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IMMUNIZATION MANUAL

for Medical Students and Physicians

DEVELOPED BY DEPARTMENT OF PAEDIATRICS, UON AND DIVISION OF FAMILY HEALTH, MOH

Edited by

D.A Mbori-Ngacha
R.K.A Sang
F.E.Onyango
D.M Mutie
M.C Wilson

FIRST EDITION

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SECTION 1

PRACTICE AND PRINCIPLES OF IMMUNIZATION

FOREWORD

This manual Is intended for use by undergraduate medical students to assist them in understanding issues involved in an immunization programme.

It is apparent that until now little attention has been paid to the teaching of immunization to the undergraduate medical students, many of whom leave medical schools with little or no knowledge regarding immunization. This anomaly needs to be corrected and it is my belief that all medical schools especially those in developing countries where immunizable diseases still present a major problem, need to include immunization into their teaching curriculum.

The role of medical personnel in promoting immunization is important. As team leaders, doctors should be knowledgeable about immunization and should develop positive attitudes, which will help them participate actively in various immunization activities.

In this manual a wide range of topics on immunization and immunizable diseases are presented. The first section of the manual deals mainly with the practice and principles of immunization as recommended by the EPI. This section will not only make the reader familiar with the philosophy behind EPI and the targets of EPI programmes but will also provide knowledge on practical aspects of immunization.

The second portion of the manual deals with the EPI target diseases. The epidemiology ,clinical presentation and preventive aspects are covered with emphasis on immunization.

It is hoped that the manual will be a useful companion to medical students. It will also provide useful reference material to other health workers, including doctors and nurses.

This immunization manual is a collaborative effort between the Department of Paediatrics and Child Health of the College of Health Sciences, University of Nairobi and the Management Unit of the Kenya Expanded Programme on Immunization (KEPI) with assistance from Resources for Child Health (REACH) to whom we are grateful.

I believe that in writing this manual, a lot of experience has been gained which will be useful in helping us compile other manuals in other Important child survival areas.

It is my sincere belief that this manual will be put to good use.

DR. FRANCIS E. ONYANGO
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1

EXPANDED PROGRAMMES ON IMMUNIZATION (EPI)

WITH SPECIAL EMPHASIS ON KENYA EPI (KEPI)

R.K.A Sang
D.M Mutie

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.
- able to describe the "Pillars of KEPI" and their importance.

"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".

Dr. Halfdan Mahler, Former WHO-Director
General on World Health Day, 1984.

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. 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, has 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- diarrnoea-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 the light of this 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 short-comings 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.

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 concern and priority to them such as yellow fever in West-Africa and Hepatitis B in most countries in sub-Saharan Africa and South East Asia. All these diseases being addressed by EPI Programmes have been termed "**EPI - target diseases**".

The **objectives** of EPI Programmes are:

- 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.

4. EPI PROGRAMME ACCELERATION

1977 was the onset of the implementation of the EPI programme. In 1982, the EPI programme's 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 dark 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. These 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, gradually started to 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 complacence, since at such

immunization coverage levels, 3 million children would still die annually, 200,000 would be paralysed and some 150,000 blinded from these diseases (5).

5. KENYA EXPANDED PROGRAMME ON IMMUNIZATION (KEPI)

5.1 Historical Background 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. Its 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. Motivation rather than coercion being the preferred approach.

5.2 Objectives

The objectives contained in the 5-year "KEPI'S Plan of Operation" proposal, prepared in 1980, were as follows:

5.2.1 Immunization Coverage

Immunization Coverage of 75% for single-shot antigens (BCG and measles) and 60% for multiple shot ones (D.P.T, Polio and Tetanus Toxoid) during the first 3 years of KEPI's operation in a given district was proposed. 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).

5.2.2 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 Mombasa 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 1234 dispensaries.

5.2.3 Training

Training was to be of three types: at Senior, Supervisory and Operational levels. The 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.

5.2.4 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.

5.2.5 Public Motivation

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

5.2.6 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.

5.2.7 Research

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

5.3 Implementation

The implementation of KEPI was planned in 3 stages namely:-

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

5.3.1 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.

It dealt with the following areas:-

- equipment
- transport, procurement and distribution
- training schedules
  - identification of trainers
  - number of cadres staff to be trained.

- training materials
  - data collection
  - public Mobilization activities.

5.3.2. 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 41 districts. An evaluation carried out at this stage was encouraging.

5.3.3. Operational Stage: Mid 1982 - 1986.

The KEPI programme was introduced step by step in the 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 been raised to 43%.
- no vaccine shortages were experienced by the programme.
- 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.

5.4 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 BCG 90%, DPT3/polio3/ measles 80% and tetanus toxoid 75%
- 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 based on cost effectiveness and sustainability 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 programme by external teams
- regular feed back to staff.

NB Sentinel Station Reporting for measles, poliomyelitis, neonatal tetanus planned to start from 1990 is yet to be implemented.

6. PROGRAMME MONITORING

Immunization returns are supplied to KEPI through the Routine Health Information System (H.I.S) of the Ministry of Health. This system still needs further strengthening if

it is to serve the programme satisfactorily. By 1984, pre-KEPI Surveys carried out in 31 of the 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)

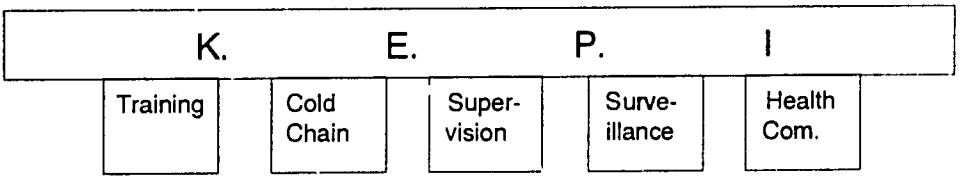
Every two years, KEPI is reviewed by External Evaluation Teams. This has been a regular feature since 1984. Their reports show a positive trend in KEPI's performance.

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

7. THE FUTURE OF KEPI

The year 1990, other than being the year to attain UCI, is the 10th anniversary of KEPI. In the past 10 years, experience has shown that KEPI rests, and will continue to rest on the, "5- Pillars of:

- training
- cold chain system
- supervision
- surveillance and
- health communications.



7.1 Training

In the recent past, refresher post-basic courses were necessary. These were costly as some of the staff trained were lost from the programme through retirements,

resignations and deployment in other areas of health provision. Therefore the future focus will be on basic training in medical schools and paramedical institutions in Kenya. On the job training by district supervisors will be vital, as well.

7.2 Cold Chain

Maintenance of the cold chain is basic to the success of an immunization programme. Accurate records of the functioning of the cold chain are necessary to enable the detection of any "breaks" in the chain. To facilitate this the computerization of Cold Chain Return Forms from all the 1250 current immunization centres, commenced in 1988.

KEPI has also included courses on the maintenance of the "cold chain" as part of the schools' curriculum for hospital equipment maintenance Trainee Technicians, in the Ministry of Health. Thus trained staff are available locally to maintain cold chain equipment.

7.3 Supervision

Meaningful Supervision at district level needs to be regular and carried out by use of "check-lists". KEPI has provided vehicles and uniform check lists for this purpose.

7.4 Surveillance

Although the Ministry's Health Information System is being re-vitalized, KEPI has requested districts to send returns directly to its Management Unit and a computer for entry of this data has been procured. It will also be necessary for KEPI to get the EPI-target disease returns, if the monitoring of disease reduction, especially of measles, poliomyelitis and neonatal tetanus is to be meaningful. Likewise, the proposed Sentinel Reporting System is a welcome activity to serve KEPI.

7.5 Health Communication

Health education and Social Mobilization activities are the combined function of the health communication component of KEPI.

KEPI has trained different cadres of health workers in communication skills and Social Mobilization.

The key person at the district level is the District Health Education Officer whose role it is to motivate people to seek immunization services and create health awareness as it pertains to immunization.

Health Education Officers organize Social Mobilization activities in collaboration with both the governmental and non-governmental sectors.

REFERENCE

1) WHO Health Magazine, Jan-February, 1987.

2) WHO-AFRO Region. EPI Mid-Decade Evaluation Report AFR/RC 35/21 of August, 1985.

3) WHO/UNICEF Joint Statement on Planning Principles for Accelerated Immunization Activities. Geneva, 1985.

4) WHO EPI Global Report. *Wkly Epidem. Rec.* (33) **62**: 241-243

5) WHO. EPI Global Advisory Group. *Wkly Epidem. Rec.* (2) **64**:5-10 (1989)

6) Min. of Health. appraisal Report on Expanded Programme on Immunization, A. Joint MOH/DANIDA Report, Kenya. 1st Edition. November, 1978.

7) Min. of Health. Report on KEPI Programme Review, 27 January to 13 February, 1986, pg. 27-28. A MOH/DANIDA Document containing restricted information. Nairobi, 1986.

8) DANIDA, KEPI Programme Review Report, 2-20 May 1988, pag 1 A MOH/DANIDA Document containing restricted information. Nairobi, 1988.

9) KEPI Management Unit. National Immunization Coverage Survey Kenya: 1987. A Min. of Health Publication, 1987.

10) Bjerregaard P. and Mutie D.M. Immunization Coverage in Kenya: *E. Afr. Med. J.*, **65**: 811-819(1988)

11) National Council for Population and Development (Min. of Home Affairs and National Development.). The Kenya Health Demographic Survey: 1989.

2

PRACTICE OF IMMUNIZATION

M.W Mwangi

Learning Objectives

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

- familiar with the National Immunization Schedule currently in force.
- capable of calculating the yearly, quarterly and monthly immunization coverage targets.
- familiar with the preparatory and implementation tasks at MCH's Immunization Site.
- capable of making calculations for adequate vaccine needs of a vaccination post.

1. INTRODUCTION

The main objective of immunization activities is to reduce morbidity and mortality caused by immunizable diseases. It is the responsibility of the supervisor to schedule immunization sessions and to ensure that they are conducted properly. He is also concerned with the overall quality of the immunization programme and its expansion to include all the eligible children and women.

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 contraindicators of the illness. Therefore, KEPI in this sense becomes a part of the PHC component which is integrated, co-ordinated and is performed in conjunction with other activities that health workers do.

2. POLICY OF IMMUNIZATION

Each country has an immunization policy which usually follows WHO's general guidelines. Immunization policies enable a country to standardise immunization procedures/practices. The policy in Kenya is to:

- integrate immunization activities into MCH/FP/PHC framework.
- sterilize all immunization equipment/supplies using steam sterilizers for the recommended period of 20 minutes.
- use one sterile syringe and needle per injection to prevent cross infection.
- use potent vaccines kept at 0^0C to $+8^0$C which meet WHO standards.
- keep vaccines on ice-packs during vaccination sessions to maintain potency during the session.
- discard all opened and unused vaccines at the end of the day. BCG should be discarded at the end of 4 hrs of reconstitution.
- hold vaccination sessions daily in fixed facilities from 8 a.m to 5 p.m supplemented by outreach services if appropriate.

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

- In case a child requires admission to hospital the decision whether or not to immunize is left to the receiving 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".

3. NATIONAL IMMUNIZATION SCHEDULE

3.1 The current schedule in use in Kenya (Fig 1) was developed in 1986 and revised in 1989. This was necessitated by the need to introduce polio birth dose and by the introduction of Hepatitis B in a pilot district in Kenya. (This is a dynamic area that will continue to evolve with new developments in immunization policies).

FIG. 1 The National Immunization Schedule

CONTACT	AGE OF CHILD	VACCINE DOSE	DOSAGE	ROUTE
1	At birth or at first contact	BCG	0.05ml (under 1 yr.) 0.1ml (over 1 yr.)	Intradermal
	At birth or at first contact (before 6 weeks)	Polio birth dose	2 drops	Oral
2	At 6 weeks or at first contact after 6 weeks	OPV I DPT II HB I	2 drops 0.5ml 0.5ml	Oral Intramuscular Intramuscular
3	At 10 weeks or 4 weeks after OPV I and DPT I	OPV II DPT II HB II	2 drops 0.5ml 0.5ml	Oral Intramuscular Intramuscular
4	At 14 weeks or 4 weeks after OPV II and DPT II	OPV III DPT III HB III	2 drops 0.5ml 0.5ml	Oral Intramuscular Intramuscular
5	At 9 months or first contact after 9 months	Measles	0.5ml	Subcutaneous

NB HB vaccination is still given on a pilot basis in one district (Kiambu) in Kenya. If results are favourable the HB vaccination will be given countrywide.

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

- most childhood vaccine-preventable diseases occur very early in life. If this schedule is followed according to specification the 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 above 9 months should enter a ward without being immunized against measles, and 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 6 weeks of life, it should not be administered. One should then start polio I at 6 weeks instead.

- regardless of the interval between the two doses of DPT 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. 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 given. For instance, if a child is seen for the first time when ten months old, one should give BCG, DPT I, OPV I and measles and ask the mother to come back four weeks later for DPT II and OPV II.

- booster doses after primary immunizations are not indicated until KEPI attains over 80% coverage for fully immunized children.

3.2. TETANUS VACCINATION FOR PREGNANT WOMEN

The current KEPI recommendation regarding tetanus vaccination for pregnant women is as follows:-

- a pregnant woman in her 1st pregnancy should receive two tetanus toxoid (TT) injections with 4 weeks interval between them. She should receive a booster dose of T.T. as soon as she is diagnosed pregnant in subsequent pregnancies.

FIG. 2 Tetanus Toxoid Schedule for Pregnant Women

DOSE	WHEN TO IMMUNIZE	PROTECTION
TT I	At first contact or as early as possible during pregnancy including first trimester.	No Protection
TT II	At least 4 weeks after TT I	3 Years
Booster	1 T.T. Dose every subsequent Pregnancy.	5 years

The purpose of the T.T. vaccination for pregnant women is not only to protect the mother against tetanus, but to protect the newborn against neonatal tetanus which has a high case fatality rate close to 90%.

3.3 WHO Proposed TT Immunization Schedule

As part of the strategy towards the elimination of neonatal tetanus by 1995, WHO has proposed a new TT immunization schedule (presented below). The target for TT in this schedule is broadened to include all women of child bearing age (15-45 years) It aims at providing life long protection of women against tetanus and hence protects the future newborn by passive immunity.

FIG. 3 WHO Recommended T.T. Immunization Schedule for Women of Child Bearing Age

DOSE	WHEN TO IMMUNIZE	PROTECTION
TT I	At first contact or as early as possible during pregnancy	Uncertain
TT II	At least 4 weeks after TT I	3 Years
TT III	At least 6 months after TT II or during subsequent pregnancy	5 Years
TT IV	At least one year after TT III	10 Years
TT V	At least one year after TT IV or during subsequent pregnancy	Life Long

4. CONDUCTING VACCINATION SESSIONS

4.1 VACCINATION SESSIONS

In Kenya, the Government Policy is to immunize on a daily basis. Ideally, vaccination sessions should be scheduled so that all children in the area served by the health facility can receive their first set of immunizations as soon as possible before the age of one year. To ensure that all children in the area are vaccinated at the earliest acceptable age, vaccination sessions for each health facility should be scheduled regularly at specified times.

In planning immunization schedules one may consider the number of children immunized by a health facility daily. If there are at least ten children immunized daily then immunization sessions should be scheduled on a daily basis. This will ensure that all eligible children are vaccinated at the earliest acceptable age.

Fewer sessions may be planned where less than ten children are immunized daily, to avoid wastage of vaccines and time. It may be useful to designate the same day of the week, for example each Wednesday, as immunization day. Local leaders should 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 the vaccination sessions the staff should be warm and friendly to both the parents and children. The immunization status of each child should be checked by asking the parents about their child's immunizations and confirmed by using the child health card. Additionally BCG scars should be looked for.

Immunizations should be administered to all children even if they are sick, unless they need hospitalization. Sick children should be referred for immunization after they have been attended to for their illness.

The time interval between doses of immunizations should be checked. Second or third doses of polio, DPT and HB should not be given if the time interval is less than a month. 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. After immunization the parents should be informed of the vaccines the child has received and the reactions to expect from the immunization.

Tally sheets should be filled accordingly after each immunization has been given. Date of immunization should be noted on the card. The mother and child permanent records should be filled in properly. The vacinator should explain clearly to the 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.

Four hours after the start of the immunization session all opened and unused BCG vials that have been removed from the refrigerator, should be discarded.

At the end of the day DPT, HB, TT, measles and OPV vials that have been removed from the refrigerator should be discarded.

4.2 ESTABLISHING THE TARGET POPULATION

The number of children that need immunization in a catchment area is the 'target' population. The aim is to protect all of these children. To be able to know how many children need immunization 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. In Kenya, one can assume that the number of children born in any catchment area is 5% of the total population. Therefore to calculate the target population one needs to know the total population.

For example let us consider health facility A in location B. The total population in location B is 26,000; therefore the number of children 0-11 months old to be immunized is 5% of 26,000 i.e. 1,300. So each year approximately 1,300 children will need immunization. This is the yearly target population.

The target population is used to calculate the requirement of vaccines, syringes and needles.

4.3 PREPARATION OF VACCINATION SITE

In the MCH/FP Area

Immunization activities are integrated with MCH/FP activities and include:-

- weighing
- history taking
- counselling
- sterilization of equipment
- treatment
- immunization
- health education
- antenatal care
- postnatal care
- family Planning
- control of communicable disease.

In selection of an immunization site a large enough 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 needed, one for letting clients in and the other for exit.

When a room does not have two doors, the staff will have to discuss and decide how best they can improvise.

- there should be a waiting area outside the room.
- where possible, keep the refrigerator in the same MCH area to minimize the health workers moving in and out of the room to get vaccines as needed.
- guide the clients into a single queue to enter the MCH/FP area to avoid confusion.
- have two chairs/stools, one for the patient/client and the other one for the health worker.
- allow only one patient/client at a time to go inside MCH/FP area, to provide privacy.
- sick children should be identified and attended to first.

Other team members should be reminded to screen and refer children for immunization before discharge. All expectant mothers must also be encouraged to attend the MCH/FP clinic for tetanus toxoid immunization as early as possible in the pregnancy.

- 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 where they will be given TT vaccine and given follow up advice.

4.4 Use of Clean and Sterile Equipment

Use disposable syringes and needles if available. If disposable needles and syringes are used:-

- use one needle and syringe per injection and discard.
- if disposable syringes and needles are not available clean vaccination equipment and sterilize it using a steam sterilizer. If immunizations are performed on daily basis, the syringes and needles should be cleaned and sterilized at the end of the sessions each day, so that they will be ready to begin the session the next day without wasting time to clean and sterilize.
- the cleaning and sterilizing procedures should be known by every health worker. Supervisors of immunization activities must see that all the rules regarding the cleaning and sterilization are adhered to.

4.5 Educating Parents about Immunization Activities.

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

- **group talk before vaccinating children.**

Parents should be comfortable and seated as they listen and participate in the discussion. It should be kept short and practical. Parents should be given time to ask questions.

- **at the vaccination station/table.**

Every effort should be made to ensure that parents can describe the important facts about immunization. Health workers should explain the age group to be immunized and which diseases the children will be immunized against. The side effects of each vaccine should be explained. Health workers should stress the need for return visits. Parents should be requested to convince other new parents of the importance of having their children immunized.

As health workers vaccinate each child, parents should be encouraged to have their questions and any queries clarified. While giving DPT, HB and polio vaccines it should be explained to them that these vaccines are not strong enough to protect their children if they receive only one dose and that three doses are needed. The health workers should remind parents to bring their children for measles immunization at the age of nine months.

- **At exit station** (or when leaving for home after immunization).

It is important that parents understand why their children are being immunized, which diseases they are being immunized against and why they have to bring their children for more injections. Therefore health workers should interview the parents about the immunization before leaving the facility.

4.6 Screening children and recording information obtained.

Screening a child determines a child's immunization status and general state of health. During this process one should determine the child's age, weight, immunization(s) already received, and the immunization to be received.

After each immunization the Child Health Card should be up-dated to indicate the child's immunization status. It is important to let the parents take the children's cards home with them and to encourage them to bring the card at each visit to the health facility.

A record of immunization should be kept by a health facility staff. This record determines which immunization the children have received, in case the parents lose their cards. These records can also be used to follow-up mothers who are not bringing their children to be immunized.

4.6.1 How to fill in the Child Health Card.

- 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, and interpret these weights to the parents.

- record any disease reported and reason for follow up and give an explanation to parents.
- determine vaccines to administer.
- if the child is too young to be immunized, 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.

4.7 Administration of vaccines:-

- hands should be washed before and after handling vaccines. All the vaccines and diluents must be kept cold. DPT, HB and TT vaccines are damaged if kept below 0^0C so they should never be frozen.
- **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 under 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**
  Route of administration - **intramuscular,**
  Dose - 0.5 ml.
  Site - upper outer part of the (R) 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).
- **Hepatitis B.** vaccine
  Route of administration - **Intramuscular**
  Dose - 0.5 ml.
  Site - as for DPT but **(L) thigh.**

4.8 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 was supposed to receive.
- ensure that parents can tell the possible reactions and what to do about them.
- ensure that mothers can tell the return dates and the importance of second and third doses of TT, DPT, HB and polio.
- parents should be given their immunization cards and encouraged to bring the cards with them each time they visit the health facility either for immunization or when ill.

4.9 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 vaccines should be dealt with, in one of the following ways:

- pour vaccines into the pit latrines
- burn them
- break the empty vials
- if disposable syringes and needles are used collect them and destroy them.

5. MONTHLY REPORTING

Monthly Monitoring

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:

No of children who received DPT1 X 100 = % immunized with DPT1,
monthly target population.

- What percentage of children who received DPT1 did not receive DPT III vaccine (i.e. the drop out rate)?

  No. who received DPT 1 - No. who are eligible for DPT III X 100 = Drop out rate in %
  number who received DPT I.

- Are children who are sick from the target diseases coming to the clinic?

If in a given month/months no cases are diagnosed this should be recorded as zero cases for that month (s).

6. EVALUATION:

The purpose of evaluation is to determine whether the set targets are being met. Evaluation should be done annually or biennially. During your evaluation ask yourself these questions:-

- did you hold immunization sessions daily?
- did you have enough vaccines?
- did you have enough syringes and needles to give a safe sterile injection?
- was the cold chain maintained and were all the refrigerator temperatures in the safe range of 0^0c- $+8^0c$
- did you check the immunization status of all children and pregnant women who came to the clinic?
- did you, then, give the women and children all the vaccine they should have had?
- did you inform them about immunizations to be given on their return date?

The cause of any identified problems detected should be rectified.

7. CALCULATING REQUIREMENTS

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

Using the example of Health Centre A in location B which had a target population of 1300 and knowing that each child will require:-

- 1 dose of BCG vaccine
- 1 dose of measles vaccine
- 4 doses polio vaccines, and
- 3 doses of DPT,

The following would be the vaccine requirements per year:-

- 1 x 1300 doses of BCG = 1300 doses or 65 twenty dose vials.
- 1 x 1300 doses of measles = 1300 doses or 130 ten dose vials.
- 4 x 1300 doses of polio = 5200 doses or 520 ten dose vials.
- 3 x 1300 doses of DPT = 3900 doses or 390 ten dose vials.

In order to cater for vaccine wastage due to the destruction of unfinished/opened vials additional stock needs to be ordered as follows:-

- BCG	50%
- DPT	30%
- Polio	30%
- TT	30%

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.

8. SUPERVISION

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

Further Reading

1. MOH/KEPI operational Training Manual for Health Workers in Kenya Ministry of Health, Nairobi, April, 1982.
2. WHO/EPI Training Manual for mid-level Managers. Conduct Vaccination Sessions.
3. WHO/EPI Sterilization Alert Highlights up-date, Geneva, July 1987.
4. R.H. Henderson. Providing Immunization: The State of the Art. In Protecting the World's Children: Vaccines and Immunization within Primary Health Care. Bellagio Conference Report March 13-15, 1984. The Rockfeller Foundation, June, 1984.
5. WHO/UNICEF Joint Statement, Planning for Accelerated Immunization Activities, WHO Geneva, 1985.
6. MOH/KEPI Immunization Activities. Immunizing Mothers and Children in MCH/FP Clinics. Ministry of Health, Nairobi, Kenya.
7. Immunization in Practice 8 modules WHO training course, Geneva.

3

VACCINE MANAGEMENT AND THE COLD CHAIN SYSTEM

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S.M Kamau

Learning Objectives

At the end of this chapter, the student should be in a position to:

- define the "Cold Chain System", know its components and importance, in an EPI Programme.
- state the safe temperature range for most vaccines, including the names of the vaccines which should not be frozen.
- broadly enumerate the different types of Cold Chain Equipment used in the Kenya EPI Programme.
- describe what one has to do during power failure or fuel shortage for refrigerators.
- briefly describe how Kenya EPI Programme procures and distributes vaccines.

1. INTRODUCTION

Vaccines are biological substances made from bacteria or viruses and are either killed or live attenuated preparations. Clinical trials and experience have shown that when some of these preparations are introduced into the body, they help in the formation of antibodies which would stop any future invasion with the particular disease causing organism.

Vaccines have been used successfully in reducing the incidence of some diseases and this has given rise to the global Expanded Programmes on Immunization (EPI) against the six EPI target diseases. The elimination of smallpox by intensified immunizations worldwide has given hope and encouragement in the fight against the six target EPI diseases.

2. IMPORTANCE OF THE COLD CHAIN FOR EPI

The main objective of EPI is the reduction of morbidity, mortality and disability due to the target diseases. In order to achieve this, potent vaccines should be given to the majority of the target population in the recommended number of doses for each type of vaccine. The vaccines are manufactured in conformity with World Health Organization (WHO) standards for biological products in addition to National requirements and regulations for each product. Field experiences have shown that full immunizing strength of these vaccines are maintained if stored as recommended up to the expiry date stated. They are otherwise very fragile and lose their potency if exposed to high temperatures and some by very low temperatures.

Heat and sunlight destroys and reduces the efficacy of all vaccines. Polio, measles and B.C.G. vaccines are more quickly damaged by heat because it kills the live particles. Freezing temperatures destroy DPT, TT and HB vaccines. Frozen DPT and TT form granules which do not form a homogenous solution even with rigorous shaking.

Due to the sensitivity of these biological products to adverse temperatures, critical attention should be paid to the recommended storage temperature for each type of vaccine at all stages of transportation and during storage.

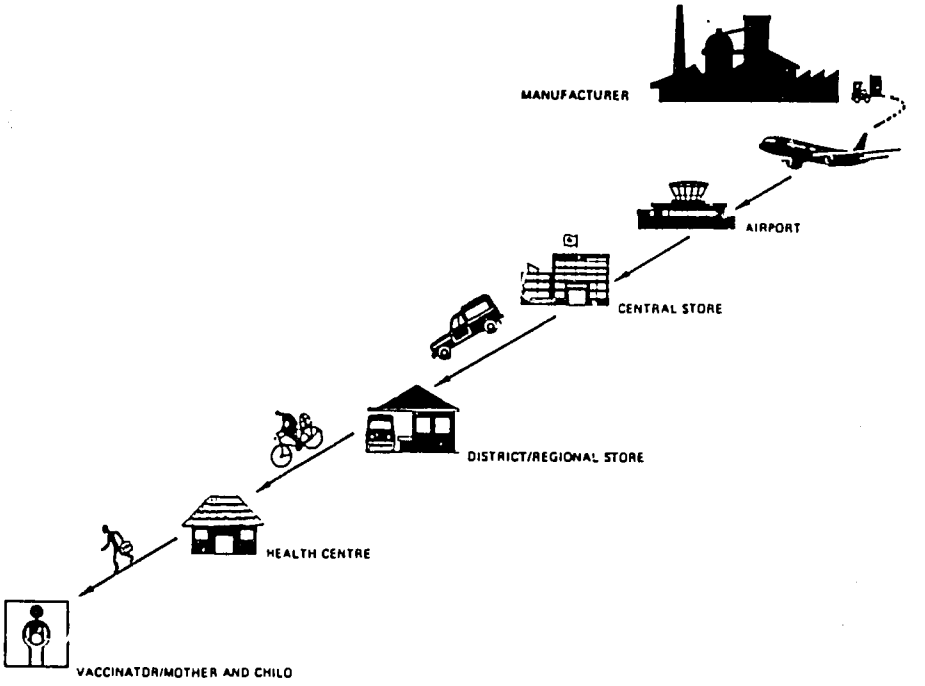
3. COLD CHAIN SYSTEM

3.1 General Principles of the Cold Chain System:

The cold chain is a system of maintaining vaccines in a potent state from the manufacturer to the consumer. In performing this activity, people, equipment and skills are required. The vaccines should always be transported and stored in the cold state

throughout the line of distribution. The cold chain has many links which should be maintained throughout. Failure at any one link can render the vaccines useless. Even short exposures are harmful since the effects are cumulative. It therefore, demands that continuous monitoring and maintenance of the cold chain must be strictly observed.

3.2 *Figure 1. The Cold chain System



*MANAGE THE COLD CHAIN SYSTEM. WHO Expanded Programme on Immunization.

The cold chain system will perform effectively if people have the skills and knowledge on how to organize and maintain the available cold chain equipment.

The equipment must be of the desired quality and quantity to enable the correct storage of vaccines, as it travels from one stage of the cold chain to the other, until it reaches the final consumer who is the mother or child.

Often the cold chain is thought to refer only to the refrigeration of vaccines. Even if the finest and most modern equipment and transportation are available, the cold chain will not be effective if people do not properly handle the vaccines.

The WHO/EPI programme has given specific guidelines on the temperatures that should be maintained at each stage (see Fig 2)

*Figure 2. Recommended Temperatures and storage time

VACCINE LEVEL: MAXIMUM STORAGE TIME:	CENTRAL STORE up to 8 months	REGIONAL up to 3 months	HEALTH CARE up to 1 month	TRANSPORT up to 1 week
MEASLES BCG ORAL POLIO	-15^0 to -25^0C			
DPT TETANUS TOXOID HB T.T.			0^0C to $+8^0$C	

MANAGE THE COLD CHAIN SYSTEM. WHO Expanded Programme on Immunization.

4. COLD CHAIN EQUIPMENT

- Cold rooms and its accessories.
- Refrigerators and deep freezers.
- Cold boxes.
- Vaccine carriers.
- Ice packs.
- Thermometers.

4.1 Cold Rooms

A cold room is a specially built, thick walled room which is mechanically kept cold, the temperature being adjustable to the level required.

Cold rooms are found at the Central Vaccine Store and the Regional Vaccine stores where the bulk of the vaccines are stored.

It would be more economical to build cold-rooms at the district level as this would increase the stock capacity and hence reduce collection and distribution costs from the Central and Regional Vaccine Stores.

4.1.1 How to Work Safely in a Cold Room:

- when more than one person is working in the cold room at a given time, care should be taken to avoid accidentally locking of anybody in the cold room.

- the cold room door is made in such a way that it can be opened from the inside. This mechanism should be checked regularly to prevent anybody being accidentally locked in the cold room.
- to avoid cold injuries minimum time should be spent working in the cold room and warm clothing worn.
- the amount of diesel in the generator fuel tank should be checked regularly and replenished as required.
- a technician should regularly check on the equipment, specifically the belts, filter drier and compressor.

4.1.2 Packing of Vaccines in the Cold-room:

- vaccines should be neatly packed on the shelves.
- it is advisable to store vaccines in order of their expiry dates to avoid the possibility of some vaccines expiring unused.
- the cold rooms should not be overstocked. The vaccines should be packed with adequate space between them to allow for adequate circulation of air.

4.1.3 How to look after the cold room

Daily care:

- the thermometer should be read on a daily basis and the temperature adjusted to the appropriate recommended level of -15^{0}c to -25^{0}c.
- the functioning of the temperature recording sheet which is fitted to the cold room should be checked.
- any unusual noise indicative of the malfunctioning of the machinery should be investigated and corrected.
- at the end of the day all lights should be switched off and the door closed securely.

Weekly care:

- the temperature recording sheet should be changed.
- the alarm that indicates undesirable temperature changes, should be tested.
- the standby generator should be checked by switching off the main electricity supply and letting the generator run for 5 minutes before switching back to the mains.

Monthly care:

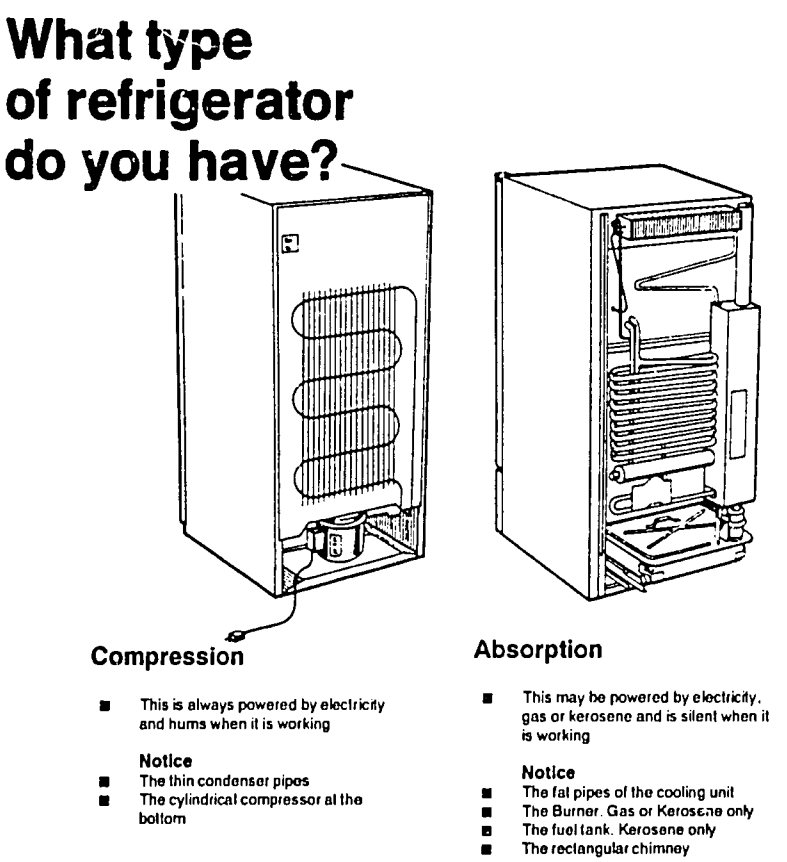
- a major check should be carried out by the maintenance technicians.

- orders should be placed for any spare parts required for the proper function of the cold room.

4.2 Refrigerators:

The compression and absorption refrigerators are currently used for vaccines storage in Kenya.

*Figure 3 Compression and Absorption Refridgerators



*MANAGE THE COLD CHAIN SYSTEM. WHO Expanded Programme on Immunization.

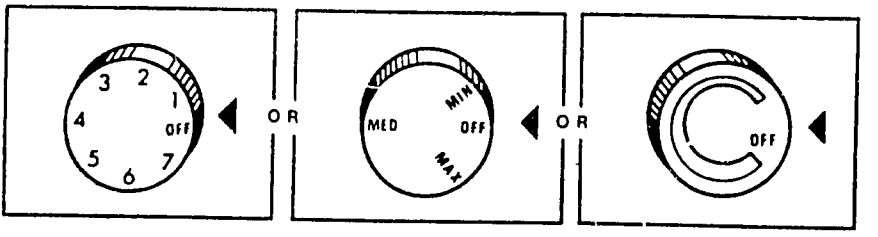
4.2.1 Compression Refrigerator

Most electric and solar refrigerators are of the compression type. A good example of a compression refrigeration system is the ice lined freezer which can also be set to operate as a refrigerator. A compression refrigerator uses an electric motor compressor to circulate a cooling fluid called refrigerant. The pump compresses the refrigerant from a gas state into a liquid state, a process which gives off heat.

The compression system circulates the refrigerant very quickly and thus has a much greater cooling effect than the absorption system. The temperature in the storage area is controlled by an automatic thermostat which switches the compressor motor on and off at the desired temperature.

The thermostat control knob can be turned towards a warmer or colder positions if necessary. It is usually marked "1" to "7",MIN, MED and MAX or with an arrow indicating how to turn for colder temperature. No "1" for "MIN" gives the warmest and No. "7" or "MAX" the coldest temperature.

Figure 4 Thermostat Control Knob



The motor of the refrigerator requires a higher power input to start than to run, but still requires a constant supply of electricity at a steady voltage. This limits where it is used to centres where there is a reliable electricity supply.

4.2.2 Absorption Refrigerator:

Absorption Refrigerators use heat produced by electricity or by burning gas or kerosene to drive a cooling cycle under pressure produced by hydrogen. The heat causes ammonia and water to circulate in a sealed system of pipes. In the evaporator inside the refrigerator, the ammonia fluid turns into gas, absorbing heat from the inside air. As a gas, it rises circulating to the outside of the refrigerator where it condenses into a liquid, releasing the heat to the outside air.

Absorption refrigerators are less efficient than compression refrigerators because of the slow circulation of the refrigerant, but they are much more suitable for stores where there is a weak, unreliable electricity supply. This type include kerosene and gas, refrigerators.

4.2.3 Models of Refrigerators:

The common models of refrigerators used in Kenya are RCW 42EG, Sibir S2323, RA1300 and VR50 Solar. It is important to know and quote the model of your refrigerator when requesting for repairs and replacements during maintenance.

4.2.4 How to install a Refrigerator:

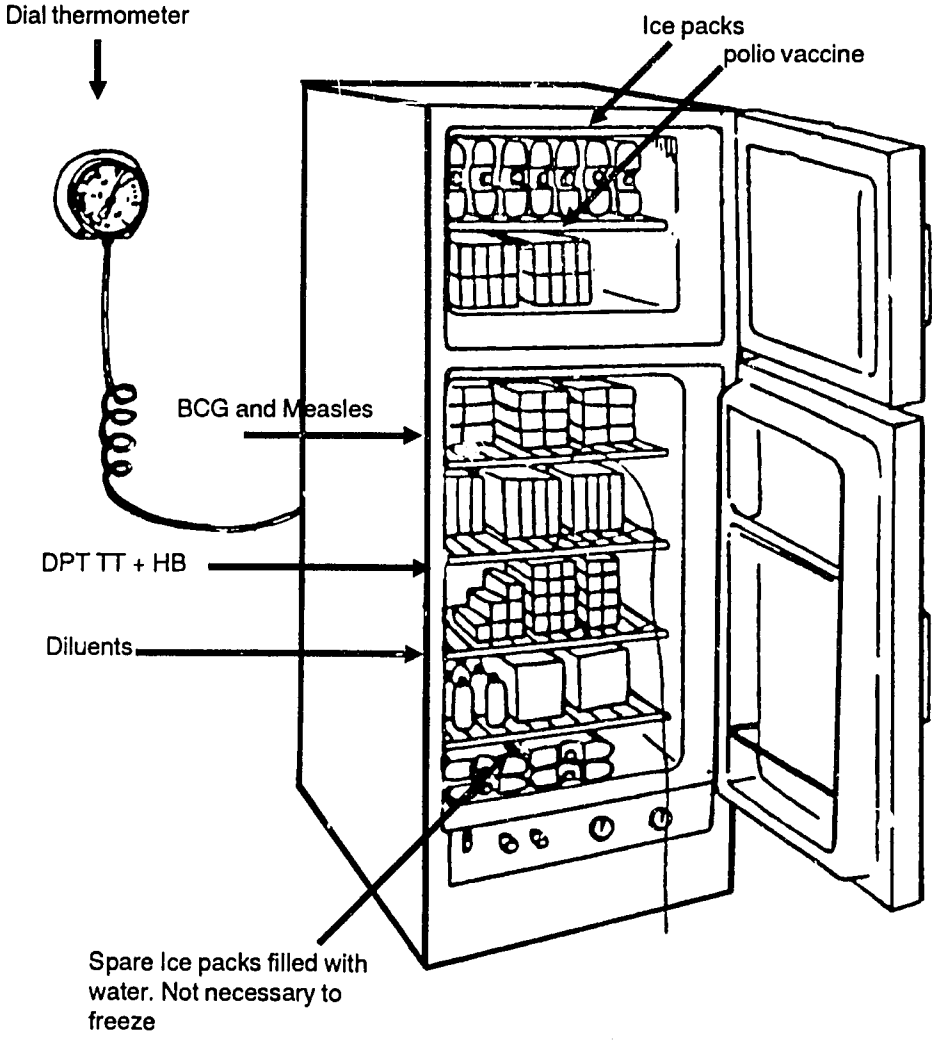
- place the refrigerator in the coolest part of the building.
- the room must be well ventilated and a good air circulation around the refrigerator is necessary but avoid draughts from doors and windows.
- keep the refrigerator in the shade and away from heat of any kind.
- clearances to wall and roof must be at least 16 inches (400mm) from the ceiling and 12 inches (300mm) from the walls.
- to keep the refrigerator dry, place it on wood blocks 1 to 2 inches (25 to 50mm) thick. The refrigerator must stand firm and level on these blocks. An absorption refrigerator must be perfectly level or it will not work properly.

4.2.5 Packing in a Refrigerator:

The vaccines are placed in the refrigerator such that polio, measles and BCG vaccines are put in the coldest part of the refrigerator. DPT, TT and HB vaccines should be put in the middle shelves away from the evaporator which would otherwise freeze them. Ice packs and diluents are placed at the bottom shelves.

The vaccines should be packed neatly in the refrigerator leaving spaces between them to allow air movement. The newest vaccine is placed on the right side of the refrigerator. As a routine practice, it is advisable then to use vaccines on the left side first, in order to make sure that oldest vaccine is used first.

*Figure 5 A Properly Packed Refrigerator at District Vaccine Store.



*KEPI Operational Level Training for Health Workers in Kenya.

4.2.6 How to care for the Refrigerator:

- make sure you don't operate the refrigerator on two sources of energy at the same time.
- check the temperature inside the refrigerator twice a day.

- check that the burner flame is blue which suggests a well functioning refrigerator that will maintain the ideal temperatures. If it is not blue the most likely reason is inadequate flow of gas therefore adjust appropriately using the gas regulators.
- check the ice formation on the evaporator. If the ice is thicker than 6 to 10mm defrost the refrigerator. Thick frosting of the evaporator will make the temperature go up.

4.2.7 How to Keep Vaccines Cold in a Refrigerator:-

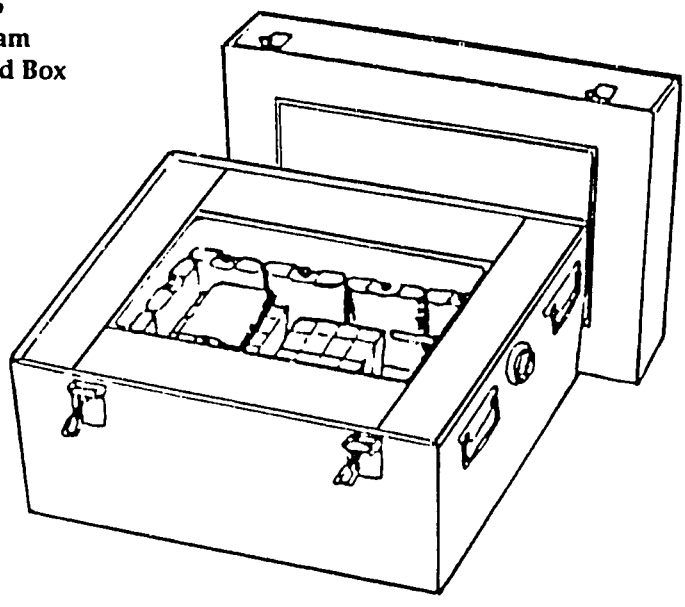
- place vaccines in the correct compartment.
- avoid opening the refrigerator unnecessarily.
- ensure the maintenance of ideal temperatures of 0 to $+8^0$c. This should be based on a twice daily temperature recording.
- defrost the refrigerator regularly.
- pack the vaccines with enough space in-between to allow circulation of air.
- avoid packing the vaccines in contact with the evaporator.

4.3 Cold Boxes and Vaccine Carrier:

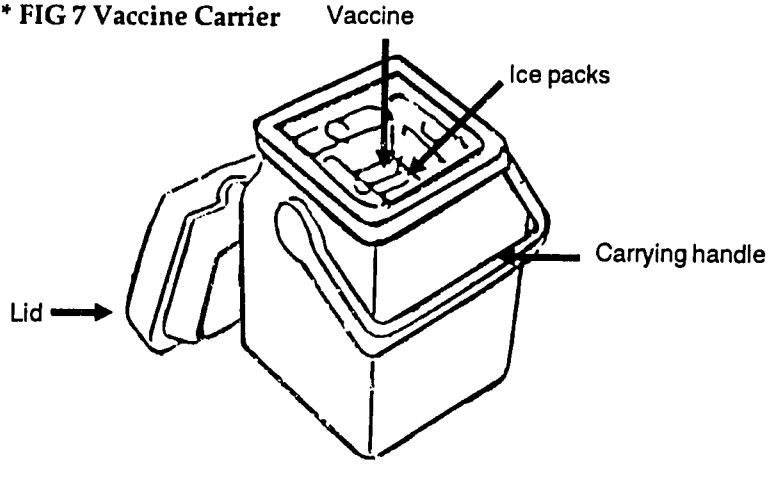
Cold boxes and vaccine carriers are used for keeping vaccines cold during transportation. These containers are designed to keep cold air inside and prevent warm air from entering. During the transportation and distribution of vaccines, one should avoid opening these containers.

Frozen icepacks are lined in inner wall of cold boxes and vaccine carriers to keep the vaccines cold. It is important that frozen icepacks be placed in a single layer on a table for 5-10 minutes after being removed from the freezer and before being used inside cold boxes and vaccine carriers. The temperature inside the icepacks will rise slightly and the icepacks will no longer pose a threat of freezing the DPT, TT or HB vaccines. (The reduction in the cold life of the icepacks which are exposed for 5-10 minutes to outside temperatures will not be significant.) DPT, TT and HB should be wrapped with foam material and not placed directly next to the icepacks to avoid the risk of being frozen.

*FIG 6
Diagram
of Cold Box



* FIG 7 Vaccine Carrier



*KEPI Operational Level Training for Health Workers in Kenya.

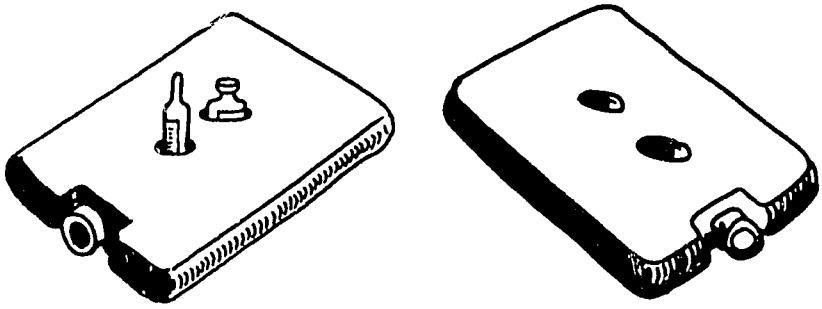
4.4 Icepacks

These are plastic containers filled with water or jelly. They are put into the freezing compartment to freeze them before they are used in cold boxes and vaccine carriers. During the vaccination session, vaccine vials are placed on the icepacks to avoid the

frequent opening of the refrigerators, cold boxes and vaccine carriers which would raise their internal temperatures.

Make sure that the caps on the icepacks are secure so water does not leak out. Icepacks should be filled to within 1" inch of the top to allow for the water to expand when frozen.

FIG 8 Diagram of Icepacks



4.5 Types of Thermometers Used in Cold Chain:

There are different types of thermometers used in monitoring the cold chain system. Those commonly used are:

- **liquid Crystal Thermometers.**

  These are inexpensive thermometers used during the vaccine transportation and in refrigerators. They do not operate at temperatures below freezing point.

- **dial Thermometers.**

  There are 2 types of dial thermometers. The first one is used in the central, regional and district vaccine stores. They have an alarm and can also record minimum and maximum temperature readings.

  The 2nd type of dial thermometers have neither an alarm nor the capacity to record maximum and minimum temperature readings. These are commonly used during vaccine transportation and in the majority of refrigerators.

- **digital Thermometers.**

  These are mainly used by engineers during evaluation to determine the functioning of the cold chain equipment.

- **thermographic Thermometers.**

  These are large thermometers in-built on the walls of cold rooms, that graphically record the temperature of the cold room on a continuous basis. They are commonly used in large vaccine stores.

5. MONITORING OF THE COLD CHAIN SYSTEM

5.1. Temperature Recording

This is done twice daily, in the morning and in the afternoon. The temperature is recorded on specially designed forms. This task is important since any failure in the functioning of the refrigerator will be noticed and action taken immediately by adjusting the thermostat. This will save the loss of vaccines and prevent administration of vaccines that might have been exposed to high temperatures.

5.2. Cold Chain Monitor Cards (3M)

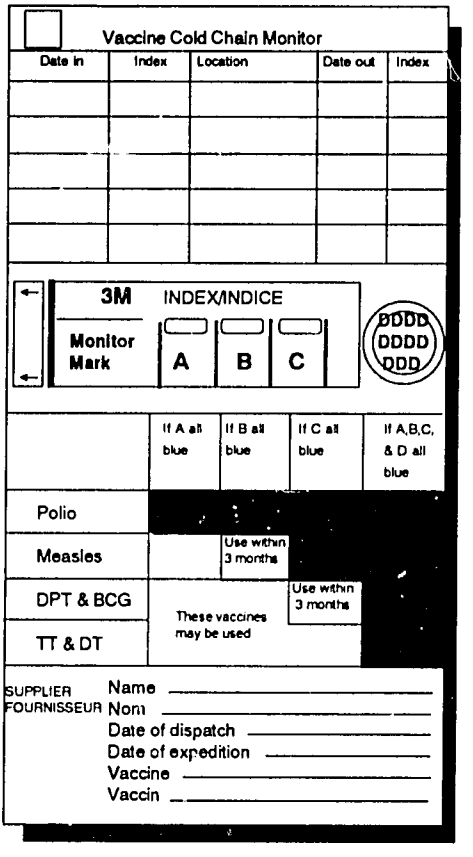
This is a special rectangular card with 4 oval windows with a "Stabilizing Strip" at the end. The monitor is activated when this strip is removed and colour changes occur corresponding to temperature rise.

5.2.1. How Cold Chain Monitor Card Works

Each cold chain monitor has a heat sensitive indicator in the form of a strip with 4 windows stuck to it. The indicator operates at two different temperatures, 10^0C and temperatures above 34^0C. The card is entirely heat stable until it has been activated by tearing off the stabilizing strip. The instructions for interpreting the readings are always printed on the monitor card. One advantage of this monitor is that the colour change is irreversible. Colour stops spreading when the temperature is below 10^0C. But it will not return down the scale even if taken to a freezer. The higher the temperature, the faster the blue colour will spread from one window to the other.

Research is being conducted to look for other types of monitors which could be attached to individual vials.

*FIG 9 Diagram of Monitor



Keep the Cold Chain Monitor with your vaccine

When the monitor arrives...
complete the top part of the card
- fill in the date
- fill in the index (A,B,C, or D)
- fill in the location

When the monitor leaves...
complete the top part of the card
- fill in the date
- fill in the index (A,B,C or D)

If windows A,B,C and D are all white use vaccines normally

If the windows A to C are completely blue, but window D is still white it means that the vaccine has been exposed to a temperature above 10°C but below 34°C for the following number of days:

	INDEX		
	A	B	C
At a Temperature of: 12°C	3 days	8 days	14 days
21°C	2 days	4 days	11 days

If only window D is blue it means that there has been a break in the cold chain of a temperature higher than 34°C for a period of at least two hours Check the cold chain - Use vaccines normally

*MANAGE THE COLD CHAIN SYSTEM. WHO Expanded Programme on Immunization.

5.3. Freeze Watch

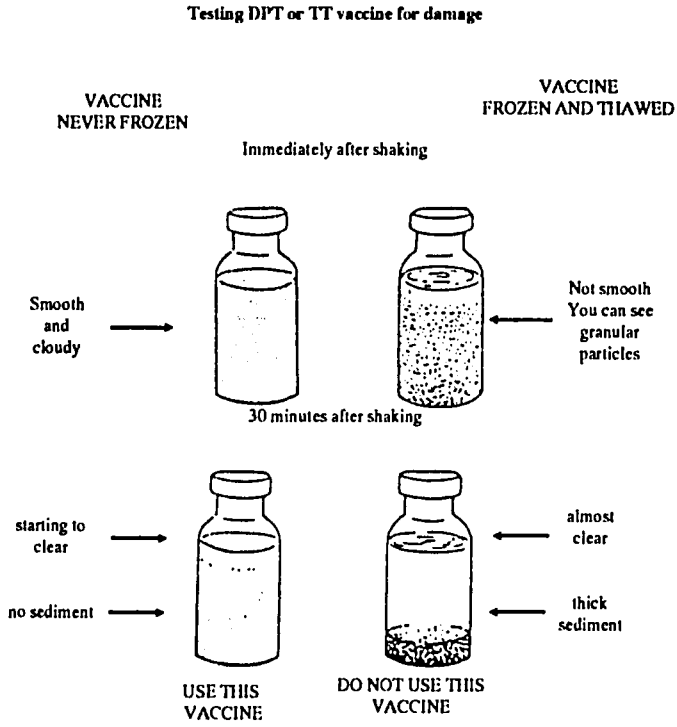
The freeze watch indicator is a small sealed glass ampoule. It is filled with a coloured liquid. If the temperature falls below-3°C, the watch will burst and stain the background red. It is therefore useful in detecting if vaccines that should not be frozen (i.e DPT, TT and HB) have been exposed to adverse temperatures. If these vaccines have been frozen they must not be used as they will have lost their potency.

5.4. Shake Test

This is a simple test that can be easily done at every stage of the cold chain. The sedimentation rate of a suspect vial is compared with a similar DPT or TT, vial which is

known to have been stored at the correct temperature. Shake the two vials vigorously and inspect carefully in strong light. Follow the instruction as described below. (Fig 10)

FIG 10 Testing DPT and TT vaccines for damage



6. POWER FAILURES

In the event of power failure one should do the following:

- if one has a gas/electric refrigerator,

  - switch on the gas regulator and light the gas.

  - check that the flame is burning correctly.

  - check that the gas cylinder has sufficient gas. If gas is insufficient and there is no spare cylinder, make arrangements to transfer the vaccine to the nearest centre where the cold chain can be maintained.

  - switch off the electricity supply.

- if the refrigerator works only on electricity and gas is not available,

  - do **nothing** to the refrigerator, and **do not** open the lid until you are ready to transfer the vaccines to another centre where the cold chain can be maintained.

  - maybe maintain 'safe' period of time.

7. VACCINE MANAGEMENT.

7.1. Vaccine Procurement - Handling and Storage

Vaccine procurement can be considered in terms of central and peripheral vaccine procurement where central procurement refers to the central KEPI vaccine store which caters for the whole country; and peripheral procurement refers to the regional and district vaccine stores including health centres.

7.1.1. Vaccine Procurement - Handling and Storage at the Central Vaccine Store:

The annual estimates for the total vaccine requirements for the whole country are done by the KEPI Management Unit annually. These estimates are based on the previous year's consumption plus about 10% which caters for:

- where there has been shortages.
- an increase of the population of the under-fives.
- an element of vaccine wastage.

The above orders are sent to the manufacturers through UNICEF which facilitates the procurement of the vaccine for the Global EPI programme.

Before the vaccines are despatched from the manufacturers to Kenya, a telex is normally sent to the KEPI Management Unit giving the following information:-

- type of vaccine to be expected.
- number of vials or doses to be expected.
- flight number of the aircraft.
- expected time of departure (Country of origin).
- expected time of arrival (Nairobi airport).
- Airway Bill (A.W.B) number.
- number of packages to be expected and the gross weight.

Once this information has been received by the KEPI Management Unit,

- it relays the same information to the Government Clearing Agents based at the Airport.
- it arranges for storage spaces in the Central Vaccine Store.
- transport is made available for immediate collection of the vaccine when it arrives.

When the vaccines arrive at the Central Vaccine Store, the following have to be done:-

- checking and recording the state of the cold chain monitors accompanying individual vaccine boxes to assess the maintenance of cold chain during shipment.
- checking and recording the condition of the ice packs accompanying individual boxes.
- checking and recording the quantities of the vaccine received and the packaging.
- once it has been confirmed that the vaccines have been transported properly they are sorted out by date of expiry and stored at the various recommended temperatures i.e. -15^{0}C to -25^{0}C for both polio and measles vaccines and 0^{0}C to +8^{0}C for BCG, DPT, tetanus toxoid and HB pending distribution.

7.1.2. How to Calculate National Peripheral Vaccines Requirements

It is important to receive the correct amount of vaccine during each supply period e.g. during each month. If too little vaccine is ordered stock may run out before the next supply arrives, and so cause delays in immunization activities. If too much vaccine is ordered, some may expire before use, and will be wasted. In addition, there is always the risk of power failure, or refrigerator breakdown, and if there is too much stock, a great deal of vaccine may be destroyed whilst the refrigerator is out of action. Therefore it is important to calculate the correct amount of vaccines required for each health facility.

The following steps help in estimation of the quantity of vaccines required:-

- estimating the size of the total population.
- calculating the target group.
- estimating the expected coverage.
- calculating the number of doses to be given.
- estimating a wastage rate.
- estimating the frequency of supply.
- adding a reserve stock

Example: Using BCG Vaccine

- estimate the size of the total population:
  for example: 100,000 people.

- calculate the target group:

  the target group for BCG immunization is all newborns. Assuming a birth rate of 35 per 1000 population: Multiply by 0.035
  100,000 x 0.035 = 3,500 children.

- estimate the expected coverage:

  assume that this may be 80%

  therefore multiply by 0.80 as follows:

  3,500 children x 0.80 immunized children = 2800 children

- calculate the number of doses to be given:

  for BCG vaccine this is one dose per child. Therefore multiply by 1.
  2800 x 1 = 2800 doses of BCG vaccine.

- estimate the wastage rate.

From KEPI field surveys, it has been established that vaccine wastage occurs at the following rates:

BCG	50%
Polio	30%
DPT	30%
Measles	30%
TT	30%

Using the same example, the wastage rate for BCG will be 50% of 2800 doses i.e 1400 doses.

Therefore, when ordering, an additional 1400 doses should be ordered.

After calculation of the vaccine requirement the estimate should be forwarded to the Central Vaccine Store for necessary action.

7.1.3 Distribution and Handling of Vaccines at the Peripheral Level

From the Central Vaccine Store the vaccines are distributed to the regional and district vaccine stores from where the peripheral health facilities draw their supply. During distribution, cold chain links must be strictly maintained.

There are 3 main vaccine distribution systems as follows:

- direct Distribution to the Districts.
- direct collection from the Central Vaccine Store by the Districts.
- distribution by public transport.

7.1.3.1. **Direct Distribution to the Districts**

Direct distribution is scheduled to be carried out at least after every two months during the months of January, March, May, July, September and November. In Kenya there are 3 established vaccine distribution routes as follows:-

- central route.
- western route.
- coastal route.

This facilitates efficient distribution, allows for cold chain monitoring and provides opportunities for supervision.

7.1.3.2. **Direct Collection from Central Vaccine Stores by the Districts**

Districts situated near Nairobi where the Central Vaccine Store is situated, are expected to continue to collect their vaccines.

7.1.3.3 **Distribution by Public Transport**

For the districts which are not easily accessible and because of lack of better alternatives of vaccine distribution, this is done by public transport such as air freight and buses.

Courtesy services of Air Kenya, Police Airwing, the Kenya Army planes and the Flying Doctors Service are utilized. In these circumstances, a telegram is sent in advance to advise the stations about the despatch of the vaccines and by which Air Charter Plane.

7.1.4 How to Keep Careful Records

In order to control the amount of vaccine being delivered to the district store and to keep a check on the vaccine as it is issued to the immunizing staff, it is necessary to keep careful records. These records will show you immediately:

- how much of each type of vaccine is in the refrigerator.
- the expiry date of each vaccine.
- which vaccines have been issued to health centres and dispensaries.
- which vaccines have been returned by health centres and dispensaries.
- how much vaccine has been delivered to the District Store and the date.

These records must be kept on a stock ledger, using one sheet for each type of vaccine.

8. VACCINE POTENCY TESTING

Vaccines are not routinely sent for potency testing except when large quantities have been exposed to a cold chain failure. It is not economical to test small quantities.

Vaccine potency and safety is tested by the manufacturer before releasing vaccines to the market. It is mandatory too that production protocols duly signed by National Authorities of the Control Laboratories are submitted with each consignment received by the KEPI Management Unit. These protocols will contain all the details of the tests performed and will include the sterility tests, innocuity tests, final concentrations, identity tests and expiry dates of each batch.

Due to the cost and complexity involved in testing the vaccines, the WHO has given guidelines on the amount under suspect justifying the test. (see Fig 12 below)

FIG. 11 Information for testing vaccine potency

Vaccine	No. of doses involved justifying test	No. of doses needed for test	Time when answer expected(allowing) for repeated test)	Conditions of transport
Poliomyelitis (Oral)	2,000	50	1 month	0^0c to 8^0c
Measles (Freeze-dried)	2,000			
BCG (Freeze-dried)	20,000	100	3 months	
Diphtheria Pertussis-Tetanus	200,000			
Tetanus Toxoid	50,000			

Note: It is not normal to take vaccines for testing from a health centre store. The quantities are not large enough to justify the cost of the transport and test.

Sometimes it is necessary to perform potency tests on vaccines being used in an immunization programme particularly when the function is suspect.

The samples needed for testing should be collected from points most likely to demonstrate the weakness of the cold chain. These samples should be clearly labelled with the date, place and the name of the person who has collected the sample. The samples are then well packed with cold ice packs and sent to the testing laboratory. The results obtained should be able to help if remedial actions are required.

FURTHER READING

1. MOH/KEPI Operational Training Manual for Health Workers in Kenya. Min. of Health, Nairobi, 1991
2. WHO/EPI Training Manual for Mid-Level Managers. Manage Cold Chain. Revision 2, February 1985
3. Resources for Child Health (REACH). The Logistics of Vaccine Management. In EPI Essentials. A Guide for Programme Officers. Chapter II. John Snow Inc. Arlington. Va. August 1989.
4. Programme for Appropriate Technology in Health (PATH). Immunization: Kenya Primary Health Care. Vol. 3 No. 1 January 1983. Washington, 1983.
5. Users handbook for gas and electric operated absorption refrigerators, WHO, EPI/LOG/84/19 Rev.1

4

MISSED OPPORTUNITIES FOR IMMUNIZATION

R.K.A Sang
J.M Wanza
G.N Kimani

Learning Objectives

At the end of this chapter, the student should be in a position to:

- define a missed opportunity for immunization.
- identify missed opportunities for immunization.
- enumerate ways to reduce missed opportunities for immunization.

1. INTRODUCTION

A missed opportunity for immunization occurs when any eligible child or woman comes to a health facility and does not receive any or all of the vaccine doses for which he or she is eligible. The opportunity to immunize eligible children is missed when:-

- the health facility does not offer immunization services.
- the health workers do not use appropriate contraindications to immunizations.
- the health workers do not routinely screen children and women for their immunization status and offer the recommended vaccines.
- the health workers do not give all the vaccines for which the children and women are eligible at the time of the visit.

2. METHODS OF IDENTIFYING MISSED OPPORTUNITIES

Identification of missed opportunities can be done through:

- Review of routine data e.g. those involving routine reporting of diseases.
- Conducting missed opportunity surveys.

2.1 Review of routine data (routine reporting of diseases)

Although all the heath facilities are required to report the occurrence of the EPI target diseases (among others), the reporting still remains quite incomplete for most diseases. A form is filled-in every week at the health facility level, then sent to the Ministry of Health headquarters for information, analysis and necessary action. It has been observed however that the reporting health facility does not generally use the data collected.

It is important to accurately diagnose the diseases and report by age. To Check the sensitivity of the reporting system the following methods may be used:-

- the number of newborns adjusted for immunization coverage may be compared with the average number of cases reported annually to estimate the completeness of the reporting of the disease.
- planned immunization surveys may also serve as a checking mechanism.

So long as they are consistent, routine reporting may be useful in evaluating disease trends. Thus persistently large proportions of reported cases without a corresponding

decrease in vaccine availability may suggest that the vaccine may not be getting to the children.

2.2 Conducting A Missed Opportunity Survey

Supervisors assess the occurrence of missed opportunities by conducting a survey. The survey measures the number of missed opportunities, identifies their causes, and helps determine where interventions are needed in an immunization programme.

The survey answers questions about the number of eligible children and women who go to the health facility during routine immunization sessions but do not receive all of the immunizations for which they are eligible. The number of eligible children and women who go to the health facility during out-patient or non-immunization sessions and are not immunized are also recorded.

Missed opportunity surveys provide supervisors with information that may be used to reduce the number of missed opportunities and increase the number of people reached with immunizations.

3. IMMUNIZATION CLINICS IN KENYA

In Kenya, immunization services are integrated with Maternal Child Health and Family Planning (MCH/FP) services in all immunizing health facilities. The Kenya Expanded Programme on Immunization (KEPI) has been charged with the responsibility of ensuring that:-

- adequate vaccines are available.
- vaccines are well maintained through storage in standardised equipment (refrigerators) that maintain the correct and recommended temperatures (maintenance of cold chain).
- Child Health cards are available.
- vehicles are available to transport vaccines.
- health workers concerned with immunization are trained and given skills to enable them to maintain correct refrigerator temperatures, safely administer vaccines to children and pregnant women and correctly enter the necessary information on Child Health cards and Antenatal cards.
- gas cylinders are provided to those facilities that use gas to run their refrigerators.
- current information, education and communications materials are developed and circulated.

As a result of KEPI's active involvement on immunization activities, there has been a definite increase on immunization coverage in children and pregnant women. From

surveys conducted in 1987 and 1990, the fully immunized rate in children 12 - 23 months of age has risen from 51% in 1987 to 71.2% in 1990 and for pregnant women from 37% in 1987 to 66% in 1990. Though this is quite encouraging, there are still a few districts with very low coverage and a notable percentage of missed opportunities for immunization.

Missed opportunity surveys that have been conducted in various districts in Kenya indicate that the major causes of missed opportunities are the use of false contraindications by health workers and poor planning of immunization sessions.

4. WAYS TO REDUCE MISSED OPPORTUNITIES

This can be done through:-

- identification of missed opportunities by examining health facility records and immunization cards (Child Health and Antenatal cards).
- conducting surveys to measure missed opportunities.
- checking immunization status of every child 0-23 months and pregnant women visiting health facilities for any reason. Those in need should be immunized before leaving.
- avoiding false contraindications to immunization e.g. fever, cold, diarrhoea, vomiting and malnutrition. There are few real contraindications. Incorrect use of contraindications denies life-saving immunizations to many infants (see Table 1).
- review of the National Immunization schedule to ensure that it provides optimal protection at the earliest age (see Table 2).
- ensuring that all eligible women and children have an immunization card and that they bring the card to every clinic visit and that these cards are checked by the health worker on every visit and the relevant details discussed with the mother.
- ensuring that those sick enough to be admitted are immunized on admission or before discharge from hospitals.

4.1 Table 1: Summary of Indications and Contraindications to EPI Vaccines

1. Immunize children who are malnourished or mildly ill
2. Immunize pregnant women with Tetanus Toxoid. Early pregnancy is not a contraindication.
3. For children who have an illness requiring hospitalization the decision whether or not to immunize should be made by the doctor admitting the child.
4. Give OPV, DPT, HB and measles to children infected with Human Immune Deficiency Virus (HIV) or who have AIDS.
5. Do not give BCG to children who have symptomatic infection with HIV.
6. Do not immunize children who have had a previous severe event (reaction) after a previous dose of the vaccine.

4.2 Table 2: Recommended Immunization Schedule to Provide Protection at the Earliest Age.

Age	Vaccine
Birth	BCG and OPV
6 Weeks	DPT,OPV and HB
10 Weeks	DPT,OPV and HB
14 Weeks	DPT,OPV and HB
9 months	Measles

REFERENCES:

1. WHO - Planning Principles for Accelerated Immunization Activities - A joint WHO/UNICEF Statement, 1985.
2. JSI - EPI Essentials - A Guide for Programme Officers - Second Edition, August 1989.
3. WHO - Expanded Programme on Immunization - Missed Opportunities for Immunization - update, February 1989.
4. MOH - KEPI - Immunization Coverage Survey, 1987.
5. MOH - KEPI - Immunization Coverage Survey, 1990.

5

SOCIAL MOBILIZATION FOR IMMUNIZATION (SMI) AND THE ROLE OF THE PHYSICIAN IN EPI

G. K Kagondu
D. M Mutie

Learning Objectives

At the end of this chapter, the student should be in a position to master:-

- the definition and the essentials of the Social Mobilization Strategy.
- the role and the importance of Social Mobilization in EPI Programmes.
- the planning for Social Mobilization.
- the outlets for Social Mobilization messages.
- the short experience of KEPI Social Mobilization activities.

1. INTRODUCTION

Social Mobilization (SM) in general, is a strategy which aims at correctly, adequately and persuasively informing the vast majority of a community to come forward to demand and use certain services.

Social Mobilization for Immunization (SMI) on the other hand, is an approach aimed at the promotion of good family and community health through efficient and effective utilization of immunization services. It is a two-pronged process which on the one hand requires that an all out effort be made to inform and support the vast majority of parents and pregnant women (or women of childbearing age) to accept, come forward, demand and use immunization services; and on the other hand mobilizing resources so as to improve the availability and access to vaccines by those eligible to use them. Thus it is a "demand - supply" situation. Social mobilization is achieved when immunization services are offered to everyone, when everyone is aware and knows about these services and finally when the eligible demand and receive the services.

2. IMPORTANCE OF SOCIAL MOBILIZATION FOR IMMUNIZATION

It is not enough to develop and maintain good physical and material infrastructure for immunization services if the communities do not reciprocate by making use of them. The ultimate objective of these services is not only the raising of immunization coverage for the target groups but also the reduction of the vaccine preventable diseases of childhood, commonly referred to as EPI - target diseases.

In 1985, a review of many country EPI - Programmes by WHO and UNICEF, revealed that the attainment of the Universal Child Immunization (U.C.I.) by 1990, was unlikely unless the programmes moved a little bit faster; there was need for country "Programme Acceleration". The aim of the Programme Acceleration was to raise the percentage of immunization coverage of the eligible and at the same time reduce the drop-out-rates so that as many as possible of the starters of the National Immunization Schedule, finally complete it. The 1987, Kenya National Immunization Coverage Report showed a drop-out rate of 17%.

To achieve an effective programme acceleration and a significant reduction of drop-out. rates, community participation is indispensable. However, it is known that one of the various reasons why people, with access to a service, do not use it is because of lack of **adequate** and **correct information**. People cannot participate in what they do not know, believe in or practice. Hence, the need, through Social Mobilization, to inform families and communities of the potential benefits of Immunization. In a similar fashion a component of Social Mobilization ought to be directed at health workers so that they become knowledgeable and skilful 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 the child has to return for the next immunization. In addition, the health worker should motivate a return visit.

3. AIMS AND OBJECTIVES OF SOCIAL MOBILIZATION FOR IMMUNIZATION

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, programme managers need to mobilize resources (human, materials and supplies) in order that the services meet and satisfy the demand created. In this connection, therefore, it is necessary to plan and implement Social Mobilization activities in a manner which favours their sustainability and not in a temporary effort, lapsing into doldrums later on.

4. COMMUNICATION SKILLS

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 mother. In Kenya it is known that the health worker is the most important and credible source of information on immunization for the mother and therefore it is crucial that they enhance this with good communication skills so as to motivate mothers to return to complete all immunizations. The experience of the mother at the health facility will determine to a large extent whether or not she returns. For instance a rude health worker will put off the mother.

The following guidelines will help health workers communicate better with mothers:-

- being polite and helpful.
- making the mothers comfortable and at ease.
- using simple language in explaining issues. Avoid medical jargon.
- listening and encouraging mothers to talk of their experiences and concerns and encouraging them to ask questions.
- asking them 'open' questions. Avoid questions which require a " yes" or "no" answer.
- using teaching aids that are available such as handouts, audio tapes, charts, posters and actual objects like vaccine vials.

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. THE ROLE OF THE PHYSICIAN IN SOCIAL MOBILIZATION FOR IMMUNIZATION (with special reference to the District Medical Officer of Health).

In Kenya, the success of any public health programme is dependent upon 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 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 Social Mobilization for Immunization process at district level. Physicians (and Clinical Officers) generally supervise rather than give immunizations, their most important EPI role is to assure quality of services.

5.1 Planning

A lot of data exists at district level, through the routine health information reporting system or through surveys. Realistic planning requires that a district **"Situation Analysis"** be done especially in terms of:

- current immunization coverage.
- knowledge attitudes and practices (KAP) of potential and real service users.
- missed opportunities for immunization.

The population profiles as well as the human and material resources at the disposal of the DHMT need to be analysed, too. In this way the MOH will be able to ascertain the existing demands, weaknesses and constraints. He will then participate, as a planner and advisor, in drawing up with his DHMT, a Social Mobilization Plan of Action. His position in the district enables him to collaborate 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.

5.2 Implementation

The keen MOH will participate not only in the planning and implementation of research survey activities to collect information and data on Social Mobilization, but also in training for those who will be involved in the health communication activities. In some instances he will be the key person in promoting health communications among government, local and political leaders to assure them of good quality immunization services and a sure supply of vaccines at the health facilities, so that those who are motivated to go for the immunization services are not disappointed.

5.3 Supervision

When Social Mobilization activities have been started, the MOH and his team will continuously monitor the progress being made, through planned supervisory visits preferably by the use of check-lists which can be used by any member of the DHMT. He will hold meetings periodically with his team and a few of the field Social Mobilization implementors to keep track of both the health communication component as well as the resultant activities at the immunization centres.

5.4 Evaluation and Feed-back

Periodic evaluation is an in-built component of the Social Mobilization Plan of Action. The MOH will facilitate the exercise by participating 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".

6. KENYA EXPERIENCE OF SOCIAL MOBILIZATION FOR IMMUNIZATION

Social Mobilization is undertaken at National, Provincial, District and Community levels. The National level provides support to the districts in terms of giving guidelines, planning, supervision, finances and materials production and dissemination. The

provincial level assists the districts in training and supervision. The district is the focus of Primary Health Care activities including Social Mobilization for Immunization.

Planning and implementation of such activities is the responsibility of the District Health Management Team headed by the Medical Officer of Health. The District Health Education Officer in collaboration, with other government ministries, Non-governmental Organizations and Private and Voluntary Organizations in the district organize Social Mobilization for Immunization activities. Generally, activities follow the Social Mobilization strategy stages as outlined below:-

6.1 Awareness Creation

Sensitization of political leaders and government officials is carried out at all levels as an entry point of Social Mobilization. This is important in order to enlist a firm commitment for Social Mobilization. This is done by holding workshops for government ministry officials, administrative, community and opinion leaders and other identified groups. These people in turn, help create awareness in the community. The use of various media, like radio, rural newspapers and posters, political gatherings and churches are other outlets for awareness creation.

6.2 Developmental Research

In order to plan appropriate Social Mobilization activities. Each district must determine the reasons why their population either accept or refuse immunization. Some of the reasons that have been found out in Kenya to account for non-acceptance of immunization 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 the reasons for non-acceptance of immunization in their particular district. These may be ascertained through KAP surveys, Focus Group Discussions, interviews and observations. Once this is known, then achievable objectives for Social Mobilization can be established.

6.3 Target Groups

Some of the target groups which have been identified for Social Mobilization include:-

- women Groups
- men, especially fathers (in barazas)
- school children
- school teachers
- administration personnel
- politicians
- extension workers
- community health workers
- traditional birth attendants
- health workers
- religious groups.

6.4 Messages

6.4.1 Development of Messages

To develop messages for Social Mobilization, areas of concern must be identified. The following were areas of concern identified in Kenya from developmental research:-

- 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 have been developed:

- immunization - A chance for every child
- an immunized child is a protected child
- immunizing your child saves time and money
- love them. Protect them. Immunize them
- a good mother has her children immunized
- immunization prevents disease - do not wait for your child to get sick
- has your brother/sister been immunized?
- every healthy child must have an up-to-date immunization card
- if you love your children, have them immunized
- every child due for immunization must be immunized even if unwell.

Messages should be targeted to particular issues and groups. They should be motivating, persuasive and credible.

6.4.2 Channels of Communicating Messages

Many channels for the dissemination of information on immunization have been identified and are used at all levels, some of these include:-

- **Mass Media**

  - Electronic media:
  Radio proved an effective channel to reach Kenyan rural populations and information on immunization is prepared in vernacular so as to reach most people. T.V. has been used mostly in urban areas.

  - Print Media:
  Posters addressing the various issues have been developed. However, these have been used more as visual aids since a portion of the population may not be able to read. Rural newspapers which are in most of the districts have been used to disseminate information but more use needs to be made of them.

- **Inter-personal Channels**

  Numerous channels have been identified in the communities and are being utilized. The main ones are:-

  - health facilities:

  this includes individual counselling and group talks given at the health facility. Health workers should be supported and encouraged to use any visual aids such as charts, audio tapes as well as the practice of good communication skills in order to motivate the mothers

- barazas, women group meetings, workshops, adult education classes, schools and churches:

all these are effective channels and outlets of passing messages to the community and are being used in the districts

- use of school children

Kenyan school pupils have been effectively used in some districts where immunization coverage is low in a "Child to Child" project. Primary school pupils with help from their teachers are asked to go to their neighbouring communities and look for eligible children for immunization and to motivate their mothers to take the children for immunization

- house to house visits:

health workers doing extension work carry out house to house visits to educate parents. Teaching aids are used for more effective communication

- use of community health workers:

community health workers have also been used not only for creating awareness and educating parents but also to look for drop-outs in the community and "channelling" them to the health facilities

many other groups have been used not only for providing Information Education and Communication (IEC) but also channeling mothers to health facilities. Some of these include Traditional Birth Attendants, Teachers, women groups

- listening groups/discussion groups:

many groups which already exist can be used as a forum for giving education on immunization. DHMT should provide necessary resources

The above are guidelines and may vary from district to district depending on the needs of the community.

6.5 Monitoring, Supervision and Evaluation

Continuous monitoring and supervision should be carried out to ensure:-

- effective distribution of materials and dissemination of messages.
- correctness and appropriateness of messages and materials.
- changes in KAP of a community.

Evaluations are carried out to assess the level of achievement of the stated goals and objectives especially the overall EPI goal of disease reduction. This is done through periodic annual or biennial reviews, preferably by groups not involved with the day to day social mobilization activities.

6.6 Training

Different groups of health workers, including community health workers in the district have been identified and trained in Social Mobilization. The training includes communication skills, EPI services and simple operations research and evaluation methods. Health Education Officers are specifically trained in materials production and distribution.

6.7 Implementation of Activities

In each district the District Health Management Team has been responsible for implementing the KEPI activities. The District Management Team has drawn up a plan of action detailing:-

- objectives to be achieved.
- target groups to be reached.
- activities planned to meet the objective.
- monitoring of Planned Activities.
- persons responsible for each activity.
- resources required including budget.

Inter-sectoral collaboration with other ministries, Non-governmental Organizations and Private and Voluntary Organizations, has been crucial during all stages of the activities.

Further Reading

1. WHO/UNICEF. Joint statement on Planning Principles for Acceleration of Immunization Activities. Geneva, 1985.
2. KEPI Management Unit/UNICEF. Battling the Six Immunizable Diseases. A Ministry of Health, Kenya, Publication 1988-90.
3. WHO. Report of EPI Global Advisory Group Meeting, 13-118 October, 1986 New Delhi. WHO/EPI/87/1.
4. WHO. Report of EPI Global Advisory Group Meeting 9-13 November, 1987 Washington. Who/EPI/Gen/88.1
5. Grant P.J. In the State of World Children, 1987. Towards Universal Immunization, Pg. 56. Published for UNICEF by Oxford University Press, New York.
6. Rasmusen M. R. el al. In Communication for Child Survival. USAID Bureau for Science and Technology, Office of Health and Education. Washington D.C. (1988).

Objectives for Chapters in Section 2

After reading these chapters, the student should be able to:

1. Identify the risk factors associated with the target diseases.
2. Outline the characteristics of the causative organisms of the diseases.
3. Identify the pertinent clinical features of the target diseases.
4. Make a "reasonably" accurate diagnosis of the diseases.
5. Successfully manage a child with any of the diseases.
6. Identify the important control measures of each disease.
7. Appropriately administer the vaccines for the target diseases.
8. Outline the qualities and characteristics of each of the vaccines.
9. Identify and manage the complications associated with the vaccines.
10. Outline the role of the vaccines in the control of the diseases.

6

MEASLES

V.A Orinda

1. INTRODUCTION

Measles is a universal disease (1), first described as an entity by the Arabian physician Rhazes in 900 A.D. (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 2.5 million children die from measles annually (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.

2. EPIDEMIOLOGY

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.

2.1 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 5020 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 Hull (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.

2.2 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.

2.3 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 to 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 immunization 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.

2.4. 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.

2.5 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.

3. 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)

4. 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 may disappear within 12-18 hours 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.

5. 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.

5.1 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).

5.2 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.

5.3 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. Dossetor 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.

5.4 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.

5.5 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.

5.6 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 form 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.

6. 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 house-hold 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.

7. PREVENTION

7.1 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 some 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 4 of 36 children after intranasal inoculation 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 attenuated 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 immunogenic 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 attenuated 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 immunization 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 Nairobi, 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).

7.2 Vaccine Storage and Handling

Measles vaccine is a freeze dried heat sensitive vaccine which must be kept at recommended temperatures 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}C. Where as at the health centres and dispensaries, it should be kept between 0 to +8^{0}C at all times. The diluent for reconstituting the vaccine should be kept cold too.

7.3 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.

7.4 Side Effects

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.

7.5 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).

8. 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.

REFERENCES

1. Wilson, G.S: **Measles as a Universal Disease.** *Am. J. Dis. Child.* **103**:49, 1962

2. Enders, J.F: **Measles Virus: Historical Review, Isolation, and Behavior in Various Systems** *Am. J. Dis. Child.* **103**: 112, 1962.

3. Christensen, P.E., Schmidt, H., Jensen, O., Bang, H.O., Anderson, V., and Jordal, B. : An Epidemic of Measles in Southern Greenland, 1951: Measles in a virgin soil, I. *Acta Med. Scand.* **144**: 313, 1952.

4. Grant, J.P. : The State of the World's Children 1985 New York, Oxford University Press, 1985, P 36.

5. Aaby, P., Bukh, J., Lisse, M.I. and Smits, A. : Severe Measles in Sunderland, 1985: A European-African Comparison of Causes of Severe Infection. *Int. J. Epidemiol.* **15**:101, 1986.

6. Morley, D : Severe Measles in the Tropics. I. *Brit. Med. J.*, **1**: 363, 1969.

7. Morley, D. Measles in Nigeria. *Brit. Med. J.*, **1**:363, 1969.

8. Morley, D., Woodland, M., and Martin, W.J. : Measles in Nigerian Children. *J. Hyg. Camb.* **61**:115, 1963.

9. Taneja, P.N., Ghai, O.P., and Bhakoo, O.N. : Importance of Measles in India. *Am. J. Dis. Child.* **103**:226, 1962.

10. Moraes, N.L. De A : Medical Importance of Measles in Brazil. *Am. J. Dis. Child.* **103**:233, 1962.

11. O'Donovan, C : Measles in Kenyan Children *E. Afr. Med. J.* **48**:526, 1971

12. Miller, C.L : Current Impact of Measles in the United Kingdom. *Rev. Infect. Dis.* **5**:427, 1983

13. Hinman, A.R., Orenstein, W.A., Bloch, A.B., Bart, K.J., Eddins, D.L., Amler, R.W. and Kirby C.D. : Impact of measles in the United States *Rev. Infect. Dis.* **5**:439, 1983.

14. Ofosu-Amaah, S : The Control of Measles in Tropical Africa: A review of Past and Present Efforts. *Rev. Infect. Dis*:24 **5**:546, 1983.

15. Aaby, P., Burk, J., Lisse, M.I., and Smits, A.J. : Measles vaccination and reduction in child mortality : a community study from Guinea-Bissau. *J. Infect.* **8**:13, 1984.

16. Fernandez de Castro, J. : Measles in Mexico. *Rev. Infect. Dis.* **5**:422, 1983.

17. Voorhoeve, A.M., Muller, A.S., Schulpen, T.W.J., Gemert, W., Valkenburg, H.A., and Ensering, H.E., : Agents affecting health of mother and child in a rural area of Kenya. III. The epidemiology of measles. *Trop. Geogr. Med.* **29**:428, 1977.

18. Williams, P.J., and Hull, H.F. : Status of Measles in the Gambia, 1981. *Rev. Infect. Dis* 24. **5**:391, 1983.

20. Borgono, J.M. : Current Impact of Measles in Latin America. *Rev. Infect. Dis.* **5**:417, 1983.

21. Krugman, S., Giles, P.J., Friedman, H. and Stone, S. : Studies in Immunity to Measles. *J. Pediatr.* **66**:471, 1965.

22. Aaby, P. Burk, J., Hoff, G., Leerhoy, J., Lisse, I.M., Mordhorst, C.H. and Pedersen, I.R. : High Measles Mortality in infancy related to intensity of exposure. *J. Pediatr.* **109**:40, 1986.

23. Aaby, P., Burk, J., Lisse I.M. and Smits, A.J. : Overcrowding and intensive exposure as determinants of measles mortality. *Am. J. Epidemiol.* **120**:49, 1984

24. Aaby, P., Burk, J., Lisse I.M. and Smits, A.J. : Measles Mortality, State of Nutrition, and Family Structure : a community study from Guinea-Bissau. *J. Infect. Dis.* **147**:693, 1983.

25. Leoning, W.E.K. and Coovadia, H.M. : Age-specific occurrence rates of measles in urban, peri-urban, and rural environments: Implications for time of vaccination. *Lancet*, **11**:324, 1983.

26. Bwibo, N.O. : Measles in Uganda. *Trop. Geogr.* Med. **22**: 167, 1970

27. Nieburg, P. and Dibley, M.J. Risk Factors for Fatal Measles Infections. *Int. J. Epidemiol* **15**: 309, 1986.

28. Koster, F.T., Curlin, G.C. Aziz K.M.A. and Hagne, A. Synergishe. Impact of measles diarrhoea on nutrition and mortality in Bangladesh. *Bull, W.H.O.*, **59**: 501, 1981

29. Reddy, V., Bhaskaram P., Raghuramulu, N., et al.
Relationship between measles, Malnutrition, and blindness: a prospective study in Indian children, *Am. J. Clin. Nutr.* **44**:924, 1986.

30. Vavavithya W., Stoecker B., Chaiyaratana W., Kittikool J., Vitamin A status of Thai Children with measles. *Trop. Geogr. Med.* **38**:359, 1986.

31. Joint WHO/UNICEF statement on Vitamin A for Measles, *Weekly Epidem. Re.* **19**: 133, 1987.

32. Sommer A., Hussaini G., Tarwotjo I., Susanto D. ncreased mortality in children with mild vitamin A deficiency. *Lancet* 11:585, 1983.

33. Sommer A., Tarwotjo I., Tilden, R., Djunaedi E., Loeden A.A.: Impact of Vitamin A. Supplementation on childhood mortality *Lancet* 1: 1169, 1986.

34. Barclay, A.G.J. Foster, A. and Sommer, A. itamin A supplementation and mortality related to measles. A randomized clinical trial. *Br. Med. J.* Vol. 294:294, 1987.

35. Hussey, G. D. and Klein, M. : A randomized controlled trial of Vitamin A. in children with severe measles. *N. Eng. J. Med.* 323: 160, 1990.

36. Scheifele, D. W. and Forbes, C.E. Biology of Measles in African Children. *E. Afr. Med. J.* 50:169 (1973).

37. Vaughan V.C. McKay, J.R., and Behrman. Nelson Textbook of Pediatrics. WB Saunders Company, West Washington Square, Philadelphia.

38. Expanded Programme on Immunization Field Evaluation of Vaccine efficacy *Wkly Epidemi Rec.* 60: 133,1985.

39. Dover, A.S., Escobar, J.A., Duenas A.L., and Leal, E.C., : Pneumonia Associated with Measles. *J.A.M.A.* 234:612, 1975.

40. Dave, K.H. : Measles in India. *Rev. Infect. Dis.* 5:406, 1983.

41. Pongrithsukda, V., Phonboon, K., and Manunpich, K. Measles - associated diarrhoea in Northeastern Thailand. *Southeast Asian J.Trop. Med. Pub. Hlth* 17: 43, 1986.

42. Feachem, F.G. and Koblisky, M.A. Interventions for the control of diarrhoeal diseases among young children; Measles Immunization. *Bull, W.H.O.* 61: 1983.

43. Editorial. Measles Mortality and malnutrition *Lancet* 11:661, 1983.

44. Scheifele, D.W. and Forbes, C.E. : Prolonged giant cell excretion in severe African Measles. *Pediatrics.* 50:867 1972.

45. Dossetor, J., Whittle, H.C. and Greenwood, B.M : Persistent Measles infection in Malnourished children. *Brit. Med. J.* 1:1633, 1977.

46. Whittle, H.C., Mee, J., Werblinska, J., Yakubu, A., Onuora, C. and Gomwalk, N. : Immunity to Measles in Malnourished Children. *Clin. exp. Immunol.* 42:144 1980

47. Enders, J.F. and Peebles, T.C. : Propagation of Cytopathogenic Agents from patients with Measles *Pro. Soc. Exp. Biol. and Med.* 86:277, 1954.

48. Enders, J.F., Katz, S.L and Halloway, A. : Development of Attenuated Measles-Virus Vaccines: A Summary of Recent Investigation. *Am. J. Dis. Child.* 103:165, 1962.

49. Hektoen, L. : Experimental Measles *J. Infect.* Dis. 2:238, 1905.

50. O'Neil, G.G., Stokes, J. Jr., Shaffer, M.F. and Rake, G. Virus of Measles grown in developing chick embryo. *Am. J. Dis, Child.* 60:757, 1940.

51. Maris, E.P., Gellis, S.S., Shaffer, F., Dunham, W.B., Stokes, J. Jr. and Rake G. : Vaccination of children with various chorioallantoic passages of measles virus: A Follow-up Study. *Paediatrics.* 4:1, 1949.

52. Stokes J. Jr., Weibel, R., Kalenda, R., Reilly, C.M. and Hilleman, M.R. : Enders Live Measles- Virus Vaccine with Human Immune Globulin. *Am J. Dis. Child.* 103:196, 1962.

53. Levin, S., Israel, R., Mosses, S., Shimansky, L. and Krugman, S. : Attenuated Measles-Virus Vaccine Studies in Israel. *Am. J. Dis. Child.* 103:193, 1962.

54. Schwartz, A.J.F., Boyer, P.A., Zirbel, L.W. and York, C.J. : Experimental vaccination against measles: I. Tests of live measles and distemper vaccine in monkeys and two human volunteers under laboratory conditions. *J.A.M.A.* 173:861. 1960.

55. A Report to the Medical Research Council by the Measles Vaccines Committee.: Vaccination Given All.

56. Krugman, S. Present status of measles and rubella immunization in the United States: A Medical progress report. *J. Pediatr.* 78:1, 1971.

57. Hayden, R. J. : The epidemiology and nature of measles in Nairobi before the impact of measles immunization. *E. Afr. Med. J.* 51.199, 1974.

58. Aaby, P., Burk, J., Leerhoy, J., Lisse, I.M., Mordhorst, C.H. and pedersen, I.R. : Vaccinated children Get Milder Measles Infection: A Community Study from Guinea-Bissau. *J. Infect. Dis.* 154:858, 1986.

59. McAleer, W.J., Markus, H.Z., McLean, A.A., Buynak, E.B. and Hilleman, M.R. : Stability on storage at various temperatures of live measles, mumps and rubella virus vaccines in new stabilizer. *J. Biol. Stand.* 8:281, 1980.

60. ikic, D.M. : Edmonston-Zagreb Strain of Measles Vaccine: Epidemiologic Evaluation in Yugoslavia. *Rev. Infect. Dis.* 5:558, 1983.

61. Sabin, A.N., Arechina, A.F., Castro, J.F., Sever, J.L., Madden, D.L., Shekarchi, I. and Albrecht, P. : Successful Immunization of Children with and without Maternal Antibody by Aerosolized Measles Vaccine. I. Different Results with Undiluted Human Diploid Cell and Chick Embryo Fibroblast Vaccines. *J.A.M.A.* 249:2651, 1983.

62. Whittle, H.E. and Rowland, M.G. M. : Immunization of 4-6 month old infants with Edmonston-Zagreb measles vaccine. *Lancet*, 11:834, 1984.

63. Measles vaccination in developing countries. A symposium on current issues. *Trans. R. Soc. Trop. Med. Hyg.* 69:21, 1975.

64. Collaborative study by the Ministry of Health of Kenya and the World Health Organization. : Measles immunity in the first year after birth and the optimum age for vaccination in Kenyan children. *Bull. WHO.* 55:21, 1977.

65. Expanded Programme on Immunization: The Optimum Age for Measles Immunization. *Weekly epidemiological Record.* 57:89, 1982.

66. Centers for Disease Control: Measles prevention: Recommendations of the Immunisation Practices Advisory Committee (ACIP). *MMWR* 38:S-9, 1989.

67. Aaby, P., Hansen, H.L., Tharup, J., Sodemann, M., Knudsen, K., Jensen, T.G., Kristiansen, H., Poulsen, A., Jakobsen, M., Da Silva, M.C., and Whittle, H., : Trial of high-dose Edmonston-Zagreb measles vaccine in Guinea-Bissau: Protective Efficacy, *Lancet*, 11:810, 1988.

68. Khanum, S., Garelick, H., Uddin, N., Mann, G., : Comparison of Edmonston-Zagreb and Chwarz Strains of Measles Vaccine Given by Aerosol or Subcutaneous Injection. *Lancet* 1:150, 1987.

69. Tidjani, O., Guerin, N., Lecam, N., Grunitsky, B., Levy-Bruhl, O., Xuereff, C. and Tatagan, K.: Serological Effects of Edmonston-Zagreb, Schwartz, and AIK-C Measles Vaccine Strains Given at Ages 4-5 of 8-10 months, *Lancet* 11:1357, 1989.

70. Markowitz, E.K., Supulveda, J., Diaz-Ortega J.I., Valpespino, J.L., Albrecht, P., Zell, E.R., Stewart., J., Zarate, M.L., and Lernier H.R.Immunization of six-month-old infants with different doses of Edmonston-Zagreb and Schwartz Measles Vaccines. *N. Eng. J. Med.* 322:580, 1990.

7

POLIOMYELITIS (INFANTILE PARALYSIS)

D.M Mutie.

1. INTRODUCTION

Poliomyelitis is an acute communicable disease caused by any of the three poliovirus types, namely: type I (Brunhilde), type II (Lansing) and type III (Leon). It occurs sporadically or in epidemics, usually affecting children aged under five years of age, and is characterized by varying degrees of paralysis.

The earliest historical record of this disease was in Egypt about 16-14 Century B.C. (almost 3500 years ago), which showed a tomb-stone engravement of a young priest with a withered, shortened leg, the characteristic deformity of paralytic poliomyelitis (1). 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.

The year 1955 was an important land mark in the control of poliomyelitis infection with the introduction of the Salk or inactivated, injectable polio vaccine (IPV). In 1961, the Sabin or live attenuated vaccine oral polio (OPV)was introduced. This resulted in a steep decline in the number of poliomyelitis cases in Europe and North America, while in developing countries, the incidence of poliomyelitis remained static or even increased.

In 1985, it was agreed that poliomyelitis should be eradicated from the Americas. Eradication means not only the elimination of the acute clinical disease but the extinction of the wild virus, as had previously been done with small-pox. Various policies were developed that rapidly raised immunization coverage and, as progress was achieved and the incidence of poliomyelitis fell, increasing emphasis was placed on surveillance, the identification of high risk areas and "mopping - up" immunization in these areas. The results were so good that, within 5 years, the incidence fell from many thousand cases to less than 15 in 1990.

In view of this success and progress in the EPI programme globally, the World Health Assembly, in 1988 agreed to target global poliomyelitis eradication by the year 2000.

The lessons learned in the Americas have allowed the development of policies and a global plan of action that provide the potential for this ambitious target to be achieved, on time.

In Kenya poliomyelitis became a public health problem after 1950. The first epidemic of significance was recorded in 1954, during which attack rates among Europeans was very high: 254 per 100,000 (2,3). Previously, as far back as 1925, the earliest year for which records are available, very few cases occurred among non-Africans. It is assumed that at that time the polioviruses were widely spread, circulated abundantly and therefore conferred a solid immunity on the indigenous population. With the improvement of personal and communal hygiene, barriers were created between wild virus in the excreta and the non-immune persons; infection was therefore postponed to older, non-immune, accumulated age-groups. Indeed since 1954 paralytic poliomyelitis epidemics began to occur at the frequency of every three years, usually around the months of October (see Table 1).

Table 1: Notified Polio Cases in Kenya:

Year	Notified cases
1954	538
1957	617
1960	1003
1963	aborted*

Source: *Bull. Wld Org. 48:421 (1973)*

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

Late in the 1960's, after several of these outbreaks, the Ministry of Health (MOH) decided to introduce OPV immunization of susceptibles at appropriate periods in a bid to prevent or abort the anticipated 3-yearly outbreaks. Early in 1972, a nation-wide immunization campaign against poliomyelitis in eligible children was carried out with the help of lay volunteers. Two rounds, one in February/March and the other in June/July, were successfully carried out (4,5). Not only did the anticipated outbreak in October, 1972 fail to occur, but since then no serious poliomyelitis outbreaks have been recorded. In addition, of course, the following other factors have come into play to further militate against outbreaks, namely:-

- introduction of routine and sustained immunization with OPV;
- Kenyans have gradually attained better standards of living;
- better disease surveillance;
- the widely used OPV vaccines have, indirectly, assisted in immunizing susceptible contacts of vaccinees especially in over-crowded urban slum areas with poor environmental sanitation.

2. 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 faeco-oral and oral-oral routes, through the so called 5F's, namely: Faeces, Fingers, Foods, Fluids and Flies. Possibly the major form of spread of poliovirus around cases is respiratory, with research showing that most household contacts of a case, show increased antibodies, even when there has been no possibility of faeco-oral spread.

In 1983, the WHO estimated that in developing countries, 400,000 paralytic polio cases occurred. In 1986, 28,773 cases of poliomyelitis were reported to WHO by 173 countries (6). It is important to note that the reported data do not reflect the actual situation, which at best has been demonstrated by "lameness surveys" carried out throughout the world since 1974. These surveys are based on the detection of residual poliomyelitis paralysis of lower limbs in school-age children (5-14 years of age), and have made it possible to estimate the discrepancy between the reported morbidity and actual morbidity in developing countries. This discrepancy varies greatly between countries, but it is such that the reported incidence could be multiplied by a factor ranging from 4 to 100. (7). Infact the 1990 WHO estimate of the global incidence of poliomyelitis is 190,000, although only 23,000 cases were officially reported. Drawing on Americas' experience, acute flaccid paralysis, other than poliomyelitis appears to occur at an incidence between 1-2 cases per 100,000 children under 15 years, reflecting cases of Guillain-Barre syndrome, transverse and traumatic myelitis. Effective surveillance should be able to pick up these, plus any vaccine associated cases.

Poliomyelitis can be viewed as having three major epidemiological phases:-

- endemic,
- epidemic and
- post-vaccination (8).

2.1 Endemic Poliomyelitis

The endemic situation occurs where polioviruses circulate abundantly as was recently the case in many developing tropical countries, with low living standards and poor environmental sanitation. In these countries, during the 1960's and 1970's virtually all children over 4 years of age and women of child-bearing age had antibodies in their blood, to one or more of the three poliovirus types. One should appreciate the protective effect of transplacental antibodies at the age when infants will initially be exposed to circulating wild or vaccine virus. Most infections were asymptomatic and paralytic cases rare, occurring sporadically mainly in infants (truly "infantile" paralysis). This rarity of clinical paralytic poliomyelitis, and absence of epidemics, led to the erroneous belief that no poliovirus existed in those countries while in fact the reverse was true: polioviruses were highly endemic and conferred solid immunity on the communities.

2.2 Epidemic Poliomyelitis

The epidemic pattern of poliomyelitis is a transition from the endemic phase, when better personal and communal hygiene create barriers between the virus excreters and the susceptible persons, so that the age at exposure is shifted from infancy to later childhood. The delay in infection also results in an accumulation of susceptibles to critical numbers sufficient to support a wide and rapid spread of the virus thus an epidemic ensues. This was the case in developed countries during the first 50-60 years of this century. It is possible that many developing countries, Kenya included, are currently undergoing this transitional phase, and hence the need to raise and sustain a high poliomyelitis immunization coverage rate to avoid possible paralytic poliomyelitis epidemics. A recent example of this situation was the 1986 poliomyelitis epidemic in the Gambia, West Africa, where more than 300 cases occurred as compared to 4-5 cases in the previous 5 years.

It should be noted that type I virus is the one most frequently responsible for known epidemics in developing countries while type III tends to become the dominant cause of cases when effective immunization has reduced the incidence of cases to a low level.

2.3 Post Vaccination

The post-vaccine era, now seen in developed countries, has ushered in a dramatic reduction in the incidence of poliomyelitis. The paralytic forms have been virtually eliminated. As a strategy for health for all by the year 2000, the European countries in 1984 and the Americas, in 1985 have both set 1990 as the target-date for the elimination of paralytic poliomyelitis from their geographical regions. In this post-vaccine era, in countries with high OPV immunization coverage, "vaccine viruses" are abundantly excreted by vaccinees and these viruses infect the unvaccinated contacts. Therefore poliovirus isolates from the few clinical cases occurring or from healthy carriers are almost all characterized in the laboratory as vaccine strains. Thus in areas with high poliomyelitis coverage, wild polioviruses are rarely identified. There are therefore an increasing number of people whose protection from poliomyelitis is vaccine-induced, who are capable of preventing viral transmission of any wild poliovirus which might exist in our surroundings. It is recommended that periodically serologic surveys are carried out to determine the persistence of vaccine-induced antibodies to each of the three poliovirus types over the years. This could indicate if there is an accumulation of susceptibles to any of the three poliovirus types which may lead to an outbreak if a wild poliovirus is introduced into the community from outside. In 1988, Israel experienced an outbreak despite a poliomyelitis vaccination coverage of 85-90% (9). Oman and Saudi Arabia still suffer from epidemics inspite of a high immunization coverage, using potent OPV.

3. PATHOGENESIS AND PATHOLOGY

Infection is not synonymous with disease as the majority of infected persons (upto 90%) are asymptomatic, while 5-10% develop febrile illness not accompanied by paralysis. Only 1:200 (about 0.5%) of children infected with wild polioviruses who develop

paralysis. The incubation period of the disease is 7-14 days, while its infectivity is 3-4 days before the end of the incubation period, and approximately one week after the onset of symptoms.

Through ingestion, the wild poliovirus gets access to the mucosal cells of the oropharynx and ileum of the gastrointestinal tract. These virus multiply mainly in the gastrointestinal tract and the body is stimulated to produce IGA secretory antibodies. Thus local gut immunity is produced and in the majority of cases the disease is arrested at this stage. However, in a few persons, the wild virus multiply, overcome the local gut immunity and gain access to and infect lymph nodes draining the infected mucosa. They further gain entry into blood stream and the lymphatic system to cause viraemia, finally reaching the anterior horn of the spinal cord's grey matter or the basal ganglia of the brain stem to destroy the motor neurons and consequently cause paralysis.

Immunity after infection with wild viruses is permanent and is directed towards the specific poliovirus type causing the infection. There is no cross protection between the three types of viruses. In the same token a child with paralytic poliomyelitis needs to be immunized, as a second infection with a different type of poliomyelitis may cause new paralysis of another limb or even involve the brain stem, with a catastrophic outcome.

4. CLINICAL FEATURES

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

- **Inapparent or asymptomatic** poliomyelitis, which forms up to 90% of infected persons. It can only be proved by the isolation of viruses from the faeces or the presence of humoral anti-bodies against the polioviruses.
- **Abortive form,** which 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,** which resembles the abortive type but, in addition, there are muscle pains and stiffness of the neck and back. This form should be born in mind during polio epidemics as different forms of strain can precipitate paralysis.
- **Paralytic Poliomyelitis** is the typical form found in only 0.5% of those infected with the wild polioviruses. Most cases in many countries are due to type I polioviruses (in Kenya type I accounts for 85% of paralytic cases), followed by type III and finally type II. 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, usually affecting one limb only. Initially the limb muscles are painful and there is an abrupt onset of flaccid paralysis as evidenced by reduced muscle tone, 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 which may result 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, thereafter it regresses to some degree. However, one should be aware of the danger of provocation paralysis as it has been shown in several studies that over 40% of children suffering from acute poliomyelitis had received an injection, (irrespective of the drug used) during the febrile incubation period. The WHO recommendation is to avoid unnecessary injections in the presence of known polio virus transmission.

5. COMPLICATIONS

Poliomyelitis is more of a crippler than a killer. Mortality rates range from 4-10% even during epidemics. Observations in Bombay City showed that 15% of paralytic cases make a complete recovery while 75% do not recover or have partial recovery (10).

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 hips and knees and dorsiflex the ankles. Contracture are common.

Bulbar poliomyelitis is associated with cardio-vascular problems because of the damage of motor nuclei of some cranial nerves and the possible involvement of the respiratory and vasomotor centres in the medulla oblangata. This leads to aspiration pneumonia, irregularities in respiratory, and pulse rates and blood pressure. All these predispose to cardio-respiratory arrest.

6. MANAGEMENT:

Being a viral disease, poliomyelitis has no specific drug treatment. Therefore prevention is the only viable option. Prevention of the disease and its complications can be grouped into two:

- **General Measures:** These measures assist to interrupt the transmission of the virus especially during epidemics or within the close contacts of an index case. They include:-

  - the promotion of personal hygiene,

  - domestic and communal hygiene,

  - the use of clean water and food,

- the isolation of active cases for a week or two after the onset of clinical signs and symptoms.

- The avoidance of intramuscular injections, oral surgery and severe muscle strain (like a child having to walk many kilometers) especially during poliomyelitis epidemics, prevents "imminent paralysis" in non-paralytic cases Confirmed cases should be notified to the health authorities.

- **Specific Measures:** These include the use of either IPV or OPV. The latter is preferred in developing countries on account of its low cost, ease of administration, induction of local gut immunity and the indirect protection of close un-immunized contacts of the vaccinee through the shed vaccine virus in stool, especially in communities living in poor environmental sanitation conditions.

7. THE DEVELOPMENT AND USE OF POLIO-VACCINES

7.1 Vaccine Development

7.1.1 **I.P.V:** this killed, formalin-inactivated, injectable vaccine was developed by an American virologist and physician Dr. Jonas Salk in 1954 and licenced in 1955. Its wide use thereafter in the U.S.A. during the period 1955-1962 reduced the incidence of paralytic poliomyelitis cases from 21,000 per year during the 5 years proceeding its introduction to less than 1,000 cases - a 95% drop. However, IPV tends to confer individual immunity mainly and very little herd immunity. Even in individual children a very limited gut immunity is produced.

Later on, van Wezel in Holland introduced the enhanced-potency IPV (E-IPV) vaccine which 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 polio virus. IPV can be combined with DPT to form the quadruple vaccine which can be useful in some tropical areas where OPV "take rate" has been found to be low.

7.1.2 **O.P.V:** is the live attenuated oral polio-vaccine developed by Dr. Albert Sabin of the U.S in 1957 and licenced in 1962. It is polyvalent, thus containing the attenuated strains derived from poliomyelitis types 1,2 and 3. These vaccine virus can multiply in the gut after oral administration of the vaccine and induce local IgA secretory antibodies, which provide resistance to re-infection by the wild poliovirus. OPV is the WHO-recommended vaccine against poliomyelitis, for both routine use, and more importantly during epidemics. The advantages and disadvantages of OPV are outlined in Table 2 on the following page.

TABLE 2

ADVANTAGES AND PROBLEMS ASSOCIATED WITH OPV VACCINE

	Advantages		Problems
(i)	Confers both humoral and intestinal immunity like natural infection	(i)	Being live viruses, the vaccine viruses do mutate and in rare instances cause paralytic polio in recipients or their contacts.
(ii)	Immunity induced may be life-long	(ii)	Vaccine progeny virus spreads to house-hold contacts (this may be an advantage).
(iii)	Induces antibody very quickly in a large proportion of vaccinees	(iii)	Vaccine progeny virus spreads from persons to persons in the community in this way "vaccinating" even persons who have not agreed to be vaccinated.
(iv)	Oral administration is more acceptable than injection and much easier to accomplish	(iv)	In certain warm climates, the induction of antibodies is unsatisfactory in a high proportion of vaccinees.
(v)	Administration requires minimum expertise	(v)	Contra-indicated in immune-compromised persons and their household associates and also for persons on immunosuppressive therapy.
(vi)	During epidemics, it not only induces antibodies quickly but also rapidly infects the gut, blocking the spread of the epidemic virus.		
(vii)	It is relatively inexpensive both to produce the vaccine itself and to vaccinate		
(viii)	Can be prepared in human diploid cells and thus not dependent on the scarce numbers of monkeys		

Source: WHO Bulletin 56:31 (1978)

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.(8)

The take rate was found to range from as low as 34.1% in Nigeria (11) to 79% in Gambia during the 1986 poliomyelitis outbreak. However, despite all this, KEPI considers the OPV in use in Kenya to have vaccine efficacy of 95%.

7.2. Vaccine Storage, Handling and Use

Both IPV and OPV need proper cold chain care. Since the latter is the only vaccine KEPI uses, the following comments are confined to it:

Of the 5 EPI vaccines (BCG, polio, measles, DPT and T.T.), OPV is the most heat-sensitive, but like the rest of the EPI vaccines, the ideal and recommended storage temperature range is 0^0C to 8^0C. At the Central, Regional and District Vaccine Stores, it can safely be stored at -20^0C and in this condition keeps its potency for several months.

In November, 1984, the EPI Global Advisory Group recommended that the first OPV dose be given at birth ("birth dose"). Although it may not be very reliable, this "bonus" dose is especially useful where:-

- poliomyelitis is an important endemic problem.
- OPV immunization coverage is low.
- poliomyelitis incidence shows a declining trend in the face of rising coverage.

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 anti-bodies. 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 OPV 2 (at 10 weeks) and OPV 3 (at 14 weeks) produce very high gut and humoral immunity.

7.3 Side Effects:

A rare OPV-associated paralytic poliomyelitis may occur in vaccinees or their close contacts. This is estimated at one case per 1 million vaccinees, (equivalent to one case per year in Kenya given, 1 million babies born per year), and 1 case in close contacts of vaccinees per 3-5 million doses of OPV distributed. Obviously the advantages of preventing paralysis from wild polioviruses far outweigh this rare complication.

8. 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 (12). 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 immunization coverage of 80-85% with protective doses of polio-vaccine would probably interrupt the poliomyelitis virus transmission.

The following six suggestions were proposed:-

- Countries to increase and sustain poliomyelitis immunization coverage as soon as possible.
- Disease surveillance (poliomyelitis as well as the other EPI-target diseases) to be improved.
- 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.
- The creation and maintenance of public awareness and provision of information and education to communities with regard to poliomyelitis and other EPI-target diseases.
- Improvement of poliomyelitis rehabilitation services for the unfortunate persons who might be inflicted by the disease.
- Promotion of research to develop better eradication strategies, improved polio-vaccines or vaccine combinations (12).

Other agencies, notably the Rotary International, has 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.

OPV, with the first dose given at birth in accordance with the revised Kenya National Immunization Schedule of 1.1.1986, should continue. By 1993, no new acute paralytic poliomyelitis due to wild poliovirus should be expected in Kenya. By 1995, the KEPI coverage with OPV3 should be raised to 80-85%, capable of breaking the chain of

transmission of wild polioviruses. By 2000AD poliomyelitis should be eradicated from Kenya.

REFERENCES

1. Dorothy M. Horstmann, Poliomyelitis. In Textbook of Pediatric Diseases. Vol. II. Philadelphia. W.B. Saunders Co., 1981.
2. Walker, A.J., Poliomyelitis in Kenya. *E. Afr. Med. J.* **33**:169-180 (1956).
3. Kaur, B. and Metselaar, D., Poliomyelitis in Kenya . *E. Afr. Med. J.* **44**: 74-86 (1967).
4. Metselaar, D. et al. Poliomyelitis: Epidemiology and prophylaxis. *Bull. Wld Org.* **48**: 429-433 (1973)
5. Koinange, W. et al. Poliomyelitis: Epidemiology and Prophylaxis. *Bull Wld. Org.* **48**:543-545 (1973)
6. WHO EPI-Poliomyelitis in 1986, 1987 and 1988. *Wkly Epidem. Rec.* (36) **64**:273-275 (1989).
7. WHO Poliomyelitis in 1985. *Wkly Epidem. Rec.* (37) **62**: 273-274 (1987)
8. Melnick, J.L Advantages and Disadvantages of killed live poliomyelitis vaccines. *Bull Wld. Org.* **56**: 22-26 (1978).
9. WHO. Poliomyelitis Outbreak in Israel. *Wkly Epidem. Rec.* (43) **63**: 325-326 (1988)
10. LaForce, F.M. et al. Clinical Survey techniques to estimate prevalence and annual incidence of poliomyelitis in developing countries. *Bull Wld. Org.* **58**:611 (1980).
11. Montefiore, D. et al. Trial of Type I Oral Poliovaccine (Sabin) in Nigerian Children. *British Med. J.* **1**:1569-1572 (1963).
12. WHO, EPI Global Advisory Group. *Wkly Epidem Rec.* (2) **64**: 5-7 (1989).

8

TETANUS

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1. INTRODUCTION

Tetanus is the clinical syndrome involving primarily the central nervous system and resulting from the toxins liberated by the vegetative form of the bacteria *Clostridium tetani* in the human body. *Clostridium tetani* is a spore producing gram positive motile bacillus which is ubiquitous in the soil but is also found carried in the intestine, skin and oral cavity and abound in animal droppings. The spore form of the organism can resist extreme physical conditions (1) Descriptions of the disease were recorded as early as the second century A.D (2).

2. EPIDEMIOLOGY

Although tetanus has a world wide distribution, the incidence in the developed countries has continued to drop rapidly while that in the warm moist parts of the world - covering largely developing countries - has remained high. In these parts of the world, neonates bear the brunt of the disease and its contribution to neonatal mortality has been noted to be between 22% and 87% (3,4,5).

Though clinical experience indicates that neonatal tetanus is prevalent in many parts of Kenya, limited reliable data exists on the magnitude of the problem. In recent district-based mortality surveys the mortality due to neonatal tetanus ranged from 3 to 15 per thousand live births. It is estimated that out of 3000 babies born alive everyday, 30 die from neonatal tetanus. This high incidence of neonatal tetanus may be attributable to the high number of births conducted at home (85%) and the low Tetanus Toxoid (TT) coverage antenatally (37%) (6,7).

Once established, neonatal tetanus is highly lethal. Even with the best facilities such as in the national referral and teaching hospital, more than 65% of the babies admitted with neonatal tetanus die (6,7,8).

3. PATHOGENESIS AND PATHOPHYSIOLOGY

The clinical syndrome associated with *Clostridium tetani* is not due to the direct invasion by the bacteria but rather to the toxins elaborated by the organism (9,10,11).

The organism gains access to the body, in spore form, at an injured site which is contaminated. This can indeed be a raw cut umbilical cord of a neonate where contamination may arise from the cutting material or animal droppings traditionally applied on the cut stump in some areas. (Other substances applied to the cord, such as ghee are associated with contamination as well). Tissue damage appears to be of crucial importance in enhancing the "germination" of the bacteria into vegetative form, without invasion of the body, probably through altered tissue oxidation - reduction potential (12,13).

The vegetative form of the bacteria liberates two types of toxins:

- **Tetanolysin,** which causes red blood cell haemolysis but otherwise plays little role in the disease process (9).
- **Tetanospasmin** an extremely lethal toxin which causes most of the signs and symptoms of the disease. In its purified form, this is a protein of molecular weight of 67,000 daltons. Each milligram contains 6.4 million lethal doses for mice, second only to Clostridium botulinum toxin in potencyl (9).

Tetanospasmin exerts its effects at four main sites in the body:-

- Motor end Plates of Skeletal Muscles:-

  There is inhibition of acetylcholine release, with resultant interference with contraction-relaxation mechanism of the muscle (11,13,15).

- Spinal cord:-

  Tetanospasmin acts within the polysynaptic interneuronal reflexes to block inhibitory reflexes, with the resultant release of uncoordinated excitatory impulses-leading to the characteristic tetanic spasms (11,13).

- Brain:-

  The toxin appears to remove the normal inhibition of cortical evoked activity, which may then lead to the observed seizures (11,14,17).

- Sympathetic Nervous System:-

  The tetanus toxin appears to have direct effect on the autonomic nervous system resulting in various signs and symptoms like profuse sweating, hypotension/hypertension, cardiac rhythm disturbances and peripheral vasoconstriction (11,16).

3.1 Clinical Presentation

The incubation period of tetanus from the time of inoculation with the spores to the onset of clinical signs appears to depend on the distance between the site of entry and the Central Nervous System, with the longer period being recorded where the distance is long and vice versa. In general, the period is between 3 to 21 days. Four clinical syndromes of tetanus are described:

3.1.2 Local Tetanus

Most patients with tetanus present with generalized manifestations; however muscle spasms can remain localised. This tends to manifest as unrelenting painful rigidity of muscles within the vicinity of the site of entry of *Cl. tetani* for weeks or months. It may also be precipitated by giving inadequate antitoxin enough to neutralise circulating toxin but not the concentrated local toxin. The syndrome has a mortality of around 1% (18).

3.1.3 Cephalic Tetanus

This is an unusual form of the disease which follows portal of entry at sites around the head. The incubation period is no more than two days and the principal manifestation is cranial nerve dysfunction - especially of the motor nerves III, IV, VII, IX, X and XII in various combinations for days or months. Mortality tends to be high largely from the complications of the cranial nerve dysfunction (19).

3.1.4 Generalised Tetanus

This is the commonest form of presentation. It is important to note that 80% of the cases may follow an apparent trivial injury - like sewing needle prick or even insect bites! The muscle spasms that follow involve the face, spine, abdomen and chest, resulting in the characteristic "Risus Sardonicus" and opisthotonus.

Characteristic seizures may occur, "tetanospasm", where there is a sudden contraction of all groups of muscles resulting in opisthotonus, clenched hands, flexed and abducted arms and extended legs - indeed a phenomenon akin to sustained valsalva manoeuvre may be noted and this is usually life threatening as it obstructs respiration. Dysphagia and hydrophobia occur with varying frequencies as do dysuria and urinary retention. Minor external stimuli including light, may trigger off the seizures. A modest elevation of temperature may follow the sustained contractions (20).

3.1.5 Neonatal Tetanus

This form of tetanus is usually generalised and occurs during the neonatal period following contamination of the umbilical stump at the time of delivery. It is associated with high mortality and although rare in the developed countries now, it is still common in the developing countries (21).

4. DIAGNOSIS

The diagnosis of tetanus is primarily clinical and is based on history of contaminated injury and presence of the clinical signs of muscle spasms.

5. COMPLICATIONS

Complications of tetanus can be minimized by strict attention to supportive care and by appropriate therapy.

The accumulation of secretions or spasm of respiratory muscles and laryngospasm may interfere with respiration leading to aspiration pneumonia, atelectasis, mediastinal emphysema or pneumothorax.

Severe tetanic seizures may result in lacerations of the tongue or buccal mucosa, intramuscular haematomas or vertebral fractures.

If the course is prolonged malnutrition and dehydration may develop unless strict attention is paid to fluid balance and caloric intake.

The case fatality of tetanus other than neonatal tetanus is high-ranging from 45% to 55% and reaching 99% in the case of tetanus neonatorum. (6,7,8,21) The shorter the incubation period, the higher the fatality. Both cephalic and neonatal forms of tetanus are associated with high mortality (22).

The cause of death in tetanus is often not clear-cut but tends to be associated with management complications. It has, however, been shown that tetanospasmin directly affects the central nervous system functions - notably the medullary and autonomic functions and may result in death in this way (20).

6. MANAGEMENT

There is no specific treatment for tetanus. The mainstay of management is supportive and the principles involved include:

- neutralisation of the circulating toxin using the human antitetanus toxin (human hyperimmune globulin) 3000-6000 units intramuscularly. This should be given early in the course of the disease since once the toxin has translocated into the neuron it is no longer accessible for neutralization (11,22,23,24).
- surgical debridement of the necrotic tissue at the portal of entry and thorough cleaning with antiseptic.

- administration of penicillin G to eliminate the vegetative bacteria still present in the body.
- maintenance of Meticulous fluid and electrolyte balance, feeding and nursing care with minimal stimulation.
- control of convulsions and spasms. This is often difficult and may require combinations of phenobarbital, chlorpromazine, meprobamate and paraldehyde (22).

7. PREVENTION

It is the modalities of preventing the disease that have been shown to be associated with significant reduction in morbidity and mortality attributable to tetanus in most parts of the world. One single target group among whom prevention contributes significantly is the neonates. Prevention depends on two premises:-

- health education.
- active immunization.

7.1 Health Education addresses itself to the issues of:-

- the need to clean contaminated wounds thoroughly with antiseptic solution (6,21).
- proper cord handling at the time of delivery: aseptic cutting, ligaturing and avoidance of treating with contaminated material (6).
- the need for booster immunizations for women of child bearing age and certainly pregnant women (22,23).
- the need to immunize all infants against tetanus routinely (21).

7.2 Active Immunization is associated with reduced incidence of tetanus and is given to:- (24)

- infants.
- pregnant women.
- injured persons.

7.2.1 Vaccines

The types of vaccines available for active immunizations are made by modifying the tetanus toxin (tetanospasmin) and are:-

- Tetanus toxoid, aluminum phosphate adsorbed

  This is the commonly used vaccine in pregnant women and injured persons. It is given as 0.5ml by intramuscular injection in three doses one month apart.

- Triple Vaccine (DPT)

  Tetanus toxoid is also available in combination with Diphtheria and Pertussis (DPT). This form is given to infants as 0.5 ml by intramuscular injection in three doses with a monthly inter-dose interval.

- Diphtheria/Tetanus Toxoid vaccine (DT)

  This is not routinely available under the KEPI programme but may be used for the very small number of children who have major adverse reactions with the pertussis component of the DPT vaccine. (see chapter 9 - Pertussis)

- Plain Tetanus Toxoid (fluid):-

  Tetanus toxoid is one of the safest antigens for immunization. Reactions are rare and include: local erythema and tenderness. Severe local reactions may occur in older persons following repeated injections.

7.2.2 The immunization schedules currently used are:-

- **Infants**:

  Three doses of tetanus toxoid one month apart given as DPT or DT starting at the age of six weeks.

- **Injured person - with contaminated wounds:**

  Booster tetanus toxoid if a previous dose has not been given in the preceding five years.

- In Kenya the current neonatal tetanus control policy targets **pregnant women** only, using the following schedule:

  TT1given during the first contact antenatally

  TT2given at least 4 weeks after TT1

  Booster for each subsequent pregnancy.

  This schedule has however been recognised to be limited in its impact particularly in developing countries where antenatal clinic attendance is not universal or consistent.

  The target population for tetanus toxoid has therefore been broadened to include not only pregnant women but all women of child bearing age.

The current WHO recommended schedule is outlined below:-

Dose	When to give	Protection
TT1	At first contact with woman of child bearing age (15-44 years) OR at first antenatal visit, as early as possible during pregnancy.	No protection or uncertain protection
TT2	At least 4 weeks after TT1	3 years
TT3	At least 6 months after TT2	5 years
TT4	At least 1 year after TT3	10 years
TT5	At least one year after TT4	Lifelong

There is no contraindication to immunization with TT at present. It is worth remembering that natural infection confers no protection. (24)

7.3 Further considerations

The goal of the KEPI programme in Kenya is to eliminate neonatal tetanus by 1995. (8)

The plan of action towards this goal include the following objectives:-

- to reduce neonatal tetanus mortality from 11 to 5 per 1000 live births by 1993
- to increase tetanus toxoid coverage (with documentary evidence) from 37% (1987) to 60% by 1990
- to eliminate neonatal tetanus mortality by 1995.

To enable these objectives to be met, KEPI plans the following "accelerated activities" to be undertaken:-

- obtain baseline data regarding neonatal tetanus morbidity and mortality by the use of neonatal mortality surveys and a reporting system where neonatal tetanus is reported separately from other forms of tetanus
- the development and use of TT cards to enable accurate evaluation of vaccination coverage
- adoption of the WHO recommended immunization schedule which targets all women of child bearing age and includes TT1 to TT5.

High coverage can therefore be achieved by vaccinating women at every health facility contact. The school health system can also be used to target school girls.

- social mobilization and training of health workers and traditional birth attendants (TBAs)

Most deliveries in developing countries take place at home attended by TBAs, therefore training and providing them with "match-box" delivery kits has been identified as a

major intervention in Kenya. This will result in an increase in the number of neonates who will benefit from clean delivery and cord care.

- using TBAs to give TT vaccinations has been proposed as another intervention that may be used. KEPI plans to introduce this on a pilot basis

- the use of surveillance systems to keep track of the progress towards elimination.

The separate reporting of neonatal tetanus and inclusion in the EPI sentinel system to monitor EPI diseases is a means for this to be done. This should include continuous monitoring and evaluation through routine supervisory visits, analysis of routine reports and community based surveys.

REFERENCES

1. Weinstein, Louis in: Textbook of Pediatric Infectious Diseases Volume 1 Feigin RD and Cherry JD (Eds) P. 843 WB Saunders 1981.

2. Aretaeus: Tetanus. In Major R.H. - Classic Descriptions of Disease 2nd Ed. P. 148-149. Springfield Ill, Thomas CC. (Eds) 1939.

3. Bildhaiya GS A study of tetanus in a hospital at Ahmedabad *J Indian Med Ass* **80**: 21-23, 1983.

4. Mazzafero V.E. et al The Distribution of tetanus in Argentina *Bull. Pan Am. Health Organisation* **15**: 327-332, 1981.

5. Ogbelde M.I. Problems of neonatal tetanus in Lagos *J Trop Pediatr* **12**: 71-79, 1966.

6. Steinglass R., Mutie D.M, Kanani G, Mjomba M., Orinda V. and Bjerregaard P Neonatal tetanus mortality in Kilifi District, Kenya: Results of a Community survey 1989 (Unpublished)- REACH/MOH

7. Melgaard B, Mutie D.M and Kimani G. A cluster Survey of Mortality due to Neonatal Tetanus in Kenya. *Int. J. Epidemiol* **17**:1,174,1988

8. Action Plan for the elimination of Neonatal Tetanus from Kenya. WHO workshop for Elimination of Neonatal Tetanus from the African Region by 1995 (Nairobi Kenya 1989)

9. Pillemer, L., Wittler RG and Grossberg DB the isolation and Crystallization of tetanal toxin *Science* **103**:615-616, 1946.

10. Roofe P.G Role of the axis cylinder in transport of tetanus toxin. *Science* **105**: 180-181, 1947.

11. Friedmann U., Zuger B and Hollander A. investigations on the pathogenesis of tetanus I and II. *J Immunol.* **36**: 473-484, 485-488, 1939.

12. Bradley K, Easton DM and Eccles JC Investigation of primary or direct inhibition *J. Physiol* **122**: 474-478, 1953

13. Brooks VB, Curtis DR and Eccles JC Mode of Action by tetanus toxin *Nature* **175**: 120-121, 1955

14. Brooks VB and Asanuma H. Action of tetanus toxin in the cerebral cortex *Science* **137**: 674-676, 1962

15. Kaeser HE and Saner A. Tetanus toxin, a neuromuscular blocking agent *Nature* **233**: 842, 1969

16. Kerr JH, Corbett JL, Prys-Roberts C et al Involvement of the Sympathetic nervous system in tetanus *Lancet* **2**: 236-241, 1968.

17. Mellanby J., Van Heyningen WE Whitaker VP Fixation of tetanus toxin by subcellular fractions of brain *J Neurochem.* **12**: 77-79, 1965.

18. Millard AH Local tetanus *Lancet* **2**: 844-846, 1954

19. Bagratuni L Cephalic tetanus *Br Med J* **1**: 461-463, 952

20. Weinstein L tetanus *N Eng J Med* **289**: 1293-1296, 1973

21. Stanfield JP and Galazka A Neonatal tetanus in the World today *Bull. WHO* **62**:647 1984

22. Textbook of Paediatric Infectious Diseases Second Edition pg 1126-1133 Feigin, R.D. and Cherry J.D., W.B. Saunders Company 1987.

23. Neonatal tetanus Elimination Issues and Future Directions Meeting Proceedings REACH/MOTHER CARE with USAID Alexandria, Virginia January 1990

24. World Health Organisation Monogram EPI/PHW/87/8

9

PERTUSSIS

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1. 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. The World Health Organization estimates that 600,000 deaths due to pertussis occur yearly; virtually all of these deaths occur in unimmunized infants and are therefore preventable (1).

2. EPIDEMIOLOGY

Pertussis is highly communicable and predominately affects children. The epidemiology is unusual in that infants are susceptible from birth due to the lack 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 (4.5).

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 (4.5).

Whooping cough is endemic in Kenya. Hospital records in the late 1960's 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 (5).

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.

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 (7).

3. 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 submucosal cells or other sites in the body (2,3).

4. 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 1gG and 1gA. Local and systemic antibodies may play a role in human protection against pertussis (8).

5. 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 rhinorrhoea, 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 a 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 intercurrent respiratory infections. Patients are usually free of *B.pertussis* organisms during the paroxysmal and convalescent stages despite persistent coughing.

6. COMPLICATIONS OF PERTUSSIS

- **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 sublobular 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 tachypnea. 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.pneumonia*. Pertussis has also been associated with activation of latent tuberculosis.(2)

- **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 (2).

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. (9-13)

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, subconjunctival hemorrhage (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 intrathoracic pressure.

Weight loss or failure to gain weight may be conspicuous especially in the young infant (2).

- **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% (4,5).

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 (4).

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 older 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 (2,3).

7. LABORATORY DIAGNOSIS

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 deciliter or greater. There may be little or no lymphocytosis in mild or moderate cases.

- **Isolation of the Organism**: Presently the "gold 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. Prior antibiotic treatment with erythromycin, chloramphenicol, trimethoprim-sulfamethoxazole or tetracycline will markedly reduce the isolation rates (14,15).

- **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 antimicrobial therapy when viable organisms are no longer present. However the sensitivity and specificity of this technique remains to be defined.

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 (14,15).

8. MANAGEMENT

8.1 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 (2,3,16).

8.2 Supportive Management

Supportive Treatment includes avoiding factors that provoke attacks of coughing and the maintenance of hydration and nutrition. Gentle suction to remove secretions and oxygen may be required, particularly in infants with pneumonia and significant respiratory distress.

9. IMMUNIZATION

9.1 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 some 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)

9.2 Vaccine Production

Most vaccines used throughout the world have been whole cell vaccines.

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. This inactivated suspension of bacterial cells is used for the pertussis vaccine component of DPT. The pertussis vaccine component is tested for purity, sterility, opacity, freedom from toxicity and potency.

DPT vaccine is formulated by combining the inactivated pertussis component with

tetanus and diphtheria toxoids. 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. The preparation of a batch of DPT vaccine from the beginning to final release, averages 9 to 11 months in duration (8).

In general most vaccines are prepared under the guidelines of the World Health Organization (15).

9.3 Vaccine Storage

The potency of the pertussis component of DPT vaccine can be decreased by temperature variability. Diminution of potency may be caused by both **high temperatures and freezing**. Stored in a refrigerator between 0^0C and $+8^0$C the pertussis component of DPT vaccine appears to have satisfactory potency over a period of two years.(18)

9.4 Immunization Schedules

The young infant is not protected from whooping cough by passive immunity from the mother. Early immunization is therefore important as young infants are at risk of developing severe form of the 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 immunization 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 immunization schedule recommends the first dose of DPT 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 (4,19,20).

9.5 Vaccine Reactions

Vaccine reactions can be divided into **minor** and **major** reactions.

9.5.1 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.

9.5.2 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 (8).

9.6 Vaccine Efficacy

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 (23).

9.7 Contraindications

No vaccine is totally without adverse reactions. It is worthwhile to note that the risk of serious complications from EPI vaccines, (of which DPT is one), are much lower than the risks from the natural diseases. 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, due to the fact that 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.

- fever of 40.5^{0}C or greater within 48 hours post-immunization.
- collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours post immunization.
- persistent inconsolable crying lasting 3 hours or more or an unusual high-pitched cry occurring 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 DPT immunization are more likely to have similar reactions of equal or greater magnitude upon subsequent immunization (8,20-23).

9.8 Recent Advances

During the last 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 routinely used in Japan in children aged 2 years and older. 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 dose of study vaccines and placebo than after the first dose of these preparations. In contrast, fever and other systemic reactions seemed to occur in lower frequency after the second dose. 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.(8,24-27)

The following important issues still need to be adressed 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.

REFERENCES

1. Six killers of children. World Health, January/February 1987 pg 7.

2. Nelson textbook of Pediatrics (Nelson, WE, Vaughan, V.C., and Berhman RE editors) 12th Edition, pg. 658-661 WB Saunders Company Philadelphia, 1983.

3. Christie A. Infectious diseases: epidemiology and clinical practice 3rd edition Edinburgh Livingston.

4. Muller A.S. MD, Leeuwenburg MPH, David S. Pratt MD FACP, Pertussis: epidemiology and control. *Bull WHO.* **64**:321-31, 1986.

5. Muller AS, Leewenburg J, Voorhoeve AM. Pertussis in a rural area of Kenya: epidemiology and results of a vaccine trial. *Bull WHO.* **62**:899-908, 1984.

6. Health and Disease in Kenya (L.C. Vogel, A.S Muller, R.S. Odingo, Z. Onyango, A. De Gens Editors,) Pg. 225-226, Kenya Literature Bureau, 1974.

7. Bjerregaard P. and Mutie D. M. Immunization Coverage in Kenya: *E. Afr. Med. J.*, **65**:811-819.

8. Report of the Task Force on Pertussis and Pertussis Immunization - 1988 *Paediatrics* **81**:6 part 2. supplement, June 1988.

9. Pollock TM, Miller E, Lobb J. Severity of whooping cough in England before and after the decline in pertussis immunization. *Arch Dis Child* **59**:162-65, 1984.

10. Pertussis surveillance-United State, 19[illegible] and 1985. *MWWR.***36**: 169-71 1987.

11. Romanus V, Jonsell R, Bergquist S.O. Pertussis in Sweden after the cessation of general immunisation in 1979. *Pediatri Inf. Dis J.* **6**:364-71,1987.

12. Report from the Swansea Research Unit of the Royal College of General Practitioners: effect of a low pertussis vaccination uptake on a large community. *Br Med J.* **282**: 23-26 1981.

13. Miller CL, Fletcher WB. Severity of notified whooping cough. *Br Med J.* **I**:117-19, 1976.

14. Manual of Clinical Microbiology Fourth Edition. Editors Lenette E.H, Balows A, Hausler Jr. W.J. Jeanshadomy. H. Fourth Edition Pg 398-399 American Society of Microbiology, Washington, DC 1985.

15. Onorato IM., Wassilak SGF: Laboratory Diagnosis of pertussis: The state of the art. *Pediatr Infect. Dis* **6**(2):145-51.1987.

16. Bass J.W. Erythromycin for treatment and prevention of pertussis. *Pediatri Infect Dis.* **5**: 154-157, 1986.

17. World Health Organization, Expert committee on Biological Standardization: Requirements for Pertussis vaccine, requirements for Biological substances No.8 16th report, WHO Technical report series No. 274. Geneva 1964.

18. Stability of vaccines. WHO/EPI/GEN 89.8

19. Galazka A.M., Lauer B.A, Henderson & Keja J. Indications and contraindications for vaccines used in the Expanded Programme on Immunization. *Bull WHO* **62**:357-366, 1984.

20. Cody CL, Baraff CJ, Cherry JD et al: Nature and rates of adverse reactions associated with DPT and DT immunization in infants and children. *Pediatrics* **68**: 650-660, 1981.

21. Hinman AR, Koplan JP: Pertussis and Pertussis vaccine Reanalysis of benefits, risks and costs. *JAMA:* **251**: 3109-3113,1984.

22. Koplan JP, Schoenbaum SC, Weinstein MC et al: Pertussis vaccine: An analysis of benefits, risks and costs *N. Eng J. Med* **10**:906, 1979.

23. Fine PEM, Clarkson JA: Reflections on the efficacy of pertussis vaccines. *Rev Infect Dis.* **9**.866-883, 1987.

24. Van Savage J., Taylor JC, Dupont WD, Hager CC, Wright PF, Evaluation of a new highly purified pertussis vaccine in infants and children. *J Infect Dis* **160**:832-7, 1989.

25. Blennow M, Granstrom, M: Sixteen month follow-up of antibodies to pertussis toxin after Primary immunization with acellular whole cell vaccine *Pediatr Infect Dis J.* **8**:621-5,1989.

26. Blennow M, Granstrom M, Adverse reactions and serologic response to a booster dose of acellular pertussis vaccine in children immunized with acellular or whole-cell vaccine as infants. *Pediatrics.***84**:62-7,1989.

27. Blennow M, Granstrom M, J: aratmaa E, Olin P, Primary immunization of infants with an acellular pertussis vaccine in a double-blind randomized clinical trial. *Pediatrics.***82**: 293-9,1988.

10

CHILDHOOD TUBERCULOSIS

F.E Onyango

1. INTRODUCTION

Tuberculosis remains a major public health problem in most developing countries. With increased industrial development, most of the developed countries for several decades had good control of the disease. However in no country was it ever eradicated.

The current prevalence of tuberculosis in the paediatric age group in Kenya is not known, but in 1987 the overall prevalence in the country, was reported at 47.7 per 100,000.

Tuberculosis affects all age groups, but has a high mortality rate in the very young and the very old.

Bacille Calmette Guerin (BCG) vaccine was developed some seven decades back. It was however put into more widespread use for control of tuberculosis some five decades ago, at a time when some of the first anti-tuberculous drugs were discovered.

Control of tuberculosis depends on health education, BCG vaccination, and treatment of those who have the disease. Since the 1940s, intensive efforts have been made to reduce the incidence of the disease using the above mentioned methods, but this has remained high in many developing countries. Due to the rising prevalence of HIV infection the incidence is likely to increase in both developed and developing countries. It has been shown that the incidence of tuberculosis is much higher in those who have HIV infection.

There is no doubt that in the foreseeable future tuberculosis will continue to affect an appreciable number of people, both young and old. It is therefore of utmost importance that all health workers especially in developing countries like Kenya should be conversant with various aspects of the tuberculous disease that are important in its control.

2. EPIDEMIOLOGY:

2.1 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 hrs and is largely a human pathogen but can cause infection in experimental animals such a guinea pigs. Rarely, it causes natural infection in other animals.

2.2 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
- fomites such as contaminated clothes; bronchoscopes and syringes, have been implicated in transmission, although rarely.

2.3 Risk Factors

These can be characterised into:-

2.3.1 Host Factors.

Age. Infection is high in infants and in adolescents.

Intercurrent conditions that may compromise immune state of the host, such as:-

- malnutrition
- measles infection
- H.I.V. infection
- lymphomas
- diabetes mellitus
- treatment with immuno-suppressants such as cytotoxic drugs and corticosteroids.

2.3.2 Bacterial Factors

- virulence

2.3.3 Environmental Factors

- overcrowding
- poor ventilation
- the presence of an open case. This is particularly important in childhood tuberculosis where a household open case is a big risk.
- poor socio-economic status.

3. PATHOGENESIS

Primary tuberculosis in children is characterised 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 mycobacteria. In a tuberculous lesion one can identify four populations of *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 a long treatment duration is needed for infections by this micro-organism to target the various populations of mycobacteria.

4. 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 **extrapulmonary** forms.

- Pulmonary tuberculosis is the most common type of tuberculosis in children, found in about 70% - 80% of children with the disease.
- Extrapulmonary 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 h
incidence of post treatment sequelae.

4.1 The common clinical features seen in children with tuberculosis are:-

- cough; usually for more than two weeks
- fever; irregular and recurrent
- loss of appetite
- loss of weight
- night sweats
- lymphadenopathy.

5. DIAGNOSIS

Unlike in the majority of adult tuberculosis where sputum is easily obtained, and diagnosis is made on Zielh Nelseen stain, the diagnosis of childhood tuberculosis is a challenging mental exercise for the clinician. It is based on several clinical and radiological factors.

This has given rise to use of a scoring system to facilitate diagnosis. Several studies have used this and found it valuable (2,3). One such scoring system in use is listed below (3):

	SCORING SYSTEM	POINTS
1.	Acid Fast Bacillus	+ 5
2.	Tubercle in biopsy	+ 5
3.	Tuberculin test	
	a) Positive = 10 mm	+ 3
	b) Borderline 5-9 mm	+ 2
	c) Conversion from negative to positive	+ 2
4.	Suggestive Radiology	+ 3
5.	Suggestive physical findings	+ 3
6.	Known contact with an open case of tuberculosis	+ 2
7.	History of contact with tuberculosis	+ 1
8.	Non-specific sign and symptoms	+ 1
9.	Non-specific X-ray findings	+ 1
10.	Non-specific granuloma	+ 1
11.	Less than 2 years of age	+ 1
12.	Response to specific anti-tuberculous treatment	+ 3
13.	BCG vaccination given	- 1

5.1 The following are definitions of some sections of the scoring system:

5.1.1 Suggestive Radiology Includes the Presence of:-

- *trachea-bronchial adenitis with or without parenchymal involvement*
- *persistent segmental lesion with mediastinal adenopathy*
- *miliary mottling.*

5.1.2 Suggestive Clinical Findings Includes:-

- *serous pleurisy*
- *papulonecrotic skin lesions*
- *cold abscesses*
- *large matted lymphnodes*

- *history of measles infection in the previous 1-3 months accompanied by cough for more than two weeks with weight loss*
- *Gibbus deformity*
- *Erythema nodosum*
- *Phlyctenular keratoconjunctivitis.*

5.1.3 Non-specific signs and symptoms

- *persistent cough*
- *measles or whooping cough infection (in recent past)*
- *weight loss/failure to gain weight*
- *protein-energy-malnutrition (P.E.M)*
- *prolonged or unresolved pneumonia.*
- *recurrent respiratory infection*
- *prolonged unexplained fever*
- *high E.S.R.*
- *meningeal syndrome*
- *hepatosplenomegaly.*

5.1.4 Non-specific X-ray findings:

- *diffuse or bizzare pulmonary shadows*
- *hilar shadows*
- *bone defects.*

5.1.5 Non-specific granuloma

- *a non-specific granuloma on biopsy of tissue.*

5.2 Utility of the point system

POINTS	INTERPRETATION
1 to 2	Tuberculosis unlikely
3 to 4	Tuberculosis possible, requires further investigations
5 to 6	Tuberculosis probable, may justify therapy
= >7	Tuberculosis unquestionable

6. MANAGEMENT

All children with tuberculosis should be put on chemotherapy early to avoid major complications and death.

Whatever treatment is given, it should be:-

- effective
- safe
- affordable and easily available.

In Kenya today, there are two major treatment regimes:-

- **Standard Regime** of:
  - Streptomycin given at a dose of 20-40 mg/kg/day intramuscularly for one to two months.
  - Thiacetazone and isoniazid are usually given in a combination tablet containing 100mg isoniazid and 50 mg thiacetazone per tablet; orally for 18 months.
  - Isoniazid is given at a dose of 10-20 mg/kg/day orally for 18 month.
- **Short-course regime** of:-
  - Streptomycin as for standard regime
  - Pyrazinamide given at a dose of 15-30 mg/kg/day orally for one to two months.
  - Isoniazid - 10-20 mg/kg/day for six months.

- Rifampicin given at a dose of 10-20mg/kg/day orally for six months.

The standard regime is effective, safe, is easily available, and cheap. However the long duration of therapy compromises its effectiveness. The short course regime is effective, and safe, but its expense may limit its use.

6.1 Contact Tracing:

Efforts must be made to:-

- identify the index case, that is the patient with open, sputum positive disease who infected the child. For young children these are usually found in the same household
- investigate other family members or contacts of the patient
- put on chemotherapy all those found to be positive.

6.2 Education

To ensure good compliance the patient put on treatment should be properly educated about:

- the disease, especially its natural history and expected response to effective chemotherapy
- the type of treatment, it's effect on the disease, the side effects and how to manage them.

7. PREVENTION AND CONTROL:

The control of tuberculosis depends on case finding, chemotherapy and immunization.

7.1 Case Finding

This is based on detecting cases who are infected and have the disease, through clinical, radiological and laboratory evaluation.

It does not benefit children in the population directly, because confirming the diagnosis in this age group is not easy. However they benefit indirectly through detection and treatment of the older people with infectious diseases who are their main source of infection.

There are two methods of Case Finding:

- passive Case Finding in which cases attending health facilities are detected and put on chemotherapy.
- active Case Finding in which the health team combs the community for cases.

7.2 Chemotherapy

- detection and treatment of those who have the open disease, reduces or eliminates, the pool of infection in a community.
- treatment of the young children with primary infection, reduces the pool of future adults with open infectious disease.
- all efforts should be applied to make sure that all patients started on anti-tuberculous treatment successfully complete the course.

7.3 IMMUNIZATION

7.3.1 The Vaccine

BCG is a live attenuated vaccine developed in 1921 from *Mycobacterium bovis*, by Calmette and Guerin at the Pasteur Institute, France.

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%.

Many laboratories all over the world produce BCG vaccines. In Kenya over the last one or two decades the following four BCG vaccine types have been used.

- Pasteur BCG vaccine
- Danish BCG vaccine
- Japanese BCG vaccine
- Glaxo BCG vaccine

Besides few and minor variations related to immunogenicity and incidence of complications these vaccines have similar characteristics. (Pasteur and Danish BCG vaccine are reported to be relatively more immunogenic and associated with slightly more complications.)

7.3.2 Storage

BCG vaccine is sensitive to light and heat. It should therefore be stored away from light at $0^{o}C$ to $+8^{o}C$.

7.3.3 Administration

The vaccine is prepared in powder form. Reconstitution should be done following carefully the instructions provided in the vaccine package from the manufacturers. The reconstituted and unused vaccine should be discarded after 4 hours.

The dosage is 0.05 mls (of the reconstituted vaccine) to newborns and infants, but 0.1 ml given to older children. However before administration of a BCG vaccine it is important to read the manufacturer's instructions carefully.

It should be given **intradermally**. This should be done using a 1ml syringe without a leak, and a 26G or 27G hypodermic needle. In Kenya, BCG vaccine is given on the anterior-lateral aspect of the upper one third of the left forearm. It must not be given subcutaneously. This is associated with high incidence of abscess formation.

During the intradermal injection one should raise a weal of about 6 mm - 10 mm in diameter. BCG vaccine can be safely given at any age without a prior tuberculin test.

Several studies have shown that BCG vaccine can be used more effectively than tuberculin test as a diagnostic tool for childhood tuberculosis (4,5,6,7,8,9).

BCG vaccine can safely be given at the same sitting (though not in the same syringe) with polio, DPT and measles vaccines.

7.3.4 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 miliary tuberculosis (9).

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% (10). However, there seems to be consistency on the reasonably good protection the vaccine affords when given to young children. Studies from Kenya (11) Togo (12) and Thailand (13) 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 (14, 15).

7.3.5 Side Effects

Side effects and complications following BCG vaccination have been observed and reported right from the early days 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 (16).

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.

7.3.5.1 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 at the vaccination site, and is characterised 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 Nelseen stain and culture are positive for AFB in about 50%. There is however no indication for treating even those who are positive.

- **Osteomyelitis:** 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).

7.3.6 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).

REFERENCES

1. Mitchison, D.A and Dichinson, J.M.: Bacteriocidal mechanisms in short course chemotherapy. *Bull. Int. Union. Against Tb.* 53: 254-259, 1978.

2. Stegen, G., Jones, K., and Kaplan, P. Criteria for guidance in the diagnosis of tuberculosis. *Paediatrics* **43**: 260 - 263, 1969.

3. Nair, P. and Philip, E. A scoring system for the diagnosis of tuberculosis in children. *Indian Paediatrics* **18**: 299- 303, 1981.

4. Udani, P.M., Paritch, K.C., Shah, P.M., and Naik P.M.: BCG test in tuberculosis, *Indian Paediatrics* **8**: 143-150, 1971.

5. Krishnaswani, K.V., Rahiru, M.A., Parthasarathy, R. and Raja M.A. BCG Test. *Ind. J. Tb* **24**: 70-74, 1979.

6. Shrivastara D.K., Shingwellar, A.G., Thawrani, Y.P. and Chondhary, A.K. Evaluation of BCG Test in Childhood Tuberculosis *Indian Paediatrics* **15**: 993-998, 1977.

7. Jaiswal, S and Bhandari, N.R. Evaluation of Diagnostic value of BCG Test in childhood tuberculosis *Indian Paediatrics* **13**:689-695, 1976.

8. Datta, T. and Sen K. BCG versus tuberculin test in the diagnosis of childhood tuberculosis. *Indian Paediatrics* *19*: 141-146, 1982.

9. Praharaj C.K. and Chondhury U. Evaluation of Mantoux and BCG Test in the diagnosis of childhood tuberculosis. *Indian Paediatrics* **14**: 99-102, 1977.

10. Clement, J.D., Chuong, J.J.H. and Feinstein A.R. The BCG Controversy. *JAMA* **249**: 2362-2369, 1983.

11. Onyango, F.E., Wafula, E.M., Ngacha, D.M., Mirza, N.M. Macharia, W.M., Musil, J., Njeru, E., Kitonyi, J.K., Magak P. and Muruka, J.: BCG Vaccine Efficacy Against Tuberculosis in Young children (Press).

12. Tidjan O., Amedome, A., ten Dam H.G. The protective effect of BCG vaccination of the newborn against childhood tuberculosis in an African community. *Tubercle* **67**: 269-281, 1986.

13. Padungchan, S., Konjanart, S., Daramas, K. and ten Dam H.G. The effectiveness of BCG vaccination of the newborn against tuberculosis in Bangkok. *Bull. World. Hlth org.* **64**: 247-258, 1986.

14. Dawodu, A.H. Tuberculin conversion following BCG vaccination in preterm infants. *Acta Paediatr Scand.* **74**: 564-567, 1985

15. WHO Document on BCG vaccination of the Newborn; Rationale and guidelines for country programmes, WHO/TB/86.147, EPI/GEN/86/10, 1986.

16. Lotte, A., Wasz-Hockert, O., Poisson, N., Dimitrescu, N., Verron, M. and Couvet E. BCG complications. *Adv. Tuberc. Res.* **21**: 107-193, 1984.

17. WHO Document on Indications and Contraindications for Vaccines used in the Expanded Programme on Immunization, EPI/GEN/83/6., 1983.

18. Tuberculosis control: A Manual on methods and Procedures for intergrated programmes. Scientific Publication No. 498, PAHO/WHO, 1986.

19. de Souza, G.R.M., Sant'Anna, C.C., Silva, J.R.L., Mano, D.B., Bethlem, N.M. Intradermal BCG vaccination complications - Analysis of 51 cases. *Tubercle* **64**: 23-27, 1983.

20. Power, J.T., Stewart, I.C. and Ross, J.D. Erythromycin in the management of troublesome BCG lesions. *Br. J. Dis. Chest* **78**: 192-194, 1984.

21. Caglayan, S., Yegin, O., Kayran, K., Timoan, N., Kasirya, E. and Gun, M. Is Medical therapy effective for regional lymphadenitis following BCG vaccination? *Am. J. Dis. Child.* **141**: 1213-1214, 1987.

22. Horowitz, O and Meyer, J. The safety record of BCG vaccination and untoward reactions observed after vaccination. *Adv. Tuberc. Res.* **8**: 245-271, 1957.

23. Van Assendelft, A.H.W. and Jukkara, A., BCG Anaphylaxis *Tubercle* **67**: 233-234, 1986.

24. Joint WHO/UNICEF statement on early immunization for HIV infected children. WHO/GPA/INF/89.6, 1989.

FURTHER READING

1. Nelson's Textbook of Paediatrics by Behrman R.E. and Vaughan V.C. 12th Edition Chapter 10.52 page 708-723, W.B Saunders Co. Philadelphia, 1983.

2. Stead, W.W. and Bates, J.H. Tuberculosis In: Harrison's Principles of Internal Medicine. 10th ed. Section 7, pg 174, McGraw-Hill Int. Book Company, Tokyo, 1983.

3. The Tuberculosis Association of India: Textbook of Tuberculosis. 2nd Revised ed. Editorial Board: Rao, K.N. Viswanathan, R., Sen. P.K., Deshmukh, M.D., Bordia, P.K., Pamra, S.P. and Dingley H.P., Vikas Publishing House Put Ltd, New Delhi, 1981.

4. Toman, K. Tuberculosis: Case Findings and Chemotherapy, Questions and Answers, WHO, Geneva, 1979.

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DIPHTHERIA

D.M Mutie

1. 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, are about 5-60%.

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. Case fatality rates are 10-15% for non-cutaneous diphtheria.

Diphtheria as a disease dates back probably to the second century (1,2), 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 (Greek, diphtheria:leather). 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.

In 1890 Von 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-antitoxin mixture to immunize children. This material was used untill 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 (2).

2. 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 6 EPI-target diseases, in Kenya as well as in other developing countries.

It has been postulated that in developing countries children acquire solid natural immunity from mild skin or chronic nasal diphtheria early in life and this prevents outbreaks of serious clinical forms of the disease despite low diphtheria immunization coverage. This might explain the seemingly uncommon occurrence of this disease in Kenya. On the other hand, it is possible that mild to moderate cases (especially faucial) do occur and are either managed as bacterial or viral throat infections or are missed altogether. Thus, inapparent infections may be many more than recognized cases.

As personal, domestic and communal hygiene improve, cutaneous diphtheria will decrease and correspondingly induced immunity will decline, too (3). This may result in the emergence of severe clinical cases. Therefore high childhood immunization coverage against the disease must be maintained to avoid this potential public health hazard.

3. 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.

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.

4. 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 of the initial infection as follows:

- nasal diphtheria
- tonsillar and pharyngeal diphtheria
- laryngeal diphtheria
- cutaneous diphtheria
- conjunctival diphtheria
- aural diphtheria.

4.1 Nasal Diptheria

Nasal diphtheria occurs commonly in infants, it initially resembles a common cold presenting with mild rhinorrhoea. The nasal discharge may become serosanguinous and then mucopurulent excoriating the nares and upper lip. A foul oduor may be noticed and careful inspection will reveal a white membrane in the nasal septum.

4.2 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 extent 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.

4.3 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.

4.4 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.

4.5 Conjunctival diphtheria

Conjunctival diphtheria lesions are usually limited to the palpebral conjunctiva which appears red edematous and membranous.

4.6 Aural diphtheria

Aural diphtheria is characterised by otitis externa with a persistent purulent and frequently foul smelling discharge.

5. COMPLICATIONS

- Respiratory obstruction may occur due to edema 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.

6. DIAGNOSIS:

6.1 Clinical Diagnosis

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.

6.2 Definitive diagnosis:

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. Other laboratory tests are of little diagnostic value.

6.3 Schick Test:

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.

7. TREATMENT

7.1 Antitoxin:

Neutralization of free toxin by the use of 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.

7.2. Antibiotics

Antibiotics are needed to stop the production of diphtheria toxin. Penicillin and erythromycin are effective against most strains of C. diphtheria.

7.3 Supportive treatment:

Supportive treatment includes the early detection and management of complications, adequate diet and bed rest when indicated.

7.4. Immunization

Immunization is necessary following recovery of the patient since recovery from diphtheria does not result in adequate immunity to prevent reinfection.

7.5 Notification:

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.

8. PREVENTION

8.1 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.

8.2 Specific Preventive Measures.

8.2.1. 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 DT vaccine is obtained but KEPI does not currently stock it. It is important to note, too, 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 0^0C to + 8^0C. 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. Its 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 DPT doses, at 4 week intervals starting at 6 weeks of age. Each DPT dose is O.5 ml 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 fact 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:

DPT 1 ..... at 6 weeks of age

DPT 2 ..... at 10 weeks of age

DPT 3 ..... at 14 weeks of age

The first dose confers no protection at all, while two doses confer a protection in 90% of the recipients. DPT3, raises the protection rate to 95%. After 3 doses of DPT, children are protected against diphtheria for 10-13 years. Immunization does not eliminate carrier states.

8.2.2. Management of contacts of a confirmed case:

If toxigenic diphtheria has been confirmed by laboratory (or is clinically highly suspected), the following steps may be useful in preventing 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 upto date with DPT 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.

If resources permit the following additional steps should be considered:-

- 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.

REFERENCES

1. Krugman, S. Diphtheria. : Infectious Diseases of Children, pg. 31 4th Edition The C.V. Mosby Co. Saint Louis, 1968.
2. Hodes, H.L. Diphtheria. : Unusual Infections *Paediatric Clinics of N. America* **26(2)**: 445-459 (1979).
3. Bwibo, N.O. Classical Diphtheria in Children. *The Uganda Fractitioner* 4:5 (1971).
4. American Public Health Association. Control of Communicable Diseases in Man. 14th Edition, Washington, 1985.
5. Miller, L.W. et al. Diphtheria Immunization. Effect on carriers and Control of outbreaks. *Am J. Dis. Child.* 123:197 (1972

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HEPATITIS B DISEASE

N.M Mirza.

1. INTRODUCTION

Hepatitis B infection is a worldwide problem with three quarters of the world's population living in areas of intermediate or high prevalence namely South East and South West Asia, Africa, Middle East, Oceania, Southern and Eastern Europe, Alaska and the Amazon region of S.America.

Worldwide it is estimated that there are 1 billion infected people, 300 million being chronic carriers with 2 million annual fatalities.

Hepatitis B is caused by a small DNA - containing virus. It is a major cause of acute and chronic hepatitis, cirrhosis and liver cancer (hepatocellular carcinoma or HCC) (1).

Origins of the virus are unknown. Man is the only known reservoir. There are no naturally infected wild animals, although chimpanzees and several other higher primates can be experimentally infected. It has never been cultured in vitro.

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.

1.1 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 (HBcAg) and Hepatitis B Surface antigen (HBsAg) respectively.

A patient with HBV infection has 3 types of particles in his serum: the Dane particle and the smaller (22nm diameter) tubular and spherical particles, thought to represent surface viral coat protein. These last two particles are non-infective.

1.2 Hepatitis B Markers

Some of the methods of detecting serum HBV markers include passive haemagglutination (PHA), Radioimmunoassay (RIA) and Enzyme-linked immunoassay (ELISA). The following hepatitis B markers have been identified:-

- HBsAg was the first HBV marker identified and was named Australian antigen by Blumberg 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 disappaers, 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 Hepatitis B core 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 infection or past infection.

- HBeAg is found in the blood. Its presence indicates viral replication and therefore high infectivity of the patient. Its antibody, the 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.

Table 1 Serological Markers Of Hepatitis B Virus*

Term	Abbreviation	Comments
Hepatitis B Virus	HBV	Aetiologic agent of "serum" hepatitis: also known as "Dane particle"
Hepatitis B surface antigen	HBsAg	Surface antigens of HBV, detectable in large quantity in serum; several subtypes identifiable
Hepatitis B e antigen	HBeAg	Associated with HBV replication, high titre HBV in serum and infectivity of serum
Hepatitis B core antigen	HBcAg	Function uncertain, no commercial test available and so cannot be detected in circulating blood
Antibody to HBsAg	Anti-HBs	Indicates infection with and immunity to HBV, passive antibody from HBIG, or immune response from HB vaccine
Antibody to HBeAg	Anti-HBe	Presence in serum of HBsAg carrier indicates lower titre of HBV
Antibody to HBcAg	Anti-HBc	Indicates prior infection especially IgG (IgG) with HBV at some undefined time
IgM class antibody	IgM anti-HBc	Indicates recent infection with HBV, and acute viral hepatitis, detectable for 4 to 6 months after infection. Such patients are highly infectious

* adapted from "Protection Against Viral Hepatitis - Recommendations of the Immunization Practices Advisory Committee (ACIP), from Morbidity and Mortality Weekly report 39(RR2):1-26, 2/9/90.

2. EPIDEMIOLOGY

2.1 Magnitude of the problem

HBV is the single most important known cause of persistent viremia in humans. The frequency of infection and carrier state has distinct geographic and ethnic variation. Areas are characterized into low, intermediate and high endemicity(2). The reason for

the difference in the different areas has been attributed to a number of factors, including social and educational standards.

- **Low Endemicity**

  Characterized by HBsAg carriage rates of less to or equal to 2%. Countries such as Britain, United States, Scandinavia, Australia and New Zealand fall in this category. Infection in these areas occurs primarily after puberty as a result of transmission from blood or blood products and from sexual contact.

- **Intermediate Endemicity**

  Carriage rates in these areas ranges between 2-5% and includes the Middle East, East and Southern Europe, Japan, N.Africa and S.America.

- **High Endemicity**

  High endemicity is characterized by carriage rates of over 5% and includes countries in Sub-Saharan Africa, China, S.E.Asia, Pacific Islands, Alaska in Northern America and the Amazon region of S.America. Infections are acquired perinatally or more commonly during early childhood.

2.2 Transmission

It was assumed that HBV was transmitted only by parenteral route hence the old name of serum hepatitis. However it has now been well established that the disease can be transmitted from person to person by close contact(3,4).

Only the whole virus (Dane particle) is capable of transmitting the infection. The HBe Antigen is associated with the Dane particle and is therefore a useful marker of infectivity.

The following body fluids have been found to have HBV DNA by molecular hybridization:

- blood (including monocytes and leukocytes)
- saliva
- urine
- seminal fluid
- vaginal secretions.

Thus, body secretions other than blood may be infectious. HBV probably replicates in other extra hepatic sites. Bone marrow cells and even human pancreas have been found to have viral antigens.

2.2.1 Perinatal transmission

Transmission of virus from carrier mothers can occur in upto 80% of babies during the perinatal period, the risk being higher in HBeAg positive mothers. Infection may be transmitted either vertically, that is from mother to unborn baby, or horizontally (from person to person by ways other than transplacental transmission).

If the mother is HBsAg positive but HBeAg negative or anti HBe - positive, the infant has only 10 - 20% chance of becoming infected with HBV perinatally, compared to 80 - 90% chance of infection if the mother is positive for both HBsAG and HBeAg (5). Perinatal transmission also seems to be influenced by unexplained racial and ethnic difference.

Intrauterine transmission is very rare accounting for only 5% of all the perinatal infections. It varies with the level of HBsAg in cord blood, being highest when HBsAg cord blood levels are greater than 20IU/L.

Transmission from mother to infant can also occur during the time of labour and delivery. This may occur either from small leaks across the placenta, trauma during birth, or maternal secretions in the birth canal.

In perinatal transmissions, most of the mothers are asymptomatic chronic carriers, but in rare circumstances the mother may have had acute HBV infection in the later part of the pregnancy or shortly after birth of the child.

Perinatal transmission depends on HBeAg status of the mother. In S.E Asia where 50%, of the mothers are HBeAg positive perinatal transmission is high. On the other hand in Tropical Africa where maternal HBeAg positivity is in the range of 5 to 15%, perinatal transmission is low, but infection with the virus occurs very early in life. The perinatal and early childhood infections lead to a large pool of cariers.

In Gambia for instance, infections of newborns is uncommon, however infection rates increase rapidly so that by the age of 2 years, 40% of children have already been infected with HBV and 15% have developed persistent infection. By the age of 10 years, 90% of the children have been infected and 20% have become chronic carriers (6).

In developing countries, after 5-6 years of age, HBV infections account for less than 10% of chronic carrier states (7).

The consequence of infection in early infancy is usually an asymptomatic chronic HBV carrier state lasting for a long time, often life-long. It is estimated that 90% of these infected infants become chronic HBsAg carriers.

Breast milk is not an important source of virus transmission(1). Although HBsAg has been detected in 71% of breast milk samples of HBsAg carrier mothers, studies have demonstrated that breast-fed infants of HBsAg carrier mothers are no more likely to be infected at 1 year of age than infants of carrier mothers, who are not breast-fed(5).

2.2.2 Parenteral

HBV is very infectious. Studies have shown a correlation between the number of injections received by children and the frequency of HBV infection. Tattooing, circumcision, ritual scarification and illicit intravenous drug use are other ways in which parenteral transmission may occur.

Some carriers have very large amounts of infectious material thus facilitating transmission by inadequately sterilized equipment.

2.2.3 Person to person (Horizontal transmissions)

The exact mechanism of transmission is not well understood but close body contact with exchange of body fluids has been suggested.

The fluids include:-

- saliva
- secretions from open wounds
- blood
- vaginal secretions
- semen.

Transmission between children is quite common in many parts of the world, since children are often more infectious than adults. This has been shown in studies where chances of being infected are much higher if a sibling is positive(8). This is because children who are HBsAg positive have a higher prevalence of HBeAg and are therefore more likely to transmit the virus through close contact with other children.

'The Gambian study (8), revealed that 86% of all children under age of 5 years who were HBsAg positive also carried HBeAg and the proportion fell to 17.6% for children aged 10 to 14 years and to 12.9% for mothers. Transmission from one sibling to another was found to be of major importance. The study further showed that the chances of a child being an HBsAg carrier are approximately 42% if an elder sibling is HBsAg positive, 27% if either the mother or the father is a carrier and 15% if neither the mother or the father is a carrier (8). Mothers who are HBsAg positive are at greatest risk of transmitting the infection to their infants.'

This mode of transmission is in contrast with what is seen in S.E. Asia where the predominant infection occurs perinatally.

In areas of high endemicity, most people are infected before they reach sexual maturity and therefore sexual transmission is probably of little importance.

Close personal contact has been incriminated as a way of infection as has been shown in institutions for mentally retarded children.

Studies have shown that chances of contracting HBV infections are much higher in spouses of infected individuals as compared to other family members (3,4). However, other studies show that family members may have upto 20 times higher carriage rate of HBsAg than spouses of persistent carriers (10). These observations indicate that sexual transmission is not the only means of spread within the family.

Other suggested modes of transmissiom are:-

- sharing of tooth brushes and razors
- it has been suggested (9) that breaks in the skin of infants and children

caused by infestation by lice and scabies, and impetigo sores may play an important role.

- insect vectors are of theoritical importance (not proven in practice). No biological transformation or propagation of the virus in vectors has been shown. If transmission occurs it is possibly only mechanical.

Studies done in rural Africa found that perinatal transmission is relatively unimportant. However in contrast to the urban African setting it was found that infection commenced early in life around 1 to 2 years of age and spread rapidly, with some regions recording 70% prevalence of HBV earlier than 5 years of age (11,12). It has been suggested that in tropical Africa nearly everyone is infected with HBV during childhood and 20% of children become chronic carriers (7,13).

The HBsAg carriage is not only a threat to the carrier (risk of developing chronic hepatitis, cirrhosis and HCC) but also to the community, as these carriers provide a source of virus for transmission to susceptible individuals.

2.3 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 out 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.

3. 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).

4. 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. Some 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 titers of anti-HBs and anti-HBe. This may be associated with features suggesting immune complex disease manifested as fever, urticarial rash and arthralgia.

4.1 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 developnig HCC.

5. 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).

5.1 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.

6. Management

The management of HBV infection will depend on whether it is acute or chronic.

6.1 Acute Infection

There is no known effective treatment and case management is geared towards supportive care.

6.2 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.

6.2.1 Chronic Hepatitis with HBeAg Positivity

Antiviral agents are administered to accelerate clearance of HBeAntiginaemia. These agents include adenine-arabinoside-monophosphate (Ara-AMP) and interferon.

6.2.2 Chronic Hepatitis with anti - HBe Positive

In asymptomatic persons or these 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 8weeks), the withdrawal of which is followed by a course of Ara-AMP or interferon has been shown to have good results.

6.2.3 Co-Infection

Co-infection or superinfection with delta virus has been associated with an increased morbidity and mortality from both acute and chronic HBV infection(8). There is relatively little information on the epidemiology of hepatitis delta (HD) and hepatitis Non A Non B(HNANB) infections in Africa. The quoted ranges of HD are 3 to 31%. HNANB is estimated to account for 8-38% cases of acute viral hepatitis throughout Africa..

In southern Africa, Kews et al observed a high association between hepatocellular carcinoma and hepatitis C (23).

7. CONTROL AND PREVENTION

7.1 Methods of Control

Methods of control include:

7.1.1 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 needles and syringes should be avoided. It should be remembered that the primary source of infection is the acutely infected individual and the chronic carrier.

7.1.2 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 (5).

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(24,25). Because of these reasons, many countries, for economic and logistic reasons would opt for HBV vaccination alone.

7.1.3 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 main stay of control of this disease depends on prevention of transmission by immunization of populations at risk.

7.1.3.1 What Levels are Protective?

Several studies have found that anti-HB titres greater than 10IU/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 and, the fact that HBV infection can occur in a patient with high anti-HBs titers indicates that protection is relative rather than absolute (27).

7.1.3.2 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.

7.1.3.3 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 some 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 (22).

- 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-endermic area. Since HBV carriage rate in hyperendemic areas is about 10-15%, death due to liver disease would therefore account for 3% of the deaths (14).

- 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 r ductions 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 inorder 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.

8. VACCINE DEVELOPMENT AND USE

8.1 Vaccine Development

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.

8.1.1. 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 antibody and the aim of vaccination is to stimulate production of anti-HBs.

To render this vaccine safe, it undergoes several purification processes. There are 3 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).

8.1.2 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 it's 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.

8.2 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.

8.3 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 $+8^{0}$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.

8.4 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.

8.5 Indications for Vaccination

- **In highly endemic areas,** indications are for new born babies.

In areas where vertical or perinatal transmission is important hyper-immune globulin (HBIG) should be given, too, in conjunction with the vaccine. HBIG is to be given within 48 hours of delivery. Administration of HBIG adds cost to the immunization programme. In Kenya, since HBV transmission is mainly horizontal, administration of HBIG together with the vaccine would not be a cost-effective measure.

- **Areas of low prevalence,** indications are for "at risk" groups which include:

  - health care staff
  - close contacts of known carriers (who are not immune)
  - immunocompromised individuals i.e patients in oncology or dialysis units
  - homosexuals
  - drug addicts
  - patients requiring frequent blood transfusion

8.6 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 some 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.

8.7 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 un-protected.

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).

8.8 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 antibody levels become undetectable, individuals seem to remain protected against clinically significant disease (HBsAg carriage or liver inflammation), provided that the initial antibody response was effective. Boostering to maintain anti-HBs levels above 10U/ml were found to be unnecessary in endemic areas. Beasley, found that in Taiwanese children the initial fall in antibody 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 programmes.

8.9 Immunogenicity:

HBsAg antigenicity is enhanced by absorption to an alum adjuvant.

Factors influencing immunogenicity:

- immune status of host. Immunologically compromised hosts (e.g AIDS or cancer patients, patients on dialysis, steroids etc) respond poorly to the vaccine
- females of all ages have a slightly better responses than males
- immune response declines with increasing age. Newborn respond as well as older children
- freezing inactivates the vaccine because it causes vaccine-adjuvant dissociation.

8.10 Non Responders

There has been some data linking non response to certain HLA haplotypes, suggesting genetic predisposition to non response. There are 5-10% non responders. It has been suggested that non response may be related to antigen presentation and conformation of vaccine.

Immunization in early childhood is more effective than in adults and immunogenicity in neonates is excellent irrespective of HBV marker status of the mother(5). Maternal antibodies or even HBIG administration does not inhibit antibody production after vaccination.

Repeated immunizations result in seroconversion in some of the initial non-responders. This effect is enhanced if larger doses are used.

The Gambian study (31) has shown that the number of non responders is low (less than 2%).

8.11 Efficacy of Vaccine

Antibodies to HBsAg develop in as many as 95% of healthy individuals given 3 doses. Once antibodies have developed, protection will be complete unless a massive inoculation of infected material occurs, as in transfusion of infected blood. Immunity lasts for at least 5 years(7).

Analysis with monoclonal antibodies suggests that qualitatively, humoral immune response to both the plasma derived and the recombinant vaccine tested was similar to that seen during recovery from natural infection.

Efficacy of vaccines have been demonstrated in a number of high-risk settings, including through sexual transmission, parenteral transmission and perinatal transmission.

In Taiwan, two pilot studies demonstrated that either 4 doses (0,1,2, and 12 months) of 5ug Pasteurs vaccine or 3 doses (0, 1, and 6 months) of Merck Sharp and Dohme (MSD) vaccine produced substantial levels of anti-HBs in 90-100% of infants. With vertical transmission being the commonest mode of transmission in Taiwan, administration of the vaccines within one week after birth was able to prevent 75% of chronic HBsAg carriers without HBIG. The protective efficacy was increased to about 90% if given in combination with HBIG soon after birth. Follow-up studies revealed that anti-HBs persisted in 90% of those vaccinated during the 5 year observation, and carriers scarcely occurred(32). Antibody production in response to the vaccine is mainly to the HBsAg, and the response is mainly to the group-specific "a" antigen. Although subtype -specific antibody may also be produced, it is probably the antibody to the common antigen that provides cross-protection against the various HBV subtypes (33).

Trial of HB vaccine in AIDS patients revealed a markedly decreased immune response in the HIV infected group. This may be related to the decreased number of T helper lymphocytes(34). It has been suggested that individuals at risk of HBV infection should be vaccinated, even if HIV - infected inorder to prevent additional virus infection which might further compromise immunity.

It has been shown that there is no difference in response to the vaccine between underweight and well nourished infants (24).

8.12 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(35).

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.

8.13 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.

8.14 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 costs 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 should be considered especially in view of the fact that cost of HBV vaccine has now been brought down to less than US$ 1 per dose, making this economically feasible, as vaccination at birth will prevent 85% of expected chronic carriers.

REFERENCES

1. Health technology Directions - Program for appropriate technology in health. PATH publication. Vol 6:No. 3

2. Beasley R.P., Palmer R. Hepatitis B Immunization strategies WHO/EPI/GEN/88.5 World Health Organization Geneva: 1988.

3. Mosley J.W. The Epidemiology of viral Hepatitis - an overview. *Am. J of Med Sci*:270: 253-270: 1975.

4. Koff R.S., Slavin M.M. Connelly L.J.D., Rosen P.R. Contagiousness of acute hepatitis B. Secondary attack rates in household contacts. *Gastroenterology* 72: 297-300: 1977.

5. Smego R.A. and Halsey N.A. The case for Routine Hepatitis B Immunization in infancy for populations at increased risk. *Pediatr. Infect. Dis.* 6: 11-19: 1987.

6. The Gambia hepatitis Study Group. The Gambia Hepatitis Intervention Study; *Cancer Research* 47: 5782-5787:1987.

7. Coursaget P., Yvonnet B., Chotard J., Sarr M., Vincelot P., N'doye R, I. Diop-mar I. and Chiron J.P. Seven year study of Hepatitis B. Vaccine Efficacy in Infants from an Endemic Area (Senegal). *Lancet* (2):1143-1144: 1986.

8. Whittle H.C., Bradley A.K., McLauctilan K. and Ajdukiewicz A.B. Hepatitis B virus infection in two Gambian villages. *Lancet* (1): 1203-1206: 1983.

9. Wainwright R.B., McMahon B.J., Bender T.R., Heyward W.L., Nakanishi S., Wainwright K.Y., Foliaki S., Erickson S. and Fields H.A. Prevalence of Hepatitis B virus Infection in Tonga: Identifying High Risk Groups for Immunization with Hepatitis B Vaccine. *Int. J. Epid;* 15:4; 567-571: 1986.

10. Szmuness W, Much M.I, Prince M., Hoofnagle J.H., Cherubin C.E. Harley E.J. and Block G.H. On the role of sexual behaviour in the spread of Hepatitis B Infection. *Ann. Int. Med.* 83: 489-95: 1975.

11. Barin F., Perrin J., Chotard J. et al. Cross-sectional and longitudinal epidemiology of hepatitis B in Senegal. *Prog. Med. Virol*, 27: 148-162: 1981.

12. Prince, A.M., Whine T. and Pollock N. Epidemiology of hepatitis B infection in Liberian infants. *Infect. Immunity* 32: 675-680: 1981.

13. Greenfield C., Wankya B.M.W, Musoke R. and Osidiana V. An age related point prevalence study of markers of Hepatitis B virus Infection in Kenya. *E. Afr. Med J.*; 63 (1): 48-53; 1986.

14. Wankya B.M, Hansen, D.P., Ndingu, A.M., Feinstone S.F. and Purcell R.H. Sero-epidemiology of Hepatitis A and B in Kenya: A rural population survey in Machakos District. *E. Afr. Med. J.* 56 (1); 134: 1979.

15. Bowry T.R. Ahmad, Z., Chemtai A.K. Hepatitis B core antibody in volunteer blood donors in Kenya. *E. Afr. Med. J.* 58:570: 1981.

16. Greenfield C, Osidiana V., Karayiannis P., Galpin S., Musoke R., Jowerr T.P., Mati P., Tukei P.M. and Thomas H.C. Perinatal transmission of hepatitis B virus in Kenya, its relation to the presence of serum HBV-DNA and anti-HBe in the mother. *J. Med. Vir.* 19(2): 135-142: 1986.

17. McMahon B.J., Alword W.M., Hall D.B., Heyward W.L., Bender T.R. Francis D.P. and Maynard J.E. Acute Hepatitis B virus Infection: Relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis* 151: 599-603: 1985.

18. Beasley R.P., Hwang L.Y, Lin C.C. and Chien C.S. Hepatocellular carcinoma and Hepatitis B virus; A prospective study of 22, 707 men in Taiwan. *Lancet* (2): 1129-1133: 1981.

19. Melnick J.L. Epidemiology. Viral Hepatitis Edited by F.B. Hollinger, J.L. Melnick, W.S. Robinson. Raven Press. New York 1985.

20. Perillo R.P., Regenstein F.G., Bodicky C.J., Campbell C.R., Sanders G.E. and Sunwoo Y.C. Comparative efficiency of adenine arabinoside 5'monophoshate and prednisolone withdrawal followed by adeninine arabinoside 5' monophosphate in the treatment of chronic active hepatitis B. *Gastroenterology.* 88(3): 780-6:1985.

21. Omata M., Imazoki F., Yokosuka O., Ito Y., Uchiumi K., Mori J. and Okuda K. Recombinant leukocyte a interferon treatment in patients with chronic hepatitis B virus infection. Pharmacokinetics, tolerance and biologic effects. *Gastroenterology;* 88(4): 870-80:1985.

22. Progress in the control of viral hepatitis; Memorandum from WHO meeting *Bulletin of the World Health Organization* 66(4): 443-455, 1988.

23. Kew M.C., Houghton M., Choo Q.L. and Kuo G. Hepatitis C virus antibodies in southern African blacks with hepatocellular carcinoma. *Lancet* I :335: 873-4:1990.

24. Beasley R.P. Hwang L.Y., Lin C.C., Stevens C.E., Wang K.Y., Sun T.S., Hsieh F.J and Szmuness W. Hepatitis B Immune globulin (HBIG) efficacy in the interruption of perinatal transmission of hepatitis B virus carrier state. *Lancet* (2): 388-393, 1981.

25. Krugman S., Giles J.P. and Hamond J. Viral hepatitis type B (MS-2) Strain; Studies on Active immunization. *JAMA* **217**: 41-45: 1971

26. Szmuness W., Stevens C.E., Harkey E.J. Hepatitis B vaccine: Demonstration of efficacy in a controlled clinical trial in a high risk population in the United States. *New Engl. J. Med.* **303**:833-841,1980

27. Summary of Clinical findings on Engerix B, a genetically engineered yeast - derived Hepatitis B Vaccine. *Postgraduate medical Journal* 63(suppl. 2) 169-178, 1987.

28. Sherentz R.J. and Hoofnagle J.H. Antibody to Hepatitis B surface antigen may not always indicate immunity to hepatitis B virus infection. *New Engl. J. Med.* **309**: 1519, 1989.

29. Greenfield C, Osidiana V.O, Tukei P.M. Musoke R., Mati J., Loucq C., Fritzell B. and Thomas H.C. Cheaper Immunization against hepatitis B. *E. Afr. Med J;* **63**(1): 3-12: 1986.

30 .Beasley R.P. Long term outcome of hepatitis B vaccination - facts and figures. Asian Pacific Association for the study of liver, Scientific Meeting, Singapore, January, 1986.

31. The Gambian Hepatitis study group: Hepatitis B vaccine in the expanded programme of Immunization; the Gambian experience. *Lancet* (1): 1057 - 1060; 1989.

32. Oon C.J., Tan K.L., Goh K.T., Wong-Yong L., Viegas O., McCarthy T., Chan S.H. and Lee H.P. Evaluation of a low dose of Hepatitis B vaccine given within a childhood immunization programme in Singapore. *J of Infect.* **13** (3): 255-267: 1986.

33. Coursaget P. et al: Proceedings of the Asian Symposium on Strategies for Large-Scale Hepatitis B Immunization, Hong Kong; June 12-13th: 1986.

34. Stevens C.E. and Taylor P.E Hepatitis B vaccine: issues, recommendations and developments. *Seminars in Liver Disease* **6**: (1): 23-27: 1986.

35. Moyes C.O, Milne A., Dimitrakakis M, et al Very Low dose Hepatitis B vaccine in Newborn Infants; an economic Option for control in Endemic areas. *Lancet* (1): 29-30: 1987.