reported AFP cases in line with the Global Polio Eradication Initiative. The figure below illustrates steps taken after a case of AFP is reported.

**Virologic Classification of AFP cases**

1. **Wild poliovirus**
   - No wild poliovirus
     - No residual weakness
     - Residual weakness, died or lost to follow-up
       - National expert committee compatible
       - Discard
     - 2 adequate specimens
       - Discard
   - Inadequate specimens
     - Discard

60 days follow should be conducted for all AFP cases and report submitted to KEPI. This will assist in final classification of all suspected cases.

### 6.6 MEASLES DISEASE SURVEILLANCE

Any person presenting with **Fever and Maculo-papular rash and Cough or Coryza or Conjunctivitis** or any case where a clinician suspects measles

**Current Situation**

Prior to the mass measles campaign in June 2002, suspected measles cases used to be line listed and only 5 specimens collected in an outbreak situation. A measles outbreak used to be confirmed when 5 or more cases are reported from one locality within duration of one month.

After the mass campaign the definition of a measles outbreak changed to **one case of confirmed measles** by laboratory investigation. In addition every case that fits the standard case definition should be investigated individually i.e case based surveillance. A serum specimen should be collected and shipped to KEMRI within 3 days of collection. In case of suspected measles outbreak in an institution, collect only 5 specimen and line list the rest (Refer measles guidelines)
Measles routine coverage is currently very low less than the required target of 80% and above. Due to this the WHO describes the transition phase from campaigns to routine will necessitate follow-up campaigns to continue until:

- national 1st measles dose coverage reach ≥90%
- annual surveillance detection rate of ≥1 suspected measles case per 100,000 population in ≥80% of districts is achieved

For surveillance indicators to guide measles control programme, WHO recommends that at the national level, the minimum detection rate for suspected measles cases with serum specimens should be increased to ≥2 cases per 100,000 population per year.

**Measles differential diagnosis**

Measles presentation resembles many other disease presentations as shown below. All suspected cases of measles must be investigated. Cases in institutions should be investigated and if linkage is confirmed then only five specimens should be collected. All the rest should be line listed but proper details included. Report any case of measles to the DMOH, DDSC or DPHN for immediate action.

NB** Note that every case of confirmed measles case is an outbreak.
What Should Health Provider Do When He/She Suspects Measles?

- Manage case (give vitamin A, encourage fluids, and treat symptoms or complications, if present)
- Collect 3-5mls of blood serum specimen
- Fill out the IDSR case investigation form

Ship specimen to KEMRI within 3 days of collection

Report case to DMOH, DDSC, DPHN

Key Information to Collect on Suspected Measles Cases

Person
- Age
- Measles vaccination status

Time
- Date of rash onset

Place
- Residence at onset
- Potential exposures (places, persons)

Transporting Serum Specimens to KEMRI measles Laboratory, Nairobi

- Place specimen in cold box below 8°C between frozen ice packs

- Complete IDSR form for each case, including the following information:
  - Date collected
  - Case identification data
  - Date of rash onset
  - Date of last measles dose (*IDSR form to be filled to completion)

- Place IDSR form, white copy, in separate and sealed plastic bag. This same form will be sent to KEPI/KEMRI. The other three copies of the form should be sent accordingly i.e pink to PMO (PDSC), Green to DMOH (DDSC) Yellow for your surveillance file in health facility.

Any confirmed case of measles by KEMRI laboratory should be considered as an outbreak and response be done. Every child in the locality should be immunized with potent measles vaccine.
Steps in Outbreak Investigation

1. Complete IDSR case investigation form and collect blood for laboratory confirmation for each suspected case
   - Linelist all cases after first 5-10 with key information if outbreak is in an institution such as schools
2. Notify district health office
   - District health office should notify all health facilities in the area
3. Conduct active case finding in health facilities and villages to identify other suspected cases
   (use clinical course of measles shown below)

**Clinical Course of Measles**

<table>
<thead>
<tr>
<th>Incubation Period (7-18 days before Rash)</th>
<th>Prodrome (about 4 days)</th>
<th>Rash (about 4-8 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-17-16-15-14-13-12-11-10-9-8-7-6-5-4-3-2-1</td>
<td>0+1+2+3+4+5+6+7+8</td>
<td></td>
</tr>
</tbody>
</table>

| Rash minus 18 days is earliest possible exposure date |
| Rash minus 4 days is probable start of infectiousness |
| Onset of rash |
| Rash plus 4 days is probable end of infectiousness |

4. Investigate other suspected cases
   - Collect blood and key information (age, vaccination status)

Analyze data and give feedback to community

Case Management
- Give vitamin A
• Control fever by giving antipyretics
• Tell mothers to return for further treatment if the patient’s general condition worsens
• Treat malnutrition and diarrhoea with sufficient fluids and a high quality diet
• Treat pneumonia with antibiotics
• Respiratory isolation of hospitalized cases

**Measles Treatment with Vitamin A**

<table>
<thead>
<tr>
<th>AGE</th>
<th>Immediately on Diagnosis</th>
<th>Next Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 months</td>
<td>50,000 IU</td>
<td>50,000 IU</td>
</tr>
<tr>
<td>6-11 months</td>
<td>100,000 IU</td>
<td>100,000 IU</td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>200,000 IU</td>
<td>200,000 IU</td>
</tr>
</tbody>
</table>

* For ocular manifestations, give a 3rd dose 2-4 weeks after the 2nd dose

**6.7 NEONATAL TETANUS SURVEILLANCE**

Normal suck & cry for the first 2 days of life + Onset of illness between 3 and 28 days of age + Inability to suck followed by stiffness and/or convulsions

**Neonatal tetanus elimination**

• Definition - Reduction of NNT cases to less than 1 per 1,000 live births in every district in the country. This should be done through
  • Identifying high risk groups/areas
  • NNT surveillance not sensitive

Need 3Cs (*Clean hands* *Clean delivery surface* *Clean umbilical cord and stump care*)
What Should Health Provider Do When He/She Suspects NNT?

- Manage case
- Report case to DMOH/DDSC/ DPHN
- Fill out the IDSR case investigation form
- One case of NNT is considered as an outbreak. Response should be done by immunizing the affected mother and all females of child bearing age in her locality.

**Note:** No specimen is collected for a case of NNT. However the IDSR form should be filled and sent respectively after confirming the outcome, (Alive, Dead, Unknown). The reason for not collecting the specimen in an NNT case is that the *clostridium tetani* spores are present in the environment and thus the source of infection is already known. The clinical presentation is explicit and does not mimic any other condition.

**How to Prevent Neonatal Tetanus**

Two complimentary strategies

Clean delivery - “3 C’s” = “3 CLEANS” (Clean hands, Clean delivery surface Clean umbilical cord and stump care)

- Immunization of mother with potent TT vaccine
- Effective surveillance

**Strategies for NNT Elimination**

- Strong routine TT immunization programme- target coverage of 80% and above
- National Immunization Days (NIDs) or SNIDs •NNT surveillance
- “Mopping-up” immunization

**6.8 HAEMOPHILUS INFuenZAE TYPE B SURVEILLANCE**

**Current Situation**

Kenya introduced *Hib vaccine* in September 2001 under the GAVI support. Surveillance for Hib surveillance is currently at one sentinel site, the Kenyatta National Hospital. However any suspected case of pediatric bacterial meningitis should be investigated through performing an LP.

**Note** that LPs should only be done by qualified staff and when laboratory services are available to process the CSF within one hour from collection. Such cases of suspected meningitis at health facility level should be referred immediately to a higher level. Kiilifi district hospital, under
Wellcome Trust, KEMRI Research activities, started Hib surveillance in 1994 even before the introduction of Hib Vaccine. Data from this unit has shown positive impact in reduction of the Hib disease since the introduction of the vaccine.

**Role of Health worker at facility/community level in Pediatric meningitis/Hib surveillance**

- Manage cases if possible *(Refer to IMCI Guidelines)*
- Ensure prompt referral of all suspected pediatric meningitis cases to a higher level
- Discourage the community from using over the counter antibiotics
- Feedback

**6.9 ROTAVIRUS SURVEILLANCE**

The aim of the surveillance is to determine the disease burden and epidemiology of rotavirus in severely dehydrated children less than 5 years admitted in Kenyatta National Hospital.

**Case Definition**

Suspected case of rotavirus diarrhea-
A child aged less than 5 years who is admitted for treatment of diarrhoea

Confirmed case of rotavirus diarrhea
A suspected case in whose stool the presence of rotavirus is demonstrated by ELISA test.

**Action to be taken**

Collect approximately ¼ full of f stool specimen using standard stool container from every child admitted with diarrhea (irrespective of the degree of dehydration)

Instructions for stool collection:

- Label the stool container with child’s name, IP number, ward and date.
- Give the mother/ guardian the pre-labeled stool container and a spatula and give instruction for stool collection
- Store the collected stool sample in the designated refrigerator in laboratory until time for processing
6.10 INTEGRATED DISEASE SURVEILLANCE & RESPONSE (IDSR)

What is IDSR?

IDSR is a comprehensive strategy for capturing health information of communicable disease for prevention and control by linking community, health facility, district, provincial and national levels. This strategy provides rational use of resources for disease prevention and control.

Currently, many intervention programs have their own disease surveillance systems. Experiences with some disease eradication and elimination programs show that disease control and prevention objectives are met when resources are dedicated to improving the ability of health officials to detect the targeted diseases, obtain laboratory confirmation of outbreaks, and use action thresholds at the district level.

The Ministry of Health lists 18 communicable diseases and conditions for integrated disease surveillance to be implemented. The diseases are recommended because they fall into one or more of the following categories:

- Are top causes of high morbidity and mortality in the African Region (for example, malaria, pneumonia, diarrhoeal diseases, tuberculosis, and HIV/AIDS);
- Have epidemic potential (for example, measles, cholera, and viral hemorrhagic fevers);
- Surveillance required internationally (for example, plague, yellow fever and cholera);
- Have available effective control and prevention interventions for addressing the public health problem they pose (for example, tuberculosis, leprosy and so on);
- Can easily be identified using simple case definitions; and
- Have intervention programmes supported by MOH for prevention and control, eradication or elimination of the diseases (for example, the Kenya Expanded Programme on Immunizations (KEPI) and the Integrated Management of Childhood Illness Strategy (IMCI))

Integrated Disease Surveillance and Response (IDSR) strategy

- IDSR strategy would help to overcome the challenges facing disease surveillance
- Strategy recommended by WHO/AFRO
- Several activities from the different vertical programs would be coordinated to make the best use of resources

Features

1. Surveillance and control closely linked
2. Uses functional approach
3. Surveillance – common public health service

**Recording and Reporting of priority diseases**

- Tools for recording
  - OPD cards
  - Registers
  - Tally sheets
- Tools for reporting
  - Case based surveillance form
  - Line list form
  - Weekly notifiable disease report form
  - Monthly communicable surveillance form
  - Others

**Reporting requirements for priority diseases**

<table>
<thead>
<tr>
<th>Reporting requirement</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report weekly (by Tuesday of following week)</td>
<td>• Cholera&lt;br&gt;• Meningitis&lt;br&gt;• Measles</td>
</tr>
<tr>
<td>Report monthly (By 5th of the following month)</td>
<td>• Cholera&lt;br&gt;• Meningitis&lt;br&gt;• Yellow fever&lt;br&gt;• Measles&lt;br&gt;• Viral hemorrhagic fever&lt;br&gt;• AFP/polio&lt;br&gt;• Guinea worm disease&lt;br&gt;• Neonatal tetanus</td>
</tr>
<tr>
<td>Report quarterly (By 5th of the month following the end of the quarter)</td>
<td>• Leprosy&lt;br&gt;• Tuberculosis&lt;br&gt;• Buruli ulcer</td>
</tr>
</tbody>
</table>

**NB:** IDSR guidelines were reviewed in 2013 and included rabies as a notifiable disease
Eighteen Recommended Diseases

Epidemic-Prone Diseases

1. Cholera
2. Diarrhoea with blood (Shigella)
3. Meningococcal meningitis
4. Plague
5. Viral hemorrhagic fevers
6. Yellow Fever
7. Typhoid fever

Diseases Targeted for Eradication and Elimination

1. Acute flaccid paralysis (AFP)/polio
2. Dracunculiasis
3. Leprosy
4. Neonatal tetanus
5. Measles

Other Diseases of Public Health Importance

1. Pneumonia in children less than 5 years of age
2. Diarrhoea in children less than 5 years of age
3. New AIDS cases
4. Malaria
5. Sexually transmitted infections (STIs)
6. Tuberculosis
7. Rabies
Objectives of IDSR

The general objective of the IDSR strategy is to provide a rational basis for decision-making and implementing public health interventions that are efficacious in responding to priority communicable diseases.

IDSR seeks to:

• Strengthen the capacity of the health system to conduct effective surveillance activities
• Integrate multiple surveillance systems so that forms, personnel and resources can be used more efficiently and effectively
• Improve the use of information for decision making
• Improve the flow of surveillance information between and within levels of health system
• Improve laboratory capacity in identification of pathogens and monitoring of drug sensitivity
• Increase the involvement of clinicians in the surveillance system
• Emphasize community participation in detection and response to public health problems
• Strengthen the involvement of laboratory personnel in disease surveillance

IDSR at district and lower levels

Disease surveillance activities at the district and lower levels is co-ordinated by a District Disease Surveillance Co-ordinators (DDSC) whose activities are as shown below

1. Supervise and co-ordinate Integrated disease surveillance for EPI target diseases and other MoH priority diseases
2. Plan and participate in Integrated disease surveillance bi-monthly meetings and other disease surveillance activities
3. Plan and conduct quarterly Integrated disease surveillance training of identified focal persons, health facility workers and sensitisation of clinicians
4. Develop social mobilisation materials and mobilise communities to participate in Integrated disease surveillance
5. Plan and implement Integrated disease surveillance activities at the community and household levels
The district disease surveillance coordinator will be expected to undertake the following activities (against which performance will be appraised)

The district surveillance coordinator should write a monthly report that should include;

1. Document the causes of late notification/investigation of AFP cases

2. Define and implement strategies to address the problem of late notification/investigation of AFP, MNT and measles cases

3. Undertake monthly sensitisation of health workers in all facilities in the district on disease surveillance

4. Train rural health facility staff on usage of permanent register for immunization and follow up of defaulters

5. Participate in activities that ensure reduction of immunization drop out rates in the district

6. Participle in IEC activities for improvement of immunization coverage in the district.

7. Conduct monthly case search visits to all health facilities (private and public) for priority diseases.

8. Ensure that routine EPI reports are received by the DMOH before the 5th day of every month

9. Conduct sixty day follow up of AFP Cases

10. Contact tracing for measles cases

11. Mobilize divisional and health facility workers to participate in public barazas convened by the provincial administration with a view to strengthening community disease surveillance.

Health Facility level

At this level frontline health workers detect and report diseases. Effort must be made to continue sensitizing them. A lot of work has gone into training on disease surveillance but constant reminders are essential to maintain vigilance on rare diseases for immediate reporting such as AFP. The larger health facilities notably hospitals should maintain a culture of weekly case search using a standard form. The forms used will be retained in the institution for at least 3 years. The district and provincial teams should verify this during their visit. Continuing medical education be initiated in all these facilities at least once every quarter. This should provide the district teams opportunity to discuss disease surveillance with staff.
Suggested benchmarks for health teams

1. Availability of monthly work plans for disease surveillance activities in the hospital
2. Evidence of weekly case search in the facility
3. Evidence of analysis of morbidity/mortality and immunization data i.e. monitoring immunization drop out rates and overages of target population
4. Evidence of follow up of immunization defaulters using the permanent register for immunization
5. Evidence of timely submission of reports to the district level before 5th of every month
6. Continuous Medical Education (CME) sessions conducted in the facility focusing on disease surveillance
7. Follow up and contact tracing for AFP, NNT and suspected measles cases

**Disease surveillance at community level**

**Divisional level**

EPI Disease surveillance at this level has been developed and is being implemented with a focus on the community. Health workers in the health facilities were sensitised in EPI disease surveillance and are reporting, investigating, and following up cases of EPI target diseases.

The provincial and district disease surveillance teams have identified focal persons at the Divisional; Location and S/Location levels presently implementing disease surveillance activities. These focal persons will be utilized to train the community actors.

Specific activities for Divisional level

1. The focal persons at each level will identify community actors to help in EPI target diseases case search.
2. The focal persons will disseminate disease surveillance messages to the community.
3. The divisional coordinator in collaboration with local health facility staff (GOK, NGO/Mission and Private) will hold at least two public social mobilization meetings to create awareness on disease surveillance.
4. Make monthly reports to the District Disease surveillance coordinator
5. Assist in the collection and submission of routine monthly Immunization reports to District level

6. Follow up of defaulters of routine immunization using the immunization register in the facilities

7. Assist in the 60 day follow up and contact tracing of suspected measles cases

8. Reporting and investigating any unusual health event in the community

**Annexes**

1. IDSR Form
2. Line listing form
3. Outbreak reporting form
4. Sixty day follow-up form for AFP cases
5. Measles contact tracing form

**REFERENCES:**

1. Integrated Disease Surveillance and Response-Technical Guidelines –Kenya- 2003
2. Integrated Disease Surveillance and Response for African Region – July 2001
3. Immunization essentials- a practical field guide (WHO)- October 2003
4. Immunization in practice – Module 1- WHO
6. Epidemiology & Surveillance of VPDs – CDC (The Pink Book)
7.1 TUBERCULOSIS (E Amukoye)

INTRODUCTION

One third of the world’s population is infected with Tuberculosis (TB). In 2010, WHO estimated there were 8.5-9.2 million cases and 1.2-1.5 million deaths due to TB. TB is the second leading cause of death from an infectious disease worldwide after HIV (which caused an estimated 1.8 million deaths in 2008).

An estimated 1.1 million died from TB among HIV-negative people and an additional 0.35 million died from HIV-associated TB. Without treatment, mortality rates are very high. In untreated cases up to 70% die within 10 years among culture-positive and 20% smear negative (in HIV negative persons).

World Health Organization (WHO) estimated approximately 1 million new cases and 400,000 deaths due to tuberculosis occur each year in children under the age of 15 years.

In Kenya case notification of all cases of Tuberculosis has been rising by an average of 16% yearly from 14,000 TB cases in 1987 to 106,000 in 2004. The prevalence has also increased from 47/100,000 to 320/100,000. This increase has been largely attributed to high prevalence of HIV in the country. This has recently changed and in 2010, the proportion of sputum smear-positive and smear negative PTB cases has decreased by 3% compared to 2009.

The situation in children is not clear due to lack of standardization in the diagnosis. The Division of leprosy tuberculosis and lung diseases(DLTLD) has consistently reported that Children under 15 years of age contributes 11% of all notified cases. Children in this age group contribute 16% of sputum negative TB cases and 3% of sputum positive.
The control of TB depends mainly in case finding and treatment to reduce the population of infectious individuals. Bacille Calmette Guerin (BCG) vaccine has been used widely in the control of TB but unfortunately it has been found to have a very low protective value against all forms of TB. Research has consistently shown high protective value against severe forms of TB such as TB Meningitis. Thus, the continued use of the BCG vaccine.

**EPI DEMIOLOGY:**

**Aetiology**

Tuberculosis is caused by *Mycobacterium tuberculosis*, an acid, alcohol fast bacillus which is resistant to drying over long periods but very sensitive to light and heat. It grows very slowly multiplying over a period of 20 – 24 hours and is largely a human pathogen but can cause infection in experimental animals such as guinea pigs. Rarely, it causes natural infection in other animals.

**Transmission**

The main route of transmission is by inhalation of infected droplets. The smaller the infected droplets (in diameter), the higher the chances of infection. Other rare modes of transmission are:-

- Transplacental or by aspiration of infected amniotic fluid by a foetus, leading to congenital tuberculosis
- Through broken skin and mucus membranes leading to regional adenitis (e.g. oral mucosa leading to TB cervical adenitis)
- Fomites such as contaminated clothes; bronchoscopes and syringes, have been implicated in transmission, although rarely.

**Risk Factors**

The risk factors can be divided into two:-

i. Risk Factor for acquiring Infection

- Over crowding
- Poor ventilation
- Poor socio economic status
- Pool of untreated TB cases

ii. Risk Factors for developing Disease

- HIV Status
- Malnutrition
- Measles
- Neoplasm (i.e. lymphomas)
- Diabetes Mellitus
- Treatment with immune suppressant such as Cytotoxic/Corticosteroid
- Virulence of the Bacteria
- Recent Infection

**PATHOGENESIS**

Primary tuberculosis in children is characterized by a focus of infection (primary or Gohn focus), lymphangitis and enlargement of regional nodes. All these combined form the Primary or Gohn complex. Tuberculosis lesions in children normally have few *Mycobacterium tuberculosis* as follows (1).

- “fast” growing population, which are easy to kill with anti-mycobacterial agents
- slow growing population, killed very slowly by anti-mycobacterial agents
- intermittently, growing population, also killed slowly (and intermittently) by the anti-mycobacterial agents
- dormant (resting phase) population, that is not killed by any anti-mycobacterial agent.

Thus long treatment duration is needed for infections by this micro-organism to target the various populations of mycobacteria.

**CLINICAL PRESENTATION**

Tuberculosis is a disease which involves all organs of the body with the exception of hair, teeth and nails. It can be divided into pulmonary and extra pulmonary forms.

- Pulmonary tuberculosis is the most common type of tuberculosis in children, found in about 70% - 80% of children with the disease.

Extra pulmonary tuberculosis is frequently seen in children, the most common of these being tuberculous adenitis, tuberculous meningitis, tuberculosis of bone, and miliary tuberculosis. Tuberculous meningitis and miliary tuberculosis have a higher incidence in children than in adults and are associated with high case fatality rates and high incidence of post treatment sequelae.

In making a diagnosis all effort should made to collect specimen for staining and culture. This would include:

- Sputum
  - Spontaneous
  - Induced
• Gastric lavage
• Fine needle aspirate (FNA)

In the Absence of the above one should always suspect Tuberculosis in any child with any two of the following:

• Fever for more than 2 weeks
• Cough for more than 2 weeks
• Unexplained weight loss or failure to gain weight
• Lethargic / fatigued

In the presence of above one can be justified to start treatment if any of the following is present:

• History of contact to open tuberculosis
• Unilateral hilar lymphadenopathy on Xray/ Ct scan
• Tuberculin skin test – TST (Mantoux test)
  • 10mm and above for well nourished immunocompetent children
  • 5mm and above for severe malnutrition or symptomatic HIV children

Other evidence includes:

• Extra pulmonary signs: Such as Cervical lymphadenopathy, meningitis, gibbus, abdominal lymphadenopathy and/or ascites, non painful joint swelling, pleural effusion
• Pneumonia or meningitis not responding response to adequate antibacterial treatment.

Please refer to national pediatric tuberculosis guidelines

**Latent Tuberculosis Infection (LTBI)**

Latent Tuberculosis Infection (LTBI) - when adults are infected, the lifelong risk of developing the disease is 15%. In children the risk is very high. It is upto 43% in infants, 24% in under 5, and 15% in adolescence in the first year of infection

In view of the high rate of developing disease in high risk groups of the population, it is suggested that if there is evidence of TB infection as shown by tests such as tuberculin skin test or gamma interferon test (Quantiferon/Eli-spot) in the following groups:

• young children under 5 years of age
• Diabetes
• HIV infection
• Neoplasm (Cancers)
• Children on immuno-suppressant drugs such as anti-cancer or steroids

They should be treated with Isoniazide preventive therapy (IPT) at dose of 10mg/kg for 6 months. Non high risk children recently exposed or with evidence of infection should be followed up for one year. Should children on IPT or on follow up become symptomatic they should be investigated for Tuberculosis disease and treated.

**TREATMENT OF CHILDHOOD TUBERCULOSIS**

Recommended first line regimen in Kenya for newly diagnosed TB is a 6 month treatment course as follows:

2RHZ 4RH

2 months: Rifampicin + Isoniazide + Pyrazivamide (Intensive phase)

Ethambutol may be added in intensive phase for severe cases (2RHZE) followed by

4 months: Rifampicin + Isoniazide (Continuation phase)

For patients with meningitis, Tb of the bones or joints (osteoarticular) the continuation phase should be extended for a total of 10 months.

The dose and common side effects of first line anti tuberculosis drugs are shown in the table below

**FIRST LINE ANTI-TUBERCULOUS TREATMENT**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Daily Dose</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>10mg (10 – 15mg) / kg</td>
<td>• Hepatotoxicity, (much less in children)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gastric Upset</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CNS effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypersensitive</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>15mg (10 – 20mg) / kg</td>
<td>• Yellow discolouration of body fluid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatitis, skin rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Induces cytochrome P450 (causing rapid metabolism of some drugs)</td>
</tr>
<tr>
<td>Pyrazimamide</td>
<td>35mg (30 – 40mg) / kg</td>
<td>• Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Arthralgias Hyper uriceamia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Skin rash</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>20mg (15 – 25mg) / kg</td>
<td>• Visual impairment (very rare if dose is below 25mg/kg)</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>15mg (12 – 18mg) / kg</td>
<td>• Ototoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Renal toxicity</td>
</tr>
</tbody>
</table>
The principle remains the same as in adults. The “Direct Observed Treatment Strategy” (DOTS) has been adopted to increase adherence and reduce treatment failure. It includes 5 elements:

1. Political Commitment

2. Passive case-finding in general health services by sputum smear microscopy examination of samples from suspected TB cases

3. Standardized short-course chemotherapy administered to at least all smear-positive TB cases under specified case-management conditions with therapy being directly observed

4. Regular uninterrupted supply of all essential anti-tuberculous drugs

5. Monitoring system for program supervision and evaluation

The person who checks and observes the child taking medication is called DOT’s Supporter and usually is the mother.

Do not delay in treating children with Tuberculosis as the risk of developing disseminated Tuberculosis is much higher in children under five.

**TREATMENT OF DEFAULTERS, OR RESISTANT TB**

Patients who default before completing their treatment regimen should be managed as follows:

Attempt to take specimens (sputum, gastric lavage, lymph node aspirate) for mycobacteria cultures. Initiate re-treatment while awaiting culture results with the following regimen:

**Streptomycin + Isoniazide + Pyrazinamid + Rifampicin**

Culture may take 2 to 4 weeks depending on the method used. Culture results guide continued therapy of the patients. Drugs to which the mycobacteria is resistant should be discontinued, and replaced with a second line drug. Second line anti-TB drugs are especially indicated for treatment of patients with mycobacteria which is resistant to first line drugs rifampicin, and/or isoniazid. These cases are difficult to treat, and should be managed by a TB specialist.

The dose and common side effects of second line anti-tuberculous drugs are shown in the following table.
**SECOND LINE ANTI-TUBERCULOUS DRUGS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Daily Dose</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capreomycin</td>
<td>15 – 30mg / kg Iv or Im</td>
<td>• Renal toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ototoxicity</td>
</tr>
<tr>
<td>Quinolones</td>
<td></td>
<td>• Tendonitis, photosensitive dermatitis</td>
</tr>
<tr>
<td>(levofloxacin,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cycloserine</td>
<td>10 – 20mg / kg Oral admin. –</td>
<td>• Emotional behavior</td>
</tr>
<tr>
<td></td>
<td>once a day</td>
<td>• Disturbance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Convulsion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Peripheral Neuropathy</td>
</tr>
<tr>
<td>Para Amino Salicylic</td>
<td>200-300mg / kg Oral in 3-4</td>
<td>• GIT disturbance</td>
</tr>
<tr>
<td></td>
<td>divided doses</td>
<td>• Hypersensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hepatitis</td>
</tr>
</tbody>
</table>

**Management of HIV infected Children**

HIV infected children are at increased risk of developing TB disease due to their deteriorating immunity. When they develop TB, they are at increased risk of developing severe and disseminated forms of TB, and of dying from TB (even after initiating anti-TB treatment) than HIV negative children. Some African studies showed that HIV infected children with TB co-infection responded more poorly to anti-TB treatment and experienced higher mortality than HIV free children. (Soeters et al, Hesseling et al).

Presence of TB defines a child to be in advanced HIV disease, pulmonary TB qualifies as a World Health Organisation HIV stage 3 condition, and extrapulmonary TB a stage 4 (Acquired immunodeficiency syndrome, or AIDS) condition. Children in WHO stage 3 or 4 disease require antiretroviral therapy, in addition to the anti-TB therapy. Treatment of TB-HIV co-infection therefore requires the following special considerations:

**Anti-tuberculosis therapy**

1. PTB – treat with standard 6 month regimen outlined above.
2. Severe, disseminated, or extrapulmonary TB, low CD4 count (CD4 < 15%) – consider more aggressive anti-TB regimen including:
   
   • Four anti-TB drugs during intensive phase (first 2 months)
   
   • Extending regimen from 6 to 9 months, especially if initial response to therapy is slow.
Antiretroviral Therapy

Concurrent antiretroviral therapy (ART) should be initiated after the child completes 2-8 weeks of anti-TB intensive phase treatment, especially if the child is under 5 years old, and/or has a low CD4 count (<20% for children under 18 months, < 15% for older children). In administering anti-TB and ART, multiple drugs will be taken concurrently, and it is important to note and limit drug interactions, and monitor closely for drug toxicity.

Interactions: Rifampicin is a potent inducer of the cytochrome P450 enzyme, and when given together with nevirapine and the majority of protease inhibitors, induces their metabolism leading to subtherapeutic levels and risk of HIV resistance to these drugs. In general, it is advisable not to avoid nevirapine and protease inhibitors (with exception of ritonavir) during anti-TB therapy.

Toxicity: Many anti-TB and ART drugs are hepatotoxic, so liver function should be closely monitored during concurrent anti-TB/ART treatment.

National recommended ART regimens to be used concurrent with anti-TB therapy:

Children < 3 years: Zidovudine or + lamivudine + abacavir
Children ≥ 3 years: Zidovudine or (stavudine )+ lamivudine + efavirenz

After completing the anti-TB regimen, for children under 3 years, abacavir should be replaced with nevirapine, which is the standard third drug for first line ART in this age group.

Immune reconstitution inflammatory syndrome:

After ART initiation the child’s immune system begins to reconstitute, CD4 cells increase, and the ability to mount an inflammatory response is restored. As a result, during the first weeks to months after ART initiation in a child with TB, an increase in inflammatory reaction to TB bacilli may occur, with “apparent” worsening of TB symptoms (e.g. worsening TB pneumonia, effusions, adenitis, expanding CNS lesions). This phenomenon is called the immune reconstitution inflammatory syndrome, and may be severe enough to warrant administration of steroids for 1-2 weeks to moderate the inflammatory response. Care should be taken in looking out for other causes of the worsening clinical signs.

Management of babies born to Sputum Positive Mothers

- Babies of mothers who are Sputum positive at time of birth should receive prophylaxis Isoniazide) for at least 6 months. should receive BCG vaccination after completing isoniazide prophylaxis. If the test is positive they should continue on prophylaxis for a total of 6 months. These babies should be followed up for at least 1 year, and look out for evidence of disease.
IMMUNIZATION

The Vaccine

BCG is a live attenuated vaccine developed in 1921 from Mycobacterium bovis, by Calmette and Guérin at the Pasteur Institute, France. Bacillus Calmette-Guérin (or Bacille Calmette-Guérin, BCG) is a vaccine against tuberculosis that is prepared from a strain of the attenuated (weakened) live bovine tuberculosis bacillus, Mycobacterium bovis, that has lost its virulence in humans by being specially subcultured (230 passages) in an artificial medium.

It has been in widespread use all over the world since the 1940’s following studies that showed its efficacy against tuberculosis to be about 80%.

Efficacy

BCG vaccine may not prevent mycobacterial infection, but has been shown to be effective in preventing the occurrence of disease and even more, preventing the occurrence of severe forms of tuberculosis such as tuberculous meningitis and military tuberculosis.

Efficacy studies done since the introduction of the vaccine in 1921 have created a lot of confusion with reported vaccine efficacy ranging from 0% to 80%. However, there seems to be consistency on the reasonably good protection the vaccine affords when given to young children. Studies from Kenya, Togo, and Thailand on children aged under six years found a BCG vaccine efficacy of 60 to 78%.

This supports continued vaccination of children as early as possible in life, preferably soon after birth, as the newborn does not get passive immunity against tuberculosis from the mother. There is evidence that BCG vaccine given to preterm children will offer adequate protection.

Side Effects

Side effects and complications following BCG vaccination have been observed and reported right from the early of BCG vaccine use, in the 1920s. However in the initial stages, these were not accepted either because the complications were not bacteriologically confirmed or because the acid-fast-bacilli were not identified beyond question as those from BCG.

Our knowledge was considerably enhanced after the Second World War, when BCG was widely applied nationally and internationally. Since then many cases with mild complications have been reported. However, severe infections have been reported rarely.
The frequency of the complications has been significantly reduced by vaccine standardization and improved operational conditions such as strict observation of the dose and intradermal administration (16).

From the available data, it is now accepted that the expected “normal” rate of occurrence of adverse effects is 0.1% to 4% (17). Rates above this may require investigations to determine the underlying reasons.

The following adverse effects have been reported:

- **Local abscesses** at the vaccination site commonly follows subcutaneous administration of BCG. They are rare with intradermal injection (17).

- **Persistent Ulcer** occurs as the vaccination site, and is characterized by discharge of serous fluid for more than four months after injection (18).

- **Regional and widespread lymphadenitis** is the most common adverse effect of BCG vaccination. This may be either suppurative or non-suppurative and occurs with an incidence of 0.1% to 4% (17). Lymphadenitis is commonly associated with administration of a larger than recommended dose (17) and has been observed to be more frequent with Pasteur and Danish types of vaccines than with the other types (17).

- In Kenya, because BCG is given on the left fore-arm, adenitis usually occurs in the left epitrochlear and left axillary glands, and occasionally at the supraclavicular region and other gland sites. Many people have used isoniazid, thiazina or erythromycin to treat this complication (19, 20). There is, however, no good evidence to support use of these drugs (21).

- Appropriate management of BCG adenitis includes reassurance of the parent and aspiration of fluctuant nodes. If the glands are red hot and tender it may suggest secondary infection especially by streptococcus or staphylococcal organisms.

- Aspirates sent for Ziehl Neelsen stain and culture are positive for AFB in about 50%. There is however no indication for treating even those who are positive.

- **Osteomyelities**: This is a rare complication and occurs at the rate of about 0.1 to 30 per 100,000 vaccinees (17). It should be treated with anti-tuberculous drugs.

- **Disseminated BCG infection**: A very rare, but at times fatal complication occurring at a rate of less than 0.1 per 100,000 vaccinees. It occurs in individuals with underlying immunodeficiency states, and should be treated with anti-tuberculous drugs (17).

- Other adverse effects include; lupus vulgaris, maculopapular skin rash, and anaphylaxis (22, 23).

**Contraindications**

There are no absolute contraindications for BCG vaccination. However, since the advent of HIV infection, it has been noticed that some children with clinical AIDS developed widespread BCG...
infection. No similar problem has been noticed in asymptomatic HIV positive children. It is therefore recommended that BCG should be given to all asymptomatic HIV infected children, but should be withheld from children with clinical AIDS (24).

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17. WHO Document on BCG vaccination of the Newborn, Rationale and guidelines for country programmes. WHO/TB/86. 147, EPI/GEN/86/10, 1986


7.2 POLIOMYELITIS (INFANTILE PARALYSIS) (E M Wafula)

INTRODUCTION

Poliomyelitis is an acute communicable disease caused by poliovirus, one of the enteroviruses, which are RNA viruses belonging to the Picornaviridae family. Poliomyelitis is caused by three distinct strains of poliovirus, namely Types 1, 2 and 3. Coxsackieviruses (named after a town in New York) and Echoviruses (enteric cytopathogenic human orphan viruses) are also enteroviruses and may cause acute illness resembling poliomyelitis1.

The earliest historical record of poliomyelitis was in Egypt about 16-14 Century B.C., which showed a tomb-stone engraving of a young priest with a withered, shortened leg, the characteristic deformity of paralytic poliomyelitis1. However, it was not until 1789, when Michael Underwood, a London paediatrician, published the first medical description of the condition. This was followed, during the second half of the 19th Century, by the firm establishment that the spinal cord was the anatomical site of the pathologic process of the disease. Finally, in 1908, Landsteiner and Popper transmitted the disease to monkeys by inoculation of human spinal cord homogenate.

Overall, in the 24 years since the Global Polio Eradication Initiative was launched in 1988, the number of cases has fallen by over 99%, from an estimated more than 350,000 cases in 1988 to 1352 reported cases in 2010. In the same time period, the number of polio-endemic countries was reduced from 125 to 4, (namely, Afghanistan, Pakistan, Nigeria, with India probably moving out of this category.

Here in Kenya, the first recorded poliomyelitis epidemic Kenya occurred in 1921–1922. Thereafter epidemics occurred on a 3 year cycle and became endemic in the country (Table 1), with specific epidemics reported by Walker A. J. 1956, Endall N. R. E. in 1958, 1960, and 1962. The last outbreak of 1965-1966 was reported by Kaur and Metsellar in East Africa Journal in 1967.

Table: Notified Polio Cases in Kenya

<table>
<thead>
<tr>
<th>Serial No.</th>
<th>Year</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1954</td>
<td>538</td>
</tr>
<tr>
<td>2</td>
<td>1957</td>
<td>617</td>
</tr>
<tr>
<td>3</td>
<td>1960</td>
<td>1003</td>
</tr>
<tr>
<td>4</td>
<td>1963</td>
<td>Aborted</td>
</tr>
</tbody>
</table>

* OPV immunisation carried out in late 1962 prevented the anticipated 1963 epidemic

Source: Bull. Wld Org. 48:421 (1973)
Late in the 1960’s, after several of these outbreaks, the Ministry of Health (MOH) decided to introduce OPV immunisation for most susceptible populations at appropriate periods in a bid to prevent or abort the anticipated 3-yearly epidemics of poliomyelitis. Early in 1972, a nation-wide immunisation campaign against poliomyelitis in eligible children was carried out with the help of lay volunteers. Two rounds were successfully carried out in February/March and June/July periods \(^5\). Not only did the anticipated outbreak in October 1972 fail to occur, but since then no serious poliomyelitis outbreaks were recorded until 2006, 2008, 2010.

A comprehensive review of patients with poliomyelitis admitted to Kenyatta National Hospital polio unit in 1969, 1970 and 1971 was carried out by Ayim E. N. in 1974 and comprised of 78 cases. Out of these, 25 cases were confirmed on stool culture as due to poliovirus with type 1 Poliovirus responsible in 15 cases and type 3 Poliovirus responsible in 10 cases. A few cases were confirmed from CSF and post mortem findings. The majority of the cases (95%) were below six years. The last case of confirmed poliomyelitis infection in Kenya before the polio importation in 2006 was in 1984 and was confirmed by stool culture when type 2 Poliovirus was isolated\(^7\). Incidentally, in the same year, the Institute of Primate Research of National Museum of Kenya reported an outbreak of poliomyelitis among black and white colobus monkeys (colobus abyscinicus Kikuyuensis) in captive environment. The outbreak was confirmed by stool culture, at KEMRI Virus Research Laboratory, to be due to type 1 Poliovirus.

The administration of polio vaccine is effective in preventing the recipients from developing or suffering from poliomyelitis. There are two polio vaccines, the oral vaccine or the Sabin variety is a live attenuated vaccine, and the inactivated vaccine or the Salk variety is administered by intramuscular injection. Both polio vaccines are given in three doses with at least a month between the vaccine doses \(^1,8\).

The Sabin or oral vaccine is the earliest vaccine to be developed and is cheaper and easier to use. The oral polio vaccine was used extensively worldwide and is highly effective and was expected to provide lifelong immunity when a full schedule of three doses are appropriately given. The immunity following the appropriate four-dose vaccination with the oral polio vaccine appeared to be lifelong while that following the vaccination with the inactivated injectable one is for many years, although the actual number of years is unknown\(^1,8\). Experience during the Polio eradication initiative has demonstrated that one needs about 5 doses in the African setting and about 10 in the Indian setting to provide complete immunisation. This is partly due to the interference of the uptake of the vaccine virus by other viruses or other health conditions.

In 1988, the forty-first World Health Assembly, consisting then of delegates from 166 member states, launched a global initiative to eradicate polio by the end of the year 2000. This followed the certification of the eradication of smallpox in 1980, progress during the 1980s towards elim-
ination of the poliovirus in the Americas, and Rotary International’s commitment to raise funds to protect all children from the disease.

In 1994, the World Health Organization (WHO) Region of the Americas (36 countries) was certified polio-free, followed by the WHO Western Pacific Region (37 countries and areas including China) in 2000 and the WHO European Region (51 countries) in June 2002. Widely endemic on five continents in 1988, polio is now found only in parts of Africa and South Asia.

Progress from 2001 to 2002 includes a reduction in polio-endemic countries from ten to four, and possibly presently to three. Over 500 million children were immunised in 93 countries during 266 supplementary immunisation activities (SIAs). Globally, polio surveillance improved in 2002, as reflected in an increase in acute flaccid paralysis (AFP) rates from 1.6 cases per 100,000 population in 2001 to 1.9 cases per 100,000 population in 2002⁹.

Despite these achievements, the Polio Eradication Initiative faced an increase in global cases in 2002 over 2001. In 2002, 1919 cases were reported (as of 16 April 2003), compared to 483 in 2001. This increase and the subsequent ones in the following years are attributed to epidemics in India and Nigeria and importation mainly from Nigeria and, in some situations, re-establishment of poliovirus circulation in a number of countries in West Africa, Central and Eastern Africa, the Middle and the Far East⁹.

To eradicate poliomyelitis from the world, the Global Polio Eradication Initiative (GPEI) spearheaded by WHO, Rotary International, the US Centers for Disease Control and Prevention (CDC) and the United Nations Children’s Fund (UNICEF) was formed and in turn formed the Global Polio Eradication Technical Consultative Group (TCG) to oversee a programme of research and consensus-building which would lead to the development of post-eradication polio immunisation policy options. On the other hand, the World Health Organisation mandated its member countries to form two critical national bodies composed of local health experts, namely the National Polio Eradication Expert Committee and the National Polio Eradication Certification Committee, to spearhead the initiative within each country⁹.

**Surveillance and Control Strategies for Poliomyelitis**

To facilitate the global eradication of poliomyelitis, the Global Polio Eradication aims at:

- interrupting transmission of the wild poliovirus as soon as possible and certifying all WHO regions polio-free by the end of 2005 (this was not achieved and is now for the future, possibly 2015);
- implementing the polio endgame programme of work, including containment of wild poliovirus, global polio-free certification, and the development of a post-eradication immunisation policy; and
• contributing to health systems development by strengthening routine immunisation and surveillance for communicable diseases.

In order to fulfil these aims the Global Polio Eradication Initiative has set out to: achieve and maintain high infant immunisation coverage with four doses of oral polio vaccine in the first year of life;

1. provide supplementary doses of oral polio vaccine to all children under five years of age during national immunisation days (NIDs);
2. carry out surveillance for wild poliovirus through reporting and laboratory testing of all cases of acute flaccid paralysis (AFP) among children under fifteen years of age;
3. carry out targeted “mop-up” campaigns once wild poliovirus transmission is limited to a specific focal area.

The Global Commission for the Certification of the Eradication of Poliomyelitis was set up by WHO with the prime purpose of carrying out independent certification of absence of wild poliovirus from all countries. The Commission subsequently developed the principles and guidelines for the certification process and established in its six regions Regional Certification Commissions.

The Global Commission for the Certification of the Eradication of Poliomyelitis established the following criteria for the certification of polio eradication:

• Absence of circulation of indigenous wild poliovirus for at least a three-year period during which surveillance activities have been maintained at the level of performance needed for certification;
• A National Certification Committee (NCC) in each country has validated and submitted the required documentation to the Regional Certification Commission (RCC or ARCC for the Afro Region);
• Appropriate measures are in place to detect and respond to importations of wild poliovirus into polio-free areas;
• Appropriate measures have been taken for laboratory containment of wild poliovirus infectious or potentially infectious materials.

Regional Certification Commission (RCC) is responsible for certification in its respective region but does so only for the whole region but not for an individual country.

The NCCs play a critical role in supporting the efforts of the ARCC for the Afro Region. They must critically review and validate all national data before submitting the national documentation.
to claim polio-free status to the ARCC. NCCs in countries that have already submitted national documentation need to provide annual update reports on the maintenance of polio-free status to the ARCC until regional certification is achieved.

The control strategies for polio eradication in Kenya are similar to those in other countries and consist of high infant immunisation coverage, supplementary doses of polio vaccine to all children under 5 years during National Immunisation Days (NIDs), surveillance for wild poliovirus through reporting and laboratory testing of all cases of acute flaccid paralysis (AFP) among children under 15 years of age.

The polio eradication initiative in Kenya is spearheaded by the National Polio Eradication Expert Committee and National Polio Eradication Certification Committee with the Kenya Expanded Programme of Immunisation providing the secretariat services earlier, but now the Division of Disease Surveillance and Response, in the Ministry of Public Health and Sanitation.

Whereas immunisation is the mainstay of eradication of polio and although enhancement of coverage is a major initiative, the polio eradication campaign is mainly a surveillance exercise, targeting polio victims. In the campaign, the polio victims are identified by acute flaccid paralysis involving one or more of the limbs of the victim.

The polio victims are identified at health institutions and in the community. The victims need to be evaluated within 2 weeks of the onset of the symptoms. This requirement is necessary because polio victims shed the highest concentration of polioviruses in their stools within 2 weeks after the onset of symptoms and thereafter the concentrations fall off. The stools of the polio victims are therefore obtained within 2 weeks after the onset of symptoms, and transported in appropriately cooled environment to KEMRI laboratories within 3 days of obtaining the stools. In the KEMRI laboratories the stools are examined and cultured for polioviruses. This arrangement maximises the isolation of polioviruses from the stools. If polioviruses are isolated, then the polioviruses are sent to South Africa for genetic mapping and sequencing to determine whether the polioviruses isolated were wild polioviruses or vaccine ones. Presently, however, the KEMRI polio laboratory is able to discriminate wild polio from vaccine polio virus and specimens are sent to South Africa only for genetic mapping and sequencing.

Normally, acute flaccid paralysis due to polio infection is asymmetrical and tends to progress over a period of a few days and does not recover, get better or regress. However, initially, victims of poliovirus infection may have some pain or discomfort in limbs and may appear to have acute flaccid paralysis when they do not actually have paralysis. The discomfort or pain in such children regresses over time and they recover their normal function. Consequently, the detailed characteristics of the acute flaccid paralysis is noted and recorded at the first review, and then a sixty-day follow-up is carried out to confirm the status of the flaccid paralysis. If the paralysis
persists at the 60-day follow up, is asymmetrical, and sensation is maintained, then the prospects of it being poliomyelitis are increased. However, the confirmatory evaluation is based on the culture results of the stool of the patient\textsuperscript{1,11}. If the stool examination does not grow any poliovirus then the acute flaccid paralysis is presumed not to have been due to poliovirus infection. When the stool is not optimal, like when the patient presents over 14 days from the onset of symptoms, or when the stool was not kept or stored in appropriately cool environment or stayed over 36 hours from the time the victim passed it to the time it arrives in KEMRI laboratories, then the clinical features and the results of 60-day follow up play a much more important role in deciding whether it was polio or not.

The major role of the National Polio Expert Committee is to go through the clinical details with regard to acute flaccid paralysis (AFP) and also the stool details (both its condition at reception in KEMRI and its culture results) of every AFP victim and classify him or her appropriately, either as victim of wild poliovirus infection or not. In a few patients with inadequate stool, or those who were identified after more than 2 weeks of symptoms it may be difficult to make such a decision. Accurate recording of the acute flaccid paralysis, timeliness of evaluating the AFP victim (namely within 14 days of onset of symptoms), the adequacy of the stool (namely appropriately transported and kept cool and received in the laboratory within 3 days of its being voided), the laboratory culture results of the stool and the condition of the victim on follow up 60 days after the onset of symptoms are crucial for classification of patients with AFP.

Victims who are reviewed after 14 days from the onset of symptoms, and/or whose stool is received in the laboratory more than 36 hours from the time it was voided, require a closer evaluation that includes physical review with all the clinical notes from the reporting institution, together with a report on their condition on review at 60 days from the onset of symptoms. After the classification of the AFP victims, the National Polio Eradication Expert Committee submits their classifications to the National Polio Certification Committee to evaluate it for certification. The National Polio Eradication Certification Committee makes their reports and submits them to the Ministry of Health and the Regional World Health Organisation.

**Epidemiology, Clinical Manifestations, Complications, Management and Prognosis**

**Epidemiology**

Man and certain species of chimpanzees are the only known reservoirs of polioviruses. The transmission of the viruses from an infected to a susceptible person is by both faecal-oral and oral-oral routes. Most infections of poliovirus in many countries are due to type 1 polioviruses and a few cases by poliovirus type 3. The type 2 poliovirus is no longer in circulation.
Poliomyelitis tends to affect mostly children under the age of five years and tends to decrease in the older age group, although it can affect any age. Infection tends to be more in crowded situations with poorer hygienic conditions. Only 1 out of 200 of those infected by poliovirus manifest flaccid paralysis of one form or another. The rest are either asymptomatic or manifest minor non-specific symptoms\textsuperscript{1,9}.

There are only a few countries that are considered to be endemic for poliomyelitis with consistent isolation of wild poliovirus from them. More countries have however experienced some polio epidemics: in some of these countries, the poliovirus has succeeded in re-establishing circulation within the population but in a few the importation has been effectively controlled and stopped\textsuperscript{9}.

Initially, there was a lot of optimism with respect to achieving the eradication of polio from the world and global efforts were seemingly bearing fruit until 2002 when some northern Muslim states in Nigeria stopped polio vaccination. This action by the Muslims in Nigeria was due to misinformation that gave the impression that polio vaccination was harmful to their children. As a result of this stoppage of vaccination, a poliomyelitis epidemic started in these states and spread to other parts of Nigeria, then to other countries in West Africa, Central Africa, Eastern Africa, the Middle East and even the far East. Although vaccination against polio was restarted in the affected states after appropriate concerted effort, the Polio Eradication Initiative suffered a major setback in its programme\textsuperscript{9}.

Life long immunity specific to the viral strains exposed to follows appropriate vaccination with the live attenuated virus (OPVV), or on recovery from an infection with the wild poliovirus. Acute flaccid paralysis may follow infection with other enteroviruses or may be due to Guillain Barre Syndrome, transverse myelitis, or trauma and may be difficult to distinguish from poliomyelitis on clinical grounds\textsuperscript{1}.

Pathogenesis

Poliomyelitis is a highly infectious disease and is acquired by ingestion. After infection, there is an incubation period of 7-14 days and the victim is infective from between 3-4 days before the end of the incubation period and sheds most viruses in the faecal material within the first 2 weeks after the onset of symptoms although viruses have been isolated from the stool as long as 3 months later. After ingestion, the wild poliovirus gets access to the mucosal cells of the oropharynx, mainly the tonsil, and Peyer’s patches in the ileum. The polioviruses multiply and stimulate the production of 1GA secretory antibodies; this immune response often arrests the disease at this stage. However the poliovirus overcomes the local gut immunity in a small percentage of those affected and gains access to the regional lymph nodes, entering the blood stream and the lymphatic system and leading to viraemia and accesses the anterior horn cells and the basal ganglia where it destroys the motor neurons and causes paralysis and related complications\textsuperscript{1}. 
Clinical Manifestations

Initial symptoms are fever, fatigue, headache, vomiting, stiffness in the neck and pain in the limbs. One in 200 infections leads to irreversible paralysis (usually in the legs). Among those paralysed, 5%–10% die when their breathing muscles become immobilised.1,10,12.

The course of the illness after infection is manifested in four clinical forms:

Inapparent or asymptomatic poliovirus infection forms up to 90% of those infected with the poliovirus and can only be identified by the isolation of wild poliovirus in the stool or presence of specific humoral viruses in the blood.

Abortive form of poliovirus infection resembles an attack of influenza and is manifested by a febrile illness with sore throat, malaise, anorexia and headache, in older children.

Non-paralytic form of poliovirus infection resembles the abortive type but has in addition muscle pains and stiffness of the neck and back.

Paralytic form of poliomyelitis is the typical form found in only 0.5% of those infected with the wild polioviruses. Paralytic poliomyelitis involves the spinal cord and the brain stem (bulbar polio) in 90% and 10% of cases, respectively. It very rarely involves the brain cortex. The spinal form of paralytic poliomyelitis in children under the age of three years affects lower limbs in over 75% of cases. It is usually asymmetrical and usually affects one limb only. Initially the limb muscles are painful and there is an abrupt onset of flaccid paralysis as evidenced by reduced muscle tone, reduced power and loss of deep-tendon reflexes. Sensation remains intact. Muscle wasting from disuse comes much later.

Bulbar poliomyelitis includes involvement of the cranial nerves and brain stem. It presents with flaccid paralysis of all four limbs and inability to swallow, cough or sneeze and often results in aspiration pneumonia. Respiratory failure may ensue. The rare cortical form presents with drowsiness, irritability or disorientation.

The paralysis of poliomyelitis progresses rapidly and is complete within 3 days and thereafter it regresses a bit. It is worth noting that several studies have shown that over 40% of children suffering from acute poliomyelitis had received an injection, (irrespective of the drug used) during the febrile incubation period. It is recommended that children with suspected poliovirus infection should not be given any injections.1,12.

Complications

Complications of paralytic poliomyelitis include melena severe enough to require transfusion as a result of superficial intestinal erosions; acute gastric dilatation occurring during the acute or conva-
lescent stage leading to embarrassment of respiration; mild hypertension probably related to lesions of the vasoregulatory centres in the medulla and especially to underventilation; skeletal decalcification with hypercalcaemia and nephrocalcinosis and electrocardiographic abnormalities suggesting myocarditis¹.

Mortality in large urban epidemics in the United States of America in the prevaccine era was 5-7% and most of the deaths occurred within the first 2 weeks after onset. Mortality and degree of disability tends to be greater after puberty. Observations in Bombay City showed that 15% of paralytic cases make a complete recovery while 75% do not recover or have partial recovery¹²(This however may not necessarily be true, because observation is not able to exclude other causes).

In spinal poliomyelitis there is atrophy of the affected limb and poor blood circulation. This results in arrested growth of the whole limb, which becomes shortened and withered. Residual paralysis usually involves the muscles that extend the hips and knees and dorsiflex the ankles. Contracture are common.

Management

Management of poliomyelitis should aim at allaying the fears and concerns of the patient and of the relatives and preparing them for what might be prolonged hospitalisation for the paralytic patient, anticipating, minimising and managing complications, including neuromusculoskeletal forms.

Patients with the abortive form of poliomyelitis should be managed with administration of analgesics, sedatives, bed rest and adequate diet. Physical exertion is discouraged for the following 2 weeks. The nonparalytic form of polio infection should be managed similarly except that hot packs and hard bed are included and analgesics are administered for a long time, sometimes for weeks. Gentle physical therapy may also be administered.

Patients with paralytic polio should be hospitalised in a quiet atmosphere. Suitable body alignment assuming a neutral position and use of sandbags, splints and boards is encouraged. As soon as pain reduces, active and passive motions are encouraged. Constipation is common and need to be managed and bladder paralysis may also occur, requiring manual compression or catheterisation under aseptic conditions. Adequate diet should be provided and the patient should receive both orthopaedic and emotional support during this period.

For patients with pure bulbar poliomyelitis, the airway must be maintained, avoiding all risks of inhalation of saliva, food or vomitus and feeding by nasogastric means. Sometimes tracheostomy may be necessary because of the vocal cord paralysis and the constriction of the hypopharynx. Intravenous infusion is given to maintain electrolyte balance. Close monitoring is necessary for these patients including blood pressure and looking out for early signs of respiratory insufficiency so that mechanical ventilation can be initiated promptly¹.⁸.
THE DEVELOPMENT AND USE OF POLIO-VACCINES

Vaccine Development

Injectable Polio Vaccine (IPV)

IPV is a killed, formalin-inactivated, injectable vaccine, developed by an American virologist and physician Dr. Jonas Salk in 1954 and licensed in 1955. Its wide use thereafter in the U.S.A. during the period 1955-1962 led to a 95% reduction of poliomyelitis from 21,000 per year before its introduction to less than 1000 per year after it was introduced. However, IPV tends to confer individual immunity mainly and very little herd immunity. Even in individual children a very limited gut immunity is produced. The longevity of protection against Polio after IPV vaccination is not quite clear but appears not to be life-long.

Later on, van Wezel in Holland introduced the enhanced-potency IPV (E-IPV) vaccine that stimulates practically 100% of recipient infants to produce protective levels of antibodies after only two doses at 2 and 4 months of age.

Advantages of IPV include its safety for administration to children with immune deficiency diseases or those on immunosuppressive therapy since it contains no live poliovirus1,13.

Oral Polio Vaccine (OPV)

OPV is the live attenuated oral polio vaccine developed by Dr. Albert Sabin of the U.S in 1957 and licensed in 1962. It is a polyvalent vaccine, containing types 1, 2 and 3 strains of poliovirus. The OPV multiplies in the gut after oral administration and induces local IgA secretory antibodies that provide resistance to re-infection by the wild poliovirus. The OPV vaccine with the three strains of polio, or trivalent vaccine, has been the WHO-recommended vaccine against poliomyelitis for both routine use and also during epidemics. Presently, with the apparent disappearance of type 2 polio and the limited circulation of type 3 polio, the monovalent polio vaccine with type 1 polio is being used preferentially in efforts to contain epidemics for polio. This preferential use of type 1 OPV is because it is the one responsible for most polio epidemics at the moment and the use of the monovalent vaccine achieves greater immune response and protection1,9. Where type 3 polio is responsible for the epidemic, then monovalent type 3 vaccine could be used.

The advantages and disadvantages of OPV are outlined in the table below:
Advantages and Disadvantages of OPV Vaccine

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Advantages of OPV Vaccine</th>
<th>Serial No.</th>
<th>Disadvantages of OPV Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Confers both humoral and intestinal immunity like natural infection</td>
<td>1</td>
<td>The vaccine viruses may mutate, though in very rare instances, and cause paralytic polio.</td>
</tr>
<tr>
<td>2</td>
<td>Immunity induced may be life-long.</td>
<td>2</td>
<td>Vaccine virus spreads to household contacts (this may be a problem in vaccine-derived poliomyelitis)</td>
</tr>
<tr>
<td>3</td>
<td>Induces antibody very quickly in a large proportion of vaccinees</td>
<td>3</td>
<td>Vaccine progeny virus spreads from persons to persons in the community in this way “vaccinating” even persons who have not agreed to be vaccinated</td>
</tr>
<tr>
<td>4</td>
<td>Oral administration is more acceptable to recipients than injection and is much easier to administer.</td>
<td>4</td>
<td>In certain warm climates, the induction of antibodies is unsatisfactory in a high proportion of vaccinees.</td>
</tr>
<tr>
<td>5</td>
<td>Administration of the vaccine requires minimum expertise.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>During epidemics, the vaccine not only induces antibodies quickly but also rapidly infects the gut, blocking the spread of the epidemic virus.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>It is relatively inexpensive both to produce the vaccine itself and to administer.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>It can use the human diploid cells in its preparation, and is not dependent on monkeys, which are scarce</td>
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<td></td>
</tr>
</tbody>
</table>


In some tropical countries, OPV “take rate” has been found lower than in temperate countries, where vaccine efficacy is 95%. Various factors have been incriminated in this, including:

- Interference by other enteroviruses already present in the gut.
- The presence of antibodies in mothers’ breast-milk.
- The presence of cellular resistance in the intestinal tract owing to previous exposure to naturally circulating polioviruses (or perhaps related viruses).
- Protein deficiency
- The presence of an inhibitor in the alimentary canal of infants.

Vaccine Storage, Handling and Use

Viability of vaccines is dependent on the maintaining of the cold chain, that is appropriately cold temperatures for the vaccines from the factory where they are manufactured to the time they are
administered to the recipients. Temperatures warmer than those recommended for the cold chain tend to inactivate or destroy the vaccines, making them to be of no protective value.

The temperatures at which the vaccines should be stored should be at -20°C at the manufacturing factory and at the central, regional and district vaccine stores, that facilitates storage for several months, while that at the health facility and other peripheral storage units should be at 0°C to 8°C since they are expected to be administered after relatively short periods.

OPV is the most heat sensitive of all the EPI vaccines.

In November 1984, the EPI Global Advisory Group recommended that the first OPV dose be given at birth (“birth dose”). Questions have been raised about the interference of the ‘take rate’ of OPV birth dose especially during the first three days of life. Maternal antibodies (transplacental or in colostrum) have been partly blamed for this, given that the level of secretory IgA antibodies in colostrum is four times the levels in breast milk after the fourth day of life. However, studies have shown that 30-80% of breast-fed babies given OPV within the first three days of life shed polioviruses in faeces (an indication of gut colonization) and 20-40% developed humoral antibodies. When the baby gets OPV1 at 6 weeks, the take rate is much better than in those children who did not get the birth dose. Thereafter OPV2 (at 10 weeks) and OPV 3 (at 14 weeks) produce very high gut and humoral immunity.

**Side Effects of Polio Vaccine**

A rare OPV-associated paralytic poliomyelitis may occur in vaccinees or their close contacts. This is estimated at one case per 4 million vaccinees. Obviously the advantages of preventing paralysis from wild polioviruses far outweigh this rare complication.

**Future Recommendations**

KEPI has already adopted the WHO Resolution 41.28 of May, 1988 calling for the eradication of poliomyelitis from the face of the earth by the year 2000 AD 14. The WHO African Regional Round Table Discussions in August 1988, in Brazzaville, urged African member countries to plan for this ambitious target after agreeing that an immunisation coverage of 80-85% with protective doses of polio-vaccine would probably interrupt the poliomyelitis virus transmission.

The following six suggestions were proposed:

1. Countries to increase and sustain poliomyelitis immunisation coverage as soon as possible
2. Disease surveillance (poliomyelitis as well as the other EPI-target diseases) to be improved
3. Laboratory capabilities to be strengthened so that they can effectively isolate and characterize polioviruses as well as to carry out vaccine quality control and viral serologic surveys
4. The creation and maintenance of public awareness and provision of information and education to communities with regard to poliomyelitis and other EPI-target diseases.

5. Improvement of poliomyelitis rehabilitation services for the unfortunate persons who might be inflicted by the disease.

6. Promotion of research to develop better eradication strategies, improved polio-vaccines or vaccine combinations.

Other agencies, notably the Rotary International, have joined WHO and UNICEF in this noble endeavour. The Rotary International in 1985, pledged to help eradicate poliomyelitis through its Polio Plus Programme, by their centenary year, 2005 AD. In Africa 30 out of 46 countries, in the WHO African Region, Kenya included, have Polio Plus Programmes supported by Rotary International.

Kenya managed to get her application for having fulfilled the requirements for polio free status approved by the WHO ARCC committee during its meeting in October 2005 in Lusaka, Zambia. The challenge is to maintain what that approval entails, given that some neighbouring countries, namely Sudan, Ethiopia, and Somalia have reported isolation of wild polio virus within their borders. This has been demonstrated by the epidemics that Kenya has had following importations from Somalia, Sudan and Uganda.

UVI in Kenya intends to introduce IPV in 2015. One of the booster doses of OPV shall be replaced by IPV.

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15. 15. WHO Bulletin 56:31 (1978)
7.3 HEPATITIS B DISEASE  (R Kamenwa)

INTRODUCTION

Approximately 350 – 400 million people worldwide are chronically infected with the hepatitis B virus (HBV), and approximately 1 million die annually of HBV-related disease. The worldwide prevalence of hepatitis B virus ranges from 0.1% to 20%. This wide range is largely due to differences in age at the time of infection. Following acute HBV infection, the risk of developing chronic infection varies inversely with age: 90% for perinatal infection, 25–35% for infection at age 1–5 years and less than 10% for adults. About 45% of the world population live in areas where chronic HBV is highly endemic (≥8% of the population are hepatitis B surface antigen (HBsAg) positive), 43% live in intermediate-endemicity areas (2–7% HBsAg-positive) and 12% live in low-endemicity areas (0.6% to <2% HBsAg-positive). In the WHO European Region the HBsAg sero-prevalence ranges from 0.3% to 12% with up to 3.5 million carriers. Central Asian republics and parts of Eastern Europe are high endemic areas. Intermediately endemic areas include eastern and southern Europe and the Russian Federation, while northern and Western Europe are low endemic areas.

More than 2 000 million people alive today have been infected with HBV at some time in their lives. Three quarters of the world’s population live in areas where there are high levels of infection. Every year there are over 4 million acute clinical cases of HBV, and about 25% of carriers, 1 million people a year, die from chronic active hepatitis, cirrhosis or primary liver cancer.

In developing countries the majority of Hepatitis B Virus (HBV) infection is acquired in early infancy or childhood. The acute infection often goes unrecognized and most of the morbidity and mortality from this disease occurs many years later. This has resulted in failure of appreciation of the full impact of this disease.

Currently, effective, affordable treatment for Hepatitis B disease is not available. Immunization is the mainstay for prevention and control of the disease.

Structure of HBV

HBV is a double stranded DNA virus belonging to a unique virus group referred to as HEPADNA. Electron microscopically, the whole virus (DANE PARTICLE) is 42nm in diameter.

The virus consists of a central core and an outer coat, both of which are antigenically represented as Hepatitis B core antigen (HBeAg) and Hepatitis B Surface antigen (HBsAg) respectively.

Hepatitis B Markers

The following hepatitis B markers have been identified:
• HBsAg was the first HBV marker identified and was named Australian antigen by Brumberg in 1967. The presence of HBsAg in blood is an indication of acute or chronic infection. Persistence of HBsAg beyond six months in the blood indicates chronic hepatitis B carriage. When it disappears, the antibodies against hepatitis B (anti-HBs) are formed. This indicates immunity to hepatitis B.

• HBcAg is deeply seated in the nucleus and is not found in the blood. It can be detected in liver tissues after liver biopsy. However its antibody, the anti-HBc antibody (anti-HBc) is found in blood. The antigen (HBcAg) and the antibody (anti-HBc) appear concurrently at the time of infection. The presence of the antibody (anti-HBc) indicates acute or chronic infection which can be differentiated by doing IgM or IgG anti-HBc. IgM anti-HBc indicates acute infection within one year and IgG indicates chronic or past infection.

• HBeAg is found in the blood and its presence indicates viral replication and therefore high infectivity of the patient. Anti-Hepatitis Be antibody (anti-HBe) appears in the blood once the antigen disappears and indicates reduced infectivity.

• DNA polymerase is an enzyme found in the blood during infection and indicates active replication of the virus.

• HBV-DNA is the most sensitive index of viral replication or infectivity.
The table below provides a summary of the markers.

Serological Markers of Hepatitis B Virus*

<table>
<thead>
<tr>
<th>Term</th>
<th>Abbreviation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B virus</td>
<td>HBV</td>
<td>Aetiologic agent of ‘serum’ hepatitis: also known as ‘Dane particle’</td>
</tr>
<tr>
<td>Hepatitis B surface antigen</td>
<td>HBsAg</td>
<td>Surface antigens of HBV, detectable in large quantity in serum; several subtypes identifiable</td>
</tr>
<tr>
<td>Hepatitis B e antigen</td>
<td>HBeAg</td>
<td>Associated with HBV replication, high titre HBV in serum and infectivity of serum</td>
</tr>
<tr>
<td>Hepatitis B core antigen</td>
<td>HbcAg</td>
<td>Function uncertain, no commercial test available and so cannot be detected in circulating blood</td>
</tr>
<tr>
<td>Antibody to HBsAg</td>
<td>Anti-HBs</td>
<td>Indicates infection with and immunity to HBV, passive antibody from HBIG, or immune response from HB vaccine</td>
</tr>
<tr>
<td>Antibody to HBeAg</td>
<td>Anti-Hbe</td>
<td>Presence in serum of HbsAg carrier indicates lower titre of HBV</td>
</tr>
<tr>
<td>Antibody to HbcAg</td>
<td>Anti-Hbc</td>
<td>Indicates prior infection especially IgG with HBV at some undefined time</td>
</tr>
<tr>
<td>IgM class antibody</td>
<td>IgM anti-HBc</td>
<td>Indicates recent infection with HBV, and acute viral hepatitis, detectable for 4 to 6 months after infection. Such patients are highly infectious</td>
</tr>
</tbody>
</table>

**Epidemiology**

**Transmission and Risk Factors**

HBV is detected in blood and body fluids (semen, saliva, nasopharyngeal fluids), and there are four major modes of transmission:

- Sexual contact
- Mother-to-child transmission in pregnancy and at birth (perinatal)
- Parenteral (blood-to-blood)
- Horizontal transmission through close personal contact or sharing of infected items. This mode of transmission is seen mainly in early childhood.

The most predominant mode of HBV transmission is perinatal. If a pregnant woman is an HBV carrier and is also hepatitis B e antigen (HBeAg)-positive, her newborn baby has a 90% likelihood of being infected and becoming an HBV carrier. Of these, 25% will die in adult life from chronic liver disease or liver cancer. Although HBsAg, HBeAg and HBV DNA have been detected in breast milk no differences in HBV transmission rate according to feeding practices in early childhood have been demonstrated.

Other conditions that favor HBV transmission include:

**Kenyan Situation**

In some parts of Kenya up to 12.5% of children under 4 years have been found to be HBsAg positive and by adolescence over 50% have some marker of HBV infection, with 7 -10% being carriers of HBsAg.(13, 14, 15). Results of different studies have varied depending on the geographic area and the diagnostic method used.

Greenfield et al (13,16) established that perinatal transmission is relatively unimportant in Kenya, as a result of low levels of circulating HBV-DNA in the maternal plasma. They found 8% of 3000 mothers to be HBsAg positive and only 4 Ol,l of 52 samples of HBsAg positive mothers were HBeAg positive and 32 were anti-HBe positive. Based on the above findings in conjunction with the: very low prevalence of anti-HBc at 12 months it would seem that in Kenyan children, perinatal transmission does not play an important role and that HBV transmission is mainly horizontal.

**PATHOGENESIS AND PATHOLOGY**

HBV is not cytopathic, but it is the immune elimination of infected hepatocytes which results in the clinical symptoms and the histopathological changes of HBV infection. Both the cell mediated immunity (CMI) and humoral immune response play a role.
The CMI response which is modulated by interferons, results in lysis of infected hepatocytes, with the cytotoxic T cells directed against the nucleocapsid protein displayed on the surface of the hepatocyte, playing a major role in this process. Humoral immune response is directed against the envelope proteins of HBV (which include the PreS1, PreS2 and S gene-encoded region).

**CLINICAL PRESENTATION**

Incubation period averages 75 days. The incubation period for infection acquired via transfusion of blood or blood products may be shorter.

Infection with HBV results in massive replication of virus in the hepatocytes. The viruses are then released into the blood. Replication of the virus in the liver, and the host immune responses to it, are responsible for the acute and chronic manifestation of the infection. Most infections go unrecognized as symptoms may be mild or non specific. Same patients develop an acute self limiting illness accompanied by jaundice and elevations of the liver enzymes.

The likelihood of developing clinical hepatitis as a result of HBV infection varies directly with age. In infancy and childhood, though fatal cases do occur, only 1 - 10% of acute infection are diagnosed clinically. While 33% of patients older than 30 years develop symptomatic disease (17). Fulminant hepatitis is also commoner in older individuals. A fulminant course may be related to enhanced immune response with rapid clearing of virus and high titors of anti-HBs and anti-HBe. This may be associated with features suggesting immune complex disease manifested as fever, urticarial rash and arthralgia.

**HBV Carriers**

A carrier is a person whose serum is repeatedly HBsAg positive over a six month period or longer. 10% of sufferers of HBV infection will become chronic carriers of the virus, with the possible later development of chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC).

The chances of developing HBsAg carrier state decreases with age. During infancy, it is as high as 90% in infants born to HBeAg positive mothers compared to 7.7% carrier state in persons infected after the age of 30 (17).

Males are 6 times more likely to become carriers than females. Development of the carrier state seems to depend on the humoral and CMI response of the patient. When these are defective, viral replication continues with an increased likelihood of chronic carrier state. This is especially important in neonates, patients with malignancies and other immuno-compromised states.

The carrier state therefore occurs more commonly in:

- males
• those acquiring infection in childhood
• those with immuno-deficiency states

It is this chronic carrier state with its associated liver damage that is of importance. It is the stage that immunization programmes are geared to eradicate.

Chronic hepatitis often occurs in carriers, with insidious progression to macronodular cirrhosis and eventual development of hepatocellular carcinoma.

The factors that eventually cause malignant transformation are unknown but viral integration into the host genome and cessation of replication in the transformed cells has been shown in liver tumours. Other incriminating evidence are:

• HBV-DNA has been isolated in the genome of HCC cells
• HCC in all parts of the world is associated with a higher HBsAg seropositivity than in age-sex matched controls
• In Taiwan a prospective study among Chinese men revealed that the risk of HCC among HBsAg carriers was approximately 100 times higher than among non-carriers(18)
• Experimental studies with woodchucks (small forest animals found in N. America) who experience natural infections with viruses which are structurally very similar to HBV, showed them to be at increased risk for developing HCC.

Complications of HBV infection

Complications of HBV infection include:

• acute hepatitis
• chronic hepatitis
• cirrhosis
• vascular disease
• glomerulonephritis
• primary hepatocellular carcinoma.

Though case fatality for acute HBV infection is estimated at 1.5 per 1000, studies have shown that the relative risk of dying among individuals with serologic markers are higher. When considering males younger than 40 years, Feret et al in Senegal found that those who were HBsAg positive were 3.5 times more likely to die than the controls.
The morbidity of HBV though as yet unmeasured, probably has even a greater negative economic impact in developing countries due to decreased productivity since chronic hepatitis, cirrhosis, and hepatic cellular carcinoma affect principally individuals from 15 to 59 years of age (8). Beasley et al (18) found that HBsAg carriers had a 280 times greater risk of developing primary liver cancer than HBsAg negative individuals. In Asia, the cumulative risk of developing HCC for HBsAg carriers over a 50 year period has been estimated to be 15% (19).

**Chronic Hepatitis**

Chronic active hepatitis develops in about 25% of HBsAg carriers with eventual progression to cirrhosis or chronic liver failure, or hepatoma.

A person with stable chronic hepatitis may suffer relapse, marked by elevations in the serum transaminase. Relapse may be spontaneous, (in 10 - 15% of patients annually), or due to super-added infection from delta virus, hepatitis A, Non-A Non-B(NANB) or may follow antiviral therapy.

During HBV infection, the viral genome becomes an integral part of the patients genome, such that viral genes are transcribed along with those of the host. Clones of these integrated cells form the basis of malignant transformation.

**MANAGEMENT**

The management of HBV infection will depend on whether it is acute or chronic.

**Acute Infection**

There is no known effective treatment and case management is geared towards supportive care.

**Chronic Hepatitis**

Two types of chronic hepatitis are distinguished as treatment varies in these 2 categories:

- Chronic Hepatitis in individuals who are HBeAg positive
- Chronic Hepatitis in those who are anti-HBeAg positive or HBeAg negative.

**Chronic Hepatitis with HBeAg Positivity**

Antiviral agents are administered to accelerate clearance of HBeAntiginaemia. These agents include adenine-arabinoside-monophosphate (Ara-AMP) and interferon.

**Chronic Hepatitis with anti - HBe Positive**

In asymptomatic persons or those with only mild symptoms, conservative measures are offered. If symptomatic, with grossly abnormal liver tests, and an active chronic
hepatitis on liver biopsy, then a short course of prednisolone (for about 8 weeks), the withdrawal of which is followed by a course of Ara-AMP or interferon has been shown to have good results.

**Co-Infection**

**Coinfection or superinfection with HDV**

Co-infection or superinfection with delta virus has been associated with an increased morbidity and mortality from both acute and chronic HBV infection. Hepatitis Delta virus (HDV) is a defective virus that is only infectious in the presence of active HBV infection. HDV infection occurs as either coinfection with HBV or superinfection of an HBV carrier. Coinfection usually resolves. Superinfection, however, causes frequently chronic HDV infection and chronic active hepatitis. Both types of infections may cause fulminant hepatitis.

**Coinfection with HIV**

- HBV infection is associated with increased severity of liver disease in HIV-infected patients.
- In HBV/HIV-coinfected patients, necroinflammatory activity in the liver tends to be milder, but higher HBV replication results in more severe liver fibrosis with increased risk for cirrhosis and a more rapid progression to end-stage liver disease.
- Patients coinfected with HIV and HBV, especially those with low CD4+ nadir counts, are at increased risk for liver-related mortality.
- HIV appears to be a risk factor for reactivation of hepatitis B in patients who have developed hepatitis B surface antibodies, especially in patients with severe immunodeficiency.

**Super-infection with Hepatitis C**

Acute HCV infection in patients with Chronic HB infection may be associated with more severe symptoms during the acute phase. Patients with HCV superinfection have higher cumulative rates of liver cirrhosis and hepatocellular carcinoma than acute HBV superinfection or CHB. Underlying HBV infection is also an important factor determining the clinical course of acute HCV infection. Fulminant hepatic failure is significantly higher among those with underlying HBV infection.

**Super-infection with Hepatitis A**

Acute Hepatitis A virus infection is severe and potentially fatal in patients with underlying chronic HBV.
CONTROL AND PREVENTION

Methods of control include:

- **Health education**

Health education aimed at change of behaviour patterns that favour spread of HBV. Blood is considered as an important vehicle for infection and thus its screening for HBV markers is essential. Sharing of razors and toothbrushes and the use of unsterilized needies and syringes should be avoided. It should be remembered that the primary source of infection is the acutely infected individual and the chronic carrier.

- **Immune Serum Globulin (Hepatitis B immunoglobulin HBIG)**

HBIG is human immune globulin prepared from pooled human plasma from persons with high titers of anti-HBs.

It is used primarily for prevention of perinatal transmission of HBV in mothers who are HBeAg positive. 90% of HBeAg positive carrier mothers infect their babies while only 5% of HBeAg negative mothers infect their babies. To be effective it should be given within 48 hours of delivery.

The dose of HBIG is 0.5mls, containing at least 300 IU and can be given concurrently with HBV vaccine using different injection sites. It has been shown that concurrent use of vaccine and HBIG for infants born to mothers with high levels of circulating HBeAg can prevent the chronic carrier state in 85-95% of such infants, whereas use of vaccine alone can prevent the chronic carrier state in 70-90% of such infants.

Limitations of HBIG include high cost and short duration of prophylaxis. In newborns, antibodies to HBsAg decline 2-3 months after HBIG therapy, leaving the infant at risk of infection. Because of these reasons, many countries, for economic and logistic reasons would opt for HBV vaccination alone.

- **Immunization**

No effective therapy has been found for treating the chronic HBV carrier state. Change of some of the behaviour patterns associated with transmission are difficult to modify, therefore the mainstay of control of this disease depends on prevention of transmission by immunization of populations at risk.

**What Levels are Protective?**

Several studies have shown that anti-HB titres greater than 10 IU/L are protective against the disease, though Szmuness in his study found that after immunization, the vaccine efficacy was protective regardless of the antibody levels.
Goal of HBV Immunization

The goal of immunization is protection against HBV carrier state with its consequent development of liver disease and hepatocellular carcinoma. HBV has been claimed to be the first anti-cancer vaccination.

Rationale for Immunization

• The goal of vaccination is particularly to prevent the carrier state and hence avoid its sequelae. The risk of developing the carrier state is highest in infancy and early childhood and drops rapidly with increasing age. The age at lowest risk of becoming a carrier is not known.

• In same areas of Kenya up to 25% of the population have HBsAg, with 90% showing markers of previous or past infection. Most of these infections start early, though perinatal transmission is not important.

• This set-up is ideal for justification of hepatitis vaccination during infancy.

• If used in early infancy, it can reduce chronic carrier rates by over 75%. HBV infection differs from other EPI-targeted diseases in that the majority of the related morbidity and mortality occurs during the adult period following relatively asymptomatic perinatal or childhood infection.

• The importance of HBV is stressed by the fact that more than 40% of persistently infected persons who survive to adult life will die as a consequence of their infection.

• Mortality from HBV must thus be viewed with regard to effect of deaths of an economically productive adult. A mortality rate of 0.5% per year from HBV related liver disease in adult carrier males has been observed in hyper-endemic area. Since HBV carriage rate in hyper-endemic areas is about 10-15%, death due to liver disease would therefore account for 3% of the deaths.

• Incorporating HBV vaccine into the existing EPI programme would be economically feasible since logistical support, cold-chain provisions, and the vaccination schedule would allow administration of other antigens at little additional cost for delivery. With reductions of cost of HBV vaccine, the cost of preventing death from the HBV related HCC and cirrhosis approaches that reported for the EPI diseases.

• Since EPI vaccination schedules differ from country to country, there should be some flexibility in dosage schedules for HBV vaccine in order to allow for integration of this vaccine with the other EPI antigens.

• In the high risk adult population HBV vaccine protects from development of acute infection which though more severe than in childhood, has lower risks of progressing to a chronic carrier state.
**VACCINE DEVELOPMENT AND USE**

Epidemiologic studies of natural hepatitis B infection showed that the development of anti-HBs conferred protection against subsequent infection. Consequently an effort was made to produce a vaccine using purified HBsAg as the immunogen. Two generations of HB vaccine have been developed namely:

- First generation plasma derived vaccine
- Second generation HB vaccine

**First Generation Vaccines**

Development of a HB vaccine was initially hampered by the inability to grow HBV in cell culture, but the pioneering work of Krugman et al established the feasibility of producing a vaccine from serum containing HBV Ag.

First generation plasma derived vaccines were developed by separating these particles from the complete virus in the blood of chronic carriers, and were licensed for use early in the 1980’s.

Usually, during HBV infection or even in the carrier state, apart from the whole virus particle (Dane particle) there are several tubular and spherical particles about 22nm diameter representing surplus viral coat protein (HBsAg). These particles are antigenic and stimulate the production of anti-HBs. Anti-HBs is believed to be the protective anti body and the aim of vaccination is to stimulate production of anti-HBs.

To render this vaccine safe, it undergoes several purification processes. major purification processes.

- heat inactivation
- formalin
- hyperosmolar urea

Each of these methods can destroy whole HBV as well as any other infective agent currently identified (including HIV).

Plasma from the donor is also screened for HIV antibodies and reverse transcriptase activity (to detect retroviruses).

**Second Generation HB Vaccines**

Three approaches have been used to produce second generation HB vaccines:
• **Recombinant DNA Technology**
Molecular cloning and sequencing of the HBV genome and the identification and cloning of the S-gene which codes for the major viral surface polypeptide led to the production of HBsAg by genetic engineering.

Currently yeast derived HB vaccines are in use and several studies have shown them to be safe, highly immunogenic and effective.

• **Synthetic Peptides**
Peptides of 8 to 12 amino acids following the amino acid sequences of hydrophilic regions of the surface antigens that are thought to be the specific antigenic sites have been produced. The main disadvantage of this type of vaccine has been its low immunogenicity. Research is currently focused on enhancing the response by attachment of the peptide to large carrier molecules.

• **HBsAg - Producing Hepatoma Cell Lines**
HBsAg particles produced by hepatoma cell lines are identical to those detected in plasma of HBsAg carriers. The main concern about the use of vaccine derived in this way has been the safety of using a vaccine that might contain oncogenes, especially since other “safer” HBV vaccines are available.

**Vaccine Dosage**
The vaccine dosage depends on the type of vaccine being used. Manufacturers process and formulate their vaccines differently, preventing meaningful comparison of dosages of vaccine from different sources.

According to data submitted to WHO/EPI/Geneva by manufacturers in 1990, an efficacious paediatric dose may include anywhere from 1.5 to 10.0 ug of active material, depending on the manufacturing process.

**Vaccine Storage and Handling**
Most HBV vaccines are moderately stable at room temperature but appear to be stable for many years at 2 to 8 degrees C. The upper limit of storage life has not yet been defined and can be expected to vary among different manufacturers. Inactivation of the vaccine occurs at high ambient temperature and by freezing. The Kenya Expanded Programme on Immunization's recommendation is 0 to +8°C.
As with other adjuvanated vaccines such as DPT, freezing results in vaccine-adjuvant dissociation. Freezing does not result in any visible changes in the vaccine, thus emphasizing the precaution to avoid freezing and to include freeze indicators during shipment and storage. HB vaccine should be handled the same way as DPT vaccine.

The prospect of using a quadruple vaccine (DPT-HB) holds great promise for facilitating the introduction of HB vaccination. It would obviate the need for a great deal more cold chain and storage space as well as for more needles and syringes.

**Compatibility with other Vaccines**

Studies monitoring post-vaccination antibody titers have shown that HB vaccine can be given with BCG, diphtheria, tetanus, pertussis, polio, measles and yellow fever vaccination, with no reduction in immune response to any of the vaccines (28,29).

A quadruple vaccine of DPT-HB is being planned. All 4 immunizing agents are proteins which are adjuvanated and handled in a similar fashion.

**Indications for Vaccination**

The hepatitis B vaccine is recommended specifically for all infants and children. It is also recommended that adults in high-risk groups be vaccinated.

The following list is a general guide for vaccination, but since every person is at some risk for infection, these guidelines should be individualized for each situation.

- All infants at birth and all children up to 18 years.
- Health care professionals and emergency personnel.
- Sexually active teens and adults.
- Men who have sex with men.
- Sex partners or close family/household members living with an infected person.
- Patients with kidney disease or undergoing dialysis.
- Residents and staff of correctional facilities and group homes.
- Any person who may fall into a high risk group due to occupation or lifestyle choices.

**Age at Vaccination**

The epidemiology of the carrier state is the primary determinant of the age at first dose. In Kenya, as in other parts of sub-Saharan Africa, transmission is primarily horizontal rather than vertical or perinatal. While early vaccination is strongly recommended to minimize the time period during which there is risk of acquiring infection, it is not essential that the first dose be given immediately after birth. Therefore, vaccination can be given at birth, or soon after birth.
For practical purposes it could be given as three doses, 4 weeks apart concurrently with DPT starting at the age 6 weeks. Reasons for giving it at this time are:

- hospital deliveries account for less than a half of all deliveries in developing countries, therefore not all babies will be seen at birth. In Kenya, only about 30% of all deliveries are conducted in hospitals, therefore this would not be an opportune time.
- giving HB vaccine at birth may meet with same obstacles, as mothers may not like their babies receiving 2 injections (BCG is normally given at birth in Kenya)
- it would be logistically simpler and more cost effective to incorporate HB vaccine into the existing KEPI immunization schedule if it was given together with the DPT. This would also improve compliance as it avoids increasing the number of hospital visits
- with the development of the quadruple vaccine (DPT,HB) this would mean administering one injection instead of two.

**Recommended Route and site**

The recommended route of administration for HB vaccine is intramuscular.

Though the intradermal route would be cheaper in terms of using a lower dosage, it is technically more difficult to administer an intradermal injection in infants. If such an injection is inadvertently given subcutaneously or intramuscularly, then it would be ineffective and leave the child unprotected.

For neonates the recommended site is the anterior aspect of the thigh. In adults it is the deltoid region (gluteal region produces an inferior immune response - probably because of thickness of fatty layer, the injection may not be truly intramuscular).

**Duration of Protection**

Following the third and last dose in the HBV immunization series, anti-HBs titres decline after about 5-6 years(7). There is individual variation in the rate of decline. In infants and children there have not been long enough follow-up studies to determine when to give booster doses.

Studies have shown that even when anti body levels become undetectable, individuals seem to remain protected against clinically significant disease (HBsAg carriage or liver inflammation), provided that the initial anti body response was effective. Boostering to maintain anti-HBs levels above 1 OU/mi were found to be unnecessary in endemic areas. Beasley, found that in Taiwanese children the initial fair in anti body titers does not continue probably because of “natural boosters”(30). Booster doses may therefore be unnecessary to maintain effective immunity and to prevent new carriers.
The vaccine has not been used long enough to establish documented evidence in prevention of chronic hepatitis, cirrhosis or HCC. However the ability of the vaccine to reduce or prevent HBV carrier state - the forerunner of HBV induced chronic hepatitis, more than justifies promotion of immunization program's.

**Immunogenicity**

HBsAg antigenicity is enhanced by absorption to an alum adjuvant.

**Factors influencing immunogenicity**

Immunization in early childhood is more effective than in adults and immunogenicity in neonates is excellent irrespective of HBV marker status of the mother. Maternal antibodies or even HBIG administration does not inhibit anti body production after vaccination. freezing inactivates the vaccine because it causes vaccine-adjuvant dissociation.

**Non Responders**

Although the majority of persons vaccinated against hepatitis B successfully respond to vaccination, an estimated 5-15% of persons may not respond. It is possible that a person who does not respond to the vaccine may already be infected with hepatitis B. Therefore, testing for the presence of the virus (HBsAg) is recommended before diagnosing a person as a “vaccine non-responder”.

- Non-responders who are HBsAg-negative should be considered susceptible to HBV infection and should be counselled regarding precautions to prevent HBV infection and the need to obtain HBIG prophylaxis for any known exposure to HBsAg-positive blood.
- Non-responders who prove to be HBsAg-positive should be counselled regarding how to prevent HBV transmission to others and regarding the need for medical evaluation.

Repeated immunizations result in seroconversion in some of the initial non-responders. This effect is enhanced if larger doses are used.

**Efficacy of Vaccine**

The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults. After 40 years, protection level drops below 90%; by 60 years protective antibody levels are achieved in only 65-75% of vaccines. The duration of protection based on current evidence is life long.

**Side Effects**

Side effects are few and are local and transient. They include pain and swelling at the injection site. Fever and flu-like symptoms have been reported in a few cases. These side effects are mainly due to the adjuvant (alum) used in the vaccine.
Acceptance and tolerance have been shown by widespread use of plasma derived vaccine in European health workers and Asian EPI Programmes. Among 8 million doses of Pasteurs vaccine no cases of AIDS, HBV, NANB or autoimmune disease has been associated with the vaccine. Anxieties have been expressed about safety of plasma derived vaccine and AIDS. However follow up of male homosexuals and medical staff vaccinated in US found no evidence to implicate the vaccine in the transmission of AIDS. This is not surprising because the processing of the plasma-derived vaccine does not permit survival of infectious agents.

**Contraindications**

There are no contraindicators to giving HB vaccine. It can be administered to patients incubating HBV, subjects positive for HBsAg, anti-HBc or anti-HBs and immunocompromised individuals.

**Cost Effectiveness of Vaccine**

When reviewing cost effectiveness of HB vaccine it should not be looked at only as preventing the acute infection but rather at the sequelae of the acute infection i.e cirrhosis and hepatocellular carcinoma which seem to affect males more, and afflicts at the prime of an individuals life. The economic impact of curtailing such productive resource persons is enormous especially in developing countries, leave alone the economic resources required for provision of health care to such patients.

Where prevalence of HBV carrier is low, targeted immunization of high risk individuals is appropriate. This, however depends upon the cost of the vaccine and of screening tools.

In areas of high endemicity or areas where acquisition of infection is in early childhood, the universal vaccination of all children in the first 6 months of life is recomended.
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7.4 HAEMOPHILUS INFLUENZAE TYPE B (D Makewa)

Introduction

Haemophilus influenzae is a gram-negative bacillus with six serotypes: a, b, c, d, e, and f. Haemophilus influenzae type b, or Hib, is responsible for 90% of the serious infections, which include bacterial meningitis and pneumonia. In addition to bacterial meningitis and pneumonia, manifestations of Hib disease include septic arthritis, osteomyelitis, septicaemia, epiglottitis, cellulitis and pericarditis.

Epidemiology

Paediatric bacterial meningitis caused by Hib, S. pneumoniae and N. meningitidis is responsible for high morbidity and mortality among children in Africa. Hib causes an estimated 450,000 child deaths each year globally and 100,000 to 160,000 child deaths each year in the WHO African region. S. pneumoniae causes 250,000 to 400,000 child deaths per year.

N. meningitidis is responsible for large epidemics (causing thousands of deaths) in many West and Central African countries (1,2). Over the last several decades, important population based studies have become available from The Gambia, Senegal, Niger, and South Africa (4-6). These studies show rates of Hib meningitis ranging from 50 to 60 cases per 100,000 children less than 5 years old. These rates are similar or higher than those seen in most of Western Europe and North America, where Hib vaccine is routinely used. It is estimated that there are at least five cases of severe pneumonia caused by Hib for every one case of Hib meningitis (8).

Transmission

Hib bacteria are passed to other children in droplets of saliva expelled when an infected child coughs or sneezes. Hib also spreads when children share toys and other things that they put in their mouths. The risk of transmission increases when children spend long periods of time in crowded households, day care settings, or crèches.

Clinical presentation-Paediatric bacterial meningitis

A child 0-59 months with the following signs and symptoms may be considered for the diagnosis of bacterial meningitis i.e.

Sudden onset of fever (>38 C axillary or >38.5 C rectal), and one of the following signs:

• Neck stiffness
• Bulging fontanelle (in children <12 months)
• Poor sucking
• Altered consciousness
• Irritability
• Other meningeal signs
• Toxic appearance
• Seizures
• Petechial or purpural rash (13)

Meningitis is not specific for Hib disease, and Hib disease cannot be diagnosed on clinical grounds.

**Diagnosis**

A lumbar puncture must be performed to obtain cerebrospinal fluid for analysis in all cases of suspected meningitis. The CSF must be analyzed within one hour of sampling.

**Laboratory criteria for diagnosis:**

1. **Culture method**
   - Isolation of Hib from a normally sterile clinical specimen, such as cerebrospinal fluid (CSF) or blood.
   - Culture of Hib from a non-sterile site, such as the throat, does not define Hib disease since the bacteria can grow in these other areas and not cause disease.

2. **Antigen detection methods**
   - Identification of Hib antigen in normally sterile fluids (CSF or blood) by antigen detection methods such as latex agglutination or counter immunoelectrophoresis (CIE)

Find below an algorithm of the diagnosis and management of a patient with suspected bacterial meningitis (14)

The specific management for Hib meningitis is antibiotics. Patients with suspected bacterial meningitis should usually be started on crystalline penicillin plus chloramphenicol preferably intravenously for a minimum of ten (10) days.

**Complications**

Children who survive Hib meningitis may develop permanent neurological disability including brain damage, hearing loss and mental retardation.
Fifteen to thirty percent of children who survive Hib meningitis are at risk for these disabilities whilst 5-10% cases of Hib meningitis are at risk of dying (12).

**Prevention**

**Vaccination**

Hib vaccine is one of the new generations of vaccines known as conjugate vaccines. With three doses, 90-99% of children vaccinated develop adequate protection against Hib infections.

Hib vaccines are available as follows:

- Monovalent liquid Hib vaccine as single- or 10-dose vials
- Lyophilised (freeze-dried) Hib vaccine, which comes only as a single-dose vial, that the vaccinator mixes with saline diluent
- Combination Hib vaccine: Liquid Hib+ DTP (tetravaccine), which comes as either single- or 10-dose vials; Liquid Hib + HepB vaccine in combination or lyophilised Hib vaccine that the user mixes with liquid DTP (to make tetravalent) or with DTP-HepB (to make pentavalent).

All Hib-containing vaccines should be stored at between +2 °C and +8 °C. Liquid Hib vaccine should never be frozen. Lyophilized vaccine may be frozen until reconstitution, but since the most commonly used diluent (DTP) cannot be frozen, it is recommended that lyophilized Hib vaccine should also be stored at temperatures between +2 °C and +8 °C to avoid errors.

**Administration**

IM injection in the outer mid thigh for infants at 6, 10 and 14 weeks as a combination of DPT-HepB-Hib (Pentavalent)

**Adverse effects**

No known serious side effects.

Mild reactions include soreness 5-15% and fever 2-10%.

In the last several years, the development of new vaccines effective in early infancy make elimination of infections and deaths due to Hib possible. These Hib conjugate vaccines have been integrated into routine infant vaccination schedules in over 70 countries globally as part of the routine infant immunization program.

Indeed in developed countries conjugate vaccines have been used for several years and have virtu-
ally eliminated invasive Hib disease. In the Gambian trial of conjugate vaccine between 1993 and 1995, the efficacy of the Hib vaccine was 95% against all Hib invasive disease after three doses and 21% protection against severe pneumonia. The vaccine was also shown to reduce asymptomatic nasopharyngeal carriage to 60%. In Africa 26 countries have incorporated the Hib conjugate vaccine in the EPI programmes.

In addition, the evaluation of Hib conjugate vaccine in The Gambia showed that immunization prevented 20% of all chest x ray confirmed pneumonia in children (4,7).

Annual comparisons-Hib isolates in KNH, 2011

However, the KEMRI/ Wellcome trust research laboratory at Kilifi has demonstrated a clear reduction in Hib disease in children less than five years in the coastal district.

In the isolates from Kenyatta National Hospital isolates we see the total number of laboratory confirmed Hib isolates since 1994 by half year periods. The numbers more or less remained around 5 to 10 isolates in each of the half year periods until the end second half of 1998 when new indications for blood culture and lumbar puncture came into force. The number isolates then exceeded the 15 level mark and often crossed the 20 level mark. This pattern was maintained even after the...
introduction of the HIB conjugate vaccine in Nov 2001. It was only in the first half of this year that the lowest number, below 5 was recorded, two years since the introduction of the vaccine.

Conjugate vaccines similar to the Hib conjugates are also being developed for prevention of pneumococcal and meningococcal disease (9-11). The pneumococcal conjugate vaccine has already been licensed in the United States and the meningococcal conjugate vaccines are under development and clinical trial. As for Hib, appreciation of these diseases, and measurement of impact of these vaccines are critical to vaccine introduction and sustaining vaccination programs.

The vaccine is now used in the routine immunization schedule of more than 100 countries and WHO recommends the use of Hib conjugate vaccines in all countries. The vaccine is available in monovalent presentation or combined with DTP and other vaccine combinations including with hepatitis B and inactivated polio vaccines.

![Global Immunization 1990-2010, 3rd dose of Hib coverage in infants, global coverage at 42% in 2010](image)

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12. WHO/V&B/03: Immunization in practice


14. Wellcome trust/Kemri

15. WHO, 1998b
7.5 IMMUNIZATION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTED CHILDREN  (E Maleche Obimbo, W Jaoko)

INTRODUCTION

The human immunodeficiency virus, also known as HIV, is a retrovirus which infects only humans. There are two major types of the HIV virus:

**Type 1:** HIV-1 is prevalent worldwide including Eastern Africa, and is responsible for the world pandemic. This form is highly virulent, transmissible from mother to child as well as horizontally, and causes a more aggressive progression of disease. Several subtypes exist, types A through to K, with subtypes A through E being the predominant ones.

**Type 2:** HIV-2 is present mainly in Western Africa, Angola and Mozambique. This form is less virulent, rarely vertically transmitted and causes a more slowly progressive disease.

**Epidemiology**

Globally, an estimated 2.5 million children are living with HIV, and 2.3 million (92%) of these children living with HIV, or dying from HIV were from Sub-Saharan Africa, and ~ 350,000 died during 2010 from HIV related causes. (UNAIDS report on the global AIDS epidemic 2009). In Kenya, during 2009, it was estimated that that there 180,000 children living with the disease.

The African epidemic is driven by HIV-1, with mainly subtypes A, C, D. In order of prevalence of specific subtype, Kenya hosts predominantly subtype A, followed by C and D; Uganda hosts subtypes C, followed by A, Tanzania subtypes D, followed by A and C. Southern Africa hosts predominantly subtype C, and western Africa predominantly subtype A. The rest of the world - Europe, the Americas and Southeast Asia host predominantly subtype B. Understanding of prevalent subtypes is important in identification of an effective vaccine against the virus.

**Transmission and natural disease course of HIV**

HIV-1 may be transmitted to children through various routes, by far the most common route being vertical transmission from mother to child either transplacentally, during birth, or through breastmilk (responsible for 95% of paediatric HIV cases). Other modes of transmission include transfusion with HIV-contaminated blood, contaminated injections, traditional scarification or circumcision with unsterile instruments.

Once in the body the virus invades body cells that have a CD4-receptor on the surface, such cells include T lymphocytes, macrophages, microglial and dendritic cells. The virus then integrates itself into the cell DNA and causes the cell to manufacture thousands of copies of virus every day, which proceed to infect other CD4 cells. Eventually the infected cells become exhausted.
and die, the process is repeated, leading to progressive depletion of CD4 cells. A “balance” may be achieved for some months to years so that the virus is controlled at a relatively constant level, during which period the child may remain relatively well, or have minor illnesses. This period is described as the relatively “asymptomatic” or early stage of disease – World Health Organization (WHO) staging system designates this as stages 1 (asymptomatic) or 2 (mild) disease. During these early stages, the immune system remains fairly competent to mount an immune response against antigens, and the number of circulating CD4 cells remains reasonably high (comprising > 25% of circulating lymphocytes). Eventually the immune system becomes significantly depleted, resulting in impaired cellular as well as humoral immunity; the child experiences moderate to severe life-threatening episodes of infection by pathogenic as well as opportunistic organisms, may develop moderate to severe impairment of growth, malignancies and major organ impairment (e.g. encephalopathy, myelopathy). This is described as WHO stage 3 (moderate) and 4 (severe) disease, or the “acquired immunodeficiency syndrome (AIDS). During this advanced stage of disease the child has loses the capability to mount effective immune responses to new antigens, and may lose immunity that was previously present. The number of circulating CD4 cells declines dangerously (to less than 15% of circulating lymphocytes).

Children appear to exhibit three patterns of disease progression - “rapid” “intermediate” and “slow” progression according to the speed at which they progress from asymptomatic/mild symptoms through to moderate/severe symptoms (AIDS). Rapid progressors develop AIDS and die before the age of 2 years, and this is seen among approximately 50% of vertically infected children and is more likely to occur among children infected before or at birth, and born to mothers who are themselves in advanced stage of HIV/AIDS. Slow-progressors tend to progress more slowly, and may remain in stages 1-2 for several years before developing AIDS, some living into teenage years. Between 5 – 25% of vertically infected children appear to be slow-progressors. Children infected after the neonatal period, through breastfeeding or other modes of transmission appear to have slower progression.

**The Immunogenicity of EPI-recommended vaccines in HIV-infected children**

There are three broad issues to consider with regards to immunogenicity of vaccines in an HIV infected child. These include:

1. **Can the child with deteriorating immunity mount an effective immune response to the vaccine?**

Two major factors influence the immune response of an HIV infected infant to vaccines:

- Their immune system is initially immature at birth, but gradually matures becoming progressively more competent over the first 2 - 5 years of life.
• The progressive destruction of the infant’s immune system by the HIV virus leading to pro-
gressive loss of capacity to mount effective immune response to antigens

The ideal timing to achieve effective immunization among HIV infected infants is a precarious
balance between these two factors. If vaccines are administered to an HIV infected child during
ey early stages of disease (WHO stages 1-2, or close to normal CD4), will generally stimulate an
adequate immune response. Vaccines administered during later stages of disease (WHO stages
3-4, or depleted CD4) may not elicit a protective immune response against the antigen.

### Immunogenicity of EPI-recommended vaccines in HIV infected individuals

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>HIV uninfected</th>
<th>HIV infected (early-late stage)</th>
<th>Comment on HIV infected children</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>++</td>
<td>+ (range 20-70%)</td>
<td></td>
</tr>
<tr>
<td>Diphtheria</td>
<td>++ (99%)</td>
<td>+ (71%)</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td>++</td>
<td>+</td>
<td>Similar to HIV-</td>
</tr>
<tr>
<td>Oral polio vaccine</td>
<td>++</td>
<td>+</td>
<td>Similar to HIV-</td>
</tr>
<tr>
<td>Haemophilus infl B</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>++</td>
<td>+</td>
<td>Seroconversion protected against serious hepatitis and chronic carriage</td>
</tr>
<tr>
<td>Measles</td>
<td>++ (89%)</td>
<td>+ (early stage 77%, late stage 36%)</td>
<td></td>
</tr>
<tr>
<td>Mumps rubella</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td>++</td>
<td>No data</td>
<td>No data</td>
</tr>
</tbody>
</table>

Parentheses represent percent of children producing protective antibody to vaccinated antigen from selected studies.

2. **How sustained is the immune response in the face of progressive deterioration of the
child’s immune system?**

During early stages (WHO stages 1-2, or CD4 above 20%) of HIV disease, the immune response
to vaccines is generally good.

As HIV disease progresses (WHO stages 3-4), and CD4 count drops

• the capacity to mount an effective immune response to new antigens declines

• there is progressive loss of previously acquired immunity against antigens/vaccines – antibody
levels and memory response against specific antigens declines
3. After initiation of antiretroviral therapy, with consequent immune reconstitution, does this child require re-vaccination against immunisable diseases?

If a child with advanced HIV disease receives highly active antiretroviral therapy (HAART) and immune reconstitution occurs (CD4 % restored to > 25%), there may be need to re-vaccinate, or give booster vaccinations to restore immunity against vaccine-preventable diseases which are prevalent in that child’s environment. Data suggests that on re-vaccination protective immunity against vaccinated antigen is restored.

The Safety of vaccines in HIV-infected children who tables update

The major concern regarding safety of vaccines in immunocompromised children is whether administering a live (albeit attenuated) organism, or a live vaccine to a child with reduced immunity may result in vaccine-associated disease, and if so, how severe could the vaccine associated disease be? This issue shall be discussed by examining each individual live vaccine separately. Emphasis shall be on individual vaccines for which there are special safety considerations for HIV infected children.

BCG (Bacille Calemette Guerin)

General comments

BCG is a live attenuated vaccine against mycobacterium tuberculosis (TB). This vaccine remains the only available immunoprophylaxis against TB, and has clearly been shown in HIV uninfected children to prevent severe forms of TB when administered early in infancy.

Children born to HIV infected parents are more likely to be exposed to TB due to high TB prevalence in their parents. HIV infected children compared to uninfected children are more likely to progress from infection to TB disease, and to develop severe forms of TB.

Safety of BCG:

There is a low incidence of adverse events from BCG vaccination when administered to children in early stages of disease. For the majority of children, BCG is given at birth before HIV symptoms set in, and the majority of HIV infected children experience no adverse events. If BCG is administered to a symptomatic HIV infected child, there is risk of multiplication and spread of the vaccine bacillus to cause regional lymphadenitis, fistula formation, osteomyelitis and disseminated BCG disease. (ref BCG). BCG is therefore contraindicated in symptomatic infants (WHO stages 3-4), and low CD4.

Immunogenicity of BCG:

The immune response to the vaccine is best when administered during early stages of HIV disease (preferably at birth). As HIV disease progresses, initial post-BCG immunity declines with de-
clining CD4 count resulting eventually in anergy to tuberculin. Between 20-72% of HIV infected children were found anergic after BCG (20 – 72% in African studies). If administered after initiation of antiretroviral therapy during the period of immune reconstitution, this vaccine may cause lymphadenitis or more disseminated BCG disease (immune reconstitution inflammatory syndrome).

**Recommendation**

The World Health Organisation’s position 2012 states “While BCG vaccination is especially important in countries with significant HIV prevalence, children who are HIV positive or unknown HIV status with symptoms consistent with HIV should not be vaccinated”. Kenya being a country with high prevalence and therefore high risk of TB, BCG should be administered to all Kenyan children at birth or as soon as possible after, regardless of HIV status of mother. BCG should not be given to children who have symptomatic HIV, or low CD4.

**POLIO VACCINES**

There are two forms of polio vaccine available today for protection against polio, oral polio vaccine (OPV) – a live attenuated orally administered vaccine; injectable polio vaccine (IPV) – a killed injectable vaccine. Both forms of vaccine have high efficacy.

For resource-limited settings, OPV is cheaper and easier to administer.

**Safety**

IPV is safe, and poses no known risks to HIV infected children. This is therefore the preferred vaccine for HIV infected children where it is affordable.

OPV poses a rare risk of 1:750,000 for vaccine associated paralytic polio, so far, only one case has been described (a Romanian HIV infected child). There are also concern about prolonged persistence of vaccine virus in the gut of HIV infected individuals, with potential of virus to revert to wild type virulent virus and cause paralytic polio. A few cases of persistence of vaccine virus have been described, but no case of paralytic polio secondary to persistence of vaccine virus has been described. Other safety concerns include the risk of transmission of OPV vaccine virus to immunosuppressed household contacts (e.g. mother) of children vaccinated with OPV.

So far however, the above mentioned risks are extremely rare, and resource poor countries which may not afford IPV, must weigh the theoretical OPV risk against wild polio transmission risk in decisions regarding polio vaccination of HIV infected children.

**Immunogenicity**

In developing countries IPV achieves higher sero-response to all 3 polio strains compared to OPV. This is thought to be related to diarrhoeal illness and other intestinal infections common in
resource-poor settings, which may interfere with the take of OPV. Progressive HIV disease is associated with reduction in sero-response to primary vaccination, and progressive loss of previous vaccine – induced immunity. After effective antiretroviral therapy with immune reconstitution, there may be benefit in re-vaccinating infants against OPV.

**Recommendation**

- Administer OPV to all Kenyan children at ages 0, 6, 10, and 14 wks.
- Booster doses of OPV after age 14 wks should not be administered if child has symptomatic HIV (stage 3-4, or low CD4)
- In symptomatic children, IPV should be given instead of OPV if affordable.

**MEASLES**

The measles vaccine is a live attenuated vaccine. In developing countries measles remains highly prevalent, and HIV infected children are at high risk of infection by wild measles virus. HIV infected children compared to HIV uninfected children have:

- Lower passive immunity (maternal measles-specific IgG) during the first year of life compared to HIV uninfected children. This is because their HIV infected mothers generally have reduced immunity, with reduced measles specific IgG, and therefore transfer inferior amount of passive immunity to their infants.
- Increased risk of severe measles infection and measles mortality even before the age of 9 months.

**Safety**

The measles vaccine is administered at age 9 months by which age many HIV infected children are symptomatic and immunosuppressed. There is however little evidence of severe post-vaccine measles; only one case of post-measles giant cell pneumonia and death in adult with CD4 < 1 has been reported in literature, despite widespread use of measles vaccine. The benefit of vaccine (protection from wild measles infection) therefore far outweighs the risks.

**Immunogenicity**

Among HIV infected children sero-response to vaccine reduces with progressive HIV disease. In one study in the Congo, sero-response was 36% in symptomatic HIV infected children, 77% in asymptomatic HIV infected children and 89% HIV uninfected children *(WHO 2001).* Antibody levels after primary vaccination fall faster in HIV infected compared to HIV uninfected children.
**Recommendation**

All children with known or suspected HIV infection should receive measles vaccine at 6 months of age, followed by a second dose at 9 months, regardless of HIV disease stage.

**YELLOW FEVER VACCINE**

This live attenuated vaccine is only administered in districts where yellow fever is prevalent in Kenya.

Safety – there is no data to inform on the safety

**Immunogenicity**

Sero-response to this vaccine deteriorates with progressive HIV disease. In one study in Cote d’Ivoire sero-response was 17% in HIV infected children, and 74% in HIV uninfected infants. There is no data regarding efficacy of vaccination to prevent yellow fever infection in HIV infected children.

**Recommendation**

- Administer yellow fever vaccine to asymptomatic HIV infected children.
- Withhold vaccination in symptomatic HIV.


<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Asymptomatic HIV infection</th>
<th>Symptomatic HIV infection</th>
<th>Optimal timing of immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>yes</td>
<td>no</td>
<td>birth</td>
</tr>
<tr>
<td>DPT</td>
<td>yes</td>
<td>yes</td>
<td>6,10,14 weeks</td>
</tr>
<tr>
<td>cPCV⁴</td>
<td>Yes</td>
<td>yes</td>
<td>6,10,14 weeks</td>
</tr>
<tr>
<td>OPV1</td>
<td>yes</td>
<td>yes</td>
<td>0, 6, 10, 14 weeks</td>
</tr>
<tr>
<td>Measles</td>
<td>yes</td>
<td>yes</td>
<td>9 or 12 months (6 months minimum)²</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>yes</td>
<td>yes</td>
<td>6,10,14 weeks</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>yes</td>
<td>no³</td>
<td>9 months</td>
</tr>
<tr>
<td>Tetanus toxoid (pregnant woman)</td>
<td>yes</td>
<td>yes</td>
<td>5 doses⁵</td>
</tr>
</tbody>
</table>

1 IPv can be used as an alternative for children with symptomatic HIV infection
2 Children in enclosed situations such as refugee camps and immune-compromised children hospitalized between the ages of 6-9 months should receive an earlier dose from 6 months, and a repeat dose after age of 9 months.
Pending further studies

cPCV conjugate Pneumococcal vaccine

Five doses of tetanus toxoid for women of child-bearing age as for non-HIV infected persons.

**OTHER NON-EPIDEMIC VACCINES**

- MMR – recommended from 12 months in HIV regardless of stage of HIV disease.
- Influenza – recommended for immunocompromised
- Varicella - unclear
- Hepatitis A - unclear
- Meningococcal – recommended when indicated
- Human Papilloma virus vaccine – girls after age 9 years only.
- Rabies - unclear

**Passive Immunization of HIV infected children**

- Intravenous immunoglobulin (IVIG) has been used in resource-rich settings as general prophylaxis for HIV-infected infants against repeated bacterial infections – with moderate efficacy
- High titre antigen-specific immune globulins (hyperimmune specific globulins) have been used for immunosuppressed patients to provide passive immunity during the period at risk e.g.
  - CMV - IVIG to bone marrow transplant patients
  - RSV - IVIG proposed for HIV patients during the RSV season
- When an immunosuppressed symptomatic HIV infected child has been exposed to a virulent infection for which IVIG is available (e.g. measles, varicella, hepatitis B), consideration to protect them by administration of hyperimmune specific globulins) where affordable
- Vaccination after administration of IVIG may be ineffective if administered within 3 months of immune globulin administration, therefore specific vaccination against the said antigen should be offered 3 or more months after the IVIG.

**HIV Vaccine Development**

**History**

It is generally believed that a safe, effective, affordable and easy to administer preventive vaccine offers the best long-term hope for controlling the HIV/AIDS epidemic. Efforts to get such a vaccine started in earnest shortly after the first case of HIV/AIDS was described.
Challenges in HIV Vaccines research and development

Attempts to develop effective preventive HIV vaccine have been difficult for several scientific reasons. These include failure to clearly define specific immune responses capable of preventing infection or limit disease progression, and the rapid rate of mutation of HIV, among others. Rational development of a vaccine against HIV requires characterization of immune correlates of infection, and delineation of the specific portions of the virus that elicit this response. Neutralizing antibodies that prevent infectivity, and cytotoxic T cells, which eliminate virus-infected cells appear to be the major elements that regulate viral clearance. Both are considered important for protection against HIV infection.

The HIV-1 virus has wide genetic diversity with known clades including clades A – E and the virus is continually mutating to produce variants of the original infecting virus. The interactions between the virus and host are also complex. Conducting clinical trials to evaluate HIV candidate vaccines is a complex process. These factors make it extremely challenging to make an effective vaccine that would prevent infection.

The first candidate HIV vaccine was tested in a clinical trial in 1987. Like the other first generation candidate HIV vaccines, this was based on gp120 genes and aimed at inducing humoral immune responses. This and other candidate vaccines which followed did not generate the required immune responses\(^1\). Newer generation candidate HIV vaccines have aimed at stimulating cellular immune responses which although may not be able to prevent infection may be able to either slow down progression to disease, or may lower viral load and thus reduce HIV transmission.

Reasons to be optimistic

There is reason to be optimistic due to the following observations:

- Immune responses to HIV in humans partially reduce HIV replication.
- In animal studies, vaccine candidates have induced some protection against simian immuno-deficiency virus (SIV) infection.
- An HIV vaccine could provide therapeutic effect in HIV infected individuals, boosting their HIV-specific immune response and control of virus, thus delaying disease progression.

Mechanisms of Immunity

An ideal vaccine will therefore be one that induces both humoral responses (evidenced by production of neutralizing antibodies) and cellular immune responses.
The ideal vaccines will induce:

- Neutralizing antibodies (humoral responses) – thereby prevent infection
- Cytotoxic T lymphocyte (CTL) cell response (cellular immune responses) – thereby eliminate virus-infected cells
- Immune activity against multiple clades (across clades A,B,C,D etc).
  - Vaccines containing conserved sections of the HIV epitope appear to achieve this.
  - Important as need to protect against various clades of virus an individual may be exposed to.
  - For a therapeutic vaccine efficacy, virus is continually mutating in infected individual.

**Candidate vaccines**

The search for an effective vaccine continues, various candidate vaccines have been tried and are under trial. Various vaccine components have been researched including:

- Synthetic or recombinant versions of the HIV proteins or peptides – which cannot reconstitute into an infectious virus
- A weakened (attenuated) virus vector such as canarypox virus or adenovirus to shuttle the non-infectious HIV gene fragments into the body
- DNA plasmid vaccination

Although many candidate HIV vaccines have been tested through phase 1 and 2 clinical trials, only 2 candidate HIV vaccines have reached phase 3 trials. It is hoped that eventually a therapeutic vaccine that slows down disease progression shall be identified, and possibly a vaccine that may prevent HIV infection.

**REFERENCES:**


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7.6 PNEUMOCOCCAL DISEASE IN CHILDREN (E Maleche Obimbo)

INTRODUCTION

Pneumonia is the leading cause of death among children, with the greatest incidence and mortality occurring in resource poor settings. Factors contributing to this disproportionate morbidity and mortality include poverty, overcrowding, indoor pollution from cooking fuel, malnutrition, HIV infection, low birth weight, and poor access to health care, including poor access to immunization.

The major causative agent is *Streptococcus pneumoniae*, followed by *Haemophilus influenzae* and viruses such as the respiratory syncytial virus (RSV). A large proportion of pneumonia is preventable through addressing the risk factors and through immunization.

This chapter shall focus on pneumococcal pneumonia with mention of other invasive pneumococcal disease, and pneumococcal vaccines. Other chapters address in more detail other aetiologic agents for pneumonia such as measles, diphtheria, pertussis and tuberculosis.

Aetiology

![Fig 6: diagram of pneumococcal bacteria](image)

*Streptococcus Pneumoniae* is a gram positive bacterium which appears as a diplococcus on gram staining. It has a polysaccharide capsule. The capsule protects it from the hosts innate immune system, evading phagocytosis. It shields underlying protein antigens on the cell surface of the organism from host antibodies and complement. As a result, organisms with reduced expression of the capsule are more likely to be cleared by the host. The capsule however, is also immunogenic and eventually stimulates the production of host antibodies directed against the capsule itself.
The capsule is comprised of polysaccharides. However, there is great diversity in the structure of these polysaccharides from one pneumococcus to another. There are over 90 different surface capsule polysaccharide types, each of which provokes a type-specific antibody response in the human host. They are described using serogroups numbered 1, 2, 3…sequentially. Each serogroup may have one or more “serotypes” denoted A, B, C,… e.g. serogroup 9 contains serotypes 9A, 9F, 9L, 9N and 9V. Some serogroups have a single serotype therefore the notation is simply a “1”. Not all serogroups cause disease, serogroups 6, 14, 18, 19, and 23 are the most prevalent, and are responsible for between 60 and 80 percent of pneumococcal infections.

**Epidemiology**

**Incidence and mortality:**

Streptococcus pneumoniae specifically is responsible for ~14.5 million episodes of serious pneumococcal disease occur per year, contributing to ~11% of all deaths in children under-five. This microbe causes invasive disease in various sites of the body, the most common being in the respiratory system-pneumonia, followed by meningitis.

Pneumonia: Children under five years in resource poor settings experience 0.29 episodes per child-year which translates to ~151 million new episodes annually. This is six-fold higher than incidence in well resourced settings (0.05 episodes per child-year, 5 million new episodes annually). In Africa children under five years experience 0.33 episodes of pneumonia per child-year, an estimated 35 million cases annually. Between 7 – 13% of these cases are severe and life-threatening requiring hospitalization, and pneumonia contributes to 19% of all under-five deaths globally, and in Africa to 21% of deaths. These estimates exclude deaths from severe neonatal infections, of which the majority are pneumonia/sepsis – so the true contribution of pneumonia to mortality is higher.

Meningitis: Incidence (cases per 100000 children) of pneumococcal meningitis is 17 globally, and 38 in sub-Saharan Africa (SSA) – which is 3-6 fold higher than in high income countries. Case fatality for pneumococcal meningitis is estimated at 59% globally, and 73% in SSA – up to 3-fold higher mortality than in high income countries.

Other invasive pneumococcal disease (non-pneumonia, non-meningitis): has incidence of 87 globally, and 192 in SSA, with case fatality for severe forms of 45% globally, and 58% in SSA – up to 3 fold higher than mortality in high income countries (next table).
Incidence and Case Fatality Rates of Invasive Pneumococcal Diseases in Children

<table>
<thead>
<tr>
<th>Site of Disease</th>
<th>Data</th>
<th>Global</th>
<th>Sub-Saharan Africa</th>
<th>High income countries** (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence*</td>
<td>2228</td>
<td>3397</td>
<td>462-1775</td>
</tr>
<tr>
<td></td>
<td>CFR (%)</td>
<td>5%</td>
<td>11%</td>
<td>2-5%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Incidence</td>
<td>17</td>
<td>38</td>
<td>6-12</td>
</tr>
<tr>
<td></td>
<td>CFR (%)</td>
<td>59%</td>
<td>73%</td>
<td>29-48%</td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other sites</td>
<td>Incidence all</td>
<td>87</td>
<td>192</td>
<td>36-71</td>
</tr>
<tr>
<td></td>
<td>Incidence severe forms</td>
<td>11</td>
<td>15</td>
<td>7-15</td>
</tr>
<tr>
<td></td>
<td>CFR (severe)</td>
<td>45%</td>
<td>58%</td>
<td>22-37%</td>
</tr>
</tbody>
</table>

* Incidence is number of annual cases per 100,000 children.
** Data for three regions – USA, Europe and West Pacific.


Transmission:

S. Pneumo is spread by contaminated respiratory droplets from person to person either through coughing or sneezing by an infected individual with subsequent inhalation of the bacteria. Another method is through contamination of hands with infected nasal secretions or sputum, and subsequent transmission of these secretions to another person’s hands which transfer the same to the face. The microbe then settles on nasal and/or pharyngeal mucosa and multiplies there colonizing it.

Risk Factors:

Environmental risk factors for transmission include overcrowding, poor ventilation, and indoor pollution by cigarette smoking, or by use of biomass fuels for cooking such as wood, charcoal and kerosene. Smoke irritates the respiratory mucosa making it more vulnerable to invasion by bacteria.

Host risk factors that increase risk of progression to disease after pneumococcal colonization of respiratory mucosa include lowered immunity due to malnutrition, progressive HIV disease, sickle cell disease, malignancy, and chronic respiratory diseases such as asthma and allergic rhino-sinusitis. Breastfeeding provides immune protection against pathogens including pneumococcus, so non-breastfed infants are at increased risk of invasive pneumococcal disease.
Pathophysiology of Pneumococcal Disease

On inhalation the pneumococcus first attaches to the nasopharyngeal mucosa, multiplies and colonises it. Colonization with most pneumococcal serotypes is asymptomatic and does not result in disease, however a minority of pneumococcal bacteria go on to spread to other sites, thus causing disease. For very invasive virulent serotypes of pneumococcus, the transit time through the nasopharyngeal mucosa may be rapid. Pneumococcus may then spread to other parts of the body as follows:

i) Direct spread along the respiratory mucosa to the ears causing acute otitis media, the para-nasal sinuses to cause sinusitis, or aspiration into the lungs to cause pneumonia.

ii) Haematogenous spread - pneumococcus may penetrate the respiratory mucosa into the bloodstream (bacteraemic stage) spread to cause disease in various sites including the lung (pneumonia), the central nervous system causing meningitis, the joints or bone causing septic arthritis and osteomyelitis, subcutaneous tissue causing cellulitis and abscesses, and the pleura causing empyema. Bacteraemia alone causes mild disease, however septicaemia (bacteraemia with concurrent invasive infection of multiple tissues and severe constitutional symptoms) causes severe illness in young children with high morbidity and mortality.

Clinical Presentation and Management of Pneumococcal Diseases

Pneumococcal infection may cause wide range of clinical disease, ranging from mild presentation with fever and bacteraemia, to severe focal disease such as pneumonia or meningitis, to severe disseminated multi-site invasive disease. The young child under two years is most vulnerable to the severe forms of invasive pneumococcal disease.

Pneumonia

*Symptoms* include cough and fever, rapid breathing, and with progression they develop difficulty in breathing or breathlessness. Young infants may also wheeze.

*Signs:* Examination reveals the following:

- Tachypnoea defined as respiratory rate:
  - Age < 2 months: ≥ 60/minute
  - Age 2 – 11 months: ≥ 50/minute
  - Age 1 – 5 years: ≥ 40/minute
• Signs of respiratory distress such as alar flaring, grunting, head nodding (infants), indrawing at subcostal, lower chest well, intercostal, supra-sternal or supraclavicular areas. In very severe disease central cyanosis may be present.

• Percussion of the chest may reveal reduced resonance over areas of consolidated lung, or effusion if present.

• Auscultation may reveal bronchial breathing, crepitations (crackles), and in infants occasionally wheezing.

• Other signs include fever, and in very severe forms of the disease, reduced level of consciousness.

Classification of severity of pneumonia is based on the symptoms and signs into (non-severe) pneumonia, severe pneumonia, and very severe pneumonia as displayed in table…

Investigations:

• Pulse oximetry – for all severe forms is useful to determine oxygen saturations at baseline and to monitor response to therapy.

• Blood culture – has low yield with only 10% of clinical pneumonia cases having a positive blood culture. Other factors contributing to low yield of culture include prior antibiotic treatment, improper handling and transport of specimens.

• Chest radiograph: is not required for the majority of cases – as the diagnosis is easily made through history and physical examination. However for children with atypical presentation, or poor response to initial treatment a chest radiograph should be taken. Classic pneumococcal pneumonia will present as lobar consolidation, however in young infants and immune-compromised patients one may see diffuse patchy opacification throughout the lungs due to widespread involvement of the lungs, or alternatively minimal abnormalities due to poor inflammatory response.

Complications of pneumonia include: respiratory failure, empyema, lung abscess, pneumatoceles and pneumothorax. Recurrent severe episodes of pneumonia as seen in HIV infected children may lead to chronic lung damage and bronchiectasis.

Treatment:

Supportive treatment: Supplemental oxygen, anti-pyretics, adequate fluids (oral or parenteral depending on severity of illness), maintain nutrition.

Specific antibiotic treatment: This is outlined in the WHO case management table following
<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>Classification</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central cyanosis</td>
<td>Very severe pneumonia</td>
<td>— Admit to hospital</td>
</tr>
<tr>
<td>Severe respiratory distress (e.g. head nodding)</td>
<td></td>
<td>— Give recommended antibiotic</td>
</tr>
<tr>
<td>Not able to drink</td>
<td></td>
<td>— Give oxygen</td>
</tr>
<tr>
<td>Chest indrawing</td>
<td>Severe pneumonia</td>
<td>— Manage the airway</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Treat high fever if present</td>
</tr>
<tr>
<td>Fast breathing</td>
<td>Pneumonia</td>
<td>— Home care</td>
</tr>
<tr>
<td>— 60 breaths/minute in a child aged &lt;2 months;</td>
<td></td>
<td>— Give appropriate antibiotic for 5 days</td>
</tr>
<tr>
<td>— 50 breaths/minute in a child aged 2–11 months;</td>
<td></td>
<td>— Soothe the throat and relieve cough with a safe remedy</td>
</tr>
<tr>
<td>— 40 breaths/minute in a child aged 1–5 years</td>
<td></td>
<td>— Advise the mother when to return immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Follow up in 2 days</td>
</tr>
<tr>
<td>Definite crackles on auscultation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No signs of pneumonia, or severe or very severe</td>
<td>No pneumonia, cough or</td>
<td>— Home care</td>
</tr>
<tr>
<td>pneumonia</td>
<td>cold</td>
<td>— Soothe the throat and relieve cough with safe remedy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Advise the mother when to return</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Follow up in 5 days if not improving</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— If coughing for more than 30 days, follow chronic cough instructions</td>
</tr>
</tbody>
</table>

Adapted from the WHO Pocket Book of Hospital Care for Children: guidelines for the management of common illnesses with limited resources. WHO 2005.
7.7 MEASLES (F. Esamai)

INTRODUCTION

Measles is a universal disease caused by the measles virus(1). It was first described as an entity by the Arabian physician Rhazes in 900 A.D. who then said ‘it was more dreaded than smallpox’(2). It is a highly infectious disease with high morbidity and mortality rates. In Greenland, an attack rate of 99.9% was reported during an epidemic in 1951 (3). It has been estimated that by 1985 there were 2.5 million child deaths per year due to measles infection(4).

Although the launching of the Expanded Programme on Immunization by the W.H.O. in 1974 has contributed to the lowering of morbidity and mortality due to measles in many developing countries, there is a need for countries and regions to develop further strategies that focus on groups at risk of developing severe disease.

The measles virus is a paramyxovirus in the genus Morbillivirus. It is 100 – 200nm in diameter with a core single stranded RNA. It has six structural proteins of which three are complexed to the RNA and three are associated with the viral membrane envelope. The envelope is made of the M – protein in the inner surface and the H and F protein in the outer surface. The H protein is responsible for the adsorption of the virus to cells while the F protein is responsible for the fusion of the virus and the host cell membranes, viral penetration and haemolysis. There is only one antigenic type of the measles virus.

EPIDEMIOLOGY

Measles occurs throughout the world and is mainly a human disease as there are no known animal reservoirs. There are no known asymptomatic carriers described to date. It is transmitted primarily from person to person by droplet infection and airborne transmission through aerosolised droplet nuclei has been documented for up to two hours after an infected person left a room or area. It is highly infectious with over 90 percent secondary attack rates among susceptible people. It is infectious 4 days before to 4 days after the onset of the rash. It is most infectious during the prodromal period through 3 -4 days of the rash. Primary viraemia occurs.

2 – 3 days after exposure with secondary viraemia occurring 3 – 4 days later. There is an initial localisation of the virus in the epithelium of the nasopharynx and conjunctiva with spread to the lymph nodes. The virus peaks at 11 – 14 days after exposure and then falls of over the following 2 -3 days.

In developing countries, measles is a severe disease affecting younger children as compared to developed countries where the pattern of measles has changed over the years (5, 6, 7). The disease
commonly occurs in epidemics every 2-3 years. In Kenya two annual epidemic peaks, during June-July and November-December, respectively, have been noted. In the absence of an immunisation program it affects everyone by adolescence.

**Clinical classification of measles cases**

A suspected case is a person with a febrile illness accompanied by a generalised maculopapular rash. A probable case meets the measles case definition of generalised maculopapular rash lasting 3 days with a fever greater than 38.3°C, a cough, coryza and conjunctivitis and has no or non-contributory serologic or virologic testing with no history of contact with a proven case of measles. A confirmed case meets the case definition and is epidemiologically linked to another confirmed case or is laboratory confirmed as measles. A laboratory confirmed case does not need to meet the clinical case definition.

Only confirmed cases should be reported to CDC but both confirmed and probable cases should be reported to the EPI program and confirmation through laboratory testing should be done.

**Epidemiological classification of measles cases**

An imported case has its source outside the country or state, rash onset occurs within 21 days after entering the country and illness cannot be linked to local transmission. An indigenous case is any case that cannot be proved to be imported.

**Mortality**

In the early 1960’s, high morbidity and mortality due to measles especially in younger children was reported in many developing countries. Morley (8) attributed 15.5% of deaths in African children under five years of age to measles. In India, during 1960, 46.1% of patients with measles admitted to an infectious diseases hospital in Delhi were below three years of age and mortality in this group comprised 80.8% of the total deaths due to measles (9). In Brazil, 80% of deaths due to measles occurred in children under 3 years of age (10). O’Donovan (11), in a review of children hospitalized with measles in Nairobi over the period 1968-1970, found that more than 50% of cases were less than 24 months of age and reported an overall case fatality rate 10.1%.

During 1970 - 1980, a reduction in morbidity and mortality rates due to measles was observed in both developed (12,13) and developing countries (14, 15, 16). The substantial reduction in morbidity and mortality which occurred in developing countries has been attributed in part to the introduction and widespread use of measles vaccine (12,13).

In a community based study in Machakos District in Kenya from 1974 to 1976 Voorhoeve. et. al. (17) found a case fatality rate in a rural setting of 6.1%. Children under 12 months of age had a higher age specific case fatality rate. In 1981, Williams and Huil (18) reported a case fatality rate
of 6.1% (19). In Guatemala and Ecuador, 6% of infant mortality and 20% of mortality in children aged 1-4 years of age, during the period 1971-1980, were attributed to measles (20). 80% of the measles deaths occurred in children under 5 years of age and 20-45% of all measles deaths occurred in children under one year of age.

**Measles attack rates**

Measles has a high attack rate in those who are susceptible (2). During the first 6 months of life, infants are largely protected against measles by maternally acquired passive immunity, but this decreases with time. Krugman et al. (21) found that passively acquired maternal antibodies were detectable in low titres in 20% of infants at 9 months of age, 12% of infants at 10 months of age, 8% of infants at 11 months of age and were not detectable at 12 months of age.

**Measles severity**

It has also been shown that measles severity is related to intensity of exposure. Aaby and co-workers (23,24,25) suggested that severity of measles was partly attributed to a greater dose of measles virus following intensive exposure. Working in an urban community in Guinea-Bissau, they found that measles mortality in the age group 0-11 months was higher among secondary cases than in index cases (22). They reported a case fatality rate of 9.4% in isolated cases of measles in the age group 6-35 months as compared to 34.7% for multiple cases of the same group (23). In an urban area of Guinea-Bissau, a case fatality rate of 25% was reported during an epidemic (37).

Loening and Coovadia (25) reported a positive correlation between population density and percentage of measles cases aged 8 months or less. They found an occurrence of measles in this age group of 20% - 45% in urban areas, 15.5% in peri-urban areas and 6-12% in rural areas. In an urban sample of 2655 children, 703 had measles and 45% of these were aged 8 month or less. Aaby and co-workers (22) suggested that intensity of exposure may lead to infection in children younger than 6 months, since a high dose of measles virus may overcome maternally acquired passive immunity, so rendering the children susceptible to infection. They observed that measles was most severe and resulted in high mortality among infants. Bwibo (26) had shown that 86.8% of deaths due 10 measles occurred in children under 3 years of age and that mortality decreased with increasing age.

Aaby and his colleagues questioned the importance of nutrition on the outcome of measles and suggested that intensity of exposure to measles virus plays a greater role than previously realized (23,24).Nieburg and Dibley (27) have reviewed the possible confounding factors in the relationship between severity of measles and malnutrition and they suggest that there is enough evidence to show that malnutrition has a role to play.
Notwithstanding this, the pattern of measles in urban and peri-urban areas (25) and the observation of increased incidence as well as increase morbidity and mortality in households where there is an index case, emphasizes the importance of intensity of exposure on the severity of measles. This, therefore, calls for the focusing of preventive measures on children who may not have reached the immunisation age, but who are at risk of high exposure to measles.

Because of this effect of intensity of exposure, all health workers should be aware of the possibility of increased risk of transmission of measles among children in crowded outpatients clinics and wards and should make every effort to minimize nosocomial infection. It should also be realized that there is a need to vaccinate all eligible children at every given opportunity. Hence all children who come to the various health facilities for whatever reason, need to be screened and immunized accordingly so as to help minimize missed opportunities for immunization.

**Delayed effect of Measles on Morbidity and Mortality**

The effect of measles on the child after the acute phase is now being recognized to be of greater significance than had been realized before. There is an increased risk of dying following acute measles infection especially for children under one year of age. The nutritional status of the affected child, prolonged diarrhoea which may occur, (28) and low vitamin A status are among other factors, besides age, which may contribute to the delayed impact of measles on morbidity and mortality.

**Measles and Vitamin A**

Measles infection is an important risk factor for the development of severe vitamin A deficiency and blindness. It has been shown that measles infection depresses serum vitamin A levels (29,30). Besides the effect on the cornea due to lowered serum vitamin A levels, the measles virus also has direct invasion of the cornea and this can also cause blindness in the acute phase of measles (31).

Supplementation of Vitamin A has been shown to reduce mortality and morbidity due to measles. Sommer and others have shown that vitamin A supplementation on pre-school children reduces mortality and morbidity associated with measles (32,33).

In Tanzania, it was shown that there was significant reduction of measles related mortality in children admitted with acute measles following Vitamin A supplementation (34). A recent study by Hussey and Klein (35) has also shown that Vitamin A reduces morbidity and mortality in measles.

WHO has recommended Vitamin A supplementation in the acute phase of measles (31) and it is evident that this strategy will help lower morbidity and mortality due to measles especially in the developing world where measles is still a major killer.
PATHOGENESIS AND PATHOLOGY

Measles virus is transmitted by droplet or contact with the secretions of the nose and throat of an infected person. The routes of entry are mainly the oro-pharynx and the conjunctivae. The vulva in the female child has been incriminated too.

When viral particles are inhaled, they land on the nasopharyngeal mucosa. They multiply and spread by infecting more and more adjacent mucosal cells in the following one week, at the end of which the whole respiratory tract is covered with infected cells. These infected cells are altered, but not destroyed, and they stick together to form large multi nucleated giant cells (36). By the tenth day of infection, cell destruction starts and this coincides with the prodromal phase of the disease. The first signs of inflammation appear.

By the twelfth day, many infected mucosal cells break apart and release measles viruses which can be coughed out or enter the blood stream to cause viraemia.

By the fourteenth day, humoral antibodies have been produced and activation of lymphocytes, which is the key defence mechanism, has taken place. These lymphocytes search and destroy infected cells throughout the body. The effect of this can be seen in the skin as the rash of measles. Forty eight hours after the onset of rash, virus elimination is complete. (36)

CLINICAL PRESENTATION

The incubation period of the disease is 7-14 days. It has a prodromal phase which usually lasts 3-5 days and is characterized by cough, runny nose, conjunctivitis and fever (37). Koplik spots usually precede the onset of the typical maculo-papular rash which starts behind the ears and then spreads to the face and downward. These Koplik spots usually occur 1 – 2 days before the rash and may disappear within 1 2 days of appearance (37). From the 3rd to the 4th day after onset the measles rash fades away leaving behind brown or dark staining in the skin. There may be desquamation of the skin as well.

According to WHO (38), measles case definition is based on clinical findings of generalized maculopapular rash of 3 days duration or more fever of 38.3°C or more and one of the following: cough, coryza or conjunctivitis.

Laboratory diagnosis

Isolation of the virus is not recommended as a routine method to diagnose measles, however virus isolation is important in molecular epidemiological surveillance to help determine the geographic origin of the virus and the strain circulating in a given location.
The measles virus can be isolated in the urine, nasopharyngeal aspirates, heparinised blood and throat swabs. The specimens should be collected within 3 days of the rash onset and not beyond 10 days of the rash onset and in Kenya these specimens are sent to KEMRI in Nairobi.

Serological testing using the ELISA is widely available and may be diagnostic if done at an appropriate time especially on the day of onset of rash. Generally a previously susceptible person exposed to the virus or vaccine will first mount an IgM response (transient usually 1 -2 months) and then an IgG response which persists for many years. Detection of IgM antibodies using the CDC IgM capture test is diagnostic. Tests done within 72 hours after the onset of rash have a 20% chance of being false negative and a repeat is recommended as the IgM antibodies are detectable for at least 28 days after the onset of the rash.

IgG testing for measles requires the demonstration of a rise in the titre against the measles virus and therefore two specimens are required with the first one taken at onset of the rash and the second 10 – 30 days later. The tests should be conducted at the same time for the two specimens using the same reagents.

MEASLES COMPLICATIONS

The high morbidity and mortality following measles infection is due to the virulence of the measles virus and to measles complication which include:

- Bronchopneumonia,
- gastroenteritis,
- malnutrition
- laryngotracheobronchitis,
- otitis media,
- encephalitis.

**Bronchopneumonia**

Bronchopneumonia is the commonest complication associated with measles.

Morley (6) found that out of 1283 children admitted to Ilesha hospital in Nigeria in 1961, 604 (47%) had bronchopneumonia. Bwibo (26) reported that 50.6% of measles cases in Mulago Hospital in Uganda had pneumonia. Dover et al (39) observed a mortality rate of 15.8% in children admitted with pneumonia associated with measles. From India, it was reported that bronchopneumonia affected 50-90% of children hospitalized with measles (40). In U.S.A., data collected during the course of several outbreaks of measles between 1969 and 1971 showed that 5.7% of patients with measles developed pneumonia (13).
**Gastro-enteritis**

Another common complication of measles is gastroenteritis. Dave reported in India (41) that gastrointestinal complications occurred in 27-62% of children hospitalized with measles. In Thailand (42) it was reported that diarrhoea occurred as a major complication in 20-72% of cases. Measles-associated diarrhoea is associated with high morbidity and mortality. In a review of studies from 11 countries (43) it was shown that in hospitals 2-29% of young children with measles and diarrhoea die. Koster, F.T. et al (44), in a one year surveillance study in Bangladesh of children under 10 years of age found that 34% of deaths due to diarrhoea were measles-associated.

**Malnutrition**

Measles and the nutritional status of the child form a complex inter-relationship. The fever, diarrhoea and loss of appetite may severely impair the nutritional status of the child with measles.

Scheifele and Forbes (44) showed that in malnourished children there was prolonged excretion of giant cells suggesting that there was a prolonged infection in these children. Dossefor and others (45) showed persistence of measles virus in lymphocytes of malnourished and that these children had depressed cell mediated immunity to measles. Whittle et al (45) suggested that mononuclear cells of malnourished children were more susceptible to infection by measles virus than in normal children.

**Laryngotracheo-bronchitis**

In measles the inflammatory process involves a great deal of the respiratory tree. In some children, the inflammation of the larynx, trachea and the bronchi, results in oedema, coupled with the production of intraluminal tenacious and purulent secretions. The end result is the narrowing of the upper airways leading to varying degrees of airway obstruction. The affected child presents often as an emergency with “barking” cough, dyspnoea, restlessness and apprehension. The dyspnoea may be progressive leading to exhaustion, cyanosis, drowsiness, respiratory failure and death.

**Otitis Media**

This results from the inflammation in the oro-pharynx and extends via the eustachian tube to the middle ear. The irritable, febrile child, often with meningismus, usually has a reddened and injected ear drum, on otoscopic examination. The ear drum may finally perforate and suppurate. Infection may spread from the middle ear to cause mastoiditis and meningitis. Deafness and Bell's palsy (paralysis of lower branch of the facial nerve) may be other complications.
**Encephalitis**

During the acute febrile illness, viraemia involving the central nervous system may result in convulsion, clouding of sensorium, stupor or even coma. Other associated long term complications may be cranial nerve palsies, hemiplegia and frank psychomotor retardation.

Besides the acute encephalitis, a chronic form of encephalitis known as subacute sclerosing pan-encephalitis (SSPE) is a major complication associated with a poor outcome. It may occur anytime from 6 months to as long as 20 years from the onset of measles infection. It is characterised at the beginning by change of behaviour, when the patient becomes careless about himself, becomes unkempt, begins to perform poorly in daily duties. If a student, it is often manifested in poor performance in class. Progresses to convulsions, develops myoclonic jerks, and the patient becomes bed ridden.

The diagnosis is confirmed by the findings of raised measles antibodies in the CSF.

**MANAGEMENT**

Measles disease is viral in origin and consequently there is no specific drug treatment once the infection strikes. However, supportive and symptomatic treatment, especially during the acute phase of the disease and for any associated complications is desirable. These will vary depending on the clinical features of each patient.

The most important aspects of management are the preventive measures aimed at the prevention and control of measles infection. These range from the general measures such as isolation of cases, avoidance of over-crowding, good household ventilation, to the specific and most important measure of immunization of children at 9 months of age with one injectable dose of live attenuated measles vaccine. After this one dose, the protection rate is approximately 95% and is thought to be life-long.

To achieve herd immunity, 95-98% of the eligible susceptible population must be effectively immunized.

**PREVENTION**

**Development of Measles Vaccine**

The story of the live attenuated measles vaccine started in 1954 when Enders and Peebles successfully propagated the measles virus in human and monkey cell-cultures (47).

It was, however, Francis Home in Edinburgh who initiated studies on immunization against measles. In 1758, based on the principle of variolation, he scarified skin of susceptible children and applied cotton soaked in the blood of patients acutely ill with measles (48,49). Home in his own
words, said: “considering how destructive this disease is, in same seasons; considering how many
die, even in the mildest epidemical constitution; considering how it hurts the lungs and eyes; I
thought I should do no small service to mankind, if I could render this disease more mild and
safe, in the same way as the Turks have taught us to mitigate the smallpox”(49).

In 1940 O’Neil et al. (50) described modified measles in 40f 36 children after intranasal inocula-
tion with measles virus adapted from the chick embryo. Maris et. al. (51) reported inoculation of
479 children with measles virus which had undergone various chorioallantoic passages and found
that 330 (69%) of them contracted the disease during follow up as compared to 44 (88%) out of
50 controls.

It was not until 1954 when Enders and Peebles developed the Edmonston B strain of live attenu-
ated measles vaccine by passing the agent through 24 passages in human renal cell cultures (47).

Studies on the Edmonston B measles vaccine during the 1960’s showed that it was highly immu-
nogenic and was protective against measles: However, it had clinical adverse reactions including
fever and rash (52,53). More studies were undertaken to develop a safer vaccine. Schwarz et. al.
(54) developed further attenuated strain of measles vaccine by passing the Edmonston strain
through 77 additional passages in chick embryo and thus developed the Schwarz further attenu-
ated live measles vaccine which had less reactions and which was shown to be efficacious (55).

Measles vaccine was licensed for worldwide use in 1963 and since then it has contributed to the
decline in morbidity and mortality due to measles. Studies have shown that measles immuni-
ization provides effective protection when given at an appropriate age. Krugman (56) found a
seroconversion rate of 86% in American children vaccinated at 9-11 months of age and 95%
seroconversion after 12 months of age. Hayden (57) found a seroconversion rate of 92% in Na-
robi, Kenya, in children vaccinated between 6-9 months of age.

Studies have shown that when measles occurs in vaccinated children, it is a milder form than in
unvaccinated children (56,58).

Further development of the vaccine has improved its stability (59) and hence its use in tropical
countries where temperatures are generally high. The Edmonston strain has more recently been
passed through human diploid cells producing the Edmonston-Zagreb strain (60) which has been
successfully tried in 4-6 month old infants (61,62).

Vaccine Storage and Handling

Measles vaccine is a freeze dried heat sensitive vaccine which must be kept at recommended tem-
peratures at all times. At the central or district vaccine stores where the vaccine is likely to be kept
longer than at the health centres or dispensaries, the vaccine should be frozen at -20°C. Where
as at the health centres and dispensaries, it should be kept between +2 to +8°C at all times. The diluent for reconstituting the vaccine should be kept cold too.

Vaccine potency is determined by the measurement of plaque forming units or by the determination of tissue culture infection doses. An international reference reagent is used to standardise the reporting of potency. The freeze-dried vaccine is heat stable with a minimal potency for one week at 37°C. It loses 50% of the potency within one hour at 22 - 25°C and is inactivated in one hour at temperatures higher than 37°C. The vaccine should therefore be kept at +2 to +8°C and be protected from sunlight as it is light sensitive.

**Optimum Age for Immunization**

The age at which measles vaccine is administered has changed over the years in response to various studies on seroconversion rates, persistence of maternal antibodies and age-specific incidence of measles.

In developing countries children are immunized at a younger age than in developed countries. This is because the measles virus circulates abundantly and these non-immune children are at high risk of contracting the disease. It was earlier recommended at a symposium on measles (63) that, since the disease was more common in younger children, vaccination be started at 6 months of age. However, based on a joint Government/WHO Collaborative Study in Kenya in 1975 (64) which found that 90% of children no longer had maternal antibodies at 7-8 months of age and that almost all the children showed seroconversion at 7.5 months, the WHO recommended that the optimum age of immunization in endemic areas be 9 months of age. It has been estimated, based on the Machakos Study in Kenya, that the proportion of cases that would be prevented by immunizing at 8, 9 and 10 months of age would be 79%, 84% and 82% respectively (65). The Kenyan recommendation is immunization with one dose of live, attenuated measles vaccine at 9 months of age.

A two-dose schedule is used in countries where the first dose is given at an early age when suboptimal seroconversion occurs due to maternal antibodies. It is therefore recommended where measles elimination is the goal with a coverage of more than 98% in the population.

The mumps measles rubella (MMR) vaccine is available in most countries of the world and is as effective as the measles vaccine. It is recommended in countries where measles coverage is high and approaching 100%.

**Adverse events following measles immunisation**

Measles vaccine is a safe vaccine which has been associated with minimal side effects.

Following vaccination against measles a child may have fever occurring between 5 and 12 days
after the vaccination. This is a low grade fever which commonly occurs around day 7 or 8 after vaccination. There may also be a mild rash. Mothers need to be assured that this is to be expected and that no harm is done to the child. These adverse events represent replication of the measles vaccine virus with subsequent mild illness. In a few cases allergic reactions to the may occur.

**Contraindications**

There are no real contraindications to the measles vaccine. It should be remembered that illness in a child such as fever should not be considered a contraindication.

Although measles is a live vaccine it is not contraindicated in children who may be infected with HIV (66).

Persons who have experienced a severe allergic reaction to measles vaccine or to a vaccine component should generally not be vaccinated. Women who are pregnant should not be given measles vaccine.

**Recent Advances**

Following recent success in the trials of the new strain of live attenuated measles vaccine, the Edmonston Zagreb vaccine, there is now hope for the young infants who get the disease before 9 months of age. Aaby and others comparing the Schwarz measles vaccine (67) and high titre Edmonston-Zagreb (EZ) measles vaccine in Guinea-Bissau in a randomized trial showed that EZ vaccine provided significant protection against measles to children both before and after the usual age of vaccination. Other studies (68,69,70) have shown that the EZ vaccine is effective in 4-6 month old infants. WHO has recommended the use of EZ vaccine especially in crowded situations where transmission rates are likely to be high and younger children are susceptible; this is expected to increase its use.

The availability of a sensitive cell line (B95a) for isolation of measles virus from clinical specimens and the establishment of automated DNA sequencing techniques have allowed for rapid genetic characterisation of a large number of wild type strains of measles virus. This data base now enables molecular epidemiological techniques to be used to identify sources of wild virus and differentiate between wild type and vaccine strains.
REFERENCES:


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7.8 ADDITIONAL IMMUNIZATION STRATEGIES (F N Were)

INTRODUCTION

The previous edition of this manuscript included some diseases that were then not covered by the KEPI program. This was in recognition of possible developments before the next edition would be possible. Some additional antigens which were in use in private institutions were not included in the booklet. This chapter has been introduced in the new edition to cover these none scheduled vaccines. The EPI program does not recommend routine use of booster immunizations even for antigens whose booster doses have been found beneficial. Nevertheless boosters are regularly administered for several antigens in the private sector albeit without a uniform schedule. This chapter will also include some recommendations towards appropriate use of boosters. The rest of the chapter covers vaccines used in epidemics and passive immunization. There is a short paragraph for those vaccines likely to be in the Kenyan market within the next five years.

The chapter is subdivided into:

1. None-EPI scheduled vaccines
2. Boosters
3. Vaccines used in epidemics
4. Passive immunization

NON-KEPI SCHEDULED VACCINES

These are vaccines used with some regularity in the private institutions and clinics but not available in the public sector. Some of them may be of known benefit but still excluded from the national schedule due to impact prioritization. They include; measles mumps rubella (MMR), hepatitis A (HAV), typhoid and influenza

Background

Measles Mumps Rubella (MMR)

Measles:

Much of this has been covered elsewhere in this book. Available evidence indicates that a second dose of measles vaccine is useful for enhanced protection. The second dose of measles improves efficacy to more than 90% protection (1). Many advanced countries have already adopted routine double dosing of measles (2). The second dose of measles vaccine is available in the triple preparation including mumps and rubella (MMR).
Rubella:
This is an RNA virus of the Togaviridae family. It causes mild to moderate disease in children. With the measles surveillance, it is becoming clear that rubella is prevalent in Kenya. About 40-50% cases of suspected measles turn out to be serologically confirmed as rubella (Source: KEPI). Rubella is usually a mild febrile maculopapular rash illness in childhood. Its importance relates to the teratogenic effects which lead to the congenital rubella infection (CRI) that can lead to miscarriage, fetal death or birth of an infant with congenital rubella syndrome (CRS) (3). Preventing CRI requires that we strengthen rubella surveillance program, identify and address the susceptible population. There is need to document susceptibility of women of child bearing age as well as conducting CRS burden study. Childhood vaccination program is not recommended in a large scale if it does not address the women of childbearing age (WCA) because of the possible shift of epidemiology of the disease to the susceptible WCA. The MMR vaccine includes a live attenuated rubella antigen.

Mumps:
Mumps is an RNA virus of the paramyxoviridae family. It causes systemic disease characterized by swelling of one or more of the salivary glands, usually the parotid glands. Approximately one third of infections do not cause clinically apparent salivary gland swelling. More than 50% of people with mumps have cerebrospinal fluid pleocytosis, but fewer than 10% have symptoms of central nervous system infection. Orchitis is a common complication after puberty, but sterility rarely occurs. Other rare complications include arthritis, thyroiditis, mastitis, glomerulonephritis, myocarditis, endocardial fibroelastosis, thrombocytopenia, cerebellar ataxia, transverse myelitis, ascending polyradiculitis, pancreatitis, oophoritis, and hearing impairment. Though not a public health concern, there is some rationale in preventing this RNA virus, at least at individual level. A live attenuated virus with life long protection is available. It is available in combination with rubella and measles (MMR).

The MMR vaccine provides a booster dose for measles while providing primary cover for rubella and mumps. It is frequently used in private facilities in Kenya albeit with no uniformity in schedules.

There have been claims that MMR may be associated with inflammatory bowel disease and developmental disorders such as autism¹, epidemiological studies have disapproved this (4-6). Concerns of the parents and health professional were not adequately addressed and there seems to be confusion regarding safety of the vaccine especially among the well-educated parents.

¹
**Hepatitis A**

A detailed background of this infection is covered elsewhere in this book. Infection causes acute viral hepatitis, occasional hepatic failure. The virus has a world wide distribution and causes about 1.5 million cases on clinical hepatitis each year (7). There are no HAV epidemiological studies done in Kenya so far but taking into consideration of the existing sanitary conditions, Kenya is categorized as HAV endemic area (8). Hepatitis A infection is usually mild and self-limiting but may occasionally result in severe disease including fulminant hepatitis in approximately 0.01% of clinical infections. This syndrome is characterized by rapid deterioration of liver functions and very high fatality rates. The predominant impact of this disease is the cost of treatment. The disease invites a wide range of costly evaluation and treatment regimens.

Several types of hepatitis A vaccines are available and are all highly immunogenic with nearly 100% of adults developing protective antibodies within one month after a single dose of the vaccine. The clinical efficacy of hepatitis A vaccine is over 90%. These vaccines can be administered together with other vaccines in the expanded program of immunization. Protective antibodies formed in response to the infection also confer life long immunity (9).

**Typhoid**

Typhoid is a serious systemic infection caused by the enteric pathogen Salmonella typhi, a gram negative bacterium. The infection is spread by the fecal-oral route and closely associated with poor food hygiene and inadequate sanitation. Due to improved sanitation typhoid has largely disappeared from industrialized countries but remains a serious public health problem in Africa and other developing regions. According to WHO, it is estimated that 16million cases occur each year resulting to 600,000 deaths (10). In endemic areas school children and young adults, peaking between 5 and 12 years, are the most frequently affected. There is not enough documentation of typhoid fever in the children aged less than 5 years. The clinical course of the disease tends to mild and non specific and the correct diagnosis may be missed in this age group. Patients with severe disease may develop cerebral dysfunction, delirium and shock and occasionally intestinal perforation and hemorrhages. Immunocomprised patients are susceptible to lower infectious doses of S. typhi and are at increased risk of death. Regardless of treatment or the risk factors the overall risk of death is 4%. Emergence of multi-drug resistance strains poses a great challenge in the treatment of typhoid fever.

The definitive diagnosis of typhoid fever requires the isolation of S. typhi from patient’s material including blood, stool, and blood cultures. More than 90% will be culture positive in the early stages of the disease. Unfortunately facilities for culturing these materials are not available in most of Kenya where typhoid fever is endemic. There has been no proper documentation of typhoid
fever even after the establishment of Integrated Disease Surveillance and Response (IDSR) team in country. In Kenya typhoid fever is classified as an epidemic prone disease.

Human are the only source of infection and the S. typhi is transmitted by fecal oral route, therefore control measures include improved sanitation and food hygiene. Improvement of these in most of the developing countries is slow and unpredictable. The ministry of Health (MOH), Kenya has put in place various measures to prevent and control typhoid fever mainly focusing on improvement of hygiene, health education, enhanced surveillance activities and provision of safe water. The MOH does not recommend mass vaccination during outbreak or for routine use. However it recommends selective immunization of groups of people at risk during an outbreak e.g. health workers. Also recommended is vaccination of specific population at risk population during an institutional outbreak (school, prisons and refuge camps).

A polysaccharide vaccine with 3-5 years protection period is available in the market (11). This safe vaccine has an efficacy of between 50 and 80%.

Influenza

The causative organism is RNA virus with 3 subtypes. The global burden is estimated to about 10% of the world’s population every year. It primarily causes respiratory disease with occasional invasion of the nervous system. Influenza affects millions of people and kills approximately one million people worldwide every year (17). The age groups most affected are children aged <2 years and adults aged >60 years. Many of these cases and deaths can be averted through the use of safe and effective vaccines. The American region has experienced success with regard to routine vaccine use in older adults, chronically ill or immunodeficient individuals, health professionals, pregnant women, and, more recently, children aged ≤23 months. Studies on disease burden, cost-effectiveness and vaccine impact are being conducted to assist decision-makers on the introduction of new vaccines and maintenance of routine immunization at the national level. The African region has also reported regular epidemics of influenza. A live attenuated vaccine with a 70% efficacy is available (18). It must however be administered annually due the frequent mutation of the influenza epidemics.
**MATRIX OF UNSCHEDULED VACCINES**

<table>
<thead>
<tr>
<th>Target population</th>
<th>Vaccine type</th>
<th>Vaccine dose</th>
<th>Vaccine safety</th>
<th>Recommended Schedules</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Influenza</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age&lt;2yrs or &gt;65.</td>
<td>Inactivated</td>
<td>0.25ml &lt;3yrs 0.5ml &gt;3yrs</td>
<td>Very good Fever/pain in 4%</td>
<td>-2doses infancy then annual booster -annual single dose in the others</td>
</tr>
<tr>
<td>Any chronic</td>
<td>Live attenuated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>illnesses</td>
<td>Live attenuated and cold protected</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis A</strong></td>
<td>Inactivated</td>
<td>0.5ml, in pre-filed syringe IM injection</td>
<td>Very Good</td>
<td>2 doses 6-18 months apart.</td>
</tr>
<tr>
<td>1-15 years Travelers</td>
<td>virus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Measles</strong></td>
<td>All the three components of this trivalent vaccine are live attenuated</td>
<td>0.5mls of reconstituted solution</td>
<td>Generally very safe.</td>
<td>15-18 months all children Booster towards 5 years</td>
</tr>
<tr>
<td>Children &lt;5yrs for all 3</td>
<td>Live attenuated</td>
<td></td>
<td>Occasional exanthema</td>
<td></td>
</tr>
<tr>
<td>All women in child bearing age for rubella alone.</td>
<td>Live attenuated</td>
<td></td>
<td>Encephalitis been reported</td>
<td></td>
</tr>
<tr>
<td><strong>Rubella</strong></td>
<td>All the three components of this trivalent vaccine are live attenuated</td>
<td>0.5mls of reconstituted solution</td>
<td>Autism reports unproven</td>
<td></td>
</tr>
<tr>
<td><strong>Typhoid</strong></td>
<td>Polysaccharide vaccine</td>
<td>0.5ml, IM</td>
<td>Very well tolerated</td>
<td>≥2 years, 3-5 yr protection</td>
</tr>
<tr>
<td>Age&gt;2yrs, professional risk</td>
<td>Live attenuated</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**BOOSTERS**

**Background**

Boosters are vaccines given after a primary one to prolong the protection period. This is particularly useful for vaccines which protect against disease with high burden and impacts. The index diseases all tend to be those that affect a wider age range of patients.

Many vaccines do not impart life long immunity on the primary schedule.

It is however known that when the antigens are re administered at the time when the protective antibody levels have reached the minimum, the full protection is restored for a further period determined by the specific vaccine dynamics. This group of vaccines includes; the DPT antigens, polio, BCG and the hemophilus influenza type b.
Some vaccines though known to impart life long protection have theoretically lower take rates during the first administration which is improved by a subsequent dose. Measles and rubella fall in the latter category.

These two factors constitute the scientific basis for boosters.

In the government supported schedule boosters are given in special circumstances only. Pregnant women, out break response and national day campaigns are the situations that regularly justify boosters supported by KEPI. Measles has been frequently supplemented in outbreak situations or during periodic national programs. The World Health Organization currently recommends a 2 dose primary schedule of measles as a strategy for elimination of the disease.

In the private sector, many antigens are given as boosters on the basis of recommendations borrowed from developed countries or the pharmaceutical industry. The table below summarizes the practice of boosters in Kenya. It covers the justification, target population, efficacy, safety and administration.

**MATRIX OF VACCINES USED AS BOOSTERS**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Target population</th>
<th>Dose/Route</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Schedule</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus</td>
<td>Pregnant Women</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Good</td>
<td>2 doses</td>
<td>Eliminate neonatal disease</td>
</tr>
<tr>
<td></td>
<td>Open Wounds</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Good</td>
<td>2 doses post trauma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All children</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Good</td>
<td>Every 5 years</td>
<td></td>
</tr>
<tr>
<td>Measles*</td>
<td>Children &lt;5yrs</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Occasionally</td>
<td></td>
<td>Improve protection to &gt;90%</td>
</tr>
<tr>
<td></td>
<td>All Children Adolescent girls Young women</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Occasionally</td>
<td>15 months before conceiving</td>
<td>Maintain heard immunity &amp; Prevent congenital rubella</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Children &lt;5yrs</td>
<td>0.5ml, IM</td>
<td>&gt;90%</td>
<td>Good</td>
<td>18 months, 5 years</td>
<td>Maintain protection to 5yrs</td>
</tr>
<tr>
<td>Antigen</td>
<td>Target population</td>
<td>Dose/Route</td>
<td>Efficacy</td>
<td>Safety</td>
<td>Schedule</td>
<td>Justification</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------</td>
<td>------------</td>
<td>----------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Children &lt;5yrs</td>
<td>0.5ml, IM</td>
<td>&gt;95%</td>
<td>Pain/fever in 20%</td>
<td>18 months, 5 years</td>
<td>Maintain protection to 5yrs</td>
</tr>
<tr>
<td>H Influenza B</td>
<td>Children &lt;5yrs</td>
<td>0.5ml, IM</td>
<td>&gt;95%</td>
<td>Occasional pain</td>
<td>18 months</td>
<td>Maintain protection to 5yrs</td>
</tr>
</tbody>
</table>

*Measles is not a true boosting but a second opportunity to elicit an immune response in those who were previously non-responsive*

**VACCINES USED IN SPECIAL CIRCUMSTANCES**

A number of diseases are or should be vaccinated against only in special situations. These include those used in response to epidemics (cholera, typhoid and meningococcal disease), specific geographic areas (yellow fever) and specific exposure of an individual (rabies). These antigens though used from time to time in the private or public sector were not reviewed in the previous edition of this manual.

**Typhoid**

A detailed background of this disease has been covered earlier in this chapter. The primary prevention of this disease should focus on hygiene issues. Mass vaccination is generally recommended in response to proven epidemics. The use typhoid vaccines to in special groups like health workers, food handlers and children’s day care facilities is also practiced and is acceptable. The polysaccharide vaccine (11) currently in use is only efficacious in children over 2 years old.

**Cholera**

Cholera is a fecal orally transmitted gram negative enterobacillus that causes a rapidly progressive diarrhea leading to severe dehydration, electrolyte imbalance and frequently death. It occurs predominantly in epidemics and is associated with poor hygienic standards. It afflicts people in all age spectra but children often suffer more mortality than adults. In addition to improved sanitary conditions two vaccines, oral (more effective) and injectable vaccines are now available. Cholera vaccine is often required by many destinations for those traveling from areas with current epidemics.

The mainstay of treatment of cases is re-hydration. Other measures used in epidemics include mass chemotherapy in household contacts. Two vaccines against cholera have been developed, killed whole cell (given orally), a killed vaccine (intramuscular) and a live attenuated oral vaccine
recently developed. The killed oral vaccine has the longest protection period (2 years) (21) while the live oral vaccine though protecting for a shorter period (6 months) has the best efficacy (>80% immunogenicity) (21). The live oral vaccine is not recommended for children under 2 years. The use of the intra muscular cholera is not encouraged presently.

**Meningoccocus**

This gram negative coccus is the cause of one of the most rapidly progressive invasive disease that leads to septicemia and meningitis (22). Five subtypes have been described (A, B, C, Y and W135). Serogroup A accounts for most of the epidemic outbreaks reported around the world. Serogroups B and C are endemic in many parts of the world while Y and W135 account for the remaining cases. Groups A causes the majority of epidemics reported in the African meningitis belt though C and W135 have also been reported (22).

The disease affects all ages but in children it is particularly common between the ages of 2 and 6 years. Types B and C are endemic in some regions of the world. Two effective polysaccharide vaccines are available in the Kenyan private market for some time now (23);

- Vaccine against serogroup A and C
- Vaccine against serogroup A, C, W135 and Y

At present, their use is limited to the following risk groups;

- Anatomical defects or absence of spleen; immune deficiencies
- Research and industrial workers who are exposed
- Military recruits and during outbreaks.
- Foreign travel where necessary

Conjugate versions of these two vaccines and a monovalent A are also now available for use in young infants in the world. Universal vaccination program for conjugate Meningococcus A was introduced in high burden countries of West Africa and is expanding towards the east.

**Yellow fever**

Yellow fever is one of the viral hemorrhagic diseases. The causative agent is a single stranded RNA virus of the flaviviridae family. It is transmitted to human by a bite of infected mosquitoes in human yellow fever virus causes mild to severe illness to fatal disease. The disease develops in 15% of these infected by the virus (24). It affects 200,000 persons worldwide each year and causes an estimated 30,000 deaths (24). Based on WHO estimates 90% of the cases in the world occur in Africa (25). Yellow fever is endemic in some regions of Africa. The yellow fever endemic zone in Africa recognized by WHO is approximately 150 north to 150 south of equator. This region
includes 34 African countries and it stretches from Southern edge of the Sahara Desert and in North to Angola in the South. Approximately 500 million people reside in this region and are at risk of acquiring fellow fever infection. Distribution of cases and epidemics is not uniform across all the regions. Most of the epidemics occur in Western African countries. A live attenuated vaccine has been developed with life long protection and over 80% efficacy.

**Rabies**

This RNA rhabdovirus is transmitted from infected animal (most commonly dogs) to man following exposure to the animal’s saliva to the broken human skin. The animal which itself be suffering an encephalitis is often out of control and may even bite its usual handlers. If the central nervous system disease develops almost all the victims die following progressive deterioration. Fortunately this is one of the few viral infections amenable to effective post exposure active immunization. The latter must however be provided early in the incubation period which varies from days to several weeks depending on the site exposed (26).

**MATRIX OF VACCINES FOR SPECIAL SITUATIONS**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Target population</th>
<th>Vaccine biology/route</th>
<th>Protection period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera</td>
<td>All during epidemic</td>
<td>Oral- Live IM- Killed</td>
<td>• Oral-killed -2yr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Oral-live 6months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• IM-6months</td>
</tr>
<tr>
<td>Typhoid</td>
<td>Special groups</td>
<td>Injectable component</td>
<td>3-5 years</td>
</tr>
<tr>
<td></td>
<td>• Anatomical defects or absence of spleen; im-</td>
<td>Oral</td>
<td>Under evaluation</td>
</tr>
<tr>
<td></td>
<td>mune deficiencies</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Research and industrial workers who are ex-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>posed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Military recruits and during outbreaks.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Foreign travel where necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal</td>
<td>All during epidemic</td>
<td>Injectable conjugate</td>
<td>For appropriate serotypes, &gt;3yr</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Regional/travel</td>
<td>Attenuated injectable</td>
<td>Life long</td>
</tr>
<tr>
<td>Rabies</td>
<td>All animal bites, susceptible animal handlers</td>
<td>Attenuated injectable</td>
<td>Uncertain. Be used per exposure</td>
</tr>
</tbody>
</table>
PASSIVE IMMUNIZATION

Passive immunization entails the use of immune-globulins to help combat the effects of already established infection/disease. This is a post exposure measure.

This section outlines some of the available agents that can be used for passive immunization. These include those used for specific infections (hepatitis A or B and rabies), toxoids elaborated by infection (tetanus), anti snake venom and polyvalent immunoglobulin for non specific infections. The matrix below summarizes the available agents.

PASSIVE IMMUNIZATION MATRIX

<table>
<thead>
<tr>
<th>Clinical syndromes/situations</th>
<th>Target</th>
<th>Preparation</th>
<th>Dose</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-snake venom</td>
<td>Gangrene, shock, muscle paralysis</td>
<td>All snake bites</td>
<td>Polyvalent antivenom</td>
<td>Depends on clinical severity</td>
</tr>
<tr>
<td>Anti Rabies Immune-globulin</td>
<td>Animal bite, Encephalopathy</td>
<td>Following bite</td>
<td>Specific human rabies immune globulin</td>
<td>20 Int Unit/kg IM or ½ IM and ½ into wound</td>
</tr>
<tr>
<td>Anti tetanus immune-globulin</td>
<td>Titanic spasms, muscle paralysis</td>
<td>Clinical disease or suspicious wound with unknown vaccination record</td>
<td>Tetanus immune globulin</td>
<td>250-500 units</td>
</tr>
<tr>
<td>Hepatitis B immune-globulin</td>
<td>Acute viral hepatitis</td>
<td>Acute infection</td>
<td>Specific immune globulin</td>
<td>0.06ml/kg to max of 5 mls. 1M</td>
</tr>
<tr>
<td>-Exposure to unscreened blood/blood products</td>
<td>-Infant of carrier mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A immune-globulin</td>
<td>Acute viral hepatitis</td>
<td>Acute hepatitis/travel to endemic area</td>
<td>Specific immune globulin</td>
<td>0.02-0.6ml/kg IM</td>
</tr>
</tbody>
</table>
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7.9 DIPHTHERIA (F N Were, D E Simiyu)

INTRODUCTION

This acute communicable disease of childhood is caused by the toxigenic strains of any of the 3 biotypes of Corynebacterium diphtheria: gravis, mitis or intermedius. It mainly attacks the mucous membranes of the upper respiratory tract (tonsils, pharynx, larynx and the nose), the skin (wounds, sores, or abrasions) and occasionally other mucous membranes such as the conjunctiva and the vulva. It is only moderately infectious as attack rates among close contacts, of clinical cases or healthy carriers. Most cases occur in un-immunized or partially immunized children, particularly between the ages of 1 and 7 years. Children born of immune mothers possess a transient passive immunity for the first 6 months of life. According to the United States’ Centers for Disease Control and Prevention (CDC) the severer forms of diphtheria come with 5-10% mortality in relatively advanced facilities (1). Nigerian workers reported >30% fatality, ascribed mainly to lack anti-toxin sera(2). This further stresses the need for sustained universal vaccination in children leaving is resource restricted environments.

Diphtheria as a disease dates back probably to the gerond century (3,4), but it was in 1826 that Brettoneau recognized and described it clinically. He called it “dephtherite” as the membrane in the throat looked like leather (diphtheria in Greek). In 1883 Klebs described the diphtheria bacillus in the membrane of a diphtheric patient and in the following year, Loeffler grew the organism and isolated it in pure culture. In 1888, Loeffler, Roux and Yersin demonstrated that the disease was due to an exo-toxin elaborated by the bacillus.

EPIDEMIOLOGY

The disease has a world-wide distribution even though intensive immunization programmes coupled with better standards of living have caused its sharp decline in developed countries between the 1920’s and 1950’s. Diphtheria is common in developing countries especially in communities where over-crowding, low levels of immunization and poor environmental and sanitary conditions, such as among the urban poor, prevail. However, the prevalence of the disease is, perhaps, the least documented among the 11 EPI-target diseases, in Kenya as well as in other developing countries.

In more recent years it diphtheria has been found to marginally commoner in females (5) and more visible among older children and adolescents (6)
PATHOGENESIS AND PATHOLOGY

Through droplet infection (during coughing, sneezing and talking) the bacilli from an infected person (a case or carrier) reach, colonize and multiply in the secretions and epithelium of the nasopharynx of a susceptible person. These bacteria produce a toxin, which necrotizes the underlying tissues. This necrosis and the resulting dead tissue enhance more growth and multiplication of the bacilli. The necrotic, inflammatory and exudative materials form a membrane.

Initially the membrane is thin, white and filmy but soon turns thick and grey with a sharply defined border and adheres to the underlying tissues. At this stage some of the toxin gets entry into the general circulation and causes damage to muscles and nervous tissue, thus causing myocarditis by the second week of illness and neuritis between the third and seventh week of illness.

The bacilli remain lodged at the site of infection and it is the toxin produced that causes the clinical illness locally or systemically. Once the toxin is deposited in muscle or nervous tissue, it cannot be neutralized.

Note The whitish membrane on the tongue and oropharynx.

Note also the surrounding Oedema

There is also a clear demarcation between the membrane and normal tissue

Natural immunity: Newborns of immune mothers acquire a transient, passive immunity lasting up to 6 months of age. Clinical disease is, however, not followed by lasting immunity because, like in tetanus infection, antibacterial antibodies are of no consequence as the immunity depends primarily on IgG anti-toxin antibodies.
**Clinical Presentation**

The incubation period is 1-6 days. The signs and symptoms of diphtheria depend on the site of the infection, the immunization status of the host and whether or not toxin has escaped into the systemic circulation. Diphtheria is classified clinically on the basis of the anatomic location as; Nasal, Tonsiler-Pharyngeal, Laryngeal, Cutaneous, Conjunctival and Aural.

**Nasal Diphtheria**

Nasal diphtheria occurs commonly in infants, it initially resembles a common cold presenting with mild rhinorrhea. The nasal discharge may become serosanguinous and then mucopurulent excoriating the nares and upper lip. A foul odour may be noticed and careful inspection will reveal a white membrane in the nasal septum.

**Tonsillar and pharyngeal diphtheria**

Tonsillar and pharyngeal diphtheria has an insidious onset presenting initially with malaise, low grade fever and pharyngitis. Within 1-2 days a membrane appears that may vary in extent according to the immune status. In partially immune individuals a membrane may not develop. The course of pharyngeal diphtheria depends on the extern of the membrane and the amount of toxin produced. In mild cases the membrane sloughs off in 7-10 days and recovery is uneventful. Severe cases however may be characterised by respiratory and circulatory collapse. The pulse rate is increased dis-proportionately to the body temperature which is generally normal or slightly elevated. Palatal paralysis may occur presenting with a nasal voice, nasal regurgitation and difficulty in swallowing food. Stupor and death may follow in 7-10 days. Less severe cases may have a slow recovery complicated by myocarditis and neuritis.

**Laryngeal diphtheria**

Laryngeal/ diphtheria is characterised by noisy breathing, progressive stridor, hoarseness and dry cough. Severe laryngeal obstruction may occur which may result in death unless alleviated. Signs of toxemia are generally not present in laryngeal diphtheria.

**Cutaneous diphtheria**

Cutaneous diphtheria usually appears as an ulcer with a sharply defined border and a membranous base. It is more common in warm climates and may serve as an important source of person to person transmission of diphtheria.

**Conjunctival diphtheria**

Conjunctival diphtheria lesions are usually limited to the palpebral conjunctiva which appears red edematous and membranous.
**Aural diphtheria**

Aural diphtheria is characterised by otitis externa with a persistent purulent and frequently foul smelling discharge.

Some of these lesions are pictured below (Ref 7)

<table>
<thead>
<tr>
<th>Cutaneous</th>
<th>Cutaneous</th>
<th>Laryngeal</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Cutaneous Image" /></td>
<td><img src="image2" alt="Cutaneous Image" /></td>
<td><img src="image3" alt="Laryngeal Image" /></td>
</tr>
<tr>
<td><strong>Note the scally whitish appearance. This is made up of the same debris as the throat membrane</strong></td>
<td><strong>The skin variety can penetrate the soft tissue to the bone</strong></td>
<td><strong>The White membrane is visible on the glotis. This child most likely has laryngeal disease</strong></td>
</tr>
</tbody>
</table>
Pharingo-tonsiler
Note the swelling of the neck due to lymph node reaction. This is also called Bullneck diphtheria

Severe Life Threatening Disease
This is a Child on life support through a tracheostomy

COMPLICATIONS

• Respiratory obstruction may occur due to oedema of the tissues and the diphtheria membrane
• Toxin induced myocarditis usually occurs between 10-14 days of illness and may follow both mild and severe disease.
• Neurologic complications which are also toxin induced usually set in between 3-7 weeks after onset of the diphtheria symptoms. They are predominantly motor and may take the form of paralysis of the soft palate, ocular palsies, paralysis of the diaphragm and of the limbs; complete resolution usually occurs.

DIAGNOSIS

Clinical Diagnosis (8)
This should be made on the basis of clinical findings because any delay in therapy poses a serious risk to the patient. In order to improve disease recognition, patient management and surveillance, the World Health Organization (WHO) has proposed the following standardized Case Definition for Diphtheria:

• **Suspect diphtheria** is a person presenting with acute pharyngitis, naso-pharyngitis or laryngitis with a membrane

• **Probable diphtheria** represents a suspect case with one of the following:
• Typical findings on physical examination by a qualified health worker.
• Air-way obstruction, possibly with a stridor.
• Myocarditis or neuritis (paralysis), 1-6 weeks after onset of symptoms.
• History of exposure to a suspect case of diphtheria in the previous 2 weeks.
• An epidemic of diphtheria currently in the area where the patient comes from.
• Other common alternative diagnoses have been appropriately ruled out by laboratory tests.
• **Confirmed diphtheria** includes the features of a “probable case” and a positive culture of *Corynebacterium diphtheria*. The demonstration of toxin production is recommended but not really required in typical cases. It is important to note that direct smears of throat swab specimens are not sufficiently accurate to substitute for cultures.

**14.6.2 Definitive diagnosis (8)**

This depends on the isolation of *C. diphtheria*. Material from beneath the membrane or a portion of the membrane should be obtained for culture. The laboratory should be notified of the suspicion of diphtheria so that appropriate loeffler tellurite and blood agar media are inoculated. **There are advanced developments towards a Polymerase Chain Reaction based test (8). This will make diagnosis easier and more accurate**

**TREATMENT**

All cases must be notified to the local Medical Officer of Health or the relevant local health authority to facilitate the tracing, identification and management of contacts.

**CASE MANAGEMENT OF DIPHTHERIA**

<table>
<thead>
<tr>
<th>Supportive care</th>
<th>Intravenous fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients with respiratory failure unlikely to tolerate oral feeds</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Tracheostomy</strong></td>
<td><strong>Useful for correcting upper airway obstruction</strong></td>
</tr>
<tr>
<td><strong>Active Immunization</strong></td>
<td>Necessary following recovery of the patient since recovery from diphtheria does not result in adequate immunity to prevent re infection.</td>
</tr>
</tbody>
</table>
**Specific acre**

**Antitoxin**

Neutralization of the toxin by the use the antitoxin given intravenously as early as possible in the course of the disease is the **specific** treatment for diphtheria. A single dose is given to avoid the risk of sensitization. Tests for sensitivity to the antitoxin must be given prior to administration.

**Antibiotics**

Antibiotics are needed to stop the production of diphtheria toxin. Penicillin and erythromycin are effective against most strains of C. diphtheria. Patients with hypersensitivity to penicillin and/or can be given Rifampicin

<table>
<thead>
<tr>
<th>Community response</th>
<th>Notification</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases must be notified to the local Medical Officer of Health or the relevant local health authority to facilitate the tracing, identification and management of contacts.</td>
<td></td>
</tr>
</tbody>
</table>

**Identify further cases**

identify all close contacts of the case during his/her infectious period (these are persons living in the same household, sharing eating/sleeping quarters, or having prolonged direct face to face contact)

Make sure contacts are up to date with diphtheria containing vaccine

watch for symptoms of upper respiratory tract infection among contacts for a period of at least 7 days, and start penicillin or erythromycin treatment immediately symptoms develop.

This skin test has been used to determine the immune status of the patient. It is not helpful in early diagnosis since it cannot be read for several days. It is however useful in determining the susceptibility of contacts.

If resources allow throat swabs for C. diphtheria on all identified close contacts to identify carriers. The rationale for this is that both vaccinated and fully vaccinated persons may be carriers and transmit the disease.

Give chemoprophylaxis to unvaccinated close contacts at the time throat swabs are performed

Give chemoprophylaxis to all identified asymptomatic carriers regardless of their age and vaccination status.
**PREVENTION**

**General Preventive Measures**

These include the avoidance of overcrowding, the speedy treatment of acute respiratory infections and the improvement of personal, domestic and communal hygiene.

**Active Immunization**

**Developmental History of Diphtheria Vaccines**

In 1890 Van Behring showed that the exo-toxin stimulated the production of an, anti-toxin when injected into animals. On Christmas day, 1891 the first injection of diphtheria anti-toxin was inoculated into a human being, a child ill with diphtheria. In 1913, Behring used a toxin-anti-toxin mixture to immunize children. This material was used until it was replaced by toxoid in the 1920’s when Ramon in 1923 showed that formalin-treated toxin had its toxicity destroyed but left it with the capacity to produce antibodies in animals. Thus the resultant treated toxin was the “toxoid”, In 1931 Glenny made an alum-precipitated toxoid, which released its toxin more gradually and in general produced a higher and more consistent anti-toxin response (4).

**Universal Infant immunization**

Experience in developed countries, where diphtheria was formerly quite prevalent, underlines that prevention through systematic immunization is the best option for developing countries. The vaccine available is DPT, which contains the adsorbed alum diphtheria toxoid, whole cell pertussis vaccine and tetanus toxoid. It is safe, affordable and efficacious. When diphtheria toxoid is combined with tetanus toxoid, the OT vaccine is obtained but KERI does not currently stock it. It is important to note that recovery from a clinical attack is not always followed by a lasting immunity. Therefore active immunization should not be ignored even after diphtheria illness.

DPT is a killed vaccine but nonetheless it requires the recommended cold chain storage of 0°C to + 8°C. **IT SHOULD NEVER BE FROZEN** as the adjuvant separates from the toxoid and this adversely affects the vaccine’s potency.

The diphtheria toxoid component of DPT is a safe, stable and cheap vaccine with hardly any side effects after its administration. It’s efficacy is 95%, this means that the rate of vaccine failures among immunized children is 5%.

Kenya adopted the 1984 WHO Revised Immunization Schedule with effect from 1st January, 1986, which recommends 3 OPT doses, at 4 week intervals starting at 6 weeks of age. Each DPT dose is 0.5 mi given intra-muscularly at the upper, lateral aspect of the child’s thigh.
A longer than 4 week inter-dose interval does not require that the schedule be restarted all over again. In tact the longer the inter-dose interval, the better the subsequent sero-conversion rates (however drop-out rates are potential problems inherent in too long inter-dose intervals). The recommended schedule is:

Pentavalent 1 …………at 6 weeks of age

Pentavalent 2 …………at 10 weeks of age

Pentavelent 3. …………at 14 weeks of age

**PREPARATIONS CONTAINING PERTUSSIS VACCINE IN KENYA**

1. The EPI preparation called PENTAVALENT containing;
   - Whole cell pertussis
   - Tetanus toxoid
   - Diphtheria toxoid
   - Haemophylus influenza type b
   - Hepatitis B

2. Non EPI preparations with accelular Pertussis
   - Diphtheria and tetanus (DT)
   - Pentavelnt with the same antigens as the EPI one
   - Hexavalent with all the Pentavelent group plus injectable Polio
   - Hexavalent A with all the Hexavalent antigens plus hepatitis A

**REFERENCES**


7.10 PERTUSSIS (F N Were, D A Mbori-Ngacha)

INTRODUCTION

Pertussis (Whooping Cough) is an endemic and epidemic disease caused by *Bordetella Pertussis.* (B. Pertussis.) The disease is a major cause of morbidity and mortality in young children throughout the world. In the year 2008, The World Health Organization estimates that 16 million cases of pertussis occurred worldwide, 95% of them in developing countries. The same report estimates 195,000 deaths from the same infection that year (1). Virtually all of these deaths occur in unimmunized infants and are therefore preventable (2). The Centres for Disease Control and Prevention of America gives even higher global estimates at 30-50 million cases and 300,000 deaths annually (3) Due to confinement of the immunization programs to infants in most countries and lack of long term immunological memory of the current vaccines, an increasing burden of disease among adolescents and adults has been observed (4)

EPIDEMIOLOGY

Pertussis is highly communicable and predominately affects children. The epidemiology is unusual in that infants are susceptible from birth due to the jack of passive immunity through the transfer of maternal antibodies. Transmission occurs by droplet infection, directly through contact with organisms coughed up by an infected person. The disease is therefore more frequently reported among people living under crowded conditions (5,6).

The incidence of whooping cough is difficult to ascertain accurately even in countries where whooping cough is a notifiable disease. Completeness of reporting varies widely from country to country. In developing countries the great majority of cases are not likely to be reported because they do not come into contact with health services. It is therefore not meaningful to attempt to compare reported attack rates between countries (5,6).

Whooping cough is endemic in Kenya. Hospital records in the late 1960’5 indicated that about 20,000 - 25,000 out-patient attendances annually were due to whooping cough (6). Population based data from a longitudinal study done in Machakos district over a 7 year period (1977-1984) reported incidence rates of 1600 per 100,000 children under 15 years. The median age among the cases was 3.5 years with females having higher attack rates than males. During the period of this study immunization coverage for pertussis was low (6). There have been no more recent burden studies in Kenya regarding pertussis.

In industrialized countries the introduction of pertussis immunization together with the improvement of socio-economic status has contributed significantly to the reduction of pertussis morbidity and mortality. Following the nearly universal control of pertussis in industrialized
countries in the 1960 through to 70s the disease has remained stable in infants. There is however a surge of disease among adult populations suggesting inherent need for long protection (7,8). Adults may even become significant reservoirs of infection (8).

In Kenya the Expanded Programme for Immunization (KEPI) has had far reaching impact on improving the immunization coverage of infants. A survey done on the national immunization coverage in Kenya in March 1987 noted that 75% of the children were fully immunized against pertussis using the DPT triple vaccine. This is encouraging and will no doubt result in a decline in the incidence of pertussis (9).

**CAUSATIVE ORGANISM**

All cases and major epidemics are due to infection with *Bordetella pertussis*, a gram negative bacteria that was first cultured by Bordet and Gengou. *Bordetella parapertussis* causes parapertussis a condition that strongly resembles pertussis in its clinical manifestations.

In vivo *Bordetella pertussis* has a marked tropism for ciliated cells of the respiratory epithelium. Bacteria attach and multiply at the tips of, between, and at the base of cilia and this leads to ciliostasis, cell death, and shedding of the epithelial cells. The bacteria are not invasive and do not infect sub mucosal cells or other sites in the body (2).

**PATHOGENESIS**

Infection follows inhalation of organisms from air-borne respiratory secretions from an ill person to the respiratory tract of the new host. The pili or surface appendages of *B. pertussis* are responsible for its attachment to epithelial cells.

The pathogenesis of pertussis in man is incompletely understood. Infection of humans with *B. pertussis* is followed by the development of antibodies to various active biological components of the pertussis organism. The antibodies which are protective are not yet known. Secretions of individuals immune to pertussis contain 1 gG and 1 gA. Local and systemic antibodies may play a role in human protection against pertussis (2,10).

**CLINICAL MANIFESTATIONS**

Pertussis can affect any susceptible host but is most common and serious in young children. The disease varies clinically from severe illness with frequent cough paroxysms to very mild illness that may be mistaken for a cold.

Symptomatic illness is generally divided into 3 stages: **catarrhal**, **paroxysmal** and **convalescent**. The clinical manifestations depend to some extent on the age of the host and will be altered by immunization.
Catarrhal Stage (lasts 1-2 weeks)

The incubation period is seven to ten days and usually not more than 14 days. The onset of the disease is subtle resembling a mild and non-distinctive upper respiratory tract infection with rhinorrhea, mild conjunctival tearing, occasional sneezing and a mild cough. There may be a slight transient fever but most commonly fever is not recognized. The cold-like symptoms continue with persistent and increasing cough. By 7 to 10 days the illness enters the paroxysmal stage.

The catarrhal stage is the most infectious period, with the risk of transmission and the ability to detect the organism decreasing rapidly through the paroxysmal stage.

Paroxysmal Stage (lasts 2-4 weeks or longer)

This stage is characterised by an increasing number of episodes of coughing. The cough becomes paroxysmal consisting of repetitive series of many coughs during one expiration. This is followed by a sudden deep inspiration with a characteristic “whoop”. The absence of the typical whoop does not exclude the diagnosis of pertussis. Infants particularly may present only with paroxysms of cough followed by choking rather than a “whoop”. A variety of stimuli may set off a paroxysm such as feeding, suction or attempted examination of the pharynx. Each paroxysm is likely to result in significant hypoxia especially in young infants. Once the paroxysmal stage is reached, the course of the illness cannot be altered.

Convalescent Stage (lasts 1-4 weeks or longer)

Parents are frequently surprised by the duration of symptoms. The paroxysmal stage lasts from 1 to 4 weeks and then gradually becomes less severe. The paroxysms decrease in frequency although they may persist for 1 to 6 months or more. Paroxysms often recur with subsequent inter-current respiratory infections. Patients are usually tree of B. pertussis organisms during the paroxysmal and convalescent stages despite persistent coughing.

COMPLICATIONS OF PERTUSSI S

Respiratory Complications

Pneumonia and patchy atelectasis may occur due to stasis of the thick purulent secretions and paralysis of cilia. In hospitalised patients lobar and sub-lobular atelectasis is frequent and bronchiectasis may occur. Obstruction of large or small airways in severely affected infants may result in interstitial or subcutaneous emphysema or lead to pneumothorax.

Secondary infection is usually associated with H. influenza, S. pneumonia, Strep. pyogenes or S. aureus. When secondary infection occurs, it is often accompanied by significant fever and tachypnoea. The presence of significant fever suggests infection with a second organism. The most
frequent complications of pertussis is pneumonia. It is responsible for more than 90% of pertussis deaths in children under 3 years of age.

Otitis media is also a frequent infectious complication of the acute disease especially in infants and is frequently due to *S. pneumoniae*. Pertussis has also been associated with activation of latent tuberculosis. (5)

**CNS Complications**

Severe CNS disturbances appear most commonly in infants during the paroxysmal stage. Signs and symptoms vary; convulsions may occur abruptly or evidence of CNS involvement may appear more insidiously but progress to convulsions, semi-coma and coma.

Acute neurologic manifestations may include persistent seizures, hemiplegia, paraplegia, ataxia, aphasia, blindness, deafness and decerebrate rigidity. The CSF is typically normal or may have mild pleocytosis or a slight to moderate elevation of protein (10mg/dl).

CNS involvement frequently results in permanent sequelae. One third of children in whom encephalopathy develops die, one third survive with sequelae, and one third survive and appear normal. Sequelae may include mental retardation, focal paralysis, focal or generalized seizures and changes in personality and behaviour (5).

The frequency of CNS complications range from 1.7% to 7% or more of pertussis cases in large series of hospitalized children. CNS involvement is relatively common; 4 per 1000 reported patients with pertussis had encephalitis in 1982-1983 and in the period 1984-1985 the rate was 5 per 1000. (11-15)

It is however worth noting that all the complication rates are based predominately on hospital statistics and reported cases and are therefore likely to be overestimates.

**Other Complications**

The prolonged and violent expiratory efforts during pertussis paroxysms may have secondary consequences, including hemorrhagic events such as epistaxis, melena, sub-conjunctival haemorrhage (which is very typical), subdural hematoma and spinal epidural hematoma. Other rare events are umbilical or inguinal hernias, rectal prolapse pneumothorax and mediastinal or subcutaneous emphysema which result from raised intra-thoracic pressure.

Weight loss or failure to gain weight may be conspicuous especially in the young infant (5).
Mortality

Reported case fatality rates are usually based on hospital figures and are therefore inflated since only serious cases are hospitalised. Figures range from 0.5 per 1000 in England and Wales to close to 14% in Uganda. Community based data in Machakos, Kenya, showed an overall case fatality rate of 1.2% but among infants it was noted to be 3.2% (5, 6).

Historically infants have always borne the brunt of pertussis mortality. Even in developed nations morbidity as measured by hospitalization, pneumonia, and other complications, and death are greatest in children under 1 year of age (5).

In small infants, pertussis is particularly severe and extracts a heavy toll in morbidity and mortality. These children have small calibre airways which are easily obstructed by the debris that form as a result of the inflammatory process and this may contribute to the higher mortality.

Atypical Manifestations

Mild atypical disease may occur in cider children and adults. This is thought to be due to partial immunity or previous immunization. The symptoms consist mainly of a persistent cough due to lingering tracheobronchitis and may persist for several weeks; complications are infrequent. Cases may be difficult to diagnose unless there is a history of contact with a case of pertussis (5, 6).

LABORATORY DIAGNOSIS

This topic has been very well summarized and published in a review article obtainable on the free internet (16).

The diagnosis of pertussis is based upon a characteristic history and physical examination and is unmistakable in a typical case. However in young infants and atypical cases, several laboratory tests as listed below are especially useful.

- **WBC Count:** Lymphocytosis and an elevated total WBC count are usually present in classical disease. The absolute Lymphocyte counts exceeds the normal range and may reach 30,000 cells per decilitre or greater. This is nevertheless a very non-specific test and there is often little or no lymphocytosis in mild or moderate cases.

- **Isolation of the Organism:** Presently the “Cold standard” for the diagnosis of *Bordetella pertussis* infection is the culture from nasopharyngeal swabs. Unfortunately the organism is fastidious and slow growing, and its culture is complicated by contamination and overgrowth by other nasopharyngeal organisms. In epidemic situations with optimal specimen collection and laboratory techniques, the isolation rates in suspected cases is 80%. However in the usual clinical situation isolation rates are considerably lower being highest during the catarrhal stage and early in the paroxysmal stage.
Specimens for culture should be obtained from the nasopharynx rather than the throat, using Dacron or Calcium Alginate swabs. Patient specimens should be directly plated onto selective media. Bordet-Gengou medium, Regan-Lowe charcoal agar and modified Stainer-Scholte agar are all effective for *B. Pertussis* culture. Isolation rates are highest during the initial 3 to 4 weeks of illness. More recently, a sensitive Polymerase Chain Reaction test has been elaborated providing rapid and accurate diagnosis (16). It is however expensive and hence still not available in Kenya.

**Other Tests**

**Direct detection of organism by Fluorescent Antibody**

Direct fluorescent antibody identification of *B. pertussis* in nasopharyngeal specimens is relatively easy to carry out. It may be particularly useful late in disease or during anti-microbial therapy when viable organisms are no longer present. However the sensitivity and specificity of this technique remains to be defined (16).

**Agglutination tests**

The agglutination test has been used to study immunity to pertussis for over 40 years. It has been a useful measure of immunity following Immunization with whole cell pertussis vaccines. In the clinical situation, the demonstration of a four-fold or greater titre increase is diagnostic. However, there may be absence of demonstrable agglutinin-titres in paired sera in bacteriologically confirmed cases (16).

**MANAGEMENT**

**Specific Management**

Erythromycin is the most effective and least toxic antimicrobial in the treatment of pertussis. It can eradicate the organism after one or two days when administered in the catarrhal or even paroxysmal stage. However 10% of the cases may continue to shed the organism unless treatment is continued for 14 days.

Erythromycin initiated during incubation, or catarrhal stage may prevent or modify clinical disease. Erythromycin 40-50 mg/kg/24hrs in four divided doses is recommended for a total of 14 days for either treatment or prophylaxis. In addition to erythromycin prophylaxis for 14 days, close contacts younger than 7 years of age should receive one dose of DPT. Children over 7 years who have been immunized should receive only prophylactic erythromycin (5, 6, 9).

**Supportive Management**

Supportive Treatment includes avoiding factors that provoke attacks of coughing and the main-
tenance of hydration and nutrition. Gentle suction to remove secretions and oxygen may be required, particularly in infants with pneumonia and significant respiratory distress.

**IMMUNIZATION**

**History of Vaccine Development**

Due to the fact that pertussis was a devastating disease with high mortality the idea of vaccine development was immediately considered following the isolation of *B. pertussis* in 1906. The first trials using a vaccine developed by Danish Serotherapeutic institute in Copenhagen was carried out in Faroe Islands from 1923-1924 by Madsen. He was able to demonstrate same degree of protection in vaccine recipients. But at the same time work done in the USA gave variable results with a variety of prepared vaccines. This led to withdrawal of the vaccine from routine use, only to be reinstated in 1944 after several vaccines tried during the 1930’s proved effective. In 1964 an international standard for pertussis vaccine was established and it was recommended that a total immunizing dose of vaccine contain at least 12 i.u. (17)

The true value of pertussis vaccination is often invisible due to the marked reduction in disease following the widespread adoption of national vaccination programs. The WHO estimates that in the year 2003 38.3 million cases and 607,000 deaths were averted by the existing pertussis vaccination programs (18)

**Vaccine Production and Formulations**

All relevant vaccines used in the developing world supported by the Global Alliance for Vaccines and Immunizations (GAVI) presently contain whole cell pertussis

The pertussis vaccine is prepared from *B. Pertussis* seed stock that are composed of several strains. Stored freeze-dried bacteria are inoculated into “seed” culture. The “seed culture” is grown to provide a volume sufficient to produce a bulk culture. When growth of the bulk culture is completed, the *B. Pertussis* cells are harvested, concentrated by centrifugation and suspended in a phosphate-buffered saline solution. The concentrated bacteria are then killed and partially detoxified by heat or addition of a chemical agent (e.g. thiomersal) or by a combination of these methods. The pertussis component of vaccines is tested for purity, sterility, opacity, freedom from toxicity and potency.

Acellular pertussis was developed in response to the need to reduce side effects presumed to due to the whole cell. The first generation was a single anti-toxoid which turned out to have inadequate efficacy. Presently there are upto 5 component preparations containing a mixture of toxoid, filamentous haemagglutinins and other surface antigens (19). All these however require the same cold chain storage conditions as the original whole cell antigen.
The Vaccine Combinations (Formulations) including Pertussis in Kenya are;

1. The EPI preparation called PENTAVALENT containing:
   - Whole cell pertussis
   - Tetanus toxoid
   - Diphtheria toxoid
   - Haemophylus influenza type b
   - Hepatitis B

2. Non EPI preparations with acelular Pertussis
   - Pentavelnt with the same antigens as the EPI one
   - Hexavalent with all the Pentavelent group plus injectable Polio
   - Hexavalen A with all the Hexavalent antigens plus hepatitis A

The Pentavalent vaccine used in the EPI program of Kenya uses inactivated pertussis component with tetanus, diphtheria toxoids and hepatitis B as the liquid diluents of the HIB powder. The toxoids are adsorbed to aluminium which is used as an adjuvant in the vaccine and is mainly responsible for the cloudy appearance of the final product.

In general all vaccines used in Kenya’s EPI program are prepared under the guidelines of the World health Organization (17).

**Vaccine storage**

The potency of the pertussis component of DPT vaccine can be decreases by temperature variability. Diminution of potency may be caused by both high temperature and freezing. Stored in a refrigerator between 0°C and +8°C the whole cell pertussis component relevant combination vaccine appears to have satisfactory potency period over two years.

**Immunization schedules**

The young infant is not protected from whooping cough by passive immunity from the mother. Early immunisation is therefore important as young infants are at risk of developing severe form of disease. Interference with the infant’s antibody response is not a problem as maternal antibodies are usually absent. Therefore for countries with a high incidence of the disease, EPI recommends starting immunisation at 6 weeks of age and providing three doses spaced at four weeks intervals. Each dose contains at least 4. I.U.

In Kenya under the KEPI programme the current immunisation schedule recommends the first dose of PENTAVALENT to be given at 6 weeks (or at first contact with the baby after 6 weeks).
Subsequent doses are given 4 weeks apart to a total of 3 doses. Inter-dose intervals of longer than 4 weeks does not require restarting the schedule. There is increasing evidence supporting the role of booster doses throughout childhood and the elderly (20).

**Vaccine Reactions**

Vaccine reactions attributable to pertussis can be divided into minor and major reactions

**Minor vaccine reactions include:**

- Pain and inflammation at the site of injection
- High fever

These reactions are very common but transient and disappear within 24-48 hours post vaccination. Parents should be made aware of the occurrence of these. Management consists of the use of analgesics/antipyretics like paracetamol.

**Major vaccine reactions include**

- Persistent crying
- Unusual high pitched cry
- Excessive somnolence
- Convulsions
- Hypotonic-hyporesponsive state (collapse, shock)
- Encephalopathy.

It is important to note that these major reactions are rare with the currently used vaccines. The estimated risk for severe neurological illness attributable to Pertussis vaccine is 1 in 170,000 doses administered while that for permanent neurological sequelae is 1 in 470,000 doses (11).

**Vaccine Efficacy/Effectiveness**

The efficacy of pertussis vaccines has been measured in several epidemiologic studies. An enormous amount of data has accumulated indicating powerful impact on disease prevention and modification. Reported efficacy of the whole cell vaccine varies from 63%-91 %. (21) Although there is considerable knowledge about *B. pertussis* antigens and toxins and a recent increased understanding about virulence factors in disease, there is a lack of specific information regarding the cause of both common and severe vaccine reactions (22).

In order to translate efficacy into effectiveness (measures by actual impact upon introduction into the national program), several factors need to be ensured including; coverage over 90%, timely scheduling and ideal cold chain management. This is the goal of the Division of Vaccines and Immunization in Kenya.
Contraindications

No vaccine is totally without adverse reactions. It is worthwhile to note that the risk of serious complications from pertussis vaccines is much lower than the risks from the natural disease. The decision to withhold immunization should be taken only after serious consideration of the potential consequences for the individual child and the community.

It is particularly important to immunize children suffering from malnutrition. Low-grade fever, mild respiratory infections or diarrhoea and other minor illnesses should not be considered as contraindications to immunization. The immunization of children ill enough to require hospitalization, should be deferred for decision by the hospital authorities. The immunization status of hospitalized children should be evaluated and they should receive appropriate immunization before discharge. The hazards of immunizing must be balanced against the risk of remaining unimmunized. Pertussis-associated convulsions, encephalopathy and death are a great deal more common than those associated with immunization. During the last decade several carefully performed studies have produced risk-benefit analyses of pertussis immunization and all indicate that the benefits of vaccination far outweigh the risks.

However, because whole cell vaccines are associated with disturbing acute morbidity, the following guidelines have been laid down after careful consideration regarding contraindications to further immunization after an initial dose:

• allergic hypersensitivity to a prior dose of vaccine.
• collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours post immunization
• convulsion with or without fever occurring within three days post-immunization
• encephalopathy occurring within 7 days of immunization.

These recommendations are based on the presumption that children who experience adverse reactions following pertussis immunization are more likely to have similar reactions of equal or greater magnitude upon subsequent immunization (21, 23-25).

Recent Advances

During the 1990s decade, much has been learned about the biology of *B. Pertussis* and this information has led to the development of new acellular vaccines that cause less local reactions. Acellular vaccines are currently routinely used in developed countries in the their national programs. Many providers in Kenya’s private sector have also shifted to acellular pertussis.

Clinical trials on the efficacy of acellular vaccines have been undertaken in the United States and Sweden in children aged 6 months. Local adverse reactions were noted to be few and mild. Local
reactions were more frequent after the second doge of study vaccines and placebo than after the first doge of these preparations. In contrast, fever and other systemic reactions seemed to occur in lower frequency after the second doge. Vaccine efficacy in studies done in Sweden was 80% when only severe cases were considered, but was 60% when all cases were considered. This is less than that reported for whole cell vaccine in previous trials. There is therefore a question as to whether acellular vaccine is as efficacious as whole cell vaccine. (23,26)

The following important issues still need to be addressed regarding the pertussis vaccines:

- The efficacy and safety of acellular vaccine in children younger than 6 months
- The efficacy of the acellular vaccine compared with whole-cell vaccines
- The optimal immunization schedule with both the whole cell” and the acellular vaccine.

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7.11 YELLOW FEVER (G Irimu)

INTRODUCTION

Yellow fever is a viral hemorrhagic disease. The etiological element is yellow fever virus. It is transmitted to human and other vertebrate by the bite of infected mosquitoes. It is termed as ‘arbovirus’ as it is transmitted between vertebrate hosts (human and monkeys) by arthropods (mosquito). The virus can also be considered as a zoonotic virus. The virus is a member of the family Flaviviridae, genus Flavivirus. The genus Flavivirus is composed of approximately 70 viruses which include dengue viruses and Japanese encephalitis virus. The yellow fever virus is small (35-45nm) and consists of a core containing a single-stranded RNA surrounded by a lipid envelop.

16.1 EPIDEMIOLOGY

Yellow fever occurs in tropical areas of Africa and South America. Yellow fever affects 200,000 persons world wide each year and causes an estimated 30,000 deaths. WHO estimates 90% of the cases in the worlds occur in Africa. This chapter therefore focuses on yellow fever in Africa.

Geographical distribution of yellow fever in Africa

Yellow fever is endemic in some regions of Africa. The yellow fever endemic zone in Africa recognized by WHO is approximately 150 N to 150 S of equator. This region includes 34 African countries and it stretches from Southern edge of the Sahara Desert in the North to Angola in the South. Approximately 500 million people reside in this region and are at risk of acquiring yellow fever infection. Distribution of cases and epidemics is not uniform across all the regions. Most of the epidemics occur in Western African countries. African countries which have had an epidemic since 2000 include Nigeria, Ivory Coast, Liberia, Senegal and Guinea 1. The first epidemic in Kenya occurred in September 1992 and was brought under control in March 1993. No other human epidemic has been recorded in Kenya since then. The yellow fever outbreak was mostly in the woodland of Kerio Valley away from human settlement due to large movement of non-immune humans into yellow fever endemic zones in search of water in period of drought. Young males were most affected. This was the last epidemic reported in Kenya. Yellow fever however continues to be continuously present in the jungles of East and Central Africa. Therefore although there has not been recent reported yellow fever activity in Kenya in the last 17 years there is still a risk of resurgence of the disease in the country.

The outbreak in Kenya was transmitted by bites caused by Ae. Africanus and Ae keniesis mosquitoes.
**Yellow fever transmission**

The reservoir of yellow fever virus (YFV) is the susceptible vector mosquito species that remains infected throughout its life and can transmit the virus transovarially. Yellow fever can persist as zoonosis in tropical areas of Africa and America, with non human primates responsible for maintaining the infection. Man plays the role of amplifiers of the amount of virus available for the infection of mosquitoes.

There are three epidemiological patterns of YFV transmission:

- **Jungle cycle** (enzootic; forest or Sylvatic cycle, endemic area)
- **Intermediate cycle** (emergency zone; cyclic epizootics and epidemics)
- **Urban cycle** (potential for epidemics)

The three transmission patterns lead to clinically identical disease since they are produced by the same virus. Each of the three cycles need a different vector, this explains why the forest cycle could be de-linked from the jungle cycle. Some of the mosquitoes however have the potential of bridging the gap between jungle and urban yellow cycles.

**Jungle cycle:** In African forest the transmission is predominantly monkey to monkey by mosquito Aedes africanus. Human infection is sporadic and large epidemics involving people are rare. Aedes africanus is a forest mosquito that breeds primarily in tree holes and is only found in jungles of Africa. The jungle cycle is similar to that in South America where the principal mosquito vectors are primarily in the genera, Hemagogus and Sabethes.

**Intermediate cycle:** Transmission is either between monkey to monkey or monkey to man. It is usually in areas with some human activity such as small human settlements, communal herding areas and farmland. It has potential for large epidemics. This cycle has only been described in the moist savannah of Africa. The cycle involves several species including Aedes furcifer, Aedes luteoccephalus, Aedes simpsoni and Aedes taylori.

**Urban cycle:** Transmission is from human to human by the mosquito *Ae. Aegypti*. It is the most deadly form of disease transmission, potentially involving thousands of human cases.

**Risk factors for yellow fever transmission**

1. Age: the distribution of cases by age depends on the immune status of the population at the time of the outbreak. If the entire population has no natural or vaccine induced immunity, the distribution of cases parallels the demographic distribution. However when the population has been exposed to an epidemic or a mass vaccination campaign several years earlier the adults still have some protection and are relatively less affected by the epidemic. This explains
why children are more affected by the non-occupational yellow fever. Similarly EPI recommends that YF vaccine be included in the routine EPI in the countries at risk for yellow fever.

2. Climatic conditions: rainy season favors abundance of breeding sites for mosquitoes. Incubation period in the vector is shortened by higher environmental temperatures.

3. Human activities: May influence host abundance, either negatively (hunting monkeys, mosquito control) or positively (creating artificial breeding places- pots, tyres etc, overpopulation). Felling of trees may increase transmission by bringing the treetop- dwelling mosquito down closer to human contact. The peak biting activity of *Ae. Africanus* occurs in the forest canopy 60ft above the ground in the early mornings before sunrise and in the evenings just after sunset. There is little activity at the ground level during the day.

4. Virulence of the YFV: The reason why there are infrequent of yellow fever outbreaks in East and Central Africa is not clear, yet YFV is continuously present in the jungles of East and central Africa. It is possible that different genotypes of YFV may vary in virulence in human being.

**CLINICAL PRESENTATION**

In human beings, yellow fever virus causes mild to severe illness to fatal disease. The clinical symptoms of the disease develop 3-6 days after mosquito bite but may be as long as 13 days. The disease develops in 15% of those infected by the virus, majority develop only a mild disease and recover quickly. Two main phases of the disease are recognized:

**First phase (period of infection):** It is characterized by sudden onset of fever, headache, muscle pain, backache, general weakness, nausea and vomiting. The patient has red eyes and positive Faget’s sign (failure for pulse rate to rise with body temperature).

The patient has viraemia and is infectious to mosquito.

A short period of remission ensues, clinical symptoms disappears for up to 24 hours after which the toxic phase begins.

**Second phase (toxic phase):** The patient develops high fever, vomiting, epigastric pains, jaundice, hemorrhagic diathesis including hematemesis, coma and death.

Yellow virus is absent from the blood of patients in this phase. Anti-yellow fever virus antibodies appear during this stage.

Case mortality rate for patients in toxic phase is 20-50% or higher. Death usually occurs within 10 days of the onset of symptoms. Disease confers lifelong immunity to the survivors.
Differential diagnosis of yellow fever

The clinical diagnosis of isolated case of yellow fever is particularly difficult because the symptoms are similar to those of may other diseases, e.g. viral hepatitis, malaria, dengue, typhoid fever, leptospirosis and Ebola disease and Lassa fever. Laboratory confirmation is therefore essential for the diagnosis of an isolated case.

LABORATORY DIAGNOSIS OF YELLOW FEVER

Presence of yellow-fever-specific IgM or a four-fold rise in serum IgG levels (acute or convalescent) in the absence of yellow fever vaccination.

Or isolation of yellow fever virus from blood.

Or positive postmortem liver histopathology.

Or detection of yellow fever antigen in tissue by immunohistochemistry.

Or detection of yellow fever virus genomic sequence in blood or organs by PCR

In persons vaccinated with yellow fever vaccine virus may be recovered from blood 6-7 days after vaccination and detectable IgM neutralizing antibodies are present as long as 18 months after immunization.

TREATMENT OF YELLOW FEVER

There is no specific treatment for yellow fever. Supportive treatment should be given as indicated by the symptoms. Person with yellow fever should be nursed in isolation to reduce disease transmission in the presence of the appropriate mosquito.

YELLOW FEVER VACCINE

Vaccine development

17D vaccine is the only yellow fever vaccine available currently. It was developed by Theiler and Smith in 1937. It is a live attenuated virus produced from human virus by passage in embryonated chicken eggs.

Vaccine storage, Handling and use

It is a stable vaccine whose shelf life at temperature -20 or 4 °C is prolonged to 2 years. At the central stores where the vaccine is likely to be kept for upto 8 months vaccine need not be frozen. It can be kept at +2 °C to + 8 °C. If lyophilized, the diluent used should be at refrigerator temperature and the reconstituted vaccine should be kept in an ice-bath. The vaccine is available as
single dose vial or multiple dose vial. Once reconstituted the vaccine should be thrown away after 6 hours or at the end of the vaccination session; multiple-dose vial policy does not apply.

17D vaccine is given at a dose of 0.5ml subcutaneously.

17D yellow fever vaccine can be administered simultaneously with any or other EPI antigens with subsequent good take rates ³.

**Optimum age of immunization**

Yellow fever vaccine is recommended for use from 6 months of age. Yellow fever vaccine should not be given to infants younger than 6 months. Immunization of infants younger than four months can produce post-vaccination encephalitis (0.5-4 per 1000 infants)³. WHO recommends that yellow fever vaccine be included in the national EPI activities in endemic countries and that it should be given to infants at the same time as the measles vaccine at 9 months of age. However it can be used to infants aged 6 months during yellow fever outbreaks. The response to yellow fever in children 6 months of age are qualitatively (seroconversion) and qualitatively (GMTs of antibodies) similar to those immunized at 9 months of age. The adverse effects are also similar ⁴.

Inclusion of yellow fever vaccination in the childhood routine immunization is required in Kenya because of the risk of resurgence of the disease. However due to logistical problems DVI has focal areas of yellow fever vaccination activity. That is in Kerio Valley and the districts around it. The vaccine is given at 9 months together with measles vaccine. The coverage is poor because of the drop out rate between Pentavalent 3 and measles. It should be maintained at 95% among children aged 1 year as should measles coverage. Including yellow fever vaccine in the routine EPI programme is more cost effective than conducting emergency campaigns in response to yellow fever epidemics.

**Yellow fever vaccine efficacy**

YF vaccine is highly effective vaccine with sero-conversion rates of 98% with minimal side effects. YV is recommended to be given every 10 years. The immunity may last as long as 30 years though ³.

**Adverse effects related to yellow fever vaccine**

Yellow fever vaccine is considered to be one of the safest vaccines.

- Mild reactions in 2-5% of the vaccines are limited to headache and low grade fever usually 6⁶th-7⁶th day after vaccination.
- Allergic reactions including skin rash and urticaria occur in less than 1:1,000,000 in persons. Mainly in persons with allergy to eggs.
• Encephalitis. 0.5 to 4 per 1000 infants aged less than 4 months. 5
• Local reactions include redness and swelling at the site of injection. 4

**Indications and contraindications of yellow fever vaccine**

**Indications**

1. In persons 9 months or older living in at risk areas. High priority is to be given to persons at risk of exposure.

2. Immigrants from non-endemic to at risk regions. They should be vaccinated at least 10 days before arrival.

**Contra-indications**

1. Children less than 6 months of age

2. Persons with severe egg allergy.

3. Symptomatic HIV positive individuals and severely immuno-compromised person. Persons testing HIV positive with CD4+ counts above 200 cells/mm3 can be safely vaccinated without added adverse effects.

**Not recommended (except during epidemics when risk of transmission is high)**

• Pregnant mothers

**YELLOW FEVER CONTROL**

Four strategies that have the potential to bring yellow fever fully under control in Africa: epidemic control, mass immunization, routine childhood immunization and surveillance.

In order to control yellow fever the following issues should be considered:

1. The yellow fever vaccination plan should target 100% of the population residing in the enzootic areas and areas that are the source of immigration into the enzootic areas. Yellow fever coverage should be maintained at >95% among the children aged one year.

2. Epidemiological surveillance system of yellow fever virus circulation should be established and in countries where it is existing it should be strengthened both in enzootic and non-enzootic areas to allow rapid implementation of outbreak control measures when a human case or an epizootic case is detected.
3. Health workers in both the enzootic and non-enzootic should be conversant with definition of febrile icteric syndrome and surveillance strategy for yellow fever to allow early detection of yellow fever virus in circulation.

4. Yellow fever laboratory network needs to be strengthened.

5. An adequate yellow fever vaccine should be maintained both for routine immunization and control for possible outbreaks.

6. In areas where yellow fever epidemics are occurring or considered at high risk inclusion of older child may be appropriate as a special ‘catch up’ programme.

7. In countries where yellow fever vaccine and measles vaccines are given simultaneously at 9 months, yellow fever vaccine should be considered in measles vaccination campaign.

**Surveillance for yellow fever**

Yellow fever surveillance is critical for monitoring the incidence of the disease and allowing the prediction and early detection of outbreaks and monitoring of control measures. Case reporting of yellow fever is universally required by the International Health Regulations. Cases should be reported to WHO within 24 hours of detection.

**WHO recommended case definition for purpose of surveillance**

**Suspected case:**
A person with acute onset of fever followed by jaundice within 2 weeks of onset of the first symptoms.

**Confirmed case:**
A suspected case that is laboratory confirmed or epidemiologically link to a laboratory-confirmed case or outbreak.

**Action taken if a single case of yellow fever is suspected**

- Report case –based information to the next level immediately.
- Treat and give patients appropriate supportive care under mosquito net and strict isolation.
- Collect specimen for laboratory confirmation.
- Investigate case to determine how transmission occurred.
- Plan for an immunization activity.
**Action taken if a single case of yellow fever is confirmed**

- Mobilize community early to enable rapid case detection and treatment.
- Conduct a mass campaign in appropriate age group in the area (age 6 months and older) and in areas with low coverage.
- Identify high-risk population groups and take steps to reduce exposure to mosquitoes.
- Improve routine and mass vaccination to include yellow fever in the high-risk areas.

Once epidemic is confirmed priority should then be given to collecting specimen from new or neighboring areas.

**Constraints on emergency vaccination in Africa**

Emergency vaccination takes place as soon as an outbreak has been confirmed in an attempt to limit the spread by immunizing all persons in the focus regardless of their former immunization status. Unfortunately in Africa, epidemic control often suffers from delay of two months or more between the onset of epidemics and their recognition, partly due to the fact occurrence of the cases in remote areas with a few medical services and unfamiliarity of medical personnel with the disease. There could also be difficulties in obtaining large supply of vaccines, syringes and needles and sudden deployment at a short notice of large numbers of health workers. Immunity after vaccination does not develop until seven days after immunization, hence vaccination does not confer immunity immediately, hence importance of isolating the cases.
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7.12 ROTA VIRUS

INTRODUCTION

Rota virus is the most common cause of diarrhoeal illness in children worldwide. It is highly infectious with high morbidity and mortality rates, especially in children from developing countries (1). It was first discovered by Ruth Bishop in 1973 from duodenal biopsies in children with diarrhoea (2).

THE VIRUS

Rota virus is a double stranded RNA virus belonging to the Reoviridae family. It has a complex wheel-like structure with a triple-layered icosahedral protein capsid composed of an outer layer, an intermediate layer and an inner core layer. The outer capsid contains 2 structural proteins, the VP4 and VP7 antigens, which are important in classification and vaccine development.

There are seven groups of the virus, A-G, with A, B, and C found in humans and animals and D, E, F and G found only in animals. Group A Rota virus is of the greatest clinical significance. There are several serotypes based on the VP4 and VP7 antigens.

EPI DEMIOLOGY

Prevalence

Rota virus is described as a “democratic” virus found throughout the world and it affects both the rich and the poor. 95% of children worldwide are infected within the first 3 to 5 years of life, irrespective of race or socioeconomic status (1).
Rota virus gastroenteritis is the leading cause of diarrhoea related illness and death among infants and young children. It is estimated that worldwide, Rota virus results in 25 million clinic visits/year, 2 million admissions/year and 527,000 deaths/year in children less than 5 years of age (3,4). It is the most common diarrhoeal pathogen causing hospitalization in both industrialized and less developed countries, accounting for approximately 40% in both. Most severe infections occur in children under the age of 2 years and nearly half of Rota virus deaths occur in Africa.

Transmission

Rota virus occurs more commonly in the dry winter months in developed nations but there is a less distinct seasonality pattern seen in tropical countries. It is highly contagious and humans are the main reservoirs although it does affect animals too.

It is spread predominantly by the fecal oral route by contamination of food, water and environmental surfaces such as toys. This is especially important in infants and young children as they frequently put their hands and toys into their mouths (5).

Due to the universality of rota virus infection, regardless of hygiene and sanitation levels, droplet transmission of the infection is also a possibility, and rota virus is known to cause respiratory systems.

Rota virus is highly stable and can survive for hours on human hands and for several days on solid surfaces. It remains infective in human stool for up to one week. It is relatively resistant to commonly used disinfectants but is inactivated by high concentrations of alcohol, chlorine or iodine (5,6). Transmission can occur before onset of symptoms and can persist for up to 8 weeks after symptoms have subsided (7).

PATHOPHYSIOLOGY (8,9)

CLINICAL PRESENTATION

The incubation period of the disease is 2-4 days. The most common clinical features are:

1. Vomiting, which usually precedes the diarrhoea.

2. Diarrhoea: profuse watery diarrhoea, upto 20 episodes/day that can last for 3-9 days.

3. Fever.

Other symptoms include abdominal pain, nausea and malaise (10). Occasionally, the child may have respiratory symptoms and CNS features like headaches and rarely convulsions.
Potential consequences of untreated severe Rota virus gastroenteritis include severe dehydration, metabolic acidosis, electrolyte imbalances, hypovolaemia, circulatory collapse and death. The greatest proportions of hospitalizations occur in children 6-24 months of age.

Lack of access to appropriate rehydration therapy during severe Rota virus gastroenteritis results in high mortality rates in the developing world.

Natural immunity to Rota virus infection develops after the first infection, which is usually the most severe. Subsequent infections are less severe (11).

**DIAGNOSIS**

Testing for Rota virus is rarely done in the clinical practice as stool tests for Rota virus antigen and PCR are expensive (12). Diagnosis is usually therefore made on clinical grounds and Rota virus should be suspected in children less than 24 months of age who present with acute onset vomiting, diarrhoea and fever.

**MANAGEMENT**

As it is a viral infection, there is no specific treatment for the disease. Early and appropriate institution of oral rehydration fluids, continued feeding and zinc supplementation are recommended. WHO and UNICEF have issued guidelines for both caregivers and health professionals on management of children with acute diarrhoea (13).

**Recommendations for parents/carers:**

**Prevent dehydration** through the early administration of increased amounts of appropriate fluids available in the home, and oral rehydrating salt (ORS) solution, if available.

- **Continue feeding** (or increase breastfeeding) during, and increase all feeding after the episode.
- **Recognise the signs of dehydration** and take the child to a health-care provider for ORS or intravenous electrolyte solution (as well as familiarise themselves with other symptoms requiring medical treatment [e.g. bloody diarrhoea]).
- Provide children with 20 mg per day of **zinc supplementation** for 10–14 days (10 mg per day for infants under 6 months old).

**Recommendations for healthcare providers**

- **Counsel mothers** to begin administering suitable available home fluids immediately upon onset of diarrhoea in a child.
- Treat dehydration with **oral rehydration salt solution** (or with an intravenous electrolyte solution in cases of severe dehydration).
• Emphasize **continued feeding** or increased breastfeeding during, and increased feeding after the diarrhoeal episode.

• Use antibiotics **only when appropriate**, i.e. in the presence of bloody diarrhoea or shigellosis, and abstain from administering anti-diarrhoeal drugs.

• Provide children with 20 mg per day of **zinc supplementation** for 10–14 days (10 mg per day for infants under <6 months old).

• Advise mothers of the need to increase fluids and continue feeding during future episodes.

In children with **severe dehydration and/or shock**, manage urgently using the WHO guidelines.

**PREVENTION**

Since Rota virus affects both the rich and the poor, and is resistant to the common anti-septics, improvement in sanitation and hygiene are unlikely to reduce the incidence of infection. Fortunately, it is now a vaccine preventable disease.

Two vaccines against the Rota virus antigen (Rotarix™ and Rotateq™) have been licenced by WHO have shown excellent clinical efficacy. They are both live attenuated liquid vaccines that are administered orally as a 2 dose or 3 dose regimens respectively to be given with the routine infant EPI vaccinations. The target age group is infants below the age of 32 weeks, and the first dose should be given no later than 15 weeks of age. The vaccine is stored at 2-8° Celsius.

**Vaccine efficacy**

The first ever vaccination against Rota virus infection, RotaShield® was withdrawn after an increased incidence of intestinal intussusception was noted. Two subsequent Rota virus vaccinations have undergone large scale trials involving total of almost 100,000 infants and there has been no increase in intussusception noted.

The two currently licensed rotavirus vaccines, Rotarix™ and RotaTeq™ have undergone worldwide clinical development programs (16, 17). Both vaccines have demonstrated:

• Efficacy of 74% against Rota virus GE of any severity
• Efficacy of 96-100% against severe Rota virus GE
• 95% reduction in incidence of Rota virus hospitalizations
• Efficacy against diverse rotavirus serotypes, that is sustained over the first few years of life
• Efficacy in co-administration with other routinely used infant vaccines

It has been noted that the vaccine immune responses in infants tend to be less robust in developing countries, with efficacy of 61-64% against severe Rota virus GE in Africa (19). This is thought
to be secondary to multiple factors including high levels of malnutrition, HIV and poverty. However, since most Rota virus deaths occur in the poorest countries of Africa and Asia, the reduced vaccine efficacy will be compensated for, as the impact on Rota virus mortality in Africa is greater than in other regions due to inequity of disease burden in terms of death rates (20, 21).

A study done on HIV-infected infants in South Africa demonstrated that Rota virus vaccination was immunogenic in HIV infected children, it did not increase immune suppression in terms of CD4 count and viral load and it also did not decrease the immune response to any of the antigens that were administered concurrently (18).

Studies on Rota virus vaccination in pre-term infants have demonstrated comparable efficacy to those on term infants (19).

Several countries have incorporated the Rota virus vaccine into their national EPI schedules. In Brazil, diarrhoea mortality fell by 17% and diarrhoea hospitalizations by 22% in the first three years of vaccination, representing 300 fewer deaths and 40,000 fewer hospitalizations annually (14). WHO strongly recommends that Rota virus vaccination be included in all national immunization programs in regions where diarrhoeal deaths account for >10% of mortality in children < 5 years of age (15).

**Adverse Events**

Pyrexia, diarrhoea, and vomiting were common adverse events noted after administration of the vaccine. Otitis media and bronchospasm occurred in more vaccine than placebo recipients. However, the frequency of adverse experiences observed was generally similar to that seen when the concomitant vaccines were administered with placebo.

Intussusception was the major adverse event noted after introduction of the first Rota vaccine (RotaShield®). Intussusception occurs when a proximal portion of the bowel telescopes into a distal portion. This can lead to oedema and compression of the mesenteric blood vessels, necrosis, perforation of the bowel and even death. The infant presents with sudden onset colicky abdominal pain, vomiting and “red currant jelly” stools. A double contrast barium enema is diagnostic (and may be therapeutic) but emergency referral is vital.

Intussusception surveillance remains ongoing and so far, there has been no overall increase in intussusception with the newer Rota virus vaccines.
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7.13 CERVICAL CANCER AND HUMAN PAPILLOMA VIRUS VACCINES (L. W Muchiri)

INTRODUCTION

Cervical cancer (CC) is the second leading cause of cancer death in women globally and the first in women in many developing countries.1, 2 In sub-Saharan Africa CC is the most common cancer in women and there are over 200 million women aged 15 years or older who are at potential risk of CC.3 Nearly 71,000 CC cases are diagnosed and approximately 62,000 deaths are caused by CC each year in sub-Saharan Africa.3 Experts believe that essentially all cases of CC are caused by infection with oncogenic types of human papillomavirus (HPV).4-6

EPIDEMIOLOGY

HPV is a very common infection that is readily transmitted during sexual contact. Therefore, most men and women become infected with HPV soon after they become sexually active. In most countries in the world, 70% to 80% of men and women will be exposed to HPV infection at some point in their lives.7 Condoms are only partially effective in preventing HPV infections.8, 9 A recent meta-analysis suggests that the overall prevalence of HPV is higher in sub-Saharan Africa than in other regions of the world with Eastern Africa having the highest adjusted HPV prevalence (31.6%).10 The prevalence and incidence of HPV infection also vary between countries in the region due to different sexual behaviours and societal norms. Even when women only become sexually active at the time of marriage and have only one lifetime partner, they are likely to acquire the infection from their husbands if they had sexual experience before marriage.

There are more than 100 types of HPV infection that infect many parts of the body, and a subset of these cause genital infections.11 Some genital HPV types (referred to as oncogenic types of HPV) cause cancers of the cervix12, vulva13, 14, vagina13, penis15, 16 and anus.17 Irrespective of global geographic region, the most common HPV types found in association with anogenital cancers are types 16 and 18.7 Cancer of the cervix is by far the most common genital cancer and HPV is the necessary cause. Studies have identified HPV in almost 100% of invasive cervical cancer cases, 89% of high-grade squamous intraepithelial (HSIL) lesions and 73% of low-grade squamous intraepithelial (LSIL) lesions.18 The most potent CC causing HPV types are HPV 16 and 18, which together cause approximately 70% of invasive cervical cancer cases19 and are the predominant HPV types identified in HSIL and LSIL lesions.18

Other genital HPV types are less likely to cause cancer but can cause other HPV-related diseases.20, 21 For example, HPV types 6 and 11 cause approximately 90% of genital wart cases.22 Decreasing the incidence of HPV-related cancers, in particular cervical cancer morbidity and
mortality, by means such as vaccination should therefore lead to a reduction in the human and financial burden of such diseases.

Most cervical HPV infections resolve spontaneously within 2 years, but in some women invasive cervical cancer develops after one or more decades of persistent infection with an oncogenic type of HPV. Intermediate stages in the development of cervical cancer include abnormal Pap smears, low-grade and high-grade cervical lesions as well as carcinoma in situ. These predate the onset of invasive cancer.

**PATHOGENESIS AND PATHOLOGY**

Over 100 HPV types have so far been characterized and about 30 of them are known to infect the uterine cervix. In general HPV types are classified into mucosotropic types, which have been found on the mucous epithelial membrane of the oropharynx and ano-genital tract, and cutaneous types, which predominantly infect the skin (112, 113). Both types can be grouped into high-risk or oncogenic and low-risk or non-oncogenic types. By definition, high-risk HPV types are most commonly found in cervical cancer and high-grade CIN, whereas, it is the low-risk that are most commonly identified in low-grade lesions (41). Based on four large combined cytological/histological and HPV detection studies using biopsies and cervical smears it appeared that the overall HR HPV prevalence rates in pre-malignant cervical lesions increase with increasing grade of CIN whereas the LR HPV prevalence rate decreases with increasing severity of the lesion (33, 38, 39, 114). A survey of HPV types in invasive cervical cancer in 22 countries around the world revealed that HPV 16 accounted for 54% of the cancer associated HPV types followed by HPV 18 (15%), HPV 45 (9%) and HPV 31 (6%) (27). Thus, these 4 HPV types account for 84% of all cancer associated HPV types and intervention against HPV 16 alone would have considerable impact in reducing cervical cancer (115).

The process of cervical carcinogenesis can be assessed by molecular means (HPV DNA detection), visually (colposcopy and related techniques) and microscopically (cytology and histology) (116). In approximately 20% of women infected with high risk HPV, a CIN lesion will develop within 2-4 years after acquisition of the virus (38, 39, and 117). The morphologic changes that occur in the epithelial cells during productive HPV infection and referred to as low-grade cervical intraepithelial neoplasia (CIN-I) will regress spontaneously and only a small proportion will progress to high-grade CIN (CIN II-III) and eventually to invasive cancer (33, 41, 44). It has been estimated that the progression rate is in the order of 12% (44). Follow up studies estimate that 4-5 years are required for the transition from CIN I to CIN III, 9-10 years from CIN III to sub-clinical invasive carcinoma and 4-5 years from sub-clinical invasive to symptomatic invasive cancer (44, 38, and 118). The above estimates are based on data from follow-up studies and from selected cancer registries and screening programs. The existence of a morphological continuum of progressive and
consecutive changes leading to invasive cervical cancer has however, been recently challenged. It has been proposed that CIN I, and CIN II-III may be two separate entities and that only CIN II-III are real cervical cancer precursors (119).

The virus replicating cells display typical cytopathic changes characteristic for low-grade squamous intraepithelial lesions, which most predominantly include koilocytosis – the presence of marked cytoplasmic vacuolation and mild nuclear changes (120). Changes that are associated with persistent HR-HPV infection are characterised morphologically by more severe changes including increased intensity of nuclear staining indicating overall changes in the overall DNA content (aneuploidy), altered chromatin texture, changes in the nuclear membrane, changes in the cell size and in the relationship between the cytoplasm and the nucleus. Histologically, the more advanced lesions are characterized by increased number of mitotic figures and extension of the actively replicating cells to the upper layers of the epithelium. These changes are apparently related to the expression of the viral genes in the epithelial stem cells, which subsequently lose in a stepwise manner the capacity to differentiate in a coordinated manner.

**Cofactors in cervical carcinogenesis**

Human papilloma virus infections are necessary but not sufficient causes of cervical cancer (37). Certainly individual differences in Immunological responses to HPV play a critical role in determining the fate of the infections. Studies of HPV and immunity are underway, but optimal biomarkers of the successful immune response are not yet available. There is a need for epidemiological studies to confirm prospectively the other etiologic cofactors that promote HPV progression. So far, multiple case-control studies have shown that smoking, multi-parity, and long-term contraceptive use significantly increase the risk of cervical cancer (137-139). Less well-defined cofactors include other sexually transmitted diseases such as *Chlamydia trachomatis*, chronic inflammation, and diet (140-142). With exception of age and immunodeficiency, no cofactor identified to date is important enough to merit separate screening or clinical management protocols.

Cervical intraepithelial neoplasia grade III lesions tend not to regress over short-term follow-up; the longer CIN III persists, the higher the risk of invasion. Thus age is a critical epidemiological factor that merits consideration in clinical management. The median age of women with CIN III is approximately 30 years (143, 144). CIN III may be diagnosed earlier than age 25 years, but cervical cancer below the age of 25 is very rare and therefore screening efforts, particularly in poor-resource setting do not justify the efforts or the investment in screening younger women (1,145).
CLINICAL PRESENTATION

Signs and Symptoms

Cervical cancer evolves slowly over time preceded by a silent pre-malignant phase that is largely asymptomatic or when the only sign of disease is shedding of abnormal cells. Invasive disease presents with post-coital/abnormal vaginal bleeding and foul-smelling (fish-odor) discharge.

Advanced disease presents with obstructive signs and symptoms such as urinary and rectal obstruction.

Management of Cervical Intraepithelial Lesions

Successful treatment of lesions detected by screening is one of the major prerequisites of a successful screening programme. There are several modalities available depending on the grade of the lesion, the resources and the clinical setting: ablative methods, excisional methods, and expectant follow-up. There is a large body of evidence that cervical cancer precursor lesions can be treated safely and efficaciously on an outpatient basis. In-patient methods such as hysterectomy, though highly effective, should only be done for micro-invasive and invasive cancers and for those cases or settings where outpatient methods are not available. In general, biopsy-confirmed LSIL can be regularly followed up by cytology, and should only be treated in case of progression. If regular follow-up cannot be guaranteed however, treatment by an ablative method is recommended.
HSIL should preferably be treated with loop electrosurgical excision procedure (LEEP) in order to provide a specimen for histological diagnosis and that will also indicate that excision of the lesion is complete (198, 199).

**Ablative forms of therapy**

Precursor lesions of cervical cancer can be destroyed using several ablative methods: cryotherapy, electrocautery and laser ablation. All three methods have similar cure rates with recurrent rates of between 13 and 19% (194). Laser ablation has proved more effective in the treatment of larger lesions than the other two methods. The main advantage is that these modes of therapy can be offered on an outpatient basis. Their main disadvantage is that there is no tissue for histological evaluation.

Cryotherapy is reliable, easy to use, does not require electrical power and is relatively inexpensive. Anaesthesia is generally not required. It can be performed during pregnancy and has relatively few complications. It also has the potential to improve the immune response since it leaves a large amount of dead HPV viral load within the disrupted cells (198). The major disadvantages include a poor estimation of the depth of tissue destroyed, and a watery vaginal discharge for up to 12 days that patients find uncomfortable. In some resource poor settings, there may be difficulty in obtaining supplies of N₂O or CO₂ (199).

Laser ablation allows for the precise destruction of cervical lesions under local anaesthesia, without the inconvenience of associated vaginal discharge. However, the equipment is very expensive, a smoke evacuation system is required; and there are complications including cervical bleeding, in up to 5% of patients.

Electrocautery, traditionally used to treat benign chronic cervicitis and erosions, has been successfully used to destroy pre-cancerous lesions of the cervix. Major side effects include pain, uterine cramping and bleeding and an increased risk of cervical stenosis. It requires electrical power and therefore may not be readily available in resource poor settings (145).

**Excision methods**

Cervical conization is a highly effective method of treating pre-cancerous lesions of the cervix and the early stages of invasive cancer. Most gynaecologists are skilled in the procedure and no special equipment is required. However, it is a procedure that requires hospitalisation and general or spinal anaesthesia. Potential side effects and complications include bleeding, infection, cervical incompetence and spontaneous second trimester abortion, cervical stenosis and obstructed labour (199).
The loop electrosurgical excision procedure (LEEP) technique, also known as large loop excision of the transformation zone (LLETZ), is an outpatient method used to remove the entire transformation zone by slowly moving the electric loop across the cervix. The cervix is then coagulated using a ball electrode. It provides for treatment and tissue sampling at one visit. Histological examination allows for evaluation for complete excision of the lesion or for invasive disease (200). Complications include peri-operative and post-operative bleeding (up to 9% of cases), which may be reduced by use of Monsel’s paste (ferric subsulfate solution), infection (2%) and stenosis (1%). It has an impressive cure rate of 95%.

**Expectant management (follow-up)**

It is now recognized that most LSIL, particularly in young women, represents a self-limited HPV infection (47). As most LSIL will not progress or will spontaneously regress, treating all LSIL would result in considerable over-treatment. In addition, the period of progression to invasive cancer is very long and would provide ample time for detection and treatment of a progressing lesion during follow-up. Many guidelines, most of them similar, are in favour of expectant follow-up of LSIL. However, women with persistent LSIL associated with HR HPV at 12 months should probably be referred for colposcopy where possible. Management options may vary if the woman is pregnant, postmenopausal or an adolescent (201).

**Management of Invasive Cervical Cancer**

The treatment of invasive cervical cancer is largely dependent on stage of disease. Clinical staging is a prerequisite, often under anesthesia. Treatment protocols generally involve surgery and radiotherapy. Chemotherapy appears to have limited efficacy.

**PREVENTION**

**Secondary Prevention**

Secondary prevention methods such as visual inspection with acetic acid (VIA), see-and-treat management of cervical dysplasia, Pap testing and HPV DNA testing will allow for detection of intermediate lesions which are amenable to treatment and hence prevention of most cases of CC in regularly screened women. Effective prevention using these methods requires high levels of screening in the population, an effective infrastructure to deliver the screening, cultural acceptance of screenings, the availability of effective treatment, access of the population to screening and treatment, and effective follow-up. Although wealthy and middle income sub-populations of women have access to this type of care in sub-Saharan Africa, most women in these countries have never received effective screening for CC prevention.
**PRIMARY PREVENTION**

Highly safe, immunogenic and effective vaccines have recently been developed that can prevent infection with HPV types 16 and 18. These vaccines have now been licensed by the national control authorities in more than 80 countries.\(^{26}\) National immunisation programmes (NIPs) (with other childhood vaccines) in sub-Saharan Africa are improving their vaccine coverage, and routine immunisations reach more than 70% of infants.\(^{27}\) However, most NIPs do not have vaccines for administration to adolescents and the older population. School and community-based programmes are therefore thought by many experts to be the correct setting for HPV vaccine administration. School and community-based adolescent vaccination programmes have been shown to have high completion rates (>80%)\(^{28, 29}\) and are ideally suited for the implementation of HPV vaccination schedules. Ideally, both HPV immunization and CC screening programmes should be in place to have maximal impact in preventing CC.

The discovery, development and testing of the new HPV vaccines is a major medical achievement. The vaccine is a virus-like particle (VLP) made by recombinant DNA technology similar to the hepatitis B vaccine: the gene for the L1 coat protein of the virus is inserted into another cell (yeast or insect cell) which is grown in great quantities in fermentation or tissue culture.\(^{25, 30}\) "The L1 coat protein of the virus is then purified and self-assembles into hollow VLPs that are highly immunogenic but non-infectious since they do not contain nucleic acid. The vaccines, which contain aluminium salts or the AS04 adjuvant, are highly immunogenic and induce an immune response in almost 100% of recipients of all ages tested to date (9 to 55 years of age).\(^{31}\) The immune response has been shown to last more than 6.4 years\(^{32-34}\) and anamnestic responses to booster doses of vaccine have been documented.\(^{35}\) The duration of protection of the vaccine is at least 6.4 years\(^{34}\) but the full duration of protection is not yet known.

The vaccines have been shown to be highly effective in preventing HPV infection and resultant disease states.\(^{32}\) Two vaccines are currently available – a bivalent and a quadrivalent – both of which contain VLPs of types 16 and 18 to prevent CC. In addition, one of the vaccines (quadrivalent) contains VLPs of types 6 and 11 to prevent genital warts. In HPV naive women, studies with both HPV vaccines have been shown to have more than 95% efficacy in preventing HPV infection and the development of lesions caused by the HPV types present in the vaccines for up to 6.4 years of follow-up.\(^{36}\) It is important to understand that the current HPV vaccines are not therapeutic and will have no effect on the disease process of currently infected women. However, the vaccines may prevent infection with vaccine-targeted HPV types in women infected with other types of anogenital HPV.

Cost-effectiveness studies in industrial countries have shown the vaccine to be highly cost-effective when used as a routine vaccine in pre-adolescent girls, adolescent girls and young women.\(^{37}\)
Few studies have been done in developing countries, but studies in Brazil have shown the vaccine to be cost-effective with a lower vaccine cost. Studies show that immunization of males and females is less cost-effective than immunization of females alone when the measured outcome is CC prevention. However, HPV infection in males can result in other HPV-related diseases (e.g. anal and penile cancer) which are a significant burden on the health care system.

Vaccination of males could therefore reduce transmission of HPV to females, resulting in a lower incidence of HPV and fewer cases of CC, and prevent male HPV-related diseases. There is concern that a female-only strategy will be less culturally acceptable in many countries. Male vaccination could therefore be a consideration in some countries.

**IMMUNISATION STRATEGIES**

**Primary immunisation strategy**

Most countries that have issued official recommendations from expert groups have recommended that the primary immunization strategy should be to immunize pre-adolescent girls in the range of 9 to 13 years of age (see Table 1). This is to ensure that the immunization is given before the onset of sexual activity, and because this group is easier to reach with the existing immunization infrastructure. School-based programmes are most effective if most girls are in school at the recommended age of vaccination and if school health programmes are operational. Community-based immunization is also used in some countries. Some countries have allowed immunization of both males and females (e.g. Austria) but so far none has implemented universal vaccination of boys. Moreover, the impact of immunizing males has not yet been demonstrated in clinical studies (which are pending). Ideally, routine immunization of pre-adolescent females should be done as part of the national immunization programme and funded by the health care system. This will ensure high coverage and is the most important strategy that will lead to control of CC at a population level.

**CATCH-UP IMMUNISATION STRATEGY**

Most countries also recommend a catch-up immunization strategy to ensure that the benefits of immunization are available to older children and young women. The age of the recommended catch-up varies from country to country and ranges from 13 to 26 years and Government funding of the catch-up is included in most countries that currently provide universal access to these vaccines (see Table 1). This strategy will ensure that cost will not be an impediment to high coverage. Even though some girls will be sexually active at these ages, they may still receive benefit from the vaccine since very few will have already been infected with the HPV types found in the vaccines.
<table>
<thead>
<tr>
<th>Country</th>
<th>Target population</th>
<th>Catch-up population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>12 to 13-year-old females</td>
<td>14 to 26-year-old females</td>
</tr>
<tr>
<td>Austria</td>
<td>Males and females aged 9 to 15 years</td>
<td>Not available</td>
</tr>
<tr>
<td>France</td>
<td>14-year-old females</td>
<td>15 to 23-year-old females (who have not yet become sexually active, or have been sexually active for less than 12 months)</td>
</tr>
<tr>
<td>Germany</td>
<td>12 to 17-year-old females</td>
<td>Not available</td>
</tr>
<tr>
<td>Italy</td>
<td>11-year-old females</td>
<td>Not available</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>12 to 13-year-old females</td>
<td>16 to 18-year-old females (from autumn 2009)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 to 17-year-old females (from autumn 2010).</td>
</tr>
<tr>
<td>USA</td>
<td>11 to 12-year-old females</td>
<td>Women aged 13 to 26 years</td>
</tr>
</tbody>
</table>

**EPI HPV vaccine recommendations**

**IMMUNISATION OF WOMEN OLDER THAN 26 YEARS OF AGE**

Initial clinical trial results have demonstrated efficacy in preventing HPV infection and clinical disease in women over 26 years of age and up to the age of 45 years.45, 46

Women in this age group continue to become infected with HPV and develop clinical disease and cancer. ‘Bridging’ studies have shown the vaccine to be highly immunogenic up to the age of 55.31 Mass vaccination of this age group is not currently cost-effective.47 It is therefore the decision of the individual female to seek vaccination if she wishes. Some countries (e.g. Australia) have made recommendations that allow for the immunization of women over the age of 26, although this is not publicly funded, and other countries are waiting for cost-effectiveness studies to be completed before they issue recommendations concerning this age group.

**INDIVIDUAL ELECTIVE IMMUNISATION**

While primary and catch-up immunization may be funded and delivered by national immunization programmes, and recommended age ranges will vary from country to country, any woman who wishes to be immunized should be offered the HPV vaccine. Women should be encouraged to discuss HPV immunization with their health care providers, and together they can decide if immunization is appropriate.
**CHALLENGES IN HPV VACCINATION**

There have been concerns that the immunization of pre-adolescents, adolescents and younger unmarried women may meet with cultural resistance among religious conservatives in a number of countries. The impact of this issue on the uptake and acceptance of vaccination will vary from country to country and communication/advocacy strategies should therefore be tailored to the needs of the individual area.

Although the infrastructure to routinely immunize adolescents does not currently exist in many African countries, this should not prevent/hinder vaccine implementation. Furthermore, African countries should seek GAVI funding to ensure HPV vaccines become available.

**VACCINE STORAGE AND HANDLING**

**HPV2:** Cervarix

**HPV4:** Gardasil

**Condition upon Arrival**

Human papillomavirus vaccine (HPV) should arrive packed in an insulated container. Examine the shipping container and contents for damage during transport. Some vaccines are shipped with a temperature monitor. If a temperature monitor is present, check and follow the instructions. The vaccine should not have been frozen or exposed to freezing temperatures. If the interval between shipment from the distributor/manufacturer and arrival of the vaccine at the facility has been more than 48 hours or you have questions about the condition of the vaccine at the time of delivery, you should take three steps.

1. Immediately place the vaccine in the refrigerator between 35°F and 46°F (2°C and 8°C).
2. Mark vaccine “Do Not Use” and separate from uncompromised vaccines. A clearly labeled paper bag can be used for this purpose.
3. Follow your immunization program policy and contact the distributor, manufacturer and/or the immunization program for guidance.

**NOTE:** Contact the distributor and immunization program regarding shipments of Vaccines for Children (VFC) or other vaccines purchased with public funds that may not have been transported properly.
**Storage Requirements**

Refrigerate immediately upon arrival. **Store between 35°F* and 46°F (2°C and 8°C).** Do not freeze or expose to freezing temperatures.

- **HPV4 (Gardasil):** Protect vaccine from light at all times by storing in the original box.

  *Storage temperatures between 36°F and 46°F (2°C and 8°C) are specified in the label and the license for these products. However, 2°C is exactly converted to 35.6°F so the manufacturer’s guidance for Fahrenheit is rounded by the manufacturer.

**Shelf Life**

Check expiration date on the container, vial or manufacturer-filled syringe. Do not use after the expiration date shown on the label.

**Preparation**

Inspect visually for extraneous particulate matter and/or discoloration. If these conditions exist, the vaccine should not be used. Just before use, shake vial or manufacturer-filled syringe well. After shaking, HPV vaccine is a white, cloudy liquid. Through agitation immediately before administration is needed to maintain suspension. Do not use vaccine if it cannot be resuspended with thorough agitation. These vaccines should not be combined or mixed with any other vaccines. Refer to the Resources section at the end of this document for information on vaccine administration.

- **HPV2 (Cervarix):** May separate to a fine, white deposit on the bottom of the vial with a clear, colorless liquid above during storage. This does not indicate deterioration.

**Beyond Use Date*: Shelf Life after Opening**

**Single-Dose Vials:** All of the vaccine should be drawn into a sterile syringe using a sterile needle at the time the vaccine is administered.

**Manufacturer-Filled Syringes:** Manufacturer-filled syringes should be activated (i.e., syringe tip removed and/or needle attached) at the time the vaccine is administered.

*The date or time after which the vaccine should not be used; determined from the date or time the manufacturer-filled syringe is activated, vial is entered or vaccine is reconstituted; may be different from the expiration date.
**Vaccines Exposed to Inappropriate Temperatures (Temperature Excursions)**

Vaccine exposed to temperatures outside the recommended range—either too warm or too cold—requires immediate corrective action! Vaccine providers should have a current emergency vaccine retrieval and storage plan that includes, but is not limited to, these four actions.

1. Place the vaccine in the recommended storage between 35°F and 46°F (2°C and 8°C).
2. Mark vaccine “Do Not Use” and separate from uncompromised vaccines. A clearly labeled paper bag can be used for this purpose.
3. Follow your immunization program policy and contact the manufacturer and/or the immunization program for further guidance.
4. Do not discard vaccine unless directed to by the immunization program and/or the manufacturer.

**NOTE:** Contact the immunization program whenever VFC or other vaccines purchased with public funds are exposed to temperatures outside the recommended range.

**Special Instructions**

Storing multiple products and presentations can be confusing to staff and increase the risk for vaccine administration errors. There are two HPV products available from different manufacturers with different indications. HPV4 can be administered to males and females. HPV2 is approved for use in females only. Consider indications and the facility’s patient population when ordering HPV vaccine.

Vaccines that sound alike are often confused. For example, HPV, HepB and Hib vaccines are often confused, increasing the risk for an error. Consider organizing vaccines in the storage unit by age group and/or color coding labels to distinguish vaccines from each other. Do not store sound-alike or look-alike vaccines next to each other. Label the space where HPV is stored with name, gender and age indications to help decrease the likelihood of a vaccine administration error. Refer to the Resources section at the end of this document for examples of labels.

**RECOMMENDATIONS FOR THE USE OF HPV VACCINES**

**TARGET POPULATIONS**

Routine vaccination with three doses of the same HPV vaccine is recommended for females from 9 to 12 years of age. The exact age of primary immunisation may however vary from country to country to fit best with the available infrastructure.
Catch-up vaccination is recommended for females 13 to 26 years of age who have not been vaccinated previously or who have not completed the full three-dose vaccine series.

Women over 26 years of age should be encouraged to discuss HPV immunisation with their health care providers, and together they can decide if immunisation is appropriate.

Male vaccination is not recommended at this time but this issue may be reassessed when data are available and high vaccination coverage in the female population has been achieved.

**CO-ADMINISTRATION**

HPV vaccine can be administered at the same visit when other age appropriate vaccines are provided. Each vaccination should, however, be administered individually during the single visit.

**HPV VACCINATION AND SCREENING**

At present, CC screening recommendations have not changed for females who receive the HPV vaccine. All women should receive regular CC screening as recommended.

Screening for cervical pathology or for the presence of HPV is not required prior to vaccination.

A woman with abnormal screening/Pap smear results is still eligible for vaccination.

**SPECIAL SITUATIONS**

The HPV vaccine can be given to females who have an equivocal or abnormal Pap test result, a positive HPV DNA or Hybrid Capture II® high risk test, or genital warts.

Vaccine recipients should be advised that the data from clinical trials do not demonstrate that the vaccine will have any therapeutic effect on existing Pap test abnormalities, HPV infection or genital warts. Vaccination of these females would provide protection against infection with vaccine HPV types 16 and 18 not already acquired.

Lactating women can receive the quadrivalent HPV vaccination.49 The bivalent HPV vaccine should be administered during breast-feeding only when the possible advantages outweigh any possible risks.50

Females who are immunocompromised either from disease or medication can receive the HPV vaccine. However, the immune response to vaccination and vaccine effectiveness might be less than in females who are immunocompetent.51
CONTRAINDICATIONS TO USE OF VACCINE

The HPV vaccine is contraindicated for people with a history of immediate hypersensitivity to any vaccine component.

Women are discouraged from becoming pregnant during the immunisation schedule.

The HPV vaccine is not recommended for use in pregnancy.25

- If a female has not finished her three-dose vaccination course and becomes pregnant, she should not receive any other vaccine doses until after the birth, at which point the remaining dose(s) can be administered.
- The vaccine has not been associated causally with adverse outcomes of pregnancy or adverse events to the developing foetus. However, data on vaccination during pregnancy are limited.

PRECAUTIONS

The HPV vaccine can be administered to females with minor acute illnesses (e.g., diarrhoea or mild upper respiratory tract infections, with or without fever). Vaccination of people with moderate or severe acute illnesses should be deferred until after the illness improves.

ADMINISTRATION

Each dose of the HPV vaccine is 0.5 mL and is administered intramuscularly.

HPV vaccine is administered in a three-dose schedule. The quadrivalent is recommended in a 0, 2, and 6-month schedule; the bivalent vaccine should be administered in a 0, 1, and 6-month schedule.

SIDE EFFECTS

Serious adverse events are exceedingly rare. The most common adverse events are pain, redness and swelling at the site of the injection which are commonly mild in nature.

RECENT ADVANCES

- Need for boosters
- Bridging studies
- Males
- HIV positive populations
- National Reproductive Health Strategy - link
REFERENCES


31. Schwarz T, Descamps D. Immune response in women up to 55 years of age vaccinated with Cervarix. Abstract SS2-3. EUROGIN. 2007

32. Gall S. Abstract 4900. AACR. 2007


34. Wheeler CM, Teixeira J, Romanowski B. High and sustained HPV 16 and 18 antibody levels through 6.4 years in women vaccinated with Cervarix. ESPID annual meeting 2008


ANNEXES

RECOMMENDED STANDARD CASE DEFINITIONS FOR REPORTING SUSPECTED PRIORITY DISEASES

Epidemic-prone diseases

1. Cholera
   Profuse, effortless, watery diarrhea p.e. more than 3 motions in 24 hours of sudden onset with or without vomiting in a person over 5 years old.
   In an area experiencing an epidemic, all cases with acute watery diarrhea including the 2 - 5 year age range are considered as cases. A sudden increase in the number of dehydrated cases (including Children aged 2 - 5 years) resulting from acute watery diarrhea should raise suspicion of a possible cholera outbreak.

2. Diarrhea with blood (Dysentery)
   Any person with diarrhea and visible blood in the stool.

3. Meningitis (Epidemic)
   Rash onset of fever, headache, vomiting and either neck stiffness or altered consciousness or bulging fontanelle (in less than one year olds with or without photophobia or purpuric rash). Confirmation by buffy coat centrifugal fluid (CFP) and isolation of gram-negative intracellular diplococci (Brucella Neisseria meningitides).

4. Typhoid fever
   Vomitus and sustained fever, severe headache,Malaise, nausea and constipation (which is more common than diarrhea in adults). With isolation of salmonella species in blood or stool of a patient.

5. Plague
   Acute fever, chills, headaches, severe malaise, prostration with palpable submaxillary lymph nodes ( bubonic type) or cough with blood contained sputum, chest pain, difficulty in breathing (pneumonic type). Confirm diagnosis by isolation of Gram Negative Bacilli (Clostridium) in clinical material (hobo aspirate, sputum, tissue and blood).

6. Viral hemorrhagic fever
   Acute onset of fever, for at least 72 hours, with headache, nausea, unexplained bleeding tendencies with the following signs: bloody stools, vomiting blood, bleeding from gums, nose, vagina. Skin diuresis. While other causes of hemorrhagic tendencies have been ruled out. Confirmation by a positive ELISA for IgM for viruses known to cause hemorrhagic fever.

7. Yellow fever
   Acute onset of fever, jaundice, and may be associated with bleeding from body orifices, altered consciousness, and renal failure (reduced urine output, proteinuria, haematuria).

Diseases targeted for eradication and elimination

8. Acute flaccid paralysis (AFP/mile)
   Any case with weakness or flaccidity of the limbs of sudden onset, not due to trauma in a child less than 15 years of age.

9. Measles
   Person with fever and maculopapular (non-vesicular) generalised rash and cough, conjunctivitis (red eyes) or any person in whom a clinician suspects measles. A measles death is a death occurring within 30 days of onset of the rash.

10. Leprosy
    Any person with one of the following cardinal signs: skin patch with loss of sensation, one or more enlarged nerves, and presence of leprosy bacilli with or without bacteriological diagnostic confirmation and requiring chemotherapy (excluding patients released from treatment).

11. Neonatal tetanus
    Any newborn with a normal ability to suck or cry during the first two days of life, and who, between 3 and 28 days of age, cannot suck normally and has generalised stiffness and/or spasms.

12. Dracunculiasis (Guinea Worm)
    Any person with a history of skin lesion and emergence of Guinea worm within one year of the skin lesion.

Other diseases of public health importance

13a. Diarrhea with some dehydration in children less than 5 years of age
    Any child less than 5 years of age with diarrhea and two or more of the following:
    - restless or irritable
    - sunken eyes
    - dry skin, thirsty
    - skin pinch goes back slowly

13b. Diarrhea with severe dehydration in children less than 5 years of age
    Any child less than 5 years of age with diarrhea and two or more of the following:
    - lethargic or unconscious
    - sunken eyes
    - not able to drink or drinking poorly
    - skin pinch goes back very slowly

14a. Pneumonia in children less than 5 years of age
    Any child aged 2 months up to 5 years of age with cough or difficult breathing, who
    - is breathing 30 breaths or more per minute in an infant 2 months up to 1 year
    - is breathing 40 breaths or more per minute for a child aged 1 to 5 years
    (patients less than 2 months with fast breathing 60 breaths or more per minute are referred for serious bacterial infection)

14b. Severe Pneumonia in children less than 5 years of age.
    Any child age 2 months up to 5 years of age with cough or difficult breathing, and with any general danger sign, or chest indrawing, or stridor in a child.
    General danger signs are: unipal to drink or breast feed, vomiting everything, convulsions, lethargy or unconsciousness.

15. New AIDS cases
    Any person with an opportunistic infection and is HIV positive

16. Malaria
    Malaria in over 5 years excluding in pregnancy: Any person with fever or fever with headache, back pain, chill, sweats, myalgia, nausea and vomiting diagnosed clinically as malaria.
    Malaria in under 5 years: Any child below 5 years with malaria
    Malaria in pregnancy: A pregnant woman with signs and symptoms of uncomplicated malaria.

17. Tuberculosis
    Chronic cough (of more than three weeks) with spumum smear positive for mycobacterium tuberculosis.

18. Sexually Transmitted Infections
    Suggested cases:
    - Genital ulcer syndrome (non-venereal): Any male with an ulcer on the penis, scrotum, or rectum, with or without inguinal adenopathy, or any female with ulcer on labia, vagina, or rectum, with or without inguinal adenopathy.
    - Genital discharge syndrome: Any male with genital discharge with or without dysuria.
    - Cervical discharge syndrome: Any suspected case confirmed by a diagnostic laboratory procedure.
    - Genital ulot syndrome (non-venereal): Any suspected case confirmed by a diagnostic laboratory procedure (for example Gram stain showing intracellular gram-negative diplococci).

Prepared by Disease Unit, National Disease Unit, Division of Communicable and Vector-Borne Disease.
DALILI ZA MAGONJWA
YANAYOSHUGHULIKIWA NA WIZARA YA AFYA

DALILI ZA UKAMBI

Joto mwilini, kuparara
na moja kati ya haya:-

• Kukohoa
• Kamasi na/au
• Macho Mekundu

PEPOPUNDA KWA WATOTO WACHANGA

Mtoto kufariki baada ya kuzaliwa,
au mtoto kukosa kunyonya.
Mtoto kukauka misuli, au mtoto kufariki
katika mda wa mwezi wa kwanza baada ya kuzaliwa.

Dalili za ugonjwa wa kupooza

Kukosa nguvu mguuni au miguuni
na mkononi au mikononi pasipo na ajali.

Peleka mgonjwa yeyote kati ya haya kwa kituo cha afya
kilicho karibu nawe kwa haraka apate usaidizi

KENYA EXPANDED PROGRAMME ON IMMUNIZATION (KEPI)
WIZARA YA AFYA
STANDARD Case Definitions

ACUTE FLACCID PARALYSIS
Any case with weakness or floppiness of sudden onset, not due to trauma,
in a child less than 15 years of age.
All suspected cases of Poliomyelitis, Guillain- Barre Syndrome, or
Transverse Myelitis should be reported as AFP.

SUSPECTED MEASLES
History or Presence of a generalized maculo-papular rash
AND
Fever
AND
Any one of the following:
• Cough
• Red Eyes
• Runny Nose

NEONATAL TETANUS
History of Normal Suck and Cry for the First 2 DAYS of life,
AND
History of onset of illness Between 3 and 28 Days of age,
AND
History of inability to suck followed by stiffness AND/OR
Convulsions
AND
OFTEN Death

* Report all cases of the above mentioned Diseases to the Medical Officer of Health or the nearest Health Facility

KENYA EXPANDED PROGRAMME ON IMMUNIZATION (KEPI)
MINISTRY OF HEALTH
Measles Contact Tracing Form

Date of investigation: _____________ Investigated by: (name) ________________________ Designation ______________________

Institution investigating: __________________________________________________________

District ____________________________________________ Neighbourhood (address details): ____________________________________________

<table>
<thead>
<tr>
<th>NAME OF AFFECTED CHILD &amp; THE PARENT/GUARDIAN</th>
<th>Age Y=Years M=Month</th>
<th>Sex M/F</th>
<th>Total number of measles vaccine doses and date of last one</th>
<th>Has the child had this problem previously Yes/No</th>
<th>If suspect case of measles</th>
<th>Other observations:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Date of rash onset</td>
<td>Date Serum Sample taken</td>
<td>Placed visited 7-18 days before rash onset (where suspect case could have been infected)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Places where the case had been 4 days before until 4 days after rash onset (infectious period)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(pos/neg)</td>
<td></td>
<td>a) Has the suspected case had contact with foreign visitors within 7-18 days before rash onset?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) Record address if different from other</td>
</tr>
</tbody>
</table>

1. Child:
   Parent:

2. Child:
   Parent:

3. Child:
   Parent:

4. Child:
   Parent:

5. Child:
   Parent:

* All usual residents of or visitors to the house or workplace must be visited (including all persons visiting at least weekly)

** Immunisation card is required. If it is not available, record “unknown” in this column.

Interview all persons who live (or work) there and those who visited this home/workplace within 7-18 days prior to rash and onset/or since beginning of first respiratory symptoms up to 4 days after rash onset. Also interview here the case-patient that originated the investigations.
**MINISTRY OF HEALTH**

**Integrated Case Based Surveillance Form**

**For Acute Flaccid Paralysis (AFP) Case Only**

<table>
<thead>
<tr>
<th>Case Response</th>
<th>Sensitize TBEs and community leaders on safe delivery practices and cord care. Provide booster TT doses to mother of NNT case and women of child-bearing age in local community around the case.</th>
</tr>
</thead>
<tbody>
<tr>
<td>37. Did a case response for the mother take place?</td>
<td>Yes/No</td>
</tr>
<tr>
<td>38. Did a case response take place in her locality?</td>
<td>Yes/No</td>
</tr>
</tbody>
</table>

**A. Name of Site Reporting & Disease being Reported**

<table>
<thead>
<tr>
<th>Site</th>
<th>Health Facility:</th>
<th>Division:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**District:**

<table>
<thead>
<tr>
<th>District</th>
<th>Province:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
</tr>
</tbody>
</table>

**B. Affected Site Reporting & Disease being Reported**

<table>
<thead>
<tr>
<th>Site</th>
<th>Health Facility:</th>
<th>Division:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**District:**

<table>
<thead>
<tr>
<th>District</th>
<th>Province:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
</tr>
</tbody>
</table>

**B. Identification**

<table>
<thead>
<tr>
<th>Patient Information</th>
<th>Name of patient:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sex:**

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Age:**

<table>
<thead>
<tr>
<th>0-2 months</th>
<th>2-5 months</th>
<th>5-10 months</th>
<th>10-20 months</th>
<th>20+ months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Date of birth:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Parent/Guardian:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Immediate Contact:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**S. Neighbor:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**T. Other:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**D. Date of last reported exposure:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**E. Vaccination History (For disease under investigation cases of Measles, AFR (exclude birth dose of OPV), NT (TT in mother) Yellow Fever and Rubella):**

**Vaccination History:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Date of Administration</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Signs and Symptoms of Measles Case Only:**

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other:**

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Is there any history of Measles?**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If yes, date visited:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Month</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Is the case etiologically linked to a laboratory-confirmed case?**

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Form completed by:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phone No.</th>
<th>Date of diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fax No.</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signature</th>
<th>Date of form completed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Suspected Measles? Report It!!**

*Healthcare Provider's Field Guide for Reporting Suspected Measles Cases*

**When to Suspect Measles**

1. Any person with **fever** and **maculopapular rash**, **PLUS**
   ONE of the following: **cough** or **coryza (runny nose)** or **conjunctivitis (red eyes)**
   
   **or**

2. Any person in whom a clinician suspects measles

---

**Step 1:** Diagnose and manage suspected measles case
- Classify the suspected case for management (depending on severity)
  - Uncomplicated
  - Complicated
- Manage case (See KEPI's Measles Job Aide)

**Step 2:** Give 2 doses of vitamin A to suspected measles case

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose of Vitamin A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediately on Diagnosis</td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>50,000 IU</td>
</tr>
<tr>
<td>6 – 11 months</td>
<td>100,000 IU</td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>200,000 IU</td>
</tr>
</tbody>
</table>

**Step 3:** Notify District Disease Surveillance Coordinator

**Step 4:** Collect a serum sample within 24 hours from each suspected case (*See Guidelines for Collecting, Processing, and Transporting Measles Specimens*).

**NOTE:** Do not collect serum if rash occurred more than 28 days ago

**Step 5:** Complete the Integrated Case-Based Surveillance Form (MOH 502) - in detail section C.IV
- White copy (original) goes with the specimen to KEMRI
- Yellow copy (duplicate 2) goes to DMOH
- Pink copy (triplicate 3) goes to the PMO
- Green copy (fourth copy) remains in the health facility file

**Step 6:** Arrange for transport of specimen and the IDS Form to KEMRI through a reliable courier service.

**NB:** Inform your DDSC immediately if unable to send specimen to KEMRI/KEPI

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*Ministry of Health – KEPI (Tel: 020-2721057 or 020-2711791)*