Surveillance Case Definitions of Epidemic-prone and Priority Communicable/ Infectious Diseases in Pakistan

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SURVEILLANCE CASE DEFINITIONS OF EPIDEMIC-PRONE AND PRIORITY COMMUNICABLE/INFECTIOUS DISEASES IN PAKISTAN

Chief FE&DSD,
National Institute of Health
Park Road, Islamabad (44000)
Pakistan

Email: eic.nih@gmail.com

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National Institute of Health, Park Road, Chak Shahzad,
Islamabad, Pakistan
Tel: +92 (51) 9255566 +92 (51) 9255237,
Fax: +92 (51) 9255099 Email: eic.nih@gmail.com,
info@nih.org.pk

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Preface

The healthcare delivery system of Pakistan is concurrently burdened both by the communicable and non-communicable diseases. Besides common infectious diseases such as Malaria, Tuberculosis, Hepatitis, bacterial and viral gastroenteritis, Pneumonia etc., emerging ailments like Multi Drug Resistance Organisms, HIV/AIDS, Dengue, Crimean Congo Hemorrhagic Fever (CCHF), Influenza and other zoonotic illnesses are continuously challenging the national health system. The Field Epidemiology & Disease Surveillance Division (FE&DSD), National Institute of Health is the lead unit for supporting provincial health departments and other stakeholders involved in infectious diseases investigation and response at the National level. In fulfillment of responsibilities assigned to it, the FE&DSD regularly disseminates requisite guidelines, advisories and seasonal awareness and alert letter (SAAL) to all concerned departments.

Due to the immense burden of communicable diseases, a Disease Early Warning System (DEWS) was initiated in Pakistan during 1999 in collaboration with World Health Organization. During the field investigations, small booklet comprising detailed introduction, case definitions, alert/ outbreak thresholds, preventive measures and case management of communicable/infectious diseases was developed. The first edition of the booklet was launched in 2001 and used throughout Pakistan as useful filed guide for surveillance officers and public health professionals. The booklet was later revised in years 2002, 2005, 2006, 2009 and 2012. However, the emerging infectious diseases and evolving challenges linked to it necessitated a thorough review of the document to meet the surveillance and response priorities.

The Disease Surveillance & Response booklet for Priority Infectious Diseases in Pakistan has been developed by the Field Epidemiology & Disease Surveillance Division, National Institute of Health, with active participation and involvement of more than 100 surveillance and disease experts representing different federal and provincial stakeholders from health and veterinary sectors, international partners and subject matter experts through multiple consultative meetings and discussions during 2018-19.

The current edition includes description on 47 infectious diseases with a list of national priority diseases including zoonotic diseases and annexures on Infection Prevention and Control (IPC), Integrated Disease Surveillance and Response (IDSR), outbreak investigation and case reporting forms. It is intended be easily understandable to facilitate the tasks being performed by clinicians, surveillance officers and other field staff including lab. technicians and health communication officers.

Professor Maj. Gen. Aamer Ikram, SI(M)
Executive Director

Introduction

The importance of surveillance data about reportable diseases cannot be overstated. Without proper data, trends cannot be accurately monitored, unusual occurrences of diseases might not be detected, and the effectiveness of intervention activities cannot be evaluated. Uniformity in reporting criteria, simplicity and timeliness of surveillance data, are fundamental to have authentic information. Developing effective and efficient national surveillance and response systems is important for national, regional and global health security.

This booklet has been developed as a comprehensive guide for surveillance and response to epidemic-prone diseases in Pakistan. It is an updated version of the “Case Definitions Booklet” published earlier by the Epidemic Investigation Cell, Public Health Laboratories Division, National Institute of Health. Based on the current operational needs of the public health, significant changes have been made to the earlier editions. It describes the steps needed for investigation of the source of the disease, sample collection, and documentation of the risk factors, cases and contactsduring outbreaks. The booklet also elaborates the signs and symptoms of the infectious diseases of public health importance to assist the healthcare professionals in timely recognition and reporting as “notifiable” diseases to the health authorities.

The surveillance case definitions given in this booklet have been modified from different authentic sources like WHO, CDC and Euro-surveillance sites and needs to be used for surveillance purposes. Clinical case categorization may be entirely different in clinical set-ups. In outbreak situations, these case definitions may further be tailored based on time, place and person.

The information and recommendations in this booklet are intended for use by the disease surveillance managers and officers, IHR focal points, health authority at point of entry, hospital managers, clinicians and infection control officers, district health management teams, nursing officers, medical and nursing educators, communication officers, laboratory personnel and public health experts.

This booklet is not an alternate to the text books rather must be used as a guidebook for decision making and guidance in the field. It is earnestly hoped that this document would augment the judgment of physicians, public health officials and create sound basis for actions to reduce morbidity and mortality associated with the epidemic-prone diseases in the country.

Dr. Rana Muhammad Safdar
Chief, FEDSD

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Annexures:

List of Acronyms

AFP	Acute flaccid paralysis
ARI	Acute respiratory infection
AES	Acute encephalitis syndrome
ART	Antiretroviral therapy
CFR	Case fatality rate
CDC	Centers for Disease Control and Prevention
CCHF	Crimean-Congo hemorrhagic fever
CSF	Cerebrospinal fluid
DHF	Denguehemorrhagic fever
DSS	Dengue shock syndrome
DHMT	District Health Management Team
EHF	Ebola hemorrhagic fever
EDOH	Executive District Officer (Health)
ELISA	Enzyme-linked Immunosorbent Assay
EPI	Expanded Program on Immunization
EEG	Electroencephalogram
GHSA	Global health security agenda
Hib	*Hemophillus influenza type b*
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HDV	Hepatitis D Virus
HEV	Hepatitis E Virus
HSV	Herpes simplex virus
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
IPC	Infection Prevention and Control
ILI	Influenza-like Illness
ITN	Insecticide treated nets
IPC	Infection prevention and control
IDSR	Integrated Disease Surveillance and Response
IEC	Information Education and Communication
IHR-2005	International Health Regulations 2005

IV	Intra Venous
JE	Japanese Encephalitis
LBW	Low birth weight
NA	Not Available
Nm	Neisseria meningitides
NNT	Neo-Natal Tetanus
NCD	Non-communicable disease
MDR	Multi-drug-resistant
MERS-CoV	Middle East Respiratory Syndrome Corona Virus
MNHSR&C	Ministry of National Health Services Regulation and Co-ordination
MRI	Magnetic resonance imaging
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PPEs	Personal protective equipments
PoE	Points of Entry
PLHIV	People living with HIV
PAGE	Polyacrylamide gel electrophoresis
PUI	Patient under Investigation
RRT	Rapid response team
SRAS	Severe Acute Respiratory Syndrome
SARI	Severe Acute Respiratory Infection
STI	Sexually transmitted infection
RT-PCR	Reverse transcriptase-polymerase chain reaction
THQs	Tehsil Headquarters Hospitals
VPDs	Vaccine preventable diseases
XDR	Extensively drug resistant
WHO	World Health Organization
XIARO	Japanese Encephalitis Vaccine, Inactivated, Adsorbed

Surveillance

Surveillance is the ongoing process of systematic data collection, collation, interpretation and dissemination from health-related events or diseases. The collected information can be used to identify the high risk populations and their behaviors, control and prevent the disease, monitor the trends of diseases, changes in infectious agents in different clusters, health planning and resource allocation to manage the issues and also will be a valuable archive to do the research/reference work in future.

Types of Surveillance: Surveillance can be classified as:

1. Active Surveillance, Passive Surveillance and Sentinel (Facility-based) Surveillance
2. Indicator and Event based Surveillance

Active surveillance: system gathers disease information through visiting health facilities, talking to health-care providers and reviewing medical records to identify suspected cases of disease under surveillance by designated staff. It is more appropriate and complete than passive surveillance and is usually done in an area where an outbreak happens or is suspected for to gather the full information of cases or when a disease is targeted for eradication or elimination. Active case finding of the disease in affected area is an example of active surveillance. It is less frequently done because it requires considerably huge resources in terms of finances and workforce and also time.

Passive Surveillance: system usually gathers disease information from all heath care facilities/providers, laboratories, hospitals and private practitioners on a prescribed format and time through regular reporting mechanism. It is the less expensive and most common type of surveillance system done for communicable diseases and in emergencies. It relies on an extensive network of health workers so it is difficult to ensure completeness and timeliness of data.

In the **Sentinel Surveillance system,** it selects either randomly or intentionally, a small group of health workers from whom to gather data. It can be the best surveillance if more intensive efforts on each case is applied to collect necessary data which cannot be obtained through a passive system. It requires more time and resources, to produce more detailed data on cases of illness. Data collected can be used to signal trends, identify outbreaks and monitor the burden of disease in a community, providing a rapid, economical alternative to other surveillance methods. Sentinel surveillance is usually conducted only in selected locations, however, it may not be as effective for detecting rare disease or diseases that occur outside the catchment areas of the sentinel sites.

Currently, two other terminologies are widely used to identify and track infectious diseases and other public health events i.e. indicator-based surveillance (IBS) and event-based surveillance (EBS) systems and both are essential components of national surveillance system.

Event-based surveillance system (EBS) is based on the rapid capture of information about events that are a potential risk to public health. A well implemented, EBS system serves as an early warning signals an outbreak. This system focuses on reports, stories, rumors and other information about health events transmitted either through formal channels, i.e. established routine reporting systems, or through informal channels, i.e. media, internet blog, health workers and nongovernmental organizations reports that could be a serious risk to public health. Information received through EBS needs rapid assessment for the risk to public health and appropriate response.

Indicator-based surveillance system (IBS) relies on collecting data of specific diseases from health care providers to public health officials through an established national system of reporting. An example of information obtained through indicator-based surveillance might be reports received on a regular basis and entered routinely into a disease-reporting database. The disease reports may be lab confirmed or based on clinical observation.

Surveillance systems aims to provide information of selected communicable diseases that is required for public health action. An effective surveillance system has the following functions:

- Detection and notification of health events
- Collection and consolidation of relevant data
- Investigation and confirmation of cases or outbreaks
- Routine analysis, interpretation and creation of reports
- Feedback of information to those providing the data by actions

- Monitor the patterns/trends
- Reporting data to the next administrative level

Surveillance Case Definition: It is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health workforce to classify and enter their required information in predefined format. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

Outbreak Case Definition: Establishing a case definition, defining the criteria by which a case can be considered can be tricky, particularly in the initial phases of the outbreak investigation. The case definition needs to be specific enough to identify true cases of disease and also should be broad and sensitive enough to be able to identify most, if not all of the cases. The case definition may also be modified during the investigation and make it more specific by adding specific clinical, radiological or lab information which can help to categorize the disease in probable and confirmed cases. Case definitions may include four types of information:

- Personal information of cases like age, gender, nature of work, address
- Clinical information like signs and symptoms (lab results, if available)
- Limits with respect to the working and residing location of the case
- Specified time period for this particular outbreak

1. Acquired Immune Deficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV) Infection

Introduction

Human immunodeficiency virus (HIV) infects cells (CD4 cell a type of T cell) of the immune system, destroying or impairing their function. Infection with the virus results in progressive deterioration of the immune system, leading to "immune deficiency." The immune system is considered deficient when it can no longer fulfill its role of fighting infection and disease. Infections associated with severe immunodeficiency are known as "opportunistic infections", because they take advantage of a weakened immune system. Acquired immunodeficiency syndrome (AIDS) is a term which applies to the most advanced stages of HIV infection and is often characterized by the presence of any of the more than 20 associated opportunistic infections, complications or cancers.

Infectious Agent—*Human Immunodeficiency Virus (HIV)* is of two types; *HIV-1* is dominant, more virulent and more infectious. *HIV-2* is less pathogenic than *HIV-1* and is largely confined to West Africa

Mode of Transmission—

- Unprotected sexual intercourse (vaginal or anal) with an infected partner,
- Contaminated needles, syringes and/or other sharp injecting equipments.
- Infected mother to her infant during pregnancy, childbirth and through breastfeeding
- Transfusion of HIV infected blood and blood products

Incubation Period—On average, the time from HIV infection to clinical AIDS is 8 to 10 years, though AIDS may be manifested in less than 2 years or be delayed in onset beyond 10 years.

Case Definition

Confirmed Diagnosis For Adults and Children above the age of 18 months—In adults and children 18 months or older, HIV infection diagnosis is based on: Positive HIV antibody testing (rapid or laboratory-based enzyme immunoassay) which is confirmed by a second HIV antibody test (rapid or laboratory-based enzyme immunoassay) relying on different antigens or of different operating characteristics; and then performing the third HIV antibody test (rapid or laboratory-based enzyme immunoassay) test to confirm the diagnosis in Pakistan and/or; positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination.

For Children younger than 18 months—HIV infection diagnosis is based on: Positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination taken more than four weeks after birth. Positive HIV antibody testing is not recommended for definitive or confirmatory diagnosis of HIV infection in children until 18 months of age.

Case Definition for AIDS—Diagnosis in Adults and children above 5 years: Diagnosis of AIDS is based on WHO clinical stages 3 and 4 and/or; Immunological criteria for diagnosing advanced HIV in adults and children five years or older with confirmed HIV infection: CD4 count less than 350 per 3 mm of blood in an HIV-infected adult or child. and/or;

Immunological criteria for diagnosing advanced HIV in a child younger than five years of agewith confirmed HIV infection:

CD4 less than 30% those younger than 12 months

CD4 less than 25% in those younger than 12–35 months

CD4 less than 20% in those younger than 36–59 months

Lab Confirmation—Lab confirmation of HIV is done by detecting HIV antibody in serum samples using Enzyme-linked immunoassay (ELISA or EIA) or WHO-recommended three rapid tests. When the first test is positive, it must be confirmed with two other tests that are methodologically and/or antigenically independent. If either the second or third assay is non-reactive, the case is “Indeterminate”.

For neonates, Viral load determination is required for confirmation.

Specimen Collection—Collect 5 ml of blood/serum observing all standard precautions.

Storage—For sero-diagnosis refrigerate specimen at 4°C then transport to lab.

For antigen detection by PCR immediately freeze the specimen at –20°C if delay is anticipated.

Transportation—Transport specimens with complete lab request form along with Biohazard label within 24–28 hrs of collection maintaining cold chain (preferably).

Case Management

- When screening test and ELISA becomes positive in a suspected patient, it should be referred to AIDS Control Program/HIV treatment Centre for further confirmation and treatment.
- In case of a confirmed case with HIV infection or AIDS provide high quality care and support to all people living with HIV (PLHIV) that includes counselling, psychosocial support, treatment for opportunistic infections (e.g. TB), palliative care and access to antiretroviral therapy.

Preventive Measures

- Reduce sexual transmission of HIV by the uptake of appropriate HIV preventive measures including safe sex practices and promotion of the use of condoms.
- Modify the risk behavior of people in the community through "behavior change communication" (BCC).
- STI control specially for sex workers, using the syndromic STI management approach with partner notification and promotion of safer sex.
- Preventing the transmission of HIV from infected pregnant women to infants by the use of antiretroviral therapy (ART) i.e. Teneforvir, Emtricitabine and Raltegravir throughout pregnancy. Women who have not received ART during pregnancy should be given intravenous Zidovudine during labor and the neonate should be given oral Zidovudine for a duration of 6 weeks. Unnecessary obstetrical invasive procedures such as artificial rupture of membranes or episiotomy should be avoided.

- Occupational exposure: If a person has had occupational exposure to HIV, the following regimen is preferred; Emtricitibine plus Tenofovir along with Raltegravir or Dolutegravir for a duration of 4 weeks depending on the type of exposure.

Blood Safety

- HIV screening of all blood products using recommended techniques
- Recruitment of safe blood donor pool.
- Avoid un-necessary blood transfusion.

Vaccination

There is a high risk of disseminated BCG disease developing in HIV-infected infants, thus BCG vaccine should not be given to infants who are known to be HIV positive.

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2. Ameobiasis

Introduction

Amoebiasis is a contagious disease, and occurs in areas or countries with poor sanitation, particularly in the tropics. Amebiasis is distributed more in adults and rare in children under the age of five. *Entamoeba histolytica* mainly exist in two forms, the persistent trophozoite and infectious cyst. It is transmitted by fecal-oral route, predominantly from tainted water or by unhygienic food handling. The ingestion of cysts which resist the chlorination of water and possibly survive for a long time in moist environments. Cysts are typically defecated with solid stools, present in diarrhoeal stools of patients with acute phase of disease. Trophozoites are fragile and cannot survive in the environment. Acute diarrhoeal patients do not pose a significant risk to other person because at that stage, primarily contain fragile trophozoites and do not survive in the HCL medium in the stomach. For appropriate management and treatment, laboratory confirmation for *E. histolytica* infection is mandatory for all patients with visible signs and symptoms.

Clinical Picture

Amoebiasis develops asymptomatic infection in most of the cases (90%), although excretions of infectious cyst potentially pose an infectious risk. Infection with *E. histolytica* can develop mild diarrhoea, and over the period chronic diarrhoea to fulminant dysentery. Extra intestinal infection may occur (e.g., hepatic abscess).

Infectious Agent—Protozoan parasite *Entamoebahistolytica*.

Host/Reservoir—The only known natural hosts are humans.

Period of Communicability—The disease is communicable for as long as the infected person excretes *E. histolytica* cysts, which can continue for years.

Mode of Transmission—Transmission may occur via ingestion of food and water contaminated by cysts (usually via contaminated water supplies), person-to-person contact, oral-anal sexual contact or by direct inoculation, such as colonic irrigation.

Incubation Period—2 to 4 weeks or but can be persists for months after exposure.

Seasonality—Throughout the year: Outbreaks have occurred following water supply contamination, as the cysts are resistant to chlorine.

Alert Threshold—Two or more suspected cases clustered in time and Place.

Outbreak Threshold—Five or more confirmed cases clustered in time and Place with a common or suspected common source.

Case Definition

Suspected Case—Intestinal Ameoebiasis: Patient with abdominal discomfort and diarrhea (often with blood and mucus) alternating with periods of remission or constipation, with or without fever.

Extra intestinal Ameobiasis: Fever, anorexia, weakness, and loss of weight steadily progress with gradually increasing pain/tenderness in right hypochondrium, or epigastrium±history of Ameoebiasis in the past.

Probable Case—Intestinal Ameoebiasis: Suspected case with demonstration of *E. histolytica*-like cysts or trophozoitesin stool.
Extra intestinal Ameobiasis: Suspected case with an abscess/cystic mass on Ultrasound or CT scans with demonstration of specific antibody against *E. histolytica* by hemagglutination or ELISA.

Confirmed Case—Intestinal Ameoebiasis: Suspected case that is laboratory confirmed.

Extra intestinal Ameobiasis: Parasitological confirmed infection of extra intestinal tissue, or among symptomatic persons (with clinical or radiographic findings consistent with extra intestinal infection), demonstration of *E. histolytica trophozoites* in extra-intestinal tissue/aspirate.

Lab Confirmation—Lab confirmation

Intestinal Ameobiasis:

Demonstration of cysts or trophozoites of *E. histolytica* in stool, OR

Demonstration of trophozoites in tissue biopsy or ulcer scrapings by culture or histopathology.

Extra intestinal Ameobiasis: Demonstration of E. histolyticatrophozoites in extra-intestinal tissue

Microscopy relies on observation of cysts and trophozoites in faeces, colonic scrapings, aspirates and tissue samples. Demonstration of trophozoites in tissue biopsy or ulcer scrapings or demonstration of E. histolyticatrophozoites in extraintestinal tissue.

Serological tests:

The detection of antibodies is of particular use in Ameobic Liver Abscess (ALA) patients and the sensitivity has been reported to be about 100%. Serum IgG antibodies will persist for years after infection, but IgM antibodies are present in the acute phase and may be detected by ELISA methods.

Molecular testing:

Both conventional and real-time PCR methods have been used for identification with real-time PCR and considered to be the "method of choice".

Timings—A minimum of 3 specimens taken on separate days is recommended to increase the yield from 50% for a single specimen to 85–90% due to the intermittent excretion of organisms in the stool. The sample should be examined within 1 hr. of collection to search for motile trophozoites which may contain RBC's however in patients who do not present with acute dysentery, trophozoites will not contain RBCs.

Specimen Collection—Submit a walnut-size (about 2 Tb. sp liquid) portion of fresh stool in a clean, leak-proof container.

Packaging—Properly packed and labelled leak proof Screw capped container.

Storage—Do not refrigerate the sample.

Transportation—Transport to lab **IMMEDIATELY** at room temperature.

Case Management

For symptomatic intestinal infection and extra intestinal disease, treatment with Metronidazole or Tinidazole with course of 10 days should be followed by treatment with Iodoquinol or Paromomycin.

Asymptomatic patients infected with E. histolytica should also be treated with Iodoquinol or Paromomycin.

Contacts Management

Contacts should be provided with advice on personal hygiene and should be tested for E. histolytica infection for the purpose of early detection. Contacts having positive microscopy or with diarrhoeal symptoms should be managed as cases.

Preventive Measures

- No vaccine is available for Amoebiasis.
- Drink boiled/safe water.
- Good personal hygiene should be practiced. Hand washing with soap and water is typically important specially after using the toilet, changing diapers, and before handling or preparing food. The toilet seats, flush handles, taps and wash basins should be cleaned with detergent and hot water after use, followed by a household disinfectant.
- Proper sanitation and chlorination of water sources should be ensured.
- It is recommended to stay away from work, school, and serving food outside the home until 48 hrs after resolution of an episodes of diarrhoea.

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3. Anthrax

Introduction

Anthrax can be found naturally in soil and commonly affects domestic and wild animals around the world. Livestock or other herbivores acquire infection from consuming contaminated soil or feed. Humans generally acquire the disease directly or indirectly from infected animals or occupational exposure to infected or contaminated animal products.

It has been categorized as an agent of bioterrorism and has a high case fatality rate.

Clinical Picture

An illness with acute onset characterized by distinct clinical symptoms based on the site of spore entry:

- **Cutaneous:** Skin lesion evolving over 2 to 6 days from a papular through a vesicular stage, to a depressed black eschar, invariably accompanied by oedema that may be mild to extensive.
- **Inhalational (pulmonary):** Brief prodrome resembling acute viral respiratory illness, followed by rapid onset of severe shortness of breath, and high temperature, with X-ray evidence of mediastinal widening.
- **Gastrointestinal:** Abdominal symptoms characterized by nausea, vomiting and anorexia followed by fever.
- **Injectional:** Recently documented, occurs through contaminated Heroin IV use, characterized as an independent disease entity or as a special type of Cutaneous Anthrax with massive edema, necrotizing fasciitis in many cases with mortality of about 30%.

Infectious Agent—Spore-forming Gram-positive, rod-shaped bacteria known as *Bacillusanthracis*.

Host/Reservoir—Animals (normally herbivores, both livestock and wildlife), contaminated soil and articles.

Mode of Transmission—

1. Inhalation of spores
2. Ingestion of spores
3. Direct or indirect contact with contaminated animals or animal products.
4. Person-to-person transmission of B anthracis does not occur with GI or Inhalational Anthrax but has been reported rarely with Cutaneous Anthrax.

Incubation Period—From 1 to 7 days, even up to 60 days is possible.

Seasonality—Animal anthrax outbreaks due to soil-borne infections usually occur during warmer seasons

Alert Threshold—One suspected (clinical) case

OutbreakThreshold—One laboratory confirmed case

Case Definition

SuspectedCase—Any case that is compatible with the clinical description of Cutaneous, Pulmonary, Gastrointestinal, Injectional or Meningeal Anthrax AND has an epidemiological link to confirmed or suspected animal cases or contaminated animal products.

Probable Case—A suspected cases that has a positive reaction to allergic skin test (in non-vaccinated individuals).

Confirmed Case—A suspected case that is laboratory confirmed by isolation of *B Anthracis,* Anthrax electrophoretic immunotransblot (EITB) reaction, or demonstration of *B. Anthracis* in a clinical specimen by immunofluorescence

Lab Confirmation:

- Laboratory confirmed by one or moreof the following:
  - o Isolation of *B. anthracis* from a clinical specimen (e.g. blood, skin lesions and discharge fluids)
  - o Demonstration of *B. anthracis* in a clinical specimen by microscopic examination of stained smears (vesicular fluid, blood, cerebrospinal fluid, pleural fluid, stool) is suggestive

- o Culture, Positive serology (ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test) and molecular tests

Note: *it may not be possible to demonstrate B. anthracis in specimens if the patient has been treated with antibiotics.*

Timings—Samples should be collected prior to antimicrobial therapy

Specimen Collection—Organisms can easily be cultured from the blood, and may also be cultured from skin lesion exudates, pleural fluid, cerebrospinal fluid (CSF) and stool.

For serological testing, serum is required and freeze the serum and Store the specimen at –20° until shipped

Packaging—Triple Packaging

Storage—2°C–8°C

Transportation—Must be transported properly packaged with a duly filled case report form

Case Management

- Isolation/Qurantine
- Patients with severe disease of Anthrax need to be hospitalized.
- Treatment of patients suspected of having Systemic/Inhalational/ Gastrointestinal Anthrax should be started urgently and should include:
  - o Antimicrobial combination therapy (Ciprofloxacin plus Meropenem plus Linezolidfor possible or confirmed meningitis, in patients with no meningitis treat with Ciprofloxacin 400 bid iv plus Clindamycin Or Linezolid x 2 weeks followed by oral Ciprofloxacin OR Doxycyclin to complete 60 days)
  - o Antitoxin (Raxibacumab, Obiltoxaximab or Anthrax immunoglobulin)
  - o Drainage of pleural effusions
  - o Supportive care, and consideration of adjunctive glucocorticoids

Preventive Measures

1. Antibiotics are recommended for those who have been exposed to anthrax but have not yet developed symptoms. Ciprofloxacin and Doxycycline are two antibiotics that can be used to prevent anthrax.
2. Public awareness programs regarding the danger of contact with contaminated animals or their meat and products should be rolled out.
3. Regular vaccination of animals for the prevention of animal anthrax is recommended along with safe disposal of anthrax-infected carcasses. The most efficient method of disposal of infected carcasses is incineration in a manner that ensures heat sterilization of the surrounding soil.

Immunization

- Anthrax Vaccine Adsorbed (AVA): Vaccines have been developed for human use and not typically available for the general public. Currently, US FDA has not approved the vaccine for use after exposure.
- Anthrax vaccine is routinely used in three groups of adults, 18 to 65 years of age who may be at risk of occupational exposure to anthrax.
- Certain laboratory workers who work with anthrax.
- People who handle livestock/animals or animal products, such as veterinarians.

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4. Bacterial Meningitis (unspecified, not meningococcal)

Introduction

A serious and fatal inflammation of the membranes (meninges) that surround the brain and the spinal cord. Death can occur in few hours if left untreated. Most people with meningitis recover, permanent disabilities such as brain damage, hearing loss, and learning disabilities can result from the infection. Pediatric bacterial meningitis is a life-threatening illness and leaves some survivors with significant sequelae. Meticulous attention must be paid to appropriate treatment and monitoring of patients.

Mortality depends on the infectious agent, the age of the patient, patient's health and the promptness of diagnosis and treatment.

Clinical Picture

The classic symptoms are; Severe headache, fever, altered mental status fits and neck rigidity. Clinical features in neonates include poor feeding, lethargy, irritability, shrill cry, fever, hypothermia, seizures, bulging fontanelle, and hypertonia.

Infectious Agent—Leading causative agents of bacterial meningitis in:

- Newborn: *Streptococcus pneumoniae, group B Streptococcus, Escherichiacoli and Listeria monocytogenes*
- Children: *Streptococcus pneumoniae, Neisseria meningitides, Haemophilus Influenzae type B, group B Streptococcus*
- Teens: *Neisseria meningitides, Streptococcus pneumoniae*
- Adult: *Streptococcus pneumoniae, Neisseria meningitides, Haemophilus Influenzae type B, Listeria monocytogenes, group B Streptococcus*

Host/Reservoir—Humans are the only natural reservoir

Period of Communicability—This depends on the bacterial pathogen causing meningitis. It may be contagious during the incubation period and for about an additional seven to 14 days. And they can be infectious for much longer (many days to months) if the person becomes a carrier.

Mode of Transmission—Bacterial meningitis is NOT spread through casual contact or the airborne route; however, some bacteria can spread from person to person via close or lengthy contact with a patient (Haemophilusinfluenza type b (Hib) meningitis) through respiratory and throat secretions. Most bacteria are not as contagious as viruses. One can get meningitis from *Listeria monocytogenes* by eating contaminated food

Incubation Period—Depends on causative agent. The symptoms of bacterial meningitis can appear quickly or over several days. Typically they develop within 3 to 7 days after exposure

Case Definition

Suspected Case—Any person with sudden onset of fever and one of the following signs:

Neck stiffness, altered consciousness/convulsions with no other alternative diagnosis, or other meningeal sign. Neonates may exhibit additional signs as mentioned above

Probable Case—A suspected meningitis case with CSF examination showing at least one of the following:

Turbid appearance; Leukocytosis (>100 cells/mm^3); OR Leukocytosis (10-100 cells/mm^3) AND either an elevated protein (>100 mg/dl) or decreased glucose (<40 mg/dl)

Note: *If protein and glucose results are not available, diagnose using the first two conditions (i.e. turbid appearance or leukocytosis >100 cells/*mm^3*)*

Confirmed Case—Any suspected meningitis case that is laboratory-confirmed by growing i.e. culture or identification through Gram stain, antigen detection, immuno-chromatography, PCR or other methods a bacterial pathogen cultured from the CSF or from the blood with a clinical syndrome consistent with bacterial meningitis.

Lab Confirmation:—Bacterial meningitis score
Components of the bacterial meningitis score as follows:

- Positive CSF Gram stain
- CSF or blood culture

Definitive Diagnosis:

Definitive diagnosis is based on the following:

Bacteria isolated from the CSF obtained via lumbar puncture

Meningeal inflammation demonstrated by increased pleocytosis, elevated protein level, and low glucose level in the CSF

Timings—Cerebrospinal fluid (CSF) should be processed within one hour after collection or inoculated into Trans-Isolate (T-I) medium for transport if processing within 2 hours is not feasible.

Specimen Collection—CSF is the best clinical specimen to use for isolation, identification, and characterization of the etiological agents.

Blood should be collected for culture when a spinal tap is contraindicated or cannot be performed for technical reasons. Bacteremia can occur with or without meningitis.

Packaging—Specimen should be collected and packaged as close to shipping time as possible. Place specimen into zip-lock type bag, seal bag and transport withtriplepackaging.

Storage—Ambient or Room Temperature. DO NOT REFRIGERATE ORFREEZE. Protect specimen by wrapping in bubble-wrap or toweling.

Transportation—Blood specimens should be immediately inoculated into a blood culture bottle and transported as soon as possible for overnight incubation and growth of bacteria.

If a delay of several hours in processing CSF specimens is anticipated and T-I medium is not available, incubating the specimens (with screw-cap loosened) at 35-37°C with ~5% CO_2 (or in a candle-jar) may improve bacterial survival.

Case Management

Treatment for Pediatric age group:

Bacterial meningitis treatment should be started as soon as possible. IV antibiotics are required; if cause is unknown, agents can be based on child's age, as follows:

- <30 days, ampicillin plus an Aminoglycoside plus a Cephalosporin. If there is high risk of MRSA than add Vancomycin.

- 30–60 days, Ampicillin plus an aminoglycoside plus a Cephalosporin. If there is high risk of MRSA than add Vancomycin
- In older children, a Cephalosporin (Cefotaxime/Ceftrioxone) plus Ampicillin or Vancomycin (if MRSA suspicion is high)

Duration of Therapy

- Vancomycin plus either Ceftriaxone or Cefotaxime
  - o *Neisseria meningitidis* – 7 days
  - o *Haemophilusinfluenzae* – 7 days
  - o *Streptococcus pneumoniae* – 10–14 days
  - o *S agalactiae (GBS)* – 14–21 days
  - o Aerobic gram-negative bacilli – 21 days or 2 weeks beyond the first sterile culture (whichever is longer)
  - o *Listeria monocytogenes* – 21 days or longer

American Academy of Pediatrics recommends that duration of therapy should not be shorter than 5 days for meningococcus, 10 days for *H influenzae,* and 14 days for *S pneumoniae*

Treatment for Adults:

A combination of Cefotaxime/Ceftrioxone plus Vancomycin plus Dexamethasone

If *listeria* is a consideration in old age add Ampicillin.

For Contacts:

Antibiotics may be recommended for close contacts of a person with meningococcal meningitis and family members of a person who develop a serious Hib infection

Preventive Measures

Antibiotics are recommended for close contacts and family members of a person with meningitis, especially if they are living in the samehouse those who have spent 4 hours or more with the index patient for at least 5 of the preceeding 7 days before hospitalization of the patient.

Preventive therapy has been shown to reduce mortality and morbidity and consists of the following:

- Chemoprophylaxis: Rifampin, Ceftriaxone and Ciprofloxacin or Ciprofloxacin and Ceftriaxone.

- *Haemophilusinfluenzae* type b (Hib): Rifampin chemoprophylaxis for contacts of index cases of invasive Hib disease; MenHibrix provides immunization against Hib and meningococcal serogroups C and Y.
- *Neisseria meningitidis*: Quadrivalent (i.e., A, C, Y, W-135) meningococcal conjugate vaccine recommended for high-risk groups.

Appropriate precautions in the hospital depending on the causative agent appropriate hand washing for bacterial meningitis, and respiratory droplet precautions are recommended until 24 hours after the start of treatment.

Vaccination:

Vaccines are available for the following meningitis causing bacteria; *Streptococcus pneumoniae* and *Haemophilusinfluenzae* type b (Hib)

Use of Hib and pneumococcal vaccines decreases the likelihood of infection from these agents. These vaccines are part of the EPI schedule and parents should be encouraged to complete the immunization schedules.

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5. Bloody Diarrhoea/Dysentry/Shigellosis

Introduction

An infection of the lower gastrointestinal tract. The disease is more dangerous than other gut pathogens because it can penetrate the lining of the intestine and cause severe inflammation of the intestine and systemic complications and can result death**.**

Clinical Picture

Gastroenteritis, bloody mucoid diarrhea, abdominal cramps, fever and rectal pain.

- *S. dysenteriae* usually causes a more severe illness possibly with marked prostration and paediatric febrile convulsions. This may also be associated with toxic megacolon and haemolytic uraemic syndrome.
- *S. flexeneri* and *S. boydii* may also cause severe diseases while *S. sonnei* usually causes mild symptoms.

Infectious Agent—*Shigella dysenteriae, Shigella flexneri, Shigella boydii and Shigellasonne*i

Host/Reservoir—Humans are the most common reservoir/host; infection has been observed in primates also.

Period of Communicability—Agents begin to be shed in feces 4 weeks after infection, and it is communicable as long as the organisms are present in faeces. Although rare, asymptomatic carriers can also spread the infection for up to some months.

Mode of Transmission—Faecal-oral route, particularly contaminated water and food and from person to person

Incubation Period—

- Depends on the serotype.
- It varies from 12 hours to 07 days but is usually 1–3 days

Seasonality—Peak in summers

Alert Threshold—03 or more cases in one location are an alert and require an immediate investigation.

Outbreak Threshold—Six (6) or more cases in one location with one lab confirmed case of *Shigella sp.*

Case Definition

Suspected Case—A case with gastroenteritis, bloody mucoid diarrhea, abdominal cramps, fever and rectal pain

Probable Case—A clinically compatible case that is epidemiologically linked, i.e. is a contact to a confirmed case or a member of a risk group defined by public health authorities during an outbreak.

Confirmed Case—A case that meets the confirmed laboratory criteria for diagnosis i.e. Isolation of *Shigella* species from a clinical specimen.

Timings—Collect specimen before the initiation of antibiotic therapy and send it to lab ASAP

Specimen Collection—

- Collect 5 gram of stool and send it to lab with request slip
- If there is delay in sample sending, insert a sterile cotton swab into stool and keep the swab in Cary-Blair transport medium and transport.

Packaging—Each individually labelled sample, should be placed in sealable plastic bags or pouches containing absorbant material and transported

Storage—

- Transport stool specimen in Cary-Blair transport medium at ambient temperature.
- Cold chain or ice packs are not required during transport

Transportation—Cary-Blair transport medium or alkaline peptone water in transport boxes. Use appropriate triple packaging. Send full patient information along with the laboratory test request.

Case Management

- Most cases of *Shigella* are mild and self-limiting, so are treated with oral rehydration therapy, rather than with antibiotics
- Treat dehydration with oral rehydration salts or intravenous fluids if severe. Treatment of dehydration is life saving in severe case.
- Treatment with antimicrobials, will decrease the severity and reduce the duration of illness in severe cases. If antimicrobials used are effective, clinical improvement should be noted within 48 hours.
- Refer seriously ill or severely malnourished patients to hospital immediately.
- Check the results of antimicrobial sensitivity tests with the laboratory. Give an antimicrobial agent suggested in positive culture and sensitivity test report. Consider Metronidazole if there is possibility of *amoebic* dysentery (suggested by Stool R/E or microscopy)

Preventive Measures

Prevention Measures and Vaccination

- General recommendations include the use of safe drinking water, chlorination of unreliable water sources, strict hand washing practices, proper cooking and refrigeration of food items.
- Eat only thoroughly cooked food that is still hot.
- Avoid use of raw vegetables and fruits that cannot be peeled without proper washing.
- Avoid consumption of salads, food and beverages from street vendors.
- Food should be kept away from flies. Hygiene sessions for safe water and food habits should be conducted in the community.
- Involve Government line departments for the proper sanitation and safe drinking water supply to the community.

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6. Botulism

Introduction

Botulism is a rare and potentially fatal illness caused by a toxin, produced by the bacterium *Clostridium botulinum*. Botulism can be spread in several different ways like Food borne botulism, Wound Botulism, Infant Botulism, Adult intestinal toxemia and Iatrogenic Botulism.

All forms of Botulism can be fatal and are considered medical emergencies. Food borne Botulism is a serious, potentially fatal disease and serious paralytic illness caused by a nerve toxin. Food borne Botulism is a public health emergency because many people can be poisoned by eating a contaminated food.

Clinical Picture

- The classic symptoms include double vision (diplopia), blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness.
- Infants with Botulism may present with lethargy, poor feeding, constipation, weak cry, and poor muscle tone.
- If untreated, these symptoms may progress to cause paralysis of the respiratory muscles, arms, legs, and trunk.
- Botulism can result in death due to respiratory failure. Patients who survive an episode of Botulism poisoning may have fatigue and shortness of breath for years and long-term therapy may be needed to aid recovery.

Case Fatality

- Food borne Botulism carries an overall mortality rate of 5–10%.
- Wound Botulism carries a mortality rate that ranges from 15–17%.

The risk of death due to infant Botulism is usually less than 1%.

Infectious Agent—*Clostridium botulinum*, and rarely *C. butyricum* and *C. baratii*

Host/Reservoir—

- Spores are found in soil
- Home-canned food, vegetables, fruit and fish products are the most common sources of botulism
- Botulinum toxin retains much of its activity in untreated water and beverages for up to 70 days

Period of Communicability—2 weeks approximately

Mode of Transmission—

- No instance of person-to-person spread have ever been documented for botulism.
- Food borne botulism caused by ingestion of botulinum toxins through ingestion of contaminated canned food is caused by *C. botulinum*.
- Wound botulism occurs when *C. botulinum* spores germinate within wounds. Injection drug users are at increased risk for wound botulism.
- Infant botulism occurs when *C. botulinum* spores germinate and produce toxin in the gastrointestinal tract of infants.

Incubation Period—

- Food borne botulism: 12–72 hours after toxin ingestion with a range of 2 hours to 8 days.
- Infants botulism: up to 30 days
- Wound botulism: 4–14 days.

Case Definition

Suspected Case—Ingestion of botulinum toxin results in an illness of variable severity. Common symptoms are diplopia, blurred vision, and bulbar weakness. Symmetric paralysis may progress rapidly.

Probable Case: Depends on type of Botulism

Food borne:

- **Probable:** A clinically compatible case with an epidemiologic link (e.g., ingestion of a home-canned food within the previous 48 hours)

- **Confirmed**: A clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food and are lab confirmed case of botulism

Infant Botulism

- Probable: A clinically compatible case with an epidemiologic link

Wound Botulism:

- **Probable:** An illness (blurred vision, diplopia, bulbar weakness, or rapidly progressing symmetric paralysis with an infected wound.
- **Confirmed:** A clinically compatible case that is laboratory confirmed
- **Food Borne:** A clinically compatible case and is laboratory-confirmed by detection of Botulism toxin in serum, stool, or patient's food/ isolation of clostridium botulinum form stool
- **Infant:** A clinically compatible case lab confirmed by detection of botulinum toxin in stool or serum/Isolation of *C. botulinum* from stool
- **Wound:** Detection of botulinum toxin in serum or isolation of *C. botulinum* from wound

Contact Investigation—Contact Investigation (Foodborne Botulism Only)

Anyone who has shared food with a case within 5 days prior to onset of symptoms should be considered a contact. Once a food has been identified, only those known to have eaten the implicated food are considered contacts.

Lab Confirmation—Samples of stool, suspected contaminated food, body fluids, vomitus, gastric aspirate etc. should be sent to the lab for confirmation of *C. botulinum* and presence of toxins OR Mouse bioassay

Timings—

- Blood and stool samples should be collected from the patient as soon after onset of symptoms as possible before antitoxin administration.
- Samples should be taken within 48 hours of start of symptoms

Specimen Collection

- 20ml venous blood in a plain specimen tube without anticoagulant. From infants collect >5ml blood.

- 25–50g faeces
- 25–50 ml gastric contents, aspirate or vomitus.
- Obtain 10–50 g suspect food sources/samples
- Exudates or tissue from suspected wound botulism cases

Packaging—Properly triple packaged and labelled with case summary

Storage—Specimens for toxin analysis should be refrigerated, but culture samples of *C. botulinum* should not be refrigerated.

Transportation—

- *C. botulinum* is classified under WHO biosafety risk group # 4.
- Cultures that are reasonably suspected to contain *C. botulinum* must be transported as "infectious substances."

Case Management

- Treatment must not await laboratory confirmation
- Supportive treatment, especially adequate mechanical ventilation
- Surgical debridement
- Antimicrobial treatment in wound botulism. (Penicillin is the drug of choice, if allergic then Metronidazole)
- Antitoxin administration
- Remove contaminated food by inducing vomiting or by using enemas or stomach lavage.
- Careful attention to peripheral and central intravenous catheters with regular site rotation to reduce the risks of thrombophlebitis, cellulitis, and line infections should be part of the patient's supportive care.

Post-exposure prophylaxis (PEP):

- Use of Antitoxin for post exposure prophylaxis is limited by its limited availability.
- Asymptomatic persons who are believed to be exposed should remain under close medical observation and, if feasible, near critical care services
- Botulinum Toxoid is not effective as post-exposure prophylaxis as its immunity is induced over several months period.

Preventive measures & Vaccination

- Modern industrial canning was developed for killing *C. botulinum* spores.
- *C. botulinum* toxin can be destroyed by boiling food/water for 5 minutes or moreor heating at 90°C for 15 minutes; heating to 115°C will inactivate spores.
- Honey (even pasteurized honey) should not be given to children younger than 12 months of age due to high risk of infant botulism. Honey is safe for children1 year of age and older.
- Refrigeration of foods to prevent bacterial growth and formation of toxin should be promoted.
- Wound botulism can be prevented by promptly seeking medical care for infected wounds, and by not using injectable street drugs.
- Public education about botulism prevention should be seeked.

Infection Prevention & control:

- Standard precautions need to be taken.
- Patients with suspected botulism do not need to be isolated.

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7. Brucellosis

Introduction

A bacterial disease, also known as "Undulant fever", "Mediterranean fever" or "Malta fever" which is caused by Brucella genus. It is Zoonotic disease of mainly cattle, swine, goats, sheep and dogs. The incidence of Brucellosis reaches as much as 200 cases per 100,000 of the population in some regions of the world. The duration of illness and its long convalescence makes it an important economic as well as a medical problem for the patient because of time lost from normal activities.

Clinical Picture

- An acute or sub-acute febrile illness characterized by an intermittent or remittent fever accompanied by malaise, anorexia, headache, pain in muscles, joint, and/or back, fatigue and prostration, may progress to a chronically incapacitating disease with severe complications and may persist for weeks or months if left untreated.
- Recurrence may happen with fever, arthritis, swelling of the testicles and scrotal area, endocarditis, neurologic symptoms (in up to 5% of all cases), chronic fatigue, depression, enlarged liver and/or spleen.
- Depending on the duration and progression of the disease, the following phases can be observed:
  - o Acute disease phase (duration <3 months)
  - o Sub-acute disease phase (duration 3–12 months)
  - o Chronic disease phase (duration >12 months).

Infectious Agent—Common types of the Brucella genus are:

- *B.melitensis*: is the type most frequently reported as a cause of human disease
- *B.abortus*: associated with much less human disease
- *B. suis*

Host/Reservoir—Domestic and wild animals

Period of Communicability—There is no evidence of communicanbility between person to person

Mode of Transmission—Transmitted by direct or indirect contact with infected animals or their products.

- Eating undercooked meat or consuming unpasteurized/raw dairy products
- Bacteria entering the body through skin wounds or mucous membranes
- Transmission from lactating mothers to their infants and vertical transmission has been reported.
- Person-to-person transmission is extremely rare.

Incubation Period—2–4 weeks (range, 5 days to 5 months).

Seasonality—No seasonal variations affect its incidence.

Case Definition

Suspected Case—An acute or insidious onset of fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia and routine workup of other common febrile illnesses is negative and is epidemiologically linked to suspected or confirmed animal cases or contaminated food of animal origin.

Probable Case—A case that is compatible with the clinical description and is epidemiologically linked to a confirmed case andt has positive rose bengal test (RBT) followed by Brucella agglutinin titer of greater than or equal to 160 in one or more serum specimens obtained after onset of symptoms.

Confirmed Case—A clinically compatible illness with definitive laboratory evidence of Brucella infection by isolation of *Brucella sp*. from a clinical specimenOR fourfold or greater rise in Brucella agglutination titer between acute and convalescent phase serum specimens obtained greater than or equal to 2 weeks apart and studies at the same laboratory/demonstration by immunofluorescence of Brucella specimen.

Lab Confirmation:—Brucella highly virulent, thus culturing methods must carried-out under required level of biosafety.

Methods:

- Isolation of *Brucella sp*. from blood or other clinical specimen
- ELISA test
- PCR and new rapid tests such as the lateral flow assay are yet to be accredited.

Timings—

- Isolation rates are much higher during the first two weeks of symptomatic disease and in blood or bone marrow cultures taken during the pyrexial phase
- IgM antibody levels rise during the first week of acute illness, peak at 3 months, and may persist up to 2 years.
- IgG antibody levels rise about 3 weeks after onset of acute disease, peak at 6-8 weeks, and can remain detectable lifelong.
- For acute specimen, collect as soon as possible after onset of disease.
- For convalescent-phase, collect >14 days after the acute specimen.

Specimen Collection—Culture: Whole blood, bone marrow, splenic aspirate, synovial fluid and abscesses. [Adult blood 7 ml (min 3 ml), Paediatric blood 3 ml (min 1 ml)].
Serology: Collect 3-5 ml blood or 1ml serum for acute and convalescent sera for serology.

Packaging—Triple packaging with case summary

Storage—Specimen should be stored at room temperature 2-8°C is for serum

Transportation

- Sterile leak-proof container
- Transport maintaining cold chain (2-8°C) on ice packs for serology.

Case Management

- Adults: Doxycycline plus Gentamicin OR Rifampacin have been used in various combinations for treatment for a minimum of 6–8 weeks. For Neurobrucellosis, combination of Doxycycline plus Rifampicin plus Ceftriaxone.
- Paediatrics: Septran plus Rifampicin
- If bacteria localized in organs and tissues and cause focal infection, surgery could be indicated. Late diagnosis and inappropriate therapy may result in chronic disease or relapse.

Preventive Measures

- The obvious way to prevent brucellosis is elimination of the disease from the animals.
- The prevention of human brucellosis is based on occupational hygiene and food hygiene.
- Barrier precautions for hunters and professionals at risk (butchers, farmers, slaughterers, veterinarians) are recommended.
- Careful handling and disposal of afterbirths, especially in cases of abortion.
- Vaccination is not generally recommended for human use.
- Serological or other testing of animals; immunization of herds/flocks may be envisaged; eliminate infected herds/flocks.
- Education to avoid consuming unpasteurized milk and milk derivatives. All dairy products should be prepared from heat-treated milk. Consumption of raw milk or products made from raw milk should be avoided.
- Meat should be adequately cooked.
- Physicians and health workers should be aware of the possibility of Brucellosis.
- Prompt diagnosis and treatment of brucellosis during pregnancy can be lifesaving for the fetus.
- Short course of post-exposure prophylaxis (PEP) antibiotics may be recommended for pregnant women exposed to brucellosis.

Infection Prevention & Control Precautions:

- Since person-to-person transmission is rare, patients do not have to be heldin isolation rooms.
- Healthcare workers should exercise standard precautions.

Necessary Precaution for Lab Staff Includes

- Laboratory workers should take necessary precautions when working with *Brucella* species.

Primary Barriers: Use safety centrifuge cups, personal protective equipment and class II or higher Biological Safety Cabinets (BSCs) for procedures with a high likelihood of producing droplet splashes or aerosols.

Secondary Barriers: Restrict access to the laboratory when work is being performed. Maintain the integrity of the laboratory's air handling system by keeping external doors and windows closed.

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8. Chikungunya

Introduction

A mosquito-borne viral disease, first described during an outbreak in southern Tanzania in 1952. The name "Chikungunya" derives from a word in the Kimakonde language, meaning "to become contorted", and describes the stooped appearance of sufferers. Clusters of cases have been reported from various regions of the country.

Infectious Agent—Chikungunya is an RNA *alpha* virus of the family of *Togaviridae*.

Host/Reservoir—Human and other primates are the main reservoirs

Period of Communicability—CHIKV infections cause high levels of viraemia, which typically last 4-6 days, but can persist for up to 12 days after the onset of illness.

Mode of Transmission—Human to human transmission is through the bite of infected female *Aedes Aegypti* and *Aedes albopictus* mosquitoes.

Incubation period—Onset of illness occurs usually between 4 and 8 days but can range from 2 to 12 days

Seasonality—Chikungunya fever epidemics display cyclical and seasonal trends.

Case Definition

Suspected Case—Any person with acute onset of measured fever >38.5°C and severe arthralgia/arthritis not explained by other medical conditions

Probable Case—A suspected plus epidemiological criteria
<u>Epidemiological criteria</u>: Residing or having visited epidemic areas within 15 days prior to the onset of symptoms

Confirmed Case—Suspected/probable cases confirmed by laboratory tests in the acute phase.

Lab confirmation—

- Virological methods by Real-time Reverse transcriptase Polymerase Chain Reaction (RT-PCR)
- Virus Isolation
- Serological testing (IgG and IgM anti Chikungunya antibodies by ELISA)

Timings—Time period for test is critical and mentioned below:

- RT-PCR within one week after onset of illness

Serological detection by IgM ELISA after 4 days of the onset of illness

Specimen Collection—Collect 3-5 ml venous blood/serum of suspected case

Use sterile venoject tubes

Packaging—Label and pack, it properly in triple packing with ice packs and transport to laboratory within 24-48 hours at 4-8*c along with complete case report form (CRF).

Transportation—Transport the sample to the Virology Department of Public Health Laboratories Division (PHLD) at National Institute of Health, Islamabad

Case Management

There is no specific antiviral drug treatment for Chikungunya. Treatment is directed primarily at relieving the symptoms, including the joint pain by using anti-pyretic, analgesics and fluids.

Preventive Measures

- No vaccination is available.
- Community surveys to determine density of vector mosquitoes is recommended.
- Identify and destroy mosquito breeding sites in nearby outdoor and indoor premises.
- Indoor residual spray in areas with high mosquito density should be done. Thermal fogging in advised in case of outbreaks.

- Conduct community mobilization through schools and religious leaders, to promoteProper solid waste management. Larval habitats may be destroyed by filling depressions that collect water, by draining swamps or by ditching marshy areas to remove standing water. Container-breeding mosquitoes are particularly susceptible to source reduction as people can remove or cover standing water in cans, cups, and rain barrels around houses.
- Protection should be sought against day biting mosquitoes by the use of screening, protective clothing and repellents.
  - o Sleeping or resting in screened or air-conditioned rooms.
  - o Use of insecticide-treated mosquito nets.
  - o Community based environmental management and health education campaigns.

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9. Cholera/ Acute Watery Diarrhoea

Introduction

An acute, diarrheal illness caused by bacterium *Vibrio cholerae* resulting in intestine infection. An estimated 3-5 million cases and over 100,000 deaths occur each year around the world. The infection is often mild or without symptoms but can sometimes be severe.

Clinical Picture

- Cholera infection is often mild or without symptoms but can sometimes be severe.
- Approximately one in ten (5-10%) infected persons will have severe disease characterized by profuse watery diarrhea, vomiting and leg cramps.
- In these people, rapid loss of body fluids leads to dehydration and shock which can be fatal if untreated

Infectious Agent—There are two serotypes for *Vibrio cholerae* O1 and O139 that produce cholera toxin and are associated with epidemics

Host/Reservoir—Humans are considered the primary reservoir and can be asymptomatic carriers.

Period of Communicability—The contagious period for cholera begins as soon as organisms are excreted in the feces. This can occur as early as about 6 to 12 hours after exposure to the bacteria and can last for about 7 to 14 days.

Mode of Transmission—Infection results from faeco-oral route and through contaminated food and water.

Incubation period—The incubation period can be from a few hours to 5 days; it is usually 2–3 days.

Seasonality—Throughout the year; higher incidence from April to November.

Alert Threshold—One suspected case/ AWD is an alert

Outbreak threshold—One lab confirmed case, or cluster of 6 or more cases of AWD in one location, is an outbreak.

Case Definition

Suspected Case—Three or more abnormally loose or fluid stools in the past 24 hours with or without dehydration.

Probable Case—Person aged over 5 years or older with severe dehydration or a death from acute watery diarrhoea with or without vomiting. OR
Person aged over 5 year or less/above 2 years with acute watery diarrhoea in an area where there is a cholera outbreak.

Confirmed Case—Any suspected case confirmed by laboratory test

Lab confirmation—Isolated toxigenic *Vibrio cholerae* 01 or 0139 from the stool/ rectal swab or vomits; serologic evidence of recent infection

Timings— Collect specimen before the initiation of antibiotic therapy and send it to lab as early as possible

Specimen Collection—Collect 5 gram of stool and send it to lab with request slip

- If there is a delay in sample transportation, soak a sterile cotton swab with stool and insert it in Cary Blair transport medium should be refrigerated (2-8c) for transportation.

Packaging—Put a label and place in sealable plastic bag or pouch containing absorbent material.

Storage—

- Store stool and specimen in Cary Blair transport medium in room temperature.
- Cold chain or ice packs are not required

Transportation—Carry-Blair transport medium or alkaline peptone water in transport boxes. Take precautions to prevent breakage of the sample containers. Send full patient information on the prescribed form along with the test request slip.

Case Management

- Low OsmolarORS should be mixed with water as per directions and 500 ml of this should be given orally every hour.
- Even with severe dehydration, intravenous electrolyte solutions should be used only for initial rehydration, including those who are in shock
- Severe dehydrated patients require administration of intravenous fluids. Ringer's Lactate Solution (or Hartman's Solution for injection) is the preferred fluid for intravenous rehydration.
- Antibiotics (Ampicillin, Amoxicillin, Tetracycline, Ceftriaxone and Quinolone group) reduce the duration of disease and period of excretion of *Vibrio cholera* in the stool of infected patients

Preventive Measures

- Ensure adequate safe drinking water supply and proper sanitation. To make the water safe for drinking, either boil the water or chlorinate it.
- All people (visitors or residents) in areas where cholera is occurring or has occurred should observe the following recommendations:
    - o Drink only bottled, boiled, or chemically treated water. When using bottled drinks, make sure that the seal has not been broken.
    - o To disinfect your own water, boil for 1 minute or filter the water and add 2 drops of household bleach or ½ an iodine tablet per liter of water.
    - o Avoid tap water, stream/fountain water and ice cubes.
- Wash your hands with soap and clean water.
- Clean your hands especially before you eat or prepare food and after using the bathroom.
- Use bottled, boiled, or chemically treated water to wash dishes, brush your teeth, wash and prepare food, or make ice.
- Eat foods that is packaged or is freshly cooked and served hot.
- Do not eat raw or undercooked meat and seafood or unpeeled fruits and vegetables.
- Proper disposal of feces to prevent contamination of water and food sources should be done.

Vaccination

- A single-dose live oral cholera vaccine called Vaxchora (lyophilized CVD 103-HgR) for adults 18–64 years old who are traveling to an area of active cholera transmission with toxigenic *Vibrio Cholerae* O1 (the bacteria strain that most commonly causes cholera) is recommended.
- Two other oral inactivated or non-live cholera vaccines, Dukoral® and ShanChol®, are World Health Organization (WHO) prequalified. However, these vaccines are not available in third world countries.
- No cholera vaccine is 100% protective and vaccination against cholera is not a substitute for standard prevention and control measures.

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10. Congenital Rubella Syndrome (CRS)

Introduction

It is a contagious disease and generally mild in children; it has serious consequences in pregnant women causing congenital defects known as Congenital Rubella Syndrome (CRS) or fetal death. The typical triad of deafness, cataract and cardiac diseases is the classical clinical manifestations of CRS.

When Rubella infection occurs during early pregnancy, serious consequences such as miscarriages, stillbirths and a constellation of severe birth defects in fetus can result. The risk of congenital infection and defects is highest during the first 12 weeks of gestation and decreases after the 12^{th} week with defects rare after the 20^{th} week of gestation.

Clinical Picture

Infection can affect all organs of the fetus and may lead to fetal death or premature delivery. Severity of damage to fetus depends on gestational age of the fetus. Rubella infection during pregnancy also causes mental retardation, microcephaly and liver and spleen damage in the fetus. Infants with CRS usually present with more than one sign or symptom consistent with congenital rubella infection.

Congenital defects include the following:

Cataracts, congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy, purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, or radiolucent bone disease.

Infectious Agent—It is caused by *Rubella virus* which is a member of the *Rubivirus* genus of family *Togaviridae*

Host/Reservoir—Humans are the only known reservoir.

Period of Communicability—

- The period of infectivity is 7 days before appearance of rash lasting up to 6 days after the onset of rash
- As infants can shed the virus for prolonged periods, (up to 1 year of age or longer); infants with CRS should be considered infectious until they are at least 2 year old or until two tests, obtained one month apart, are negative for rubella in infants who are older than 3 months.

Mode of Transmission—By direct contact, droplet spread or vertical transmission

Incubation period—13–20 days (average 14 days)

Case Definition

Suspected Case—An infant <1 year of age who does not meet the criteria for a probable or confirmed case but who has one or more clinical manifestations of CRS.

Probable Case—An infant who does not have laboratory confirmation of Rubella infection,

a) Has at least two of the following; cataracts or congenital glaucoma, congenital heart disease, hearing impairment, or pigmentary retinopathy without a more plausible etiology ; or

b) Has at least one or more of the following; cataracts or congenital glaucoma, congenital heart disease, hearing impairment, or pigmentary retinopathy AND one or more of the following: purpura, hepatosplenomegaly, microcephaly, developmental delay, meningoencephalitis, or radiolucent bone disease without a more plausible etiology.

Confirmed Case—An infant with at least one of the symptoms clinically consistent with CRS listed above and laboratory confirmation of Rubella virus. **or** Any stillborn with laboratory confirmed Rubella virus test.

Lab confirmation

Enzyme immunoassays (EIA) for Rubella IgM and IgG

Virus detection by PCR

Timings—Clinical specimens for virus isolation from infants should be obtained at the time of the initial investigation. In infants with CRS, IgM antibody can be detected in the infant's cord blood or serum and persists for about 6-12 months

Specimen Collection—Blood/ Serum for detection of IgM and IgG by ELISA method

Nasal/ Throat swabs/ Saliva/ Urine for antigen/virus detection by PCR

Packaging—Uniquely labeled, sealed vials should be placed in sealable plastic bags or pouches containing absorbent materials such as cotton wool to soak up any leakage that may occur (triple packaging).

Storage—Must be stored at 4 to 8°C for up to 24 hours but it must not be frozen. When kept for longer periods, serum samples should be frozen at −20°C or lower.

Transportation—Specimens should be transported to the laboratory as soon as possible maintaining reverse cold chain.

Case Management

There is no specific treatment for Rubella. Treatment should be symptomatic

Preventive measures

- Laboratory confirmation of contacts of pregnant woman with suspected rubella infection.
- Isolation of infants less than one year old, with CRS from pregnant women and children or until the infant is no longer considered infectious.
- Documented vaccination of health care providers of CRS cases.
- Increase community awareness on the importance of preventing rubella and CRS.

Vaccination:

- Two doses of MMR vaccine are recommended routinely for children with the first dose at age 12 through 15 months and the second dose at age 4 through 6 years.
- Live attenuated viral rubella vaccine: one dose given by the intramuscular or subcutaneous route as monovalent, MR or MMR for women of childbearing age, but not during pregnancy.

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11. Diphtheria

Introduction

An acute, toxin-mediated upper respiratory illness affects the throat and sometimes tonsils. Disease may involve any mucous membrane. Classification based on site of disease; anterior nasal, pharyngeal and tonsillar, laryngeal, cutaneous, occular and genital. Diphtheria forms pseudomembrane (thick covering) on throat. Diphtheria affects people of all ages, but most often it strikes unimmunized children younger than 5 years of age.

Clinical Picture

Symptoms range from sore throat to toxic life-threatening diphtheria of the larynx or of the lower and upper respiratory tracts. Infected person may present with sore throat, low grade fever (rarely high), swollen glands (making breathing and swallowing difficult) and an adherent greyish white pseudomembrane on the tonsils, pharynx or nasal cavity. Systemic presentation is rare and may have myocarditis and polyneuritis.

Infectious Agent—*Corynebacterium diphtheriae*, anaerobic toxin producing gram positive bacillus
C. diphtheriae has 4 biotypes i.e. *gravis, intermedius, mitis and belfanti*

Host/Reservoir—Humans are the reservoir for *C. diphtheriae* and are usually asymptomatic

Period of Communicability—Organisms usually persist 2 weeks or less and seldom more than 4 weeks. Chronic carriers may shed organisms for 6 months or more.

Mode of Transmission—Transmitted from person to person, usually through respiratory droplets (coughing or sneezing). Infection may come by contact/touching open sores (skin lesions) and material objects (toys or clothes) used by the person who already is sick with diphtheria.

Incubation period—Usually 2-5 days, occasionally longer

Seasonality—Throughout the year; higher incidence in winter and spring

Alert Threshold—One probable case is an alert

Outbreak threshold—One lab Confirmed case is an outbreak

Case Definition

Suspected Case—Not applicable

Probable Case—Any person who meets the clinical case definition for respiratory diphtheria i.e. upper respiratory tract illness characterized by laryngitis **or** pharyngitis **or** tonsillitis, and a visible adherent "membrane" on the tonsils, pharynx and/or nose and without epidemiological linkage and laboratory confirmation.

Confirmed Case—Any confirmed case is a probable case that has been laboratory confirmed or linked epidemiologically to a laboratory confirmed case. Persons with positive *C. Diphtheria* culture but asymptomatic, should not be reported as suspected or confirmed cases.

Carrier—A person with no symptoms but has laboratory confirmation of a toxigenic strain

Discarded—Any suspected or probable case in whom other compatible organisms are isolated or if C. diphtheriae/ C. ulcerans is isolated but is confirmed to be a non-toxigenic strain

Lab confirmation

Bacteriologic culture testing
Polymerase Chain reaction (PCR)

Timings—Specimens for culture should be obtained immediately as diphtheria (involving any site) is suspected, even if treatment with antibiotics has already begun.

Specimen Collection—

- Collect nasopharyngeal and throat swabs by using polyester, rayon or nylon swabs for culture.
- The swabs should be placed in transport media such as Amies or Stuart and shipped overnight with ice packs.
- Pieces of pseudo-membrane may also be submitted in sterile saline (not formalin) in hospital settings and if shipped should be in ice packs

Packaging—Triple packaging

Storage—

- 4-8°C for 48-72 hours
- Long term storage should be at –20°C

Transportation—Transport swabs and pieces of pseudo-membrane in Amies transport Medium and sterile saline, respectively, on ambient temperature

Case Management

For Patients:

- Isolate all cases promptly and use universal and droplet precautions to limit the number of possible contacts. Do not wait for laboratory results before starting treatment/ control activities. All cases must receive diphtheria antitoxin (DAT)
  - o Mild pharyngeal or laryngeal disease : 20,000 – 40,000 units
  - o Moderate nasopharyngeal disease : 40,000 – 60,000 units
  - o Severe, extensive or late (3 or more days) : 80,000 – 100,000 units
- I.V route is penetrated dose should be mixed with 2-100 ml saline and given slowly over 2-4 hour.
- Secure definite airway for patients with impending respiratory compromise or the presence of laryngeal membrane. Removal of membrane by direct laryngoscopy or bronchoscopy may be necessary to prevent or improve airway obstruction.
- Maintain close monitoring of cardiac activity for early detection of rhythm abnormalities.
- Erythromycin and penicillin are both recommended for the treatment of diphtheria. Initiate prompt antibiotic coverage for eradication of organisms, thus limiting the amount of toxin production. Antibiotics hasten recovery and prevent the spread of the disease to other individuals.
- Azithromycin or Clarithromycin is probably as effective as Erythromycin (40 mg/kg/day; maximum, 2 gm/day)
- The patient should be isolated until three consecutive cultures at the completion of therapy have documented elimination of the organism from oropharynx.

Note: *Clinical diphtheria does not necessarily confer natural immunity, and patients should thus be vaccinated before discharge from a health facility with either primary or booster doses. Unless immunized, children and adults may repeatedly be infected with the disease.*

For Contacts:

- All close contacts, regardless of vaccination status, should have nose and throat cultures, receive a single dose of Benzathine Penicillin I/M (600,000 units for children <6; 1.2 million units for 6 or older) or a 7-10 day course of Eythromycin (PO) and remain under surveillance for 7 days.
- If cultures are positive and person is symptomatic, admit to hospital and begin treatment as confirmed case.
- If cultures are positive and person is asymptomatic, begin treatment as carrier mentioned below.

For Carriers:

- All must receive a single dose of Benzathine Penicillin G IM. (600,000 units for children <6 years; 1.2 million units for 6 years or older).
- If allergic to Penicillin, use Erythromycin (40-50 mg/kg/day) in divided doses.
- Antibiotic treatment should be continued for total of 14 days and patient should be culture negative before handling milk or working with school children.

Preventive Measures

- Standard precautions along with droplet precautions are recommended with single room isolation.
- Primary prevention of disease by ensuring high population immunity through immunization.
- Secondary prevention of spread by the rapid investigation of close contacts to ensure their early and proper treatment.
- Tertiary prevention of complications and deaths by early diagnosis and proper management.

Vaccination

- Routine immunization consists of 3 doses of 0.5 ml DPT-Hep-B-Hib (Pentavalent Vaccine) administered IM to all the children less than one year of age with the schedule of:
  a. 1st dose at the age of 6 weeks;
  b. 2nd at 10 weeks;
  c. 3rd at 14 weeks, a booster DTP at 18 months to 4 years.
- If children or adults have not been immunized with three-dose series, children <5 years should receive DT vaccine, and children ≥5 years and adults should receive Td vaccine to complete a series of three doses.

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12. Gonorrhea

Introduction

A common sexually transmitted disease (STD). Highest frequency occur between 15-29 years of age. Male-female ratio is approximately 1:1.2. Globally an estimated 200 million new cases occur annually

Clinical Picture

Commonly manifested by urethritis (burning micturition &purulent discharge), cervicitis, proctitis, salpingitis, or pharyngitis. Infection may be asymptomatic.

- **Males:** urethritis and proctitis.
- **Females:** Cervicitis, urethritis, proctitis.
- **Neonates:** Conjunctival infections acquired during passage through birth canal.

Complications:

- PID, ectopic pregnancy and tubal infertility in females
- Epididymitis, prostatitis and urethral stricture in males
- Occasionally disseminated infections, artheritis, perihepatitis etc

Infectious Agent—*Neisseria gonorrhoeae* (a gram-negative, intracellular, aerobic diplococcus)

Host/Reservoir—Humans are the only known reservoir

Period of Communicability—May extend up to months in untreated patients

Mode of Transmission—Unprotected sexual (during vaginal, anal, oral sex) Vertical transmission in neonates

Incubation period—1–14 days

Case Definition

Suspected Case—NA

Probable Case—Demonstration of gram-negative intracellular diplococci in a urethral smear obtained from a male or an endo-cervical smear obtained from a female

Confirmed Case—A probable case with laboratory confirmation of isolation of typical gram negative diplococci from clinical specimen/ by detection of antigen or nucleic acid/observation of gram negative diplococci in urethral smear from men

Lab confirmation—

- Direct smear preparation for gram staining and identification of intra-cellular, gram-negative, kidney-shaped diplococci in polymorphonuclear leukocytes
- Culture
- Enzyme Immunoassay (EIA) specially for gonococcal urethritis
- Nucleic acid amplification tests(NAATs) for rectal and pharyngeal swabs

Note: *Culture is most preferred method however over long distance shipment and due to high temperature culture is less sensitive than nucleic acid detection.*

Timings At the time of presentation

Specimen Collection

- Take urethral/ high vaginal/ cervical /rectal specimen with rayon/Dacron swab for culture(inoculated immediately on selective media: modified Thayer Martin medium)
- Urine sample especially for nucleic acid identification. Collect in leak proof container.
- Conjunctival secretions

Precautions: No urination for 2 hours before a urine sample is collected. Women should not douche or use vaginal creams or medicines for at least 24 hours before having a gonorrhea test.

Packaging—Triple packaging

Storage—Ideally specimen should be inoculated onto culture medium immediately to preserve viability of gonococci for isolation

Transportation—

- For transportation to local laboratory, the plates should be held at room temperature for no more than 5 hours in CO_2 rich atmosphere
- For long-distance shipment, specimen should be inoculated onto CO_2 rich media and incubated for 18-24hrs and have visible growth on the plate before shipping.

Case Management

Dual therapy is recommended. A single dose of 250mg of intramuscular Ceftriaxone AND 1 gram of oral Azithromycin

Preventive Measures

- Health education regarding adopting safe sex practices should be given.
- Sexual contact with the case should be avoided for atleast a week after the treatment is completed.
- All sexual partners need to be tested for early detection and treatment of infection.
- Other sexually transmitted infections should also be excluded.

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13. Haemophilus influenzae Type B (Hib)

Introduction

H. influnzae can cause pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, otitis media, purulent pericarditis, and other less common infections such as endocarditis, osteomyelitis and other potential life-threatening

Infections primarily among children aged 3 months to 5 years. It can also affect adults with certain medical conditions.

If the pathogens stay in the child's nose and throat, the child probably will not get sick. But sometimes the germs spread into the lungs or the bloodstream, and then Hib can cause serious problems. This is called invasive Hib disease.

Unimmunized children under 4 years of age, as well as household contacts and daycare classmates of a person with Hib disease, patients with sickle cell anemia, asplenia, HIV and certain immunoglobulin and complement component deficiencies, recipients of hematopoietic stem cell transplant and chemotherapy or radiation therapy for malignant neoplasms are at increased risk for invasive H. influenzae disease.

Infectious Agent—*Haemophilus influenzae type* b (Hib) is a pleomorphic gram-negative coccobacillus

Host/Reservoir—Humans are the only reservoirs

Period of Communicability—Hib is communicable for as long as the organisms are present in the nasopharynx.

- Patients are no longer infectious once they have received 24–48 hours of appropriate antibiotic therapy.

Mode of Transmission—Spread from person to person through respiratory droplets.

- Direct contact with respiratory droplets from nasopharyngeal carrier or case patient.
- Neonates can acquire infection by aspiration of amniotic fluid or contact with genital tract secretions containing the bacteria.

Incubation period—The incubation period is uncertain. It is probably 2–4 days.

Case Definition

Suspected Case—N/A

Probable Case—Meningitis, bacteremia or epiglottitis any clinical syndrome with detection of H. influenzae type-B antigen in cerebrospinal fluid.

(Antigen detection tests can be positive in urine and serum of persons without invasive Hib disease is unreliable and should not be reported as cases)

Confirmed Case—Probable case confirmed by culture **or** PCR

Lab confirmation:

Culture: Gold standard for confirming *Haemophilus influenzae* from a normally sterile site

Serotype testing (serotyping): Serotyping distinguishes encapsulated strains, including Hib, from un-encapsulated strains, which cannot be serotyped.

Antigen detection: type b capsular antigen can be detected in body fluids. Antigen detection may be used as an adjunct to culture, particularly in the diagnosis of patients who have received antimicrobial agents before specimens are obtained for culture.

Real-time PCR assays: to detect DNA of all six Haemophilus influenzae serotypes in blood, CSF, or other clinical specimens. When the organisms are nonviable following antimicrobial treatment, PCR can still detect H. influenzae DNA.

Specimen Collection—Normally sterile-site specimens for isolation of invasive H. influenzae include CSF, blood, joint fluid, pleural effusion, pericardial effusion, peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid.

Packaging—Triple packaged with case summary and lab request form

Storage—Dorset Transport medium or Transisolate medium can be used for H. influenzae at room temperature (25°C). On Dorset Transport medium, H. influenzae can be stored for approximately 3 weeks.

Note: Selection of a storage method depends on the length of time the organisms are to be stored depending on laboratory equipment and facilities.

Case Management

Chemoprophylaxis: (RIFAMPICIN)

- Respiratory isolation procedures are recommended for 24 hours after the start of treatment.
- H. influenzae, including Hib, disease is treated with antibiotics usually for 10 days.
- For Non-life threatening: Augmentin/Cefuroxime/Quinolones/Macrolides
- For Life threatening use Intravenous Ceftriaxone or Cefotaxime for empirical therapy until antibiotic sensitivities are known.

Preventive Measures

Chemoprophylaxis: (dose)

- Chemoprophylaxis is recommended for close household contacts. All people in the same household should receive chemoprophylaxis. Inadequately vaccinated children should receive age-appropriate Hib vaccination.
- Vulnerable individuals defined as:
  - o Infants under 7 months of age, regardless of vaccination status
  - o Children aged 7 months to 5 years who are not age-appropriately immunized against Hib.
- Immunosuppressed or asplenic individuals of any age. Chemoprophylaxis should also be given to all children and staff of a day-care centre who shared the same room as the case in the 7 days preceding the onset of illness.

Vaccination:

- Children over 5 years old and adults usually do not need Hib vaccine, but it may be recommended for children and adults with asplenia, sickle cell disease, before surgery to remove the spleen or following a bone marrow transplant.
- It may also be recommended for people 5 to 18 years of age with HIV/AIDS. A child will receive either 3 or 4 doses, depending on the type of vaccine used.

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14. Hepatitis A & E

Introduction

Acute viral hepatitis is a diffuse liver inflammation caused by specific hepatotropic viruses that have diverse modes of transmission. Hepatitis A and E infections are endemic in Pakistan. Both infections occur in their sporadic form due to poor water and sewage systems.

Clinical Picture

Acute jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper quadrant tenderness. A variable proportion of adult infections are asymptomatic. Lab findings include increased urine urobilinogen and >2.5 times the upper limit of serum alanine aminotransferase.

Infectious Agent—*Hepatitis A virus*

Hepatitis E virus

Host/Reservoir—Humans are the only reservoir of the Hepatitis A virus (HAV).

Humans and non-human primates are the reservoirs of Hepatitis E virus (HEV)

Mode of Transmission—Faecal-oral route

Incubation period—Hepatitis A: Ranges from 15 to 50 days.

Hepatitis E: Ranges from 15 to 64 days

Seasonality—Occur regularly during monsoon rains and floods due to major contamination of drinking water with sewage

Alert Threshold—3 or more cases in one location

Outbreak threshold—A cluster of cases: 6 or more cases in one location + Lab confirmation of type of Virus

Case Definition

Suspected Case—A case that is compatible with the clinical description of an acute illness with jaundice, dark urine, extreme fatigue, anorexia/upper right quadrant tenderness with raised serum alanine Aminotransferase (ALT)

Confirmed Case—A suspected case that meets the clinical case definition and is laboratory confirmed i.e. IgM anti HAV antibody positive

OR

A case compatible with the clinical description who has an epidemiological link with a laboratory-confirmed case of hepatitis A (i.e. household or sexual contact with an infected person during the 15-50 days before the onset of symptoms.

Lab confirmation

ELISA: positive for IgM anti-HAV/HEV
Polymerase Chain reaction (PCR): Antigen detection

Timings—Pack the specimens and send by overnight

Specimen Collection—Collect 5 ml blood during acute phase of illness observing all safety precautions. Separate serum by centrifugation technique in a tube.

Packaging—An insulated box with ice or frozen refrigerant packs

Storage—Can be stored at 2-8°C for 48-72 hours
Long term storage at –20°C, with complete lab request form

Case Management

- There is no specific management for acute uncomplicated hepatitis but general supportive measures are recommended like bed rest, fluid replacement, nutritional support, and avoidance of use of all the hepatotoxic drugs during the illness. If within 2 weeks of exposure Hepatitis A vaccination is equally effective as IVIG.
- Hospitalization is required for fulminant hepatitis (a rare syndrome of massive necrosis of liver parenchyma and a decrease in liver size) and should be considered for Hep E infected pregnant women.

Preventive Measures

Control procedures for epidemic-prone diseases, Hepatitis A and E should include;

- Provision of safe drinking water and proper disposal of sanitary waste.

- Important measures to reduce the risk of disease transmission includegood personal hygiene including frequent and proper hand washing after bowel practices and before food preparation, avoiding drinking water and/or ice of unknown purity, avoiding eating uncooked fruits or vegetables that are not peeled, high quality standards for public water supplies and proper disposal of sanitary waste.
- **Vaccination:**

  Hepatitis A vaccine is available both for adults and children aged 2 years or older and is administered I/M with a recommended vaccination schedule of 0, 1, and 6-12 months apart.

  Hepatitis E vaccine is currently available in China only.

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15. Hepatitis B, C & D

Introduction

Hepatitis B &C are potentially life-threatening liver infections. Both viruses lead to chronic hepatitis, liver cirrhosis and liver cancer in a significant number of patients. Hepatitis D, also known as "delta hepatitis," is a liver infection caused by the Hepatitis D virus (HDV). HDV increases risk of severe acute disease and progression to chronic hepatitis after Hepatitis B virus infection. Hepatitis "B" and "C" have emerged as major public health problems in the country.

Risk Factors: Frequent use of therapeutic injections (30% of the population have more than 10 injections per person per year), and reuse of syringes unsafe instrumentation speceially during dental procedures.

Clinical Picture

Symptoms of all types of viral hepatitis are similar and can include one or more of the following: fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, gray colored stools, joint pain and jaundice.

Note: Most infections occur asymptomatically.

Infectious Agent—*Hepatitis B Virus*
Hepatitis C Virus
Hepatitis D Virus

Host/Reservoir—The main reservoirs of infection are the chronic carriers of the virus among humans.

Mode of Transmission—

- **Hepatitis B:** Vertical (from mother to infant at the time of delivery) unsafe injections (use and re-use of unsterilized needles, syringes, drip sets); blood transfusions; and sexual or household contact with infected person.
- **Hepatitis C**: Primarily by direct contact with human blood through an unscreened transfusion, practise of reuse of shaving blades by barbers, re-use of inadequately sterilized needles, syringes or other medical

equipment, or through needle-sharing among drug-users. Sexual and perinatal transmission may also occur.

- **Hepatitis D:** HDV is transmitted similar to HBV and affects only those who have HBV, as co-infection or super-infection of HBV.

Incubation period—

- Hepatitis B: Average 75 days, ranges from 45 to 180 days (HBsAg may appear in 14 days).
- Hepatitis C: Ranges from 14 to 180 days (6 months), usually within 2 months
- Hepatitis D: Approximately 2-10 weeks

Alert Threshold—3 or more cases in one location

Outbreak threshold—A cluster of cases: 6 or more cases in one location + Lab confirmation of type

Case Definition

Suspected Case—A case that is compatible with the clinical description of an acute hepatitis such as fever, headache, nausea, vomiting, jaundice and abdominal pain. HBV and HCV-infected persons may be asymptomatic if virus remains dormant

Probable Case—A case that is anti-HCV or HBSAg positive (repeat reactive) by enzyme immunoassay (EIA) and with epidemiological link.

Confirmed Case—A suspected case that meets the clinical case definition
AND
Laboratory confirmation by any authentic method

Lab confirmation

Lab confirmation: Continued HBsAg seropositivity (>6 months) is an indicator of chronic infection.

- Hepatitis B: positive for IgM anti-HBc (antibody to Hep B core antigen) or HBsAg (Hepatitis B surface antigen/NAT (PCR including genotyping) positive two times at least 6 months apart.
- Hepatitis C: positive for anti-HCV antibody

- **Hepatitis D**: positive for IgM anti-HBc or HBsAg plus antiHDV positive (only co-infections occur)

Timings—Batch the specimens and send by overnight as soon as possible via courier

Specimen—Collect 5ml blood, Separate serum by centrifugation technique

Packaging—Observing all safety precautions with complete lab request form

Storage—4°C

Transportation—Transport serum specimens either refrigerated at 4°C (for serology), or frozen immediately (for antigen detection by PCR) with complete lab request form.

Case Management

Patients with acute hepatitis C should be treated with a combination of Sofosbuvir and Ledipasvir (genotypes 1, 4, 5 and 6), a combination of Sofosbuvir and Velpatasvir or Daclatasvir (all genotypes) with/without Ribavirin depending on underlying liver disease.

Tenofovir and Entecavir are preferred therapeutic options for patients with chronic hepatitis B. Lamivudine and interferon are other treatment options.

However, it is important to note that the management of chronic hepatitis (B, C and D) requires specialist consultation as this is one of the most rapidly changing subject

Preventive Measures

Prevention of HBV,HCV and HDV:

- **Vaccination:**
    - o Hepatitis B vaccine: It is an integral part of the National EPI schedule, with a standard three doses administered IM concurrently with DPT-Hib vaccine (Pentavalent) at weeks 6, 10 and 14.
    - o All the adults who are at high risk including health care workers needs a three dose regimens a booster for certain select groups if titres drops over a 10 years time
    - o Hepatitis C and Hepatitis D: No vaccines exist against HCV or HDV.

- Implement and maintain infection control practices in health care settings, including appropriate sterilization of medical and dental equipment, screening and testing of blood and organ donors and virus inactivation of plasma derived products.
- Promote behavioural change among the general public and health care workers to avoid overuse of injections and shaving blades Safe injection practices should be adopted.
- Build public awareness for safe sex practices.
- For post-exposure prophylaxis or suspected perinatal transmission, Hepatitis B Immunoglobulin (HBIG) 0.5ml I/M is effective; followed by hepatitis B vaccine 1 and 6 months later.

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16. Influenza (Seasonal and Pandemic)

Introduction

A contagious viral respiratory illness caused by an influenza virus that can cause both seasonal, epidemics and pandemics. Influenza virus has an RNA genome and it has three types named as Influenza virus A, B and C. Only influenza A and B viruses cause clinically important human disease and seasonal epidemics. The circulating strains of viruses are included in seasonal influenza vaccines that are formulated annually for both Northern and Southern hemispheres.

Influenza-A viruses

Pose a zoonotic infection risk, as they have a very varied host range and rapid evolutionary rate. Consequently, Influenza-A viruses cause the most severe clinical disease and are the commonest cause of seasonal epidemics and pandemics in human population.

- Influenza-A viruses are subdivided into different serotypes based on the antigenic properties of Hemagglutinin (HA) and neuraminidase (NA) respectively which are surface glycoproteins. The serotypes that have been confirmed in humans are H1N1 (caused Spanish Flu in 1918 & Swine Flu in 2009), H2N2 (caused Asian Flu in 1957), H3N2 (caused Hong Kong Flu in 1968), H5N1 (caused Bird Flu in 2004), H7N7, H1N2, H9N2, H7N2, H7N3, H10N7 and H7N9.
- Minor changes that occur in viral proteins between influenza seasons (known as antigenic drift) result in annual epidemics, with winter peaks in temperate regions (November-April in the northern hemisphere, and May-October in the southern hemisphere. In tropical and subtropical regions the seasonality of influenza is less well defined.

Influenza-B viruses

Are responsible for a significant morbidity and mortality and circulate along with Influenza-A viruses. Influenza-B viruses can be divided into two main lineages, referred to as B/Yamagata and B/Victoria. Influenza B viruses almost exclusively infect humans and is less common than influenza A and mutates at a rate 2–3 times lower than type A. This reduced rate of antigenic change, combined with its limited host range ensures that pandemics of influenza B do not occur.

Influenza type C virus

Is detected much less frequently and usually causes mild infections and thus presents less significant public health implications.

Clinical Picture

Seasonal influenza is characterized by a sudden onset of fever, cough (usually dry), headache, muscle and joint pain, severe malaise (feeling unwell), sore throat and a runny nose. The cough can be severe and can last 2 or more weeks. Most people recover from fever and other symptoms within a week without requiring medical attention. But influenza can cause severe illness or death especially in people at high risk.

Infectious Agent—Influenza Virus type *A, B,* or *C*

Mode of Transmission—Droplets, Air Borne&Contact

Incubation period—1-4 days (Average 2 days)

Seasonality—

- Peak during winter in temperate regions; in Pakistan the influenza activity increases from late autumn (October/November)
- Seasonal peak is observed in last week of December and January, with return to inter-seasonal levels by end of March

Alert Threshold—3 or more cases in one location

Outbreak threshold—A cluster of 6 or more cases in one location, with at least one lab confirmed

Case Definition

Case definitions for influenza surveillance—WHO global influenza surveillance standards define the surveillance case definitions for influenza-like illness (ILI) and severe acute respiratory infections (SARI)

Influenza like Illness (ILI)—An acute respiratory infection with:

- measured fever of ≥38°C and cough

With onset within the last 10 days

Severe Acute Respiratory Infection (SARI)—An acute respiratory infection with:

- history of fever or measured fever of ≥38°C and cough;
- with onset within the last 10 days
- If Disease severity requires hospitalization.

Lab confirmation

- Real-time RT-PCR
- Viral culture
- Serology

Timings—Respiratory samples must be collected within 1-5 days of symptom onset

Specimen Collection—Throat Swab

- Nasal swabs
- Nasopharyngeal aspirates
- Tracheal aspirate/Bronchoalveolar lavage fluid from intubated patients
- Collect specimen in Viral Transport Medium (VTM).
- Collect 5 ml blood or serum for serology (acute and convalescent if possible).

Packaging—Triple packaging

Storage—

- Sample for virus isolation collected in VTM must be sent to lab as soon as possible, kept at +4°C and frozen at –70°C in lab.
- Blood/serum samples should be frozen at –20°C or lower for antibody determination or –70°C for PCR

- In case transportation is delayed the samples can be stored at +4°C for about one week.
- Specimens for influenza virus isolation should not be stored or transported in dry ice unless they are sealed, taped and double plastic-bagged as CO2 (dry ice) can rapidly inactivate the virus if it gains access to the specimens.

Transportation—Transport specimens with ice packs

Case Management

Mild to moderate illness

- The goal of treatment is to alleviate the symptoms. Bed rest is advisable until the fever subside.
- Antimicrobial agents are not effective against viruses.
- Mild analgesic (Paracetamol 0.5-1g every 4-6 hours) usually relieves headache and generalized pains and warm fluids help to relieve the discomfort of symptoms.
- Pholcodine 5-10 mg 3-4 times daily may be used to suppress unproductive cough. Specific treatment of complications such as bronchitis and pneumonia may be necessary.
- Currently, most seasonal Influenza A/H3N2 and A/H1N1Pdm09 viruses are sensitive to Neuraminidase Inhibitors, Oseltamivir (Tamiflu) and Zanamivir), Peramivir.
- Antiviral treatment should be initiated within the first 2 days of symptoms to treat people who are sick with flu symptoms and who are at increased risk of severe flu illness, such as pregnant women, young children, people 65 and older and people with certain chronic health conditions. Patients not considered being at higher risk of developing severe or complicated illness need not be treated with antiviral agents.
- Recommended antiviral medications are not licensed for treatment of children (restrictions are for under 1 year of age for Oseltamivir and under 7 years of age for Zanamivir).

Hospitalized patients

- Patients with atypical pneumonia not responding to antibiotics should be suspected for seasonal influenza (A or B) infection.
- Patients who have severe or complicated influenza should receive appropriate clinical care and treatment.
- The antivirals (Oseltamivir or Zanamivir or Peramivir) should be started within 48 hours of symptoms onset after taking sample for laboratory diagnosis to achieve positive clinical outcome (however it may be used at any stage of active disease if an ongoing viral replication is anticipated). Higher doses are not of any extra benefit, standard dose should be used for all i.e. 75 mg twice daily for Oseltamivir.
- Seasonal influenza and past influenza pandemics have been associated with an increased risk of secondary Staphylococcus aureus infections, which may be severe, rapidly progressive, therefore, wherever possible, antibiotic should be used for suspected bacterial co-infection in patients with seasonal influenza infection

Note: *Patients not considered being at higher risk of developing severe or complicated illness and who have uncomplicated illness due to confirmed or strongly suspected influenza virus infection need not be treated with antivirals.*

Preventive Measures

- Vaccination remains an important means of reducing the morbidity and mortality caused by influenza viruses. Prompt voluntary immunization of the high-risk groups including the health workers, pregnant women, children under 5 years, and those with chronic cardiopulmonary diseases is recommended.
- Following are the important points in immunizing the high-risk population:
  - o A yearly influenza vaccine is recommended as the first and most important step in protecting against influenza viruses.
  - o Vaccination of high risk persons is especially important to decrease their risk of severeinfluenza illness.
  - o Two weeks following vaccination, antibodies develop that protect against influenza virus infection.

Other preventive measures

i) Respiratory etiquette for healthy persons

- Cover nose and mouth with a tissue during coughing or sneezing. Throw the tissue in the trash covered by a llid.
- Hand washing with soap and water or with an alcohol-based hand rub.
- Avoid touching eyes, nose and mouth.
- Try to avoid close contact with sick people and crowded settings.
- Practice good health habits including good sleep, nutritious food with plenty of fluids and be physically active.

ii) Respiratory etiquette for sick persons

- For people sick with flu–like illness, it is recommended for them to stay home for at least 24 hours after the fever is settled.
- Limit contact with others.
- Use of face mask while coughing and sneezing.
- Infected persons should avoid travelling.
- Improve ventilation in closedplaces.
- Hospitalized patients should be put in isolation.

iii) Infection control at health-care facility managerial activities

- Standard operating procedures should be developed to ensure proper implementation of administrative & environmental controls and use of personal protective equipments (PPEs).
- Administrative policies that address adequate staffing and supplies, training of staff, education of patients and visitors, and a strategy for risk communication are particularly needed.

Basic infection control:—Standard and Droplet Precautions should be used when caring for a patient with an acute, febrile, respiratory illness.

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17. Japanese Encephalitis (JE)

Introduction

Japanese encephalitis is a zoonotic disease caused by a mosquito-borne virus. First case of Japanese encephalitis viral disease (JE) was documented in 1871 in Japan. JE is the leading cause of vaccine-preventable encephalitis in Asia and the western Pacific. JE virus is maintained in a cycle involving mosquitoes and vertebrate hosts, mainly pigs and wading birds. Humans can be infected when bitten by an infected mosquito. About 1 in 4 cases are fatal. There is no specific treatment for JE. Patient management focuses on supportive care and management of complications. Its prevention is to prevent mosquito bites and vaccination. CFR is 20% – 30%. Some recovered patients may (30%-50%) continue to have neurologic, cognitive, or psychiatric symptoms. Limited data is available from Pakistan; however human cases have been reported from around Karachi(CDC)

Clinical Picture

Majority of the Japanese encephalitis (JE) cases are asymptomatic; <1% of patients develop clinical disease.

Acute encephalitis presents as aseptic meningitis or undifferentiated febrile illness. The classical description of JE includes a Parkinsonian syndrome with mask like face, tremor, cogwheel rigidity, and choreo-athetoid movements. Acute flaccid paralysis, with clinical and pathological features similar to those of poliomyelitis, Seizures are common, especially among children. In endemic countries, where adults have acquired immunity through natural infection, JE is primarily a disease of children.

Infectious Agent—Single-stranded RNA virus that belongs to the genus *Flavivirus*

Host/Reservoir—

- The virus is maintained in an enzootic cycle between mosquitoes and amplifying vertebrate hosts, primarily pigs and wading birds.
- Humans are incidental or dead-end hosts, because they usually do not develop a level or duration of viremia sufficient to infect mosquitoes.

Mode of Transmission—Through the bite of an infected mosquito, primarily Culex species.

Incubation period—5-15 days

Seasonality—During or shortly after the rainy season in temperate regions and year-round in tropical regions (peak transmission during summer months).

Alert Threshold—One suspected or travel associated case is an alert

Outbreak threshold—One indigenous confirmed case is an outbreak

Case Definition

Acute Encephalitis Syndrome (AES)—A person of any age, at any time of year with the acute onset of fever and at least one of:

- Change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk)
- New onset of seizures (excluding simple febrile seizures).
- Other early clinical findings may include irritability, somnolence or abnormal behavior

Suspected—A case that meets the clinical description like headache, fever, meningeal signs, stupor, disorientation, coma, tremors, hypertonia, loss of coordination. or Any AES case with recent travel to or residency in an endemic country

Probable Case—A suspected case with four-fold or greater rise in JE virus-specific IgG antibody in paired sera (acute and convalescent phases), ELISA, haemagglutination inhibition test or virus neutralization test, in patient with no history of recent yellow fever vaccination and where cross-reactions to other flaviviruses have been excluded.

OR

JE virus specific IgM antibody in single blood sample in late acute phase or early convalescence.

OR

A suspected case that occurs in close geographic and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak is considered epidemiologically-associated

Confirmed case—A clinically compatible case (AES) with JE virus specific IgM antibody in the CSF by IgM capture ELISA or
Detection of the JE virus, antigen or genome in brain, spinal cord by immunochemistry or immunofluorescence or PCR.

Lab confirmation—Laboratory criteria for diagnosis of Japanese Encephalitis:

Presumptive:

- Four-fold or greater rise in JE virus-specific IgG antibody in paired sera (acute and convalescent phases), ELISA, haemagglutination inhibition test or virus neutralization test, in patient with no history of recent yellow fever vaccination and where cross-reactions to other flaviviruses have been excluded.
- JE virus specific IgM antibody in single blood sample in late acute phase or early convalescence.

Confirmatory:

- JE virus specific IgM antibody in the CSF by IgM capture ELISA

Detection of the JE virus, antigen or genome in brain, spinal cord by immunochemistry or immunofluorescence or PCR.

Methods:

- **Blood picture**: Include a moderate leukocytosis, mild anemia, and hyponatremia.
- **ELISA**: Virus–specific IgM-capture ELISA on CSF or serum
- **Neutralizing antibody testing**: confirmatory test for patients with JE virus IgM antibodies,
- **PCR:** In serum, plasma, blood, CSF or tissue
- Isolation of JE virus in serum, plasma, blood, CSF or tissue
- **Cerebrospinal fluid (CSF)** typically has a mild to moderate pleocytosis with a lymphocytic predominance, slightly elevated protein, and normal ratio of CSF to plasma glucose.
- **Magnetic resonance imaging (MRI)** detects JE virus-associated abnormalities such as changes in the thalamus, basal ganglia, midbrain, pons, and medulla. Thalamic lesions are the most commonly described abnormality;

EEG abnormalities may include theta and delta coma, burst suppression, epileptiform activity, and occasionally alpha coma.

Timings—For serology, the sample should be collected after the 5th day of the illness.

For PCR the CSF is the best sample and has to be collected within the first 4 days of illness

Specimen Collection—At least 0.5 mL of serum and/or 1.0 mL of CSF is required for lab testing. CSF specimens are routinely tested undiluted and therefore require larger amounts.

Packaging—Triple packaging with ice packs in a reverse cold chain

Storage—Storage and transportation should at 4°C, and transported with ice packs in a reverse cold chain with a duly filled request form

Transportation—Storage and transportation should at 4°C, and transported with ice packs in a reverse cold chain with a duly filled request form

Case Management

No specific treatments have been found to benefit patients with JE, but hospitalization for supportive care and close observation is generally required. Treatment is symptomatic. Rest, fluids, and use of pain relievers and medication to reduce fever may relieve some symptoms.

Preventive Measures

Take precautions to avoid mosquito bites by using insect repellent, wearingproper clothing and reducing exposure to mosquitoes during peak biting hours (The mosquitoes that transmit JE virus feed mainly outside during the cooler hours from dusk to dawn). Stay in well-screened rooms or use a bed net oraerosol room insecticides.

Vaccination:

- Inactivated vero cell culture-derived Japanese encephalitis (JE) vaccine (manufactured as IXIARO) is the only licensed JE vaccine available. IXIARO is given as a two-dose series, with the doses spaced 28 days apart. The last dose should be given at least 1 week before travel.

- For persons aged 17 years and older, if there is a continued risk for JE viral infection for potential for exposure; a booster dose may be given (if the person has received the two-dose primary vaccination series within the past one year)
- The recommended vaccination dosage is;

o 1-3 years old: 0.25 ml

o Overhead 3 years of age: 0.5 ml

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18. Leishmaniasis

Introduction

Leishmaniasis is a parasitic vector borne disease and the most common forms are cutaneous and visceral.

Found in focal areas in 90 countries in the tropics, subtropics, and southern Europe.The annual incidence of new cases is estimated between 1.5 and 2 million. Geographical distribution of the diseases depends on sand fly species acting as vectors, their ecology and the conditions of internal development of the parasite

Clinical Picture

Cutaneous

Skin lesions without mucosal involvement; generally localized on exposed areas of body accessible to sand flies. Appearance of one or more skin lesions, typically on uncovered parts of the body. The face, neck, arms and legs are most common sites. A nodule may appear at the site of inoculation and may enlarge to become an indolent ulcer. The sore may remain in this stage for a variable time before healing - it typically leaves a depressed scar.

Visceral

Affect several internal organs (usually spleen, liver and bone marrow) presenting with fever, splenomegaly, hepatomegaly, ascites, diarrhea, cough, anemia, bleeding etc. Post-kala-azar dermal Leishmaniasis (PKDL) is a sequel of visceral Leishmaniasis that appears as macular, papular or nodular rash usually on face, upper arms, trunks and other parts of the body.

Mucocutaneous

Primarily localized cutaneous lesion followed by mucosal involvement (nasal mucosa is primarily involved followed by buccal mucosa, lips , palate and larynx)

Infectious Agent—

- *Cutaneous: L. tropica and L. major*
- *Visceral: L. donovani and L. infantum*

Host/Reservoir—Classified into zoonotic and Anthroponotic in animal and human reservoir respectively. Most common reservoir among animals are dogs, jackals, foxesmice, hamsters, sloths, opossums and small forest rodents

Period of Communicability—Not directly transmitted from reservoir to person, but infectious to sand flies as long as parasites remain in lesions in untreated cases, usually a few months to 2 years

Mode of Transmission—Bite of phlebotomine sand fly

Incubation period—Considered to be at least a week but may extend up to several months.

- Zoonotic: 4 months
- Anthroponotic: 6-12 months

Seasonality—May and October, with a usual peak in June.

Case Definition

Cutaneous Leishmaniasis

Operational Definition—A case of cutaneous Leishmaniasis is a person showing clinical signs (skin or mucosal lesions) with parasitological confirmation of the diagnosis (positive smear or culture) and/or, for mucocutaneous Leishmaniasis only, serological diagnosis

Suspected Case—Appearance of one or more lesions, typically on uncovered parts of the body; the face, neck, arms and legs, the most common sites. At the site of inoculation a nodule appears, and may enlarge to become an indolent ulcer. The sore remains in this stage for a variable time before healing, and typically leaves a depressed scar. Certain strains may disseminate and cause mucosal lesions. These sequelae involve nasopharyngeal tissues and can be very disfiguring.

Probable Case—A person showing clinical signs (skin or mucosal lesions) without parasitological confirmation of the diagnosis (positive smear or culture)

Confirmed Case—A person showing clinical signs (skin or mucosal lesions) with parasitological confirmation of the diagnosis (positive smear or culture).

Visceral Leishmaniasis

Suspected—A Person with prolonged irregular fever >2 weeks, splenomegaly, weight loss, with fever, splenomegaly, hepatomegaly, ascites, diarrhea, cough, anemia, bleeding etc.

Probable—A suspected case of VL with serological evidence of infection

Confirmed—A suspected/ probable case of Visceral Leishmaniasis with parasitological confirmation

Note: *In endemic malarious areas, visceral leishmaniasis must be suspected when fever is not responding to anti-malarial drugs and persists for more than two weeks (assuming drug-resistant malaria has also been considered).*

Lab confirmation—Serological Testing

- Immunofluorescence assays
- ELISA
- Direct agglutination methods
- Immunochromatography

K-39 based antigen testing for visceral disease
Parasitological Confirmation

- Culture from aspirated material/ biopsy
- Smear(aspiration) preparation from spleen, liver, bone marrow, lymph node
- Biopsy and special stains for confirmation of L.D bodies
- Molecular methods including PCR

Timings—Whenever possible, specimens should be collected before treatment is initiated. Since the parasitemia may fluctuate, multiple smears might be needed. These can be taken at 8 to 12 hour intervals for 2 to 3 days

Specimen Collection—Cutaneous

- Skin biopsy is the standard dermatologic technique for obtaining specimen.
- Slit-skin preparation or aspiration from the edge of the lesion by a well-trained staff is the alternate.

Visceral

- Collect 5ml clotted blood or serum for serologic studies
- Splenic or bone marrow aspirate collected in a tube with anticoagulant is required for demonstration of amastigotes.

Packaging—Triple packaging

Storage—4-8˚C

Transportation—Specimen can be transported at 22-25°C without delay. Do not transport cultures on cold packs or dry ice, and keep the cultures away from heat.

Case Management

Mild:

- Observe only, as spontaneous healing is preferred in most cases.
- Paromomycin ointment
- Heat/thermo therapy
- Intralesional antimony 20mg/kg/week for 5-10 weeks
- Cryotherapy or laser therapy

Complex:

- Sodium Stibogluconate or Meglumine antimoniate 20 mg/kg/day IV/IM for 20 days
- Liposomal Amphotericin B

Visceral:

- Amphotericin B

Other options of treatment include Fluconazole, Ketoconazole, Miltefosine

Preventive Measures

- The best way for travelers to prevent infection is to protect themselves from sand fly bites. Personal protective measures include minimizing nocturnal outdoor activities, wearing protective clothing and applying insect repellent to exposed skin, under the ends of sleeves and pants. The most effective repellents are those that contain the chemical DEET (N, N-diethyl meta toluamide).
- **Anthroponotic Leishmaniasis:** Usepermethrin treated bed nets and residual spraying of indoor rooms by insectisides.
- **Zoonotic Leishmaniasis:** Poison or dig up the burrows of reservoir rodents.

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19. Leprosy

Introduction

A chronic infectious disease usually affecting the skin, peripheral nerves, respiratory/ nasal mucosa and eyes. According to official reports received from 138 countries from all WHO regions, the global registered prevalence of leprosy at the end of 2015 was 176 cases (0.2 cases per 10, 000 people These bacteria grow very slowly and it may take up to 20 years to develop signs of the infection.

Clinical Picture

- **Skin manifestations**:
  - o **Paucibacillary**: characterized by one or a few hypopigmented skin macules that exhibit loss of sensation.
  - o **Multibacillary**: characterized by multiple symmetrically-distributed skin lesions that might not exhibit loss of sensation, nodules, plaques, thickened dermis, frequent involvement of the nasal mucosa resulting in nasal congestion and epistaxis.
- **Neuronal manifestations**: Muscle weakness or paralysis, enlarged nerves, loss of sensations leading to unnoticed injuries.
- **Blindness**
- **Epistaxis**, stuffy nose

Classification based on Clinical Features:

Tuberculoid: (Paucibacillary) One/few well-demarcated, hypopigmented, and hypo aesthetic or aesthetic skin lesions; peripheral nerves may also be involved

Lepromatous: (Multibacillary) A number of erythematous papules and nodules or infiltration of face, hands and feet progressing to skin thickening

Borderline: Skin lesions are characteristic of both the tuberculoid and lepromatous forms

Indeterminate: Early lesions, usually hypopigmented macules without developed tuberculoid/ lepromatous features but with definite identification of acid-fast bacilli in Fite stained sections

Infectious Agent—*Mycobacterium Leprae*

Host/Reservoir—

- Humans
- Armadillo, Chimpanzees, Cynomolgus Macaques, and Sooty Mangabey monkeys

Period of Communicability—In prolonged contact with untreated leprosy patient, one could get infected

Mode of Transmission—

- The exact mechanism of transmission is not well understood
- Person to person spread via nasal droplets is believed to be the main route

Incubation period—The incubation period varies widely from months to 30 years;

- An average of 4 years for tuberculoid leprosy
- 10 years for lepromatous leprosy.

Seasonality—Dry seasons with low humidity

Alert Threshold—WHO considers leprosy as a public health problem if the national prevalence rate is below one case per 10, 000 population.

Case Definition

Probable Case—A person having one or more of the following symptoms

- Hypo pigmented or reddish skin lesion(s) with definite loss of sensation
- Damage to the peripheral nerves, as demonstrated by loss of sensation and mobility to hand, feet or face.

Confirmed case—Probable case with laboratory confirmation

Lab confirmation—

- Histopathological examination
- Modified acid fast staining with 1% decolorizer
- Serological assay
- Molecular testing (PCR)

Timings—At time of presentation

Specimen Collection—

- Skin/Nerve biopsy
- Skin/nasal smears
- Blood/Serum

Packaging—Triple Packaging maintaining reverse cold chain

Storage—4-8°C for blood/serum. Formalin fixation for biopsy specimen

Transportation—Transport in cold chain to relavant lab

Case Management

Paucibacillary: Once daily Dapsone and Rifampicin once in a month for 6 months

Multibacillary: Dapsone for 12-24 months once daily, Rifampicin and Clofazimine once in a month

Single lesion paucibacillary leprosy: Rifampicin (600 mg) and Ofloxacin (400 mg) stat dose

Preventive Measures

Isolation of infected case:

- Isolation of tuberculoid cases is not indicated.
- Untreated cases of lepromatous leprosy should be isolated with contact precautions for at least 72 hours after the treatment is commenced.

- Identification and investigation of contacts by annual examinations for five years after the last contact with the infected person is recommended.
- Early detection and treatment of new cases.
- Prophylactic BCG injection in neonates born to infected mothers by a single dose of rifampicin as prophylaxis is indicated.

Note: *The best way to prevent leprosy is to avoid long-term, close contact with an untreated, infected person.*

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20. Malaria

Introduction

A vector borne parasitic disease transmitted by female Anopheles mosquito species. With an estimated 1 million cases annually, Pakistan remains one of the highest malaria burden sharing countries in WHO-EMRO and has been grouped with Sudan, Yemen, Somalia and Afghanistan. An estimated 98% of Pakistan population (185 million) is at varying risk for malaria while population at high risk is around 29% (54.6 million). The highest endemic districts/agencies are located in bordering regions with Iran and Afghanistan. Every year >3.6 million malaria suspects are treated as malaria cases in health facilities without confirmatory tests. The overall reported Annual parasites incidence API/1000 in 2015 was 1.08 with a high variation within provinces (Sindh 1.06, KP 2.28, Balochistan 5.39, FATA 8.63 and Punjab 0.03). Currently 59% of detected cases are >14 years, without any significant gender difference.

Clinical Picture

Fever, chills, sweats, headache, nausea and vomiting, body aches and general malaise

Un-complicated

The classical (but rarely observed) malaria attack lasts 6-10 hours. It consists of Classically (but infrequently observed) the attacks occur every second day with the "tertian" parasites *(P. falciparum, P. vivax, and P. ovale)* and every third day with the "quartan" parasite *(P. malariae)*

Complicated

- Cerebral malaria, with abnormal behavior, impairment of consciousness, seizures, coma, or other neurologic abnormalities
- Severe anemia due to hemolysis

- Hemoglobinuria
- Acute respiratory distress syndrome (ARDS)
- Abnormalities in blood coagulation
- Low blood pressure caused by cardiovascular collapse
- Acute kidney failure
- Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites
- Metabolic acidosis
- Hypoglycemia

Infectious Agent—

- Plasmodium falciparum
- Plasmodium vivax
- Plasmodium ovale
- Plasmodium malariae
- Plasmodium knowlesi (rarely infect humans)
- Plasmodium Simium

Note: *First two of the above species are prevalent in Pakistan.*

Host/Reservoir—Humans are the only known reservoir for the species prevalent in Pakistan

Period of Communicability—Humans may infect mosquitoes as long as infective gametocytes are present in the blood. Anopheles mosquitoes remain infective for life.

Mode of Transmission—

- Bite of an infective female Anopheles mosquito
- Rarely through blood transfusion from infected person

Incubation period—P. falciparum 9-14 days, P. malariae 18-40 days, P. ovale and P. vivax 12-18 days

Seasonality—Peak occur during rainy season (August-September)

Alert Threshold—

- Number of cases reaches two times the mean number of Confirmed cases of the previous 3 weeks for a given location.
- A single new specie in a given location

Outbreak threshold—In endemic area: Slide positivity rate above 50% or falciparum rate above 40%; while in non-endemic area, evidence of indigenous transmission of falciparum.

Case Definition

Suspected Case—Uncomplicated malaria

Patient with fever or history of fever within the past 48 hours (with or without other symptoms such as nausea, vomiting and diarrhoea, headache, back pain, chills, myalgia) in whom other obvious causes of fever have been excluded.

Severe malaria

Patient with symptoms as for uncomplicated malaria, as well as drowsiness with extreme weakness, associated signs and symptoms related to organ failure such as disorientation, loss of consciousness, convulsions, severe anaemia, jaundice, haemoglobinuria, spontaneous bleeding, pulmonary oedema and shock.

Probable Case—A suspected case with history of similar manifestations among other household/neighbourhood

Confirmed Case—Demonstration of malaria parasites in blood film by examining thick or thin smears, or by rapid diagnostic test kit

Lab confirmation—

- Peripheral blood smear (gold standard, thick and thin smears)
- Rapid Diagnostic Test (Immunochromatography), RDT kit with sensitivity of 95% is recommended for use.
- PCR
- Serology (Indirect Immunofluorescence and ELISA)

Timings—Within hours of presentation (Preferably during shivering)

Specimen Collection—Peripheral blood film: Collect 3-5 ml blood in a tube with anticoagulant (EDTA). Immunodiagnostic test kit: Sample may also be used to demonstrate parasite antigen.

Storage—Blood in EDTA tube may be refrigerated up to 2-3 days, but prolonged exposure to EDTA can alter parasite morphology.

Transportation—Transport the specimen at room temperature preventing sample spillage or damage to the tubes. Slide should be made from blood within one hour. If transport time is longer thick and thin slides should be made at bedside.

Case Management

Chloroquine Phosphate, Artemisinin-based combination therapies (ACTs) are the recommended treatments for uncomplicated P. falciparum malaria however Artemisinin and its derivatives should not be used as monotherapy.

The following ACTs are recommended:

- Artesunate plus sulfadoxine-pyrimethamine.
- Artemether plus lumefantrine,
- Dihydroartemisinin and Piperaquine Phosphate
- Artemether-Lumefantrine is currently available as a fixed-dose formulation with dispersible or standard tablets containing 20 mg of Artemether and 120 mg of lumefantrine. The recommended treatment is a 6-dose regimen Twice Daily (BD) over a 3-day period. The dosing is based on the number of tablets per dose according to predefined weight bands (5–14 kg: 1 tablet; 15–24 kg: 2 tablets; 25–34 kg: 3 tablets; and > 34 kg: 4 tablets)

In case of pregnant women, during first trimester quinine plus Clindamycin to be given for 7 days (Artesunate plus Clindamycin for 7 days is indicated if this treatment fails).

Uncomplicated Vivax Infections

Chloroquine combined with Primaquine is the treatment of choice for Chloroquine-sensitive infections. Dosage is as given below:

- Chloroquine Phosphate: 04 tablets STAT, 02 after 6 hours, then 12 hourly for 02 days
- Primaquine base: 30 mg of primaquine base once daily for 14 days. For G6PD deficiency 45 mg baseweekly for 8 weeks, (30mg of primaquine base is equal 52.6 mg primaquine phosphate)
- Pediatric dose: 0.5 mg/kg for 14 days (do not exceed 30mg of base/day)

COMPLICATED MALARIA

Adult: Artesunate based parental therapy followed by "complete" course of oral therapy

Or Quinine 20 mg/kg loading dose followed 10 mg/kg 8 hourly with doxycycline 100mg twice daily for 7 days (use clindamycin in pregnant or paediatric population.)

- **Warning:** Do not give Primaquine to pregnant women and children <6 months of age and it is advisable to do a glucose-6-phosphate dehydrogenase test before giving this drug.
- Do not give undiluted Chloroquine or quinine by I/M or I/V route, as it can cause sudden cardiac arrest, especially in children
- Do not give Sulfadoxine/ pyrimethamine to children <2 months of age or during first trimester of pregnancy
- Suspected/Probable case of severe Malaria and high risk groups should be treated immediately

Preventive Measures

Travelers and their advisers should note the four principles – the ABCD – of malaria protection:

- Beaware of the risk, the incubation period, the possibility of delayed onset and the main symptoms.

- Avoid being **bitten** by mosquitoes.
- Take antimalarial drugs (**Chemoprophylaxis**) when appropriate, to prevent infection from developing into clinical disease.
- Immediately seek **Diagnosis** and treatment if a fever develops 1 week or more after entering an area where there is the risk of malaria and up to 3 months (or, rarely, later) after departure from a high-risk area.

a) Personal protection

- Wear long sleeves and trousers outside the houses in the evening. Use mosquito repellent creams and sprays.
- Use mosquito coils or vaporizing mat containing pyrethrin.
- Use of insecticide-treated mosquito nets (ITNs) should be promoted.

b) Vector control

- Indoor spraying with residual insecticides(IRS).
- Reduce mosquito breeding sites.
- Improve vector surveillance.

C) Chemoprophylaxis (Malaria control program)

- Recommended chemoprophylaxis: Atovaquone-proguanil, Doxycycline or Mefloquine.

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21. Measles

Introduction

An acute viral respiratory illness and is still a common and often fatal disease in developing countries. The most common causes of death are pneumonia in children and acute encephalitis in adults. Measles in developing countries has resulted in high attack rates among children younger than 12 months of age. The case-fatality rate may be as high as 25%.

Clinical Picture

- The prodromal phase lasts 2–4 days (range 1–7 days) characterized by fever, followed by the three "C"s i.e. cough, coryza (runny nose), or conjunctivitis. The measles rash is a maculopapular eruption that usually lasts 5–6 days. It begins at the hairline, and then involves the face and upper neck. During the next 3 days, the rash gradually proceeds downward and outward, reaching the hands and feet.
- Koplik's spots, is considered to be pathognomonic for measles. It occurs 1–2 days before the rash to 1–2 days after the rash, and appears as punctate blue-white spots on the bright red background of the buccal mucosa.

Complications

- Measles can cause serious complications in malnourished children and people with reduced immunity; complications include diarrhea, dehydration, stomatitis, inability to feed, Sub- acute sclerosing panencephalitis (SSPE) and bacterial infections (skin and elsewhere).
- Measles illness during pregnancy results in a higher risk of premature labor, spontaneous abortion, and low-birth weight infants.

Infectious Agent—*Morbillivirus* in the *Paramyxoviridae* family

Host/Reservoir—Human is the only reservoir

Period of Communicability—Measles may be transmitted from 4 days before to 4 days after rash onset.

Mode of Transmission—Transmits via large respiratory droplets in closed areas or by direct contact with the nasal and throat secretions of infected persons

Incubation period—7 to 21 days.

Seasonality—Peak Incidence is usually in April and May

Alert Threshold—One suspected case

Outbreak threshold—Five or more clinical cases in a single location over a 30 day time period with at least one lab confirmed case

Case Definition

Suspected Case—Any person in whom clinician suspects measles Infection, or any person with fever, maculopapular rash (i.e. non-vesicular), cough, conjunctivitis and coryza i.e. runny nose or conjunctivitis

Probable Case—Any person with history of fever, rash and linked with a confirmed case of measles

Confirmed Case—Suspected or probable case confirmed through

- Polymerase chain reaction (PCR) for Measles RNA virus (RT PCR): 1 to 3 days appearance of rash OR
- Measles specific IgM: 3 days after appearance of rash OR
- IgG: (4 Fold increase between acute and convalescent phase)

Note: Patients with history of measles (satisfying case definition) within past one month should also be reported as suspected measles case. Hence, it is important for physicians to routinely ask patients (or parents) who presents with common complications of measles e.g. pneumonia, diarrhoea, otitis media, corneal scarring and malnutrition about history of rash illness.

Lab confirmation—Presence of measles-specific IgM antibodies or PCR for Measles RNA virus by real-time polymerase chain reaction (RT-PCR)

Timings—

- Five samples should be taken from fresh cases, less than five days from rash onset, in documented outbreaks
- RT PCR: 1 to 3 days after appearance of rash
- Measles specific IgM: 3 days after appearance of rash

Specimen Collection—

- Collect throat swab (Nasal/Nasopharyngeal) for virus isolation and genotyping, preserved in VTM.
- Collect 5 ml blood, centrifuged for serum separation at 3000 rpm for 5 minutes. If only two or three fresh cases are available that is sufficient.
- If centrifugation is not possible, blood should be kept in refrigerator until there is complete retraction of the clot from the serum.
- Carefully remove the serum and transfer aseptically to a sterile labelled vial.

Packaging—Triple package

Storage—Store serum at 4-8^{O}C for not more than 48 hours. Do not freeze the whole blood.

Transportation—Transport the specimens with complete request form maintaining cold chain.

Case Management

- There is no specific treatment for measles and most people recover within 2–3 weeks.
- Refer complicated cases to tertiary care settings for further management.
- All children 6 months - 5 years of age should also receive prophylactic Vitamin A in two doses given 24 hours apart. Vitamin A supplementation for two days is:
    - o Less than 6 months: 50,000IU
    - o 6 to 11 months: 100,000 IU
    - o Older than 12 months: 200,000 IU

- For children with ophthalmologic evidence of vitamin A deficiency, doses should be repeated administered on day 2 and day 28.
- Ensure adequate nutrition and liquids
- Symptomatic treatment is also recommended live measles vaccine

Preventive Measures

- Measles can easily be prevented through 2 doses of the measles-containing vaccine. Measles routine immunization first dose is given at at 9 months and second at 15 months of age.
- During a measles campaign; the priority is to immunize children 6 months to 5 years old, regardless of vaccination status or history of disease.

Post Exposure Prophylaxis

- Live measles vaccine provides permanent protection and may also prevent disease if given within 72 hours of exposure. (Always ensure vaccine safety for specific groups).
- Immunoglobulin (IG) may prevent or modify disease and provide temporary protection if given within 6 days of exposure. The dose is 0.5 mL/kg body weight, with a maximum of 15 ml intramuscularly and the recommended dose of IG given intravenously is 400 mg/kg. IG may be especially indicated for susceptible household contacts of measles patients, particularly contacts younger than 1 year of age. IG should not be used to control measles outbreaks.
- If the child is 12 months of age or older, live measles vaccine should be given about 5 months later when the passive measles antibodies have waned away.

Infection Control

- Measles is transmitted through aerosols, thus contact, droplet and aerosol precautions are recommended along with standard precautions.
- Healthcare providers should follow respiratory etiquette and airborne precautions should be adopted in healthcare settings.

- Regardless of presumptive immunity status, all healthcare staff entering the room should use respiratory protection consistent with airborne infection control precautions (use of an N95 respirator or a respirator with similar effectiveness in preventing airborne transmission).

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22. Meningitis

Meningitis is characterized by sudden onset of febrile illness with signs and symptoms of meningeal involvement. The inflammation may be caused by infection with viruses, bacteria, parasites, fungi and other non-infectious agents such as nonsteroidal anti-inflammatory drugs.

Neisseria meningitides, *S. pneumoniae* and Hib constitute more than 75% of all cases of bacterial meningitis in most studies, and 90% of bacterial meningitis in children.

Viral meningitis (aseptic meningitis): With multiple viral aetiologies, Viral meningitis occurs worldwide and sporadically or as an epidemicdisease. Case fatality rates are generally low. Infection may have potential of long-term sequelae inthose affected (mostly children) but the disease is rarely severe, and recovery is usually complete. Arash, transient paresis and encephalitic manifestations may be present. Active illness seldom exceeds10 days. Neuromuscular residual signs may occur for about 1 year and usually clear up completely. Aseptic meningitis has a reported incidence of 10.9 cases per 100,000 person-years. It occurs inindividuals of all ages but is more common in children, especially during summer and 3 times more common in males.

Etiology:

- o **Bacterial:** *Listeria spp.* (monocytogenes), Staphylococci, enteric bacteria, group B streptococci, *Mycobacterium tuberculosis*, syphilis, Leptospirosis, *Borrelia burgdorferi, T. pallidum, Brucella spp.*, *Francisellatularensis.*
- o **Viruses:** Mumps, Enterovirus, coxsackievirus, arboviruses, measles, herpes simplex and varicella viruses and lymphocytic choriomeningitis.
- o **Fungi:** *Cryptococcus neoformans, Coccidioidesimmitis, Blastomycesdermatitidis, Histoplasma capsulatum, Candida albicans, Aspergillus spp.* and *Sporothrixschencki (the dimorphic fungi are not yet reported from the country)*
- o **Parasites:** *Acanthamoebaspp.,Naegleriafowleri,Angiostrongyluscantonensis, Gnathostomaspinigerum*, *Baylisascarisprocyonis*, *Schistosomaspp.*, *Strongyloidesstercoralis* and *Echinococcusgranulosus*

Case definition

Suspected

Acute onset of fever ≥38.5°C and one or more of the following:

- Neck stiffness and pain
- Severe headache
- Nausea and vomiting
- Photophobia
- Altered mental status

In children <2 years of age a case with sudden onset of fever ≥38.5°C and irritability or bulging fontanels should be clinically defined as a case of meningitis.

Suspect viral meningitis: A suspected case with one or more of the following features seen in the CSF examination:

- Normal glucose and normal or mild increase (>50 mg/dl) in protein
- Moderate increase cells (<500/mm^3) and lymphocyte predominance (>50%)
- Epidemiological link to a confirmed case

Suspect bacterial meningitis: a suspected case with one or more of the following features seen in theCSF examination:

- Turbid
- Decreased glucose (<50 mg/dl) and increase of protein (100-500 mg/dl)
- Increased cells (>500/mm^3) and polymorph predominance (>50%)
- Positive microscopy
- Epidemiological link to a confirmed case

Confirmed

A suspect case that is epidemiologically linked to a confirmed case, or a case that is laboratory confirmed by serology/microscopy/culture/isolation.

23. Meningococcal Meningitis

Introduction

It is a bacterial form of meningitis. It can cause severe brain damage and is fatal in 50% of cases if untreated.

Several different bacteria can cause meningitis. *Neisseria meningitidis* is the one with the potential to cause large epidemics. There are 12 serogroups of *N. meningitidis* that have been identified, 6 of which (A, B, C, W, X and Y) can cause epidemics. Geographic distribution and epidemic potential differ according to sero-groups.

Clinical Picture

Sudden onset of fever >38°C, Neck stiffness, altered consciousness, other signs of Meningeal irritation or petechial or purpuric rash. Babies may be slow or inactive, irritable, vomiting, or feeding poorly. In young children, doctors may also look at the child's reflexes for signs of meningitis. The disease is still associated with a high mortality rate and persistent neurologic defects, particularly among infants and young children.

Patients also may complain of skin rash, which usually points to disease progression. Elderly patients are prone to have an altered mental state and a prolonged course with fever.

Meningococcal septicemia, which is characterized by rapid circulatory collapse and a hemorrhagic rash, is a more severe, but less common, form of meningococcal disease.

Infectious Agent—*Neisseria meningitidis,* Gram-negative diplococci, sero groups A, B, C, Y, W135

Host/Reservoir—Humans are the only host

Mode of Transmission—

- It is transmitted person to person through droplets of respiratory or throat secretions.

- Close and prolonged contact such as kissing, sneezing or coughing on someone, or living in close quarters (such as a dormitory, sharing eating or drinking utensils) with an infected person facilitates the spread of the disease.
- The most important source of infection is asymptomatic carriers.

Incubation period—Between 2 to 10 days, most commonly 3-4 days

Seasonality—Throughout the year with higher incidence during cold months

Alert Threshold—Three or more suspected cases in one location; or one confirmed case of *N. meningitidis*is an alert.

Outbreak threshold—Two or more lab confirmed cases of meningococcal meningitis from a single location is an outbreak.

Case Definition

Suspected—A case that meets the clinical case definition

(Sudden onset of fever >38°C, neck stiffness, altered consciousness, other signs of meningeal irritation or petechial or purpuric rash.)

In infants under one year of age, suspect meningitis when fever is accompanied by bulging fontanelle

Probable Case—Turbid/ purulent cerebrospinal fluid (CSF) (with or without Gram-negative diplococci visible on microscopy), OR

Ongoing epidemic and epidemiological link to a confirmed case.

Confirmed case—Positive CSF culture with or without positive blood culture of a suspected or probable case.

OR

Positive antigen detection in CSF by agglutination tests or by polymerase chain reaction (PCR),

Note: *The identification of the serogroups and susceptibility testing to antibiotics are important to define control measures*

Lab confirmation—Presumptive identification of *N. meningitidis*, *S. pneumoniae*, and *H. influenzae* can be made on the basis of a cytological examination of the CSF, specific colony morphology on blood and/or chocolate agar, staining properties on a Gram stain, or by detection of specific antigens in the CSF by a latex agglutination test or using a rapid diagnostic test (RDT)

Timings—Ideally within one hour after time of collection.

Specimen Collection—

- Collect 2-3 ml of CSF under aseptic measures through Lumbar puncture in a sterile screw-capped container for chemical analysis, latex particle agglutination test and culture for *Neisseria meningitidis*.
- Blood should be collected when a spinal tap is contraindicated or cannot be performed for technical reasons

Packaging—TIM (Trans Isolate Medium) Bottle

Storage—If delay is anticipated, sample should be inoculated in Trans Isolate Medium (TIM) [4] at 35-37°C. Do not expose the CSF to sunlight or extreme heat or cold

Transportation—Transport the specimen immediately (within one hour) to the lab. If delay is anticipated, incubate the CSF (with screw-caps loosened) at 35°C in a 5% CO_2 atmosphere (or candle-jar).If same-day transport to the laboratory is not possible, CSF should be inoculated aseptically into a TIM medium with a syringe and held overnight at, or close to 35°C.

Case Management

- Meningococcal disease is potentially fatal and should always be viewed as a medical emergency. Admission to a hospital or health centre is necessary.
- Isolation of the patient is not necessary. Appropriate antibiotic treatment must be started as soon as possible, ideally after the lumbar puncture has been carried out if such a puncture can be performed immediately.
- If treatment is started prior to the lumbar puncture it may be difficult to grow the bacteria from the spinal fluid and confirm the diagnosis.
- However confirmation of the diagnosis should not delay treatment.
- A range of antibiotics can treat the infection, including penicillin, ampicillin and ceftriaxone.

- During epidemics of confirmed meningococcal disease, case management needs to be simplified to permit the health system to respond to rapidly increasing numbers of cases.
- Diagnosis: as the flood of patients could make the routine use of lumbar puncture to confirm meningitis impossible, every suspected case of meningitis should be considered and treated as one of meningococcal meningitis.
- Treatment: simplified treatment protocols are appropriate: Use appropriate empirical antibiotics followed by culture sensitivity report.

Preventive Measures

For Contacts:

Antibiotics may be recommended for close contacts of a person with meningococcal meningitis and family members of a person who develops a serious Hib infection.

Contact management would include: Surveillance for signs and symptoms and prophylaxis depending on the causative agentEducation of contacts regarding the signs and symptomsof the disease and case management incase of appearance of symptoms. Immunization of contactsvaries according to the specific infectious agent.

Vaccination

To prevent secondary cases, of meningococcal diseasedue to serogroup A, C or W135, vaccine can be used for close contacts. Vaccination should be targeted to areas where the epidemic threshold is reached. There are three types of vaccines available:

- **Polysaccharide vaccines** are used during a response to outbreaks and are not effective before 2 years of age. This offers a 3-year protection but does not induce herd immunity.
- **Conjugate vaccines** are used in prevention (into routine immunization schedules and preventive campaigns) and outbreak response. They confer long-lasting immunity (5 years and more), prevent carriage and induce herd immunity. Theycan be used as early as one year of age.

- **Protein based vaccine**, against N. meningitidis B. has been used in outbreak response.

Chemoprophylaxis

Antibiotic prophylaxis is recommended for close contacts. When given promptly, it decreases the risk of transmission. Ciprofloxacin is the antibiotic of choice but resistance against ciprofloxacin has been emerged since 2007-8 and ceftriaxone or rifampin can be given alternative. Chemoprophylaxis is recommended for the following contacts:

- Household members (i.e. persons sleeping in the same dwelling as the case)
- Institutional contacts (i.e. persons who share sleeping quarters ege roommates in boarding schools; persons sharing barracks in military camps); nursery school or childcare centre contacts (i.e. children and teachers who share a classroom with the case)
- Other persons who have had contact with the patient's oral secretions through kissing or sharing of food and beverages.

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24. Middle East Respiratory Syndrome Corona Virus (MERS-CoV)

Introduction

A newly identified respiratory illness that has recently been emerged in the Middle East in September 2012. It is supposed to be a Zoonotic infection due to link of all MERS cases infected with dromedary camels. Since its emergence, autochthonous MERS cases have been detected mostly in the Middle East (Saudi Arabia, United Arab Emirates, Jordan, Qatar, Oman, Kuwait, Yemen, Lebanon and Iran). Travel associated cases have also reported from Europe (United Kingdom, Germany, France, Italy, Greece and the Netherlands), Africa (Tunisia and Algeria), Asia (Malaysia and Philippines) and from USA.

Clinical Picture

MERS-CoV infection ranges from asymptomatic to severe pneumonia with acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure resulting in death.

Typically, the disease starts with fever, cough, chills, sore throat, myalgia and arthralgia followed by dyspnea and rapidly progresses to pneumonia, often requiring ventilator and other organ support.

Infectious Agent—A novel coronavirus called "Middle East Respiratory Syndrome Corona virus" *Betacoronavirus* genus (*Coronavirinae*subfamily)

Host/Reservoir—Dromedary camel are likely to be a major reservoir

Mode of Transmission—MERS-CoV is thought to spread from an infected person's respiratory secretions, such as through coughing or sneezing.

Incubation period—Generally less than one week, but can be as long as 14 days (2–14 days)

Alert Threshold—One probable case

Outbreak threshold—One confirmed case

Case Definition

Suspected Case—Individuals with acute respiratory illness of any degree of severity, and/or indications of pulmonary parenchymal disease (e.g. pneumonia or ARDS), based on clinical or radiological evidence, who requires admission to hospital, with no other etiology that fully explains the clinical presentation.

Probable Case—Individuals with acute respiratory illness of any degree of severity who, within 14 days before onset of illness, had any of the following exposures:

- Close physical contact with a confirmed or probable case of MERS-CoV infection, while that patient was ill;
- A healthcare facility in a country where hospital associated MERS-CoV infections have been reported
- Direct contact with dromedary camels or consumption or exposure to dromedary camel products (raw meat, unpasteurized milk, urine) in countries where MERS-CoV is known to be circulating in dromedary camel populations or where human infections occurred as a result of presumed zoonotic transmission

OR

Suspected patient who has travelled within 14 days before onset of illness to the Middle East or countries where MERS-CoV is known to be circulating in dromedary camels or where human infections have recently occurred.

Confirmed Case—A probable case with laboratory confirmation of MERS-CoV infection (rRT-PCR assays)

Patient Under Investigation (PUI)—A person who has both clinical features and an epidemiologic link should be considered a patient under investigation (PUI).

Epidemiological link:

The epidemiological link may have occurred within a 14-days period before or after the onset of illness:

- A history of travel from countries in or near the Arabian Peninsula
- Close contact with a symptomatic traveler from countries in or near Arabian Peninsula.

- Health care associated exposure to a confirmed or probable case
- Visiting patients or staying in same close environment with MERS-CoV infected case.
- Traveling together with individual(s) infected with MERS-CoV
- Living in the same household as individual(s) infected with MERS-CoV

Inconclusive testing:

- A positive screening test on a single rRT-PCR target without further confirmation
- Evidence of sero-reactivity by a single convalescent serum sample ideally taken at least 14 days after exposure by a screening assay (ELISA or IFA) and a neutralization assay, in the absence of molecular confirmation from respiratory specimens.
- Patients with an inconclusive initial testing should undergo additional virologic and serologic testing to determine if the patient can be classified as a confirmed MERS-CoV case.

Lab confirmation—

- Real-time reverse-transcription polymerase chain reaction (rRT-PCR) assays
- ELISA test
- Immunofluorescence assay (IFA)

Note: *Serologic test is for research/ surveillance purposes and not for diagnostic purposes.*

Interpretation:

- Laboratory confirmation of MERS-CoV infection requires either a positive rRT-PCR result for at least two specific genomic targets, or a single positive target with sequencing of a second target.
- MERS patient to be considered negative for active MERS-CoV infection following two consecutive negative rRT-PCR tests on all specimens.
- Antibody-positive by ELISA, needs IFA assay and/or micro-neutralization assay to confirm the positive result

- A positive test both by ELISA and IFA, determines to be positive.
- A positive test by ELISA but indeterminate or negative by IFA needs additional confirmatory testing.

Timings

- If symptom onset was less than 14 days ago, a single serum NP/OP specimen and lower respiratory specimen should be collected rRT-PCR testing.
- If symptom onset was 14 or more days ago, a single serum specimen for serologic testing in addition to a lower respiratory specimen and an NP/OP specimen are recommended.

Specimen Collection—

- Collect 2-3 ml of clinical sample into a sterile, leak-proof, screw-cap cup or sterile dry container
- Specimen of sputum, bronchoalveolar lavage, tracheal aspirate, pleural fluid, nasopharyngeal swab (NP), oropharyngeal swab (OP), nasopharyngeal wash/ aspirate or nasal aspirate may be collected for lab testing

Serum:

- 5-10 ml of whole blood in a serum separator tube from adults.
- Minimum 1 ml of whole blood in a serum separator tube from pediatric patients

Packaging—All samples must be properly labeled, packed, sealed and placed in triple packaged container with patient summary sheet.

Storage—For short periods (≤24–48 hours), most specimens should be held at 2-8°C rather than frozen.

For delays exceeding 48 hours, blood specimens should be frozen at -20°C while NP/OP specimen should be stored at –70°C.

Transportation—All specimens must be pre-packed as triple packaging to prevent breakage and spillage.

Case Management

There is no specific antiviral treatment. Treatment is supportive and based on the patient's clinical condition. For severe cases, current treatment includes care to support vital organ functions.

Patient Placement:

- Single room with toilet and sink,
- Appropriate ventilation (e.g. level of air filtration and direction of air flow) should be maintained.
- Appropriate supply and accessibility to PPE
- Only patients who are confirmed to have MERS-CoV infection can be kept together 2 meter apart
- Accompanying individuals should be frequently observed for symptoms of acute respiratory infection
- Respiratory hygiene should be encouraged for patient and accompanying individuals
- Patient movement and/or transport should be restricted to essential diagnostic and therapeutic tests.
- Transfer within and between facilities should be avoided unless medically unavoidable
- Use dedicated equipments
- The number of visitors should be minimized to essential visitors only.

Preventive Measures

- Currently, there is no vaccine to prevent MERS-CoV infection.
- People must protect themselves from respiratory illnesses by taking everyday preventive measures such as;
  - o Properly washing hands with water and soap orusing alcohol-based hand sanitizer.
  - o Covering the nose and mouth with a tissue paperwhile coughing or sneezing and then throwing the tissue paper in the trash.
  - o Avoiding touching the eyes, nose and mouth with unwashed hands.

- o Avoiding personal contact such as kissing or using the same utensilsas the sick people.
- o Avoiding touching camels and raw meat in endemic areas.

Health Education

- All HCWs should receive education on MERS-CoV includingits symptoms, measures to control its spread, reinforcement of routine practices, contact and droplet precautions including selection and safe removal of PPE, safe work practices, sample collection, transportation and reporting.
- Patients, families and visitors should receive education about the precautions being used, the duration of precautions, the prevention of transmission of infection to others, appropriate use of PPE and hand hygiene.

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25. Mumps

Introduction

Mumps (infectious parotitis) is an infection caused by a virus and spread human-to-human via direct contact or by airborne droplets. It most often affects children between 5-9 years old. But the mumps virus can infect adults as well. When it does, complications are more likely to be serious. Mumps virus is present throughout the world.

Clinical Picture

Infection with mumps virus is asymptomatic in one-third of cases. Nonspecific prodromal symptoms include low grade fever, anorexia, malaise, and headache. Pain, tenderness, and swelling in one or both parotid salivary glands. Swelling usually peaks in 1 to 3 days and then subsides during the next week. Up to 10% develop aseptic meningitis, less commonly encephalitis leading to death or disability and permanent deafness, orchitis and pancreatitis.

Infectious Agent—*Rubulavirus* of *paramyxovirus* family

Host/Reservoir—Humans are the only reservoir

Period of Communicability—Before and within five days of parotitis onset.

Mode of Transmission—Spreads through direct contact with respiratory secretions or saliva or through fomites.

Incubation period—03 days before to 5 days after the onset of salivary gland swelling (range 12-25 days)

Seasonality—Summer, warm climate

Alert Threshold—Unusual presentation may require investigation

Outbreak threshold—Three or more cases linked by time and place

Case Definition

Suspected Case—Acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland, lasting two or more days and without other apparent cause.

OR

Parotitis, acute salivary gland swelling, orchitis, or oophoritis unexplained by another more likely diagnosis,

OR

A positive lab result with no mumps clinical symptoms (with or without epidemiological-linkage to a confirmed or probable case).

Probable Case—Acute parotitis or other salivary gland swelling lasting at least 2 days, or orchitis or oophoritis unexplained by another more likely diagnosis, in:

- A person with a positive test for serum anti-mumps immunoglobulin M (IgM) antibody, OR
- A person with epidemiologic linkage to another probable or confirmed case or linkage to a group/community defined by public health during an outbreak of mumps.

Confirmed Case—Suspected mumps patient with laboratory confirmation (ELISA, Isolation of Mumps Virus, RT-PCR)

Epidemiologically confirmed—A case that meets the clinical case definition and is linked epidemiologically to a laboratory-confirmed case

Lab confirmation—Serological assay (IgM by ELISA).

Isolation of mumps virus real time RT-PCR assays

Timings—Serology on the fifth day of illness

Real time RT-PCR assays from day of presentation

Specimen Collection—Blood specimen and buccal/oral swab be collected from patients with clinical features compatible with mumps.

Mumps virus can be isolated from throat swabs, urine and cerebrospinal fluid (CSF).

Packaging—Triple Packaging

Storage—At 4°C, For delays exceeding 48 hours, blood specimens should be frozen at –20°C.

Transportation—Transport with ice packs maintaining reverse cold chain within 24-48 hours

Case Management

Mumps typically resolves on its own (self-limiting) without the need for specific treatment. Pain-relieving medications, such as ibuprofen or acetaminophen, may be used to relieve symptoms. The patient should drink plenty of fluids and take antipyretic agents to manage any fever that takes place. Rest in bed is still one of the best tools to facilitate recovery from this disease. Complications are treated according to the standard guidelines.

Preventive Measures

- The child must be kept at home for 5 days after development of symptoms.
- Adults and children should wash their hands regularly with soap and water.
- Household members and other close contacts should not share eating or drinking utensils with the patient.
- Cover mouth and nose during coughing and sneezing.

Vaccination:

- MMR vaccine should be given at ages 12 to 15 months and a second dose at 4 to 6 years of age.
- Women who are pregnant should not receive MMR vaccine.
- For contacts of patients sufferings from mumps, it is advised that two doses of MMR vaccine be given, one at 0 and the second at 28 days. (If there is no contraindication such as pregnancy)

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26. Naegleria fowleri, Primary Amebic Meningoencephalitis (PAM) (Amoebic Encephalitis)

Introduction

A rare and devastating infection of the central nervous system that is almost always fatal. The fatality rate is over 97%. First case was reported in 1965 in Australia and more than 300 cases have so far been reported globally. In Pakistan, since 2012, a total of 45 cases have been reported from different tertiary care hospitals of Karachi. Because of the severity of the infection and difficulty in initial detection, about 75% of diagnoses are made after the death of the patient.

Clinical Picture

Signs and symptoms mimic those of bacterial meningitis, especially in the early stages. Stage 1 symptoms are headache, fever, nausea, and vomiting, stage II symptoms include neck stiffness, lethargy, confusion/disorientation, photophobia, seizures, and cranial nerve abnormalities

Infectious Agent—Naegleria fowleri(a thermophilic**,** brain-eating amoeba)

Host/Reservoir—

- The amoeba can be found in bodies of warm freshwater, such as lakes and rivers, Geothermal water/hot springs, warm water discharge from industrial plants, swimming pools, water heaters and soil
- Naegleria fowleri grows best at higher temperatures up to 115°F (46°C) and can survive for short periods at higher temperatures.
- Naegleria is free living in aquatic and soil habitats

Period of Communicability—PAM progresses rapidly and frequently leads to coma and death in 1-18 days (median 5 days for getting infection) after onset of symptoms

Mode of Transmission—Naegleria infection can be acquired by exposure of the nasal passages (by diving or swimming) to contaminated (usually warm) for inadequately treated water. No person-to-person transmission and does not spread via water vapor or aerosol droplets (shower mist or vapor from a humidifier).

Incubation period—3-7 days

Seasonality—Infections linked to freshwater swimming mostly occur during the heat of summer in May to September.

Alert Threshold—One suspected/probable case

Outbreak threshold—One confirmed case

Case Definition

Probable Case—Any case having sudden onset of symptoms including headache, fever, nausea, vomiting, photophobia, mental-state abnormalities and stiff neck within 1 to 14 days after any water related activities like swimming and rapid progression of disease resulting in loss of consciousness or death within 3 to 7 days.

Confirmed case—Probable case that is laboratory confirmed

Lab confirmation:

Pre-Mortem Diagnosis Post-Mortem and Autopsy Diagnosis—PAM and Naegleria fowleri infection can be diagnosed in the laboratory by detecting:

- **Direct Visualization**: Naegleria fowleri organisms in cerebrospinal fluid (CSF), biopsy, or tissue specimens. *Wet mount On CSF should be requested specifically*
- **Antigen Detection**: Naegleria fowleri antigen in CSF, biopsy, or tissue specimens through immunohistochemistry or indirect immunofluorescence.
- **Polymerase Chain Reaction (PCR):** Amplification of DNA from the ameobae in CSF or tissue

- **Ameoba Culture:** The amebae can be grown in culture to increase the likelihood of detecting the ameoba by direct visualization or PCR

Environmental Detection: Spring, well, water tank and pools samples. CDC does not recommend testing rivers and lakes for Naegleria fowleri

Timings—As suspected

Specimen Collection—

The CSF is the specimen of choice for demonstration of the amoeba.

- Fresh CSF sample
- Fresh brain tissue
- Formalin-fixed and paraffin embedded tissues
- Three stained H&E slides
- Biopsy or autopsy tissue collected from the area surrounding the nasal-olfactory bulbs in the brain.
- Extra CNS tissue: lung tissue, skin, and corneal biopsy. minimize the possibility of cross-tissue contamination between CNS and extra-CNS tissues
- Environmental samples be collected in sterile glass bottles and labeled with date, time, and place of collection.

(Please DO NOT FREEZE and DO NOT REFRIGERATE as this kills the ameobae)

Packaging—Properly packaged to avoid leakage and loss of sample

Storage—Should be stored in leak-proof containers

Transportation—Must be transported to lab at the earliest.

Case Management

In 02 documented cases of survival, the combination of three drugs; Amphotericin B (IV/Intrathecal), Rifampicin (Oral 10 mg/kg/day) and Fluconazole (IV/oral 10 mg/kg/day) was used along with steroids.

Azithromycin has both in vitro and in vivo efficacy against Naegleria fowleri and may be tried as an adjunct to Amphotericin B.

Miltefosine may be given along with other drugs and aggressive case management of brain swelling. Miltefosine has shown ameba-killing activity invitro against free-living amoebae, including Naegleria fowleri.

Preventive Measures

- The trophozoites and cysts (more resistant) of N. fowleri are sensitive to disinfectants like chlorine. Chlorine is the most common disinfectant used to treat drinking water and swimming pools. Swimming pools containing residual-free chlorine of 1–2 ppm are considered safe.
- Filtration and UV treatment systems may be effective in controlling Naegleria fowleri, but specialist advice should be sought.

To prevent infection:

- Avoid jumping or diving into bodies of warm fresh water or thermal pools.
- Empty and clean small collapsible wading pools daily.
- Ensure swimming pools and spas are adequately chlorinated and well maintained.
- Flush stagnant water from hoses before allowing children to play with hoses or sprinklers.
- Don't allow water to go up your nose when bathing, showering or washing your face.
- Potentially contaminated water should not be used for any form of nasal irrigation or nasal lavage.

Chlorination

- o Water supplies at risk of *Naegleria fowleri* must ensure adequate primary disinfection (C.t >30 mg/L.min) and maintain a chlorine residual of at least 0.5 mg/L at all times, in all parts of the distribution system. (CT means disinfectant concentration multiplied by the contact time)
- o Chlorine at 1 ppm at 25^{o} C (77^{o} F) will achieve four logs of reduction of the trophozoites in 12 minutes (CT = 12). However, the cyst requires about 53 minutes (CT = 53). That is about the same sensitivity as

giardia cysts, but much less effective than chlorine on bacteria or viruses (CT ~6 for virus at 10^{o} C).

- Regularly monitor water temperature and chlorine residual throughout the entire distribution system. Periodic testing for *Naegleria fowleri* can be carried out in at risk systems.
- Proper design, management and cleaning of assets (e.g. pipes and storage tanks) is required to minimise sediment (which may harbour *Naegleria* cysts) and reduce water stagnation (which may lead to loss of disinfectant residual).

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27. Neonatal Tetanus

Introduction

Neonatal tetanus is a form of generalized tetanus in newborn infants that do not have protective passive immunity because the mother is not immune. It usually occurs through infection of the unhealed umbilical stump, particularly when the stump is cut with an unsterile instrument. The most common life threatening consequences of uncleandeliveries and un-hygeinicumbilical cord care practices.

The disease is caused by the action of a neurotoxin, produced by the bacteria when they grow in the absence of oxygen, e.g. in dirty wounds or in the umbilical cord, if it is cut with a non-sterile instrument. Tetanus occurring during pregnancy or within 6 weeks of the end of pregnancy is called “Maternal Tetanus”, while Tetanus occurring within the first 28 days of life is called “Neonatal Tetanus”. Neonatal Tetanus has a very poor prognosis.

Neonatal tetanus is estimated to kill over 200,000 newborns each year; almost all these deaths occur in developing countries

Clinical Picture

At the end of the first week of life, infected infants become irritable, feed poorly, and develop rigidity with muscle spasms. With progression mild stimuli may trigger generalized tetanic seizure-like activity, which contributes to serious complications and eventually death unless supportive treatment is given.

Infectious Agent—*Clostridium tetani* - Gram-positive, spore-forming, anaerobe

Host/Reservoir—Soil and intestinal tracts of animals and humans

Period of Communicability—It is the only vaccine-preventable disease that is infectious but not contagious.

Mode of Transmission—Contaminated wounds and if childbirth takes place in an unhygienic environment OR may result from infection of the umbilical stump

Incubation period—3-21 days

Seasonality—Peak in summer or wet season

Case Definition

Suspected Case—Any neonatal death between 3-28 days of age in which the cause of death is unknown or any neonate reported as having suffered from Neonatal Tetanus (NNT)between 3-28 days of age and not being investigated.

Confirmed Case—Any neonate with normal ability to suck and cry during the first 2 days of life, and who between 3 and 28 days of age cannot suck normally and becomes stiff or has convulsions or both. Hospital-reported cases are considered confirmed.

Note: *The diagnosis is entirely clinical and does not depend on bacteriological confirmation by the laboratory. However, investigators should examine NNT case records during annual hospital record reviews.*

Lab confirmation—No laboratory findings are characteristic of Tetanus. Culture of the wound stuff may yield growth of bacteria

Case Management

- Debridement of any associated wound
- Give Tetanus Immune Globulin (TIG) to neutralize the toxin (250 IU/Kg)
- Give Inj: Penicillin 600 mg 6 hourly IV for 7 days (Metronidazole if allergic to Penicillin) to kill the toxin producing *C. tetani.*
- Muscle spasms may be treated with muscle relaxants such as Chlorpromazine (50-150 mg every 4-8 hours in adults) and Diazepam (2-20 mg IV every 2-8 hours) to control spasms and convulsions.
- Bed rest with a non-stimulating environment is also recommended (dim light, reduced noise and ambient temperature).
- Respiratory support with oxygen, endotracheal tube and mechanical ventilation may be necessary.
- General measures: Maintain hydration, nutrition and treat secondary infections

Preventive Measures

- The various immunization preparations for tetanus available are:
- Diphtheria toxoid, Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP); Tetanus toxoid (TT); and Tetanus and Diphtheria Toxoid Adsorbed (Td).
- Pregnancy: At least three primary doses given by intramuscular route to the mother before or during pregnancy should be given. Clean delivery and cord care needs to be ensured.
- Tetanus is completely preventable by active tetanus immunization, which begins in infancy as a series of Diphtheria, Pertussis and Tetanus (DPT) shots. The immunization is done at 6 weeks, 10 weeks and 14 weeks of the child. Boosters are given to teenagers and older adults specially who have been injured.
- Thorough cleaning of all injuries and wounds and the removal of dead or severely injured tissue (debridement) may reduce the risk of developing tetanus.
- After injuries in those who are not immunized Tetanus Antitoxin should be given and an intramuscular injection of toxoid that should be repeated 1 month and 6 months later. For those already protected; only a booster dose of toxoid is required

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28. Nipah Virus

Introduction

Nipah virus (NiV) infection is an emerging Zoonosis that causes severe disease in both animals and humans and endemic in South-East Asia Region. NiV was initially isolated and identified in 1999 during an outbreak of encephalitis and respiratory illness among pig farmers and people with close contact with pigs in Malaysia and Singapore. NiVis capable of causing severe disease in pigs and other domestic animals.

Clinical Picture

- Encephalitis: fever and headache, followed by drowsiness, disorientation and mental confusion. These signs and symptoms can progress to coma within 24-48 hours.
- Some patients have a respiratory illness/Influenza Like Illness
- Long-term sequelae following Nipah virus infection have been noted, including persistent convulsions and personality changes.

Surveillance goal

Infectious Agent—*Nipah virus* (NiV), family Paramyxoviridae, genus Henipavirus

Host/Reservoir—Fruit Bats of genus Pteropus
Pteropusgiganteus species of Bats is found in Pakistan.

Mode of Transmission—Direct contact with sick pigs or their contaminated tissues (throat or nasal secretions), sick bats or from human to human through respiratory droplets

Incubation period—4–45 days

Seasonality—Outbreaks in South-East Asia occurred during winter and spring (December-May).

Alert Threshold—One suspected case is an alert and requires prompt investigation

Outbreak threshold—One lab confirmed case

Case Definition

Suspected Case—A person with the following criteria:

- With respiratory features (cough, breathing difficulty) with acute encephalitis symptoms as acute onset of fever AND altered mental status OR seizure OR any other neurological deficit
- Epidemiological linkage like Drinking raw date, palm sap OR travel to Nipah endemic areas

Probable Case—Any suspected case with epidemiological link or positive serological testing

Confirmed case—Any suspected/probable case with laboratory confirmation of the disease

Cluster—Two or more suspected cases living within a 30 minute walk of each other who develop symptoms within 21 days of each other.

Lab confirmation—

- RT-PCR
- IgG and IgM by ELISA
- Virus Isolation
- Histopathology and Immunohistochemistry (IHC) on tissues collected

Timings—Specimens for virus isolation should be collected every second day of infection

Specimen Collection—PCR: Throat and nasal swabs, cerebrospinal fluid, urine and blood

Serology: At least 5 ml of serum required for serological testing

Packaging—Tissues fixed in 10% neutral buffered formalin for 48 h prior to histological processing. Viral transport medium for other samples.

Storage—Stored at −80°C until processing for antigenor viral isolation

Transportation—Storage and transportation should at 4°C in Viral transport medium (VTM), and transported with ice packs in a reverse cold chain with a duly filled request form

Case Management

- Supportive care
- Ribavirin may alleviate symptoms of nausea, vomiting and convulsions. (limited data available)
- Treatment is mostly focused on managing fever and the neurological symptoms.
- Severely ill individuals need to be hospitalized and may require use of ventilator.

Preventive Measures

- Contact and droplet precautions
- No vaccination for human use is available.
- Can be prevented by avoiding exposure to sick pigs and bats in endemic areas and not drinking raw date palm sap.
- Raising public awareness of transmission and symptoms is important in reinforcing standard infection control practices to avoid human-to-human infections in hospital settings.

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29. Pertussis (whooping cough)

Introduction

A toxin-mediated disease that can affect people of all ages,but can be very serious even deadly among infants.Worldwide, it is estimated that there are 16 million Pertussis (whooping cough) cases and about 195,000 Pertussis deaths in children per year. Despite generally high coverage with childhood Pertussis vaccines, Pertussis is one of the leading causes of vaccine-preventable deaths worldwide.

Clinical Picture

The clinical course of the illness is divided into three stages: Catarrhal, Paroxysmal and Convalescent. Characterized by uncontrollable, violent coughing which often makes it hard to breathe. The disease usually starts with cold-like symptoms and maybe a mild cough or fever. Infants may have a symptom known as "apnea." Pneumonia is the most common complication in all age groups; seizures and encephalopathy generally occur only among young infants.

Infectious Agent—*Bordetella pertussis/ Bordetella parapertussi*s

Host/Reservoir—Humans are the only known reservoir

Period of Communicability—

- Highly communicable in the early catarrhal stage and gradually decreases after paroxysmal cough.
- Untreated patients may be contagious for up to 3 weeks after the onset of paroxysmal cough or up to 5 days after onset of treatment.

Mode of Transmission—

- By direct contact with discharges from respiratory mucous membranes of infected persons
- Airborne/aerosols

Incubation period—

- 9 -10 days (range 6-20 days)

Seasonality—Pertussis has no distinct seasonal pattern

Alert Threshold—One suspected case

Outbreak threshold—Five suspected with one lab confirmed case

Case Definition

Suspected Case—A person with a cough lasting at least 2 weeks with at least one of the symptoms i.e. paroxysms/ fits of coughing, Inspiratory "whooping", Post-tussive vomiting and apnoea in infants with or without cyanosis

Probable Case—A clinical suspected case with an epidemiological linkage

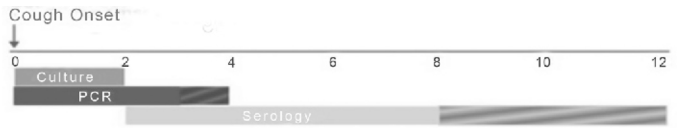
Confirmed case—Suspected/probable case with laboratory confirmation

Lab confirmation—

Methods:

- Culture is the gold standard
- Detection of genomic sequences by polymerase chain reaction (PCR)
- Positive paired serology

Timings—



Specimen Collection—Minimum: 0.3 mL of Nasopharyngeal aspirate collected in a sterile vial, or nasopharyngeal swab collected in Liquid Amies collection tube (preferred) or in a V-C-M medium (green-cap) tube, or equivalent UTM or multi-microbe media (M4), or eSwabs (Liquid Amies)

Packaging—Triple packaging, seal in biohazard bag

Storage—Can be stored at room temperature for 48 hours, refrigerated for 7 days. And frozen for 30 days

Transportation—Use UTM. Refrigerate and ship as soon as possible in a cooler containing ice packs.

Case Management

- Antimicrobial treatment is more effective in the catarrhal phase, prior to paroxysmal coughing.
- Antibiotic treatment should be initiated in all suspected cases. Treatment options include:
    - o Erythromycin 500mg, QiD for 14 days
    - o Azithromycin 500mg orally for 5 days **OR** Clarithromycin 500mg orally BID for 14 days
    - o Trimethoprim-Sulfamethoxazole, 160-800 mg orally BID for 7 days
- Young infants particularly those younger than 6 months of age should be hospitalized
- Supportive case management including cough suppressant and good nursing care
- Maintenance of proper water and electrolyte balance, adequate nutrition and sufficient oxygenation.

Preventive Measures

- Timely treatment of petussis decreases the risk of disease transmission.
- Chemoprophylaxis: Erythromycin 40-50 mg/kg per day in four divided doses for 14 days should be given.
- Immunization:
    - o Active primary immunization against B. pertussis infection with the whole-cell vaccine (WP) is recommended.
    - o Children who have received at least 3 doses are estimated to be protected especially against severe disease. However, protection begins to wane after about 3 years.

Vaccination during pregnancies

It is important for women to get the whooping cough vaccine during 27th week through 36th week of pregnancy.

Return to school : Infected children should avoid school orday care until they have completed 5 days course of therapy. In case of no treatment, the children should avoid school for atleast 21 days after the onset of symptoms.

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30. Plague (Pestis)

Introduction

One of the oldest zoonotic diseases widely distributed in the tropical, subtropical and in warmer areas of temperate countries. It may reoccur in areas that have long remained silent**.** Case-fatality ratio remained 30%-60%. Globally 3248 cases were reported including 584 deaths (2010 – 2015).Currently, the 3 most endemic countries are Madagascar, the Democratic Republic of the Congo and Peru.

Clinical Picture

Fever, chills, abdominal pain/diarrhoea, nausea, headache and extreme exhaustion.

Clinical forms

Bubonic plague, Septicemic plague, Pneumonic plague, Pharyngeal plague, Cutaneous plague, Meningeal plague

Infectious Agent—*Yersinia pestis-the plague bacillus*

Host/Reservoir—Rodents and Humans

Period of Communicability—2 to 6 days

Mode of Transmission—

- Flea bite: Bite of infected fleas especially *XenopsyllaCheopis* (rat fleas).
- Contact with contaminated fluid or tissue: Person to person transmission is rare but possible through direct exposure to infected tissues(handling sick animals or those died of plague)
- Respiratory droplets: from animal to humans and from humans to humans

Incubation period

- Bubonic plague:1-7 days
- Pneumonic plague: 1-4 days

Seasonality—Cases can occur any time during the year

Alert Threshold—One probable case is an alert and requires an immediate investigation

Outbreak threshold—One lab confirmed case is an outbreak

Case Definition

Suspected Case—Any case with rapid onset of fever, chills, headache, severe malaise with extreme painful swelling of lymph nodes (bubonic form)

OR

Cough with blood-stained sputum, chest pain, difficult breathing (pneumonic form)

Probable Case—A probable case is a suspected case with:

- A positive Fluorescent Antibody test for *Yersinia pestis* in clinical specimen; or
- Phytohemagglutinin (PHA) test, with antibody titre of > 1:10, specific for the F1 antigen of Y. *pestis* determined by HI; or an epidemiological link with a confirmed case.

Confirmed case—A confirmed case is a suspected or probable case which is laboratory- confirmed by:

- Isolation by culture of *Y. pestis* from buboes aspirates, cerebrospinal fluid, blood or sputum; or
- PHA test demonstrating a fourfold change in antibody titre, specific for F1 antigen of *Y. pestis* (HI test) in paired sera.

Note: *Case report universally required by International Health Regulations (2005)*

Lab confirmation—

- Culture
- Serological testing by ELISA
- PCR
- Fluorescent antibody testing
- Phyto Haem Agglutinin testing (PHA)

Timings—Send sample when patient is symptomatic
Serology not before 7 days as antibodies appear between 5-7 days

Specimen Collection—

- Bubonic plague: bubo aspirate for culture
- Pneumonic plague: exported sputum swab
- Serum/whole blood for serology(IgA and IgM) & PCR
- CSF(When meningeal plaque is suspected)

Packaging—Triple packaging

Storage& Transportation—Cold chain (4°–8°C). Maximum storage and transportation time is 72 hours.

Case Management

Rapid diagnosis and treatment is essential to reduce complications and fatality. Effective treatment methods enable almost all plague patients to be cured if diagnosed in time. These methods include the administration of antibiotics and supportive therapy.

- Gentamicin and Doxycycline are typically first-line treatments and duration of treatment is 10 to 14 days, or until 2 days after fever subsides. Oral therapy may be substituted once the patient improves.
- Streptomycin is the most effective antibiotic against *Y. pestis* and the drug of choice for treatment of plague, particularly the pneumonic form.
- Alternatively Doxycyclin 100 mg orally or intravenously, may be used for 10 days.

Preventive Measures

Vaccines are not recommended for immediate protection in outbreak situations.

Vaccination is only recommended as a prophylactic measure for high-risk groups e.g. laboratory personnel who are constantly exposed to the risk of contamination.

The objective of preventive measures is to inform people to be aware of the areas where zoonotic plague is active and to take precautions against flea bites and handling cases while in plague-endemic areas.

- People should avoid having direct contact with infected tissues. Exposure to patients with pneumonic plague should be avoided.
- The exposure source should be taken care of.
- Dissemination of information to health workers.
- Appropriate antibiotic treatment should be given to those affected.
- Isolation of plague patients and use of PPEs while attending the patient.
- Strict bio-safety measures while handling laboratory specimens.

Post-exposure Prophylaxis

People should receive antibiotic prophylactic therapy;i.e. Tetracycline 2g daily or Chloramphenicol for a week within 6 days of exposure if they have:

- Been in close contact with pneumonic plague patients.
- Been exposed to Y. pestisinfected fleas.
- Had direct contact with body fluids or tissues of a Y. pestis-infected mammal.
- Been exposed during a laboratory accident to known infectious material.

Environment measures

- Rodents and vector control measures should be adopted.
- Powder containing 1.5% Dieldrin or 2% Aldrin should be applied to household floor and blown into rat holes to kill all the fleaswhich remain active for 9-12 weeks.

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31. Polio

Introduction

The word Polio (Grey) and myelin (marrow, indicated spinal cord) are derived from the Greek. It is the effect of Polio virus on the spinal cord that leads to the classic manifestations of paralysis.It mainly affects children under 5 years of age. The Poliovirus is rapidly inactivated by heat formaldehyde, chlorine and ultraviolet light.

Pakistan is one of the three countries in the world with ongoing wild Poliovirus transmission, alongside Afghanistan and Nigeria.

Clinical Picture

There are three basic patterns of Polio infection: subclinical infections, non-paralytic, and paralytic. Clinical Poliomyelitis affects the CNS and is divided into non paralytic and paralytic forms. All 3 types of wild Poliovirus may cause Acute Flaccid Paralysis (AFP), although most infections (at least 95%) remain asymptomatic. Weakness is ascending and may vary from one muscle or group of muscles, to quadriplegia, and respiratory failure. Tone is reduced, nearly always in an asymmetric manner. Proximal muscles usually are affected more than distal muscles and legs more commonly than arms. Reflexes are decreased or absent. The sensory examination is normal.

1 in 200 infections leads to irreversible paralysis. Among those paralyzed, 5% to 10% die when their breathing muscles become immobilized.

Infectious Agent—Polioviruses belong to Enterovirus subgroup, family *Picornaviridae*, having three serotypes of Poliovirus, labelled P1, P2, and P3.

Host/Reservoir—Poliovirus infects only human beings and there is no animal reservoir.

Period of Communicability—Soil:Summer: 1.5 days, Winter: 20 days

Sewerage: 26 days at 23°C

Mode of Transmission—Faecal-oral contact and rarely Person-to-perso*n*

Note: *After initial infection with poliovirus, the virus is shed intermittently in faeces for several weeks.*

Incubation period—7-14 days for paralytic cases (range: 3-35 day**s**)

Seasonality—The ability of the Polio virus to infect children increases in high temperature due to which most of the cases are reported from May to September. The period is called the high transmission season (HTS). In low temperature, from October to April, the virus remains less active

Alert Threshold—One case is an alert requires an immediate notification and sample for confirmation.

Outbreak threshold—One lab confirmed case is an outbreak.

Case Definition

Clinical Case Definition—Sudden/acute onset of floppy weakness in a child less than or equal to 15 years of age due to any cause including Guillain–Barré syndrome (GBS) Syndrome.

OR

Any paralytic illness in a person of any age whom Polio is suspected by the clinician

Suspected Case—A case that meets the clinical case definition

Probable Case—AFP clinically compatible with Poliomyelitis, in the absence of adequate virological evidence

Confirmed case—AFP with laboratory-confirmed wild Poliovirus in stool samples

Discarded—A discarded case is an AFP case, which is neither diagnosed as confirmed nor compatible with a Polio case definition.

Lab confirmation—Laboratory confirmation by isolation of wild Polio virus in stool samples

Timings—Collect samples within 14 days of onset of weakness/paralysis

Specimen Collection—Collect 2 stool samples about 8 grams each (about the size of the tip of thumb) at an interval of 24 hours for virus isolation

Packaging—Transport medium like Minimal Essential Medium or Eagle's medium OR in a cold box with frozen ice packs.

Storage—Place samples immediately after collection in a refrigerator by maintaining cold chain at 2-8°C

Transportation—Transport stool specimens to the National reference Laboratory (National Institute of Health, Islamabad) maintaining reverse cold chain with duly filled request form within 24-48 hours after collection of samples.

Case Management

Management depends on the severity of infection and includes recognition of disease (differential diagnosis) and extent of damage it has caused.

Preventive Measures

Four pillars of Polio eradication:

1. Achieving a high level of coverage with at least 3 doses of the oraltrivalent poliovirus vaccine (OPV) and one OR three doses of inactivated or killed Polio vaccine (IPV).
2. Providing supplementary doses of OPV to all children less than 5 years of age during supplementary immunization activities.
3. Surveillance for all cases of acute flaccid paralysis.
4. House-to-house OPV campaigns are recommended targeting areas in which transmission of wild poliovirus persists, based on surveillance studies.

Following the Polio End-game Strategy 2013-2018, the OPV will be excluded from routine immunization in 2020 and after that only IPV will be used to immunize the children against Polio.IPV started in Pakistan in 2016 and is now being given with the third dose of DPT in EPI.

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32. Rabies

Introduction

A viral disease of mammals most often transmitted through the bite of a rabid animal. More than 3.3 billion people worldwide live in areas where rabies is enzootic. 40% of people bitten by suspect rabid animals are children under 15 years of age. Human mortality from endemic canine rabies in Africa and Asia is estimated to be 55,000 deaths/year. The rabies virus infects the central nervous system, ultimately causing death

Clinical Picture

Any person with history of dog bite/suspected rabid animal bite/scratch with acute encephalomyelitis and any of the following sign and symptoms:

Paresis or paralysis, spasms of swallowing muscles, hydrophobia, delirium, convulsions, anxiety, sensory changes referred to the site of a preceding animal bite.

Without medical attention, death occurs in about 6 days following appearance of clinical sign and symptoms, usually due to respiratory paralysis

Infectious Agent—Rabies virus, a *Rhabdovirus* of the genus Lyssavirus

Host/Reservoir—All species of mammals are susceptible to rabies virus infection, but only a few species are important as reservoirs for the disease. Virus has been identified in raccoons, pigs, foxes, jackals and coyotes. Several species of insectivorous bats are also reservoirs for strains of the rabies virus.

Period of Communicability—

- Rabid animal excret infectious agent in Saliva usually 3-7 days before onset of clinical signs and throughout the course of the disease.
- Cats excrete virus for 1 to 5 days before the signs appear, cattle for 1 to 2 days, skunks for up to 14 days and bats for 2 weeks.
- Longer periods of infected saliva/excretion before onset of clinical signs have been observed with other animals.

Mode of Transmission—

- Through the bite and virus-containing saliva of an infected host
- Spread when an infected animal scratches or bites another animal or human.
- Saliva from an infected animal can also transmit rabies if the saliva comes into contact with the eyes, mouth, or nose.
- Transmission has been rarely documented via other routes such as contamination of mucous membranes (i.e., eyes, nose, mouth), aerosol transmission, and corneal and organ transplantations.
- In developing countries, 99% of rabies cases are caused by dog bites
- Through bite of other infected mammalian species i.e. cat, monkeys, fox, bat, cattle, etc.
- Human saliva contains the rabies virus; person-to person transmission is theoretically possible but rare. Bite by a rabid patient may transmit rabies infection to others.

Incubation Period—

- 2-10 days.
- Highly variable but usually 3-8 weeks depending upon wound severity and location/distance from brain
- It can be longer sometimes up to 7 years.

Seasonality—No specific seasonality reported

Alert Threshold—One case in a susceptible animal species and /or human must lead to an alert

Outbreak threshold—One confirmed casen (clinically or laboratory based)

Case Definition

Suspected Case—Any case with acute onset of neurological syndrome (encephalitis) dominated by any or more of the following symptoms; excitability, aerophobia, paralysis, hydrophobia, delirium, convulsions, or hyperactivity (furious rabies) or paralytic syndromes (dumb rabies) that progresses towards respiratory failure, coma and death with history of bites or scratches or contact with saliva from a suspected animal during last 30 to 90 days.

Probable Case—A suspected case plus history of contact with a suspected rabid animal.

Confirmed Case—Any person meeting the clinical and the laboratory criteria

Lab confirmation—

One or more of the following:

- Rabies virus isolation from clinical specimens and confirmation of rabies viral antigens
- Identification of viral antigens by PCR on fixed tissue collected post mortem or in a clinical specimen (brain tissue, skin, cornea or saliva)
- Detection by FA (Fluorescent antibodies) on skin or corneal smear (collected ante-mortem)
- FA positive after inoculation of brain tissue, saliva or CSF in cell culture in mice
- Detectable rabies antibody titre in the CSF and serum of an unvaccinated person
- Detection of rabies viral antigens by direct fluorescent antibody (FA) brain tissue (collected post-mortem)

Specimen Collection—Ante-mortem Samples: Saliva, serum and cerebrospinal fluid (CSF), neck biopsy, brain biopsy, post-mortem samples or fresh tissue samples from the central nervous system

Packaging—Triple Packaging

Storage—2-8°C for short duration 24-48 hours
Frozen at -20°C (In case of antibodies detection)
Frozen at -70°C (In case of antigen detection)

Transportation—Transport specimens to the lab in triple container packing with ice packs or frozen with dry ice (for long distance) along with a prominent biohazard label and complete lab request form with brief history of the patient.

Case Management

There is no proper treatment once the clinical signs appear. Treatment should be started as early as possible after exposure, but in no case should it be denied to exposed persons whatever time interval has elapsed.

- **Treatment**

  Post-exposure prophylaxis consists of immediate wound cleansing and disinfection, followed by rabies vaccination and the administration of human rabies immunoglobulin.

- **Wound care**: One of the most important initial steps to prevent rabies is wound care.
- Application of Ethanol, Tincture or aqueous solution of Iodine is recommended in case of bite by infected animal.
- Suturing should be postponed.
- Where indicated, anti-Tetanus treatment, antimicrobials and drugs should be administered to control other infections.
- Anti-rabies vaccine should be given as soon as possible. For severe cases (Category III exposures) Anti-rabies immunoglobulin should be applied.

Recommended treatments according to type of contact with suspected animal:

Category	Type of contact with suspect animal	Recommended treatment
I	Touching or feeding an animal Licks on intact skin	None, if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Administer vaccine immediately, and stop if 10-day observation or laboratory techniques confirm suspect animal to be rabies negative
III	Single or multiple transdermal bites or scratches Contamination of mucous membrane with saliva	Administer rabies immunoglobulin and vaccine immediately and stop if suspect animal confirmed as rabies negative

- If a person develops the disease, death is inevitable.
- Universal nursing barrier practices are necessary for the sick people.

Preventive Measures

- Continous education of health and veterinary professionals regarding rabies prevention and control is recommended.
- Domesticated animals (especially dogs, cats and ferrets) should be vaccinated against rabies.
- Stray animals should be vaccinated or stirilized.
- Wild animals should not be handled or fed. Wild animals behaving abnormally should particularly be avoided.
- Public health educational strategies at the community level within endemic regions should be adopted.

Immunization

- Pre & post exposure prophylaxis should be given as per WHO recommendations.
- Rabies post exposure prophylaxis is an urgent medical intervention and should begin as soon as possible after the presumed exposure.
- Human preventive mass vaccination is generally not recommended but can be considered under certain circumstances for the age group 5 to 15 years.

Post Exposure Prophylaxis dose

Intra Muscular Schedule: Tissue-culture or purified duck-embryo vaccines of potency at least 2.5 IU per single intramuscular immunizing dose should be applied. One dose of the vaccine should be administered on days 0, 3, 7 and 14 (in immunocompetent, with an extra dose at 28 in immunocompromised). All intramuscular injections must be given into the deltoid region or in case of yound children into the anterolateral area of the thigh muscle. Vaccine should never be administered in the gluteal region.

Intra Dermal Schedule: For centers with 4 or more patients per day this is a very cost-effective way, ID vaccination is more immunogenic, shorter duration and improves compliance. The recommended schedule is 0.1ml into both the deltoids on day 0, 3 and 7.

Combined immunoglobulin-vaccine

Rabies immunoglobulin (RIG) should be given for all category III exposures with in the first week, irrespective of the interval between exposure and beginning of treatment. Immunoglobulin should be given in a single dose of 20 IU per kg of body weight for human anti-rabies immunoglobulin, and 40 IU per kg of body weight for heterologous (equine) immunoglobulin (this is the maximum recommended dose). The first dose of vaccine should be inoculated at the same time as the immunoglobulin, but in a different area of the body. Administration of rabies immunoglobulin (RIG) should be infiltrated into the depth of the wound and around the wound only much as anatomically feasible, if a wound is properly infiltrated there is no need to infiltrate the remaing at other sites.

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33. Rota Virus Disease (Gastroenteritis)

Introduction

The most common cause of diarrhea in children up to 5 years worldwide. First identified as the cause of diarrhea in 1973, responsible for up to 500,000 diarrheal deaths each year worldwide. Rotavirus is a contagious virus that can cause gastroenteritis. Infants and young children are most likely to get rotavirus disease. They can become severely dehydrated and need to be hospitalized and can even die if not timely/properly managed. Vaccinated and unvaccinated children may develop rotavirus disease more than once because neither vaccine nor natural infection provides full immunity (protection) from future infections. First infection with rotavirus tends to cause the most severe symptoms

Clinical Picture

Infecting almost all children by the age of 3-5 years, characterized by vomiting and watery diarrhea for 3 to 8 days. Fever and abdominal pain also frequently occur. Additional symptoms include loss of appetite and sometimes severe dehydration which include decrease in urination, dry mouth and throat with feeling dizzy when standing up.

Infectious Agent—Double-stranded RNA-virus, family *Reoviridae*

Host/Reservoir—Gastrointestinal tract and stool of infected humans

Period of Communicability—2 days before to 10 days after onset of symptoms. Rotavirus may be detected in the stool of immune-deficient persons for more than 30 days after infection

Mode of Transmission—The primary Mode of Transmission is the fecal-oral route, usually through close contact. The virus is stable in the environment, transmission also can occur through ingestion of contaminated water or food and contact with contaminated surfaces or objects.

Incubation period—Approximately 2 days

Seasonality—Have been reported during all season especially early and late calendar months. This may be attributed to the rainy and post-monsoon season.

Case Definition

Suspected Case—Any child aged 0-59 months admitted for treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhea (Excluded are children with bloody diarrhea).

Probable Case—Suspected case with an epidemiological link with a laboratory-confirmed case.

Confirmed Case—A suspected case in whose stool the presence of rotavirus is demonstrated by means of an enzyme immunoassay

Lab confirmation—

- Rapid detection of rotavirus antigen in stool specimens
- Enzyme-linked immunoassay (EIA)
- Enzyme-linked immunesorbent assay,
- Reverse transcriptase-polymerase chain reaction (RT-PCR).
- Polyacrylamide gel electrophoresis (PAGE)

Timings—The sample should be collected within 48 hours of admission to the hospital.

Specimen Collection—A stool sample obtained from a suspected case during the first contact with the patient. The following steps should be taken:

Collect 5-10 ml of stool (approximately the size of a thumb) and place in a vial using a spatula or disposable tongue depressor.

Stimulate the anal sphincter of children aged under 1 year with a sterile swab and wait for an evacuation, placing a disposable diaper inside out so that the sample is not absorbed

Packaging—

- Package it in a clean, screw-top vial bearing a label with the name of the case, the date, and the name of the hospital.

- Place the vial in a small individual plastic bag to avoid accidental spillage of the material.

Storage—

- Sample storage at a maximum of 7 days in a refrigerator between 2-8°C prior to transfer to the reference laboratory.
- Freezing/thawing/freezing cycles should be avoided to ensure the viability of the virus in the frozen material. In the case of storage for more than 4 months, a temperature of –70°C is recommended.

Transportation—Send immediately to the microbiology laboratory, with case summary form and lab request

Case Management

Self-limited, lasting for only few days. Treatment consists of replenishing lost fluids. Oral rehydration therapy is necessary and, in case of severe dehydration or frequent vomitings, start intravenous rehydration as per peadiatric guidelines. About 1 out of 70 children with rotavirus disease will require hospitalization for intravenous fluids. Antibiotic use is inappropriate.

Preventive Measures

- Good hygiene like hand washing and maintaining general cleanliness are important for infants and care takers but are not enough to control the spread of the disease.
- Safe sanitary disposal of diapers of infected children is recommended.

Vaccination

- The rotavirus vaccine was added as the 10th vaccine in the EPI Pakistan in 2016. It is administered in two oral doses to children between 6 weeks and 10 weeks of age; with a 4-week interval between the two doses.
- For the first year of an infant's life, rotavirus vaccination provids 85% to 98% protection against severe rotavirus illness and hospitalization; and 74% to 87% protection against rotavirus illness of any severity.

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34. Scabies

Introduction

A highly contagious parasitic skin infestation occurs worldwide regardless of age, sex, race, socioeconomic status or standards of personal hygiene. It is more likely to spread in situations of overcrowding.

Clinical Picture

Skin infection characterized by rash or lesions and intense itching especially at night. Lesions prominent around finger webs, wrists, elbows, axillaries, beltlines, thighs, external genitalia, nipples, abdomen, lower portion of buttocks, head, neck, palm and soles of infants may be involved.

Crusted scabies is a severe form of scabies that can affect the elderly, persons who are immunocompromised, or persons who have conditions that prevent them from itching and/or scratching (spinal cord injury, paralysis, loss of sensation, Type II Diabetes Mellitus, Mental debility/frailty).

Infectious Agent—*SarcoptesScabiei* var. hominis, a mite

Host/Reservoir—Humans are the primary reservoir. Other species of mite from animals or birds can also live on humans but do not reproduce in the skin.

Period of Communicability—Scabies is communicable until mites and eggs are destroyed by treatment, usually two courses 1 week apart. Itching may persist for 2 or more weeks after successful eradication of the mite.

Mode of Transmission—Transfer of parasites is by direct contact with infested skin of an infected person (person to person contact) or contact with towels, bedclothes and undergarments contaminated by infected persons within last 4-5 days

Incubation period—Ranges from 2 to 6 weeks before itching occurs in a person not previously exposed. Symptoms develop more quickly if a person is re-exposed, often within 1 to 4 days

Seasonality—Not specified and documented. Most cases have been reported in winter in Pakistan.

Alert Threshold—Case count greater than 2 times; the mean number of cases over the previous 3 weeks requires immediate investigation.

Outbreak threshold—Clustering of cases in a single location above the alert threshold.

Case Definition

Suspected Case—Anyone having symptoms with history of close skin-to-skin contact with a scabies case including household, sexual and close contacts during one month prior to the onset of symptoms

Probable Case—Any individual with clinical symptoms of scabies (persistent pruritic rash)

Confirmed Case—Any individual who has skin scraping with identified mites, mite eggs or mite feces

Lab confirmation—Most diagnoses of scabies infestation are made based upon the appearance and distribution of the rash and the presence of burrows.

Isolating the mites, ova or feces in a skin scraping.

Specimen Collection—Skin scraping. Scrapings should be made at the burrows, especially on the hands between the fingers and the folds of the wrist. Scrapings are best performed at the end of the burrows in non-excoriated and non-inflamed areas using a sterile scalpel blade containing a drop of mineral oil. The mineral oil enhances the adherence of the mites to the blade and can then be transferred to a glass slide. An additional 1-2 drops of mineral oil can be added to the slide, followed by a coverslip for microscopic examination. Skin scrapings should be screened at 40x or 100x magnification and then evaluated at 200 to 400x magnification for confirmation

Packaging—Properly labeled, covered and packed slides

Storage—Can be stored at room temperature

Transportation—Can be transported at room temperature

Case Management

- Application of Permethrin cream (2 days) or lotion (3 days) is treatment of choice. It should be applied to all cutaneous surfaces, particularly the hands, fingernails, waist and genitalia at bedtime after taking shower.
- Ivermectin is another option as oral antiparasitic agent approved for the treatment of scabies especially in immunocompromised patients.
- Put on clean clothing daily.
- All bed linen and clothing should be washed in hot water and dried in sun and ironed on both sides. If not possible, then place bed linen and clothing in a plastic bag, tie the bag and took it away from the family for 5 days.
- All members of the house including regular guests should be treated simultaneously.
- Treatment of patients is with Acaricide ointments preceded by a hot bath with liberal use of soap. Infested clothing should be sterilized or washed in hot soapy water. Bedding, mattresses, sheets and clothes may require dusting with Acaricides
- Room used by crusted scabies patients should be thoroughly cleaned and vacuumed after use.
- If secondary infection occurs, antibiotics may be indicated.

Preventive Measures

- Health education and promotion about the disease is the most effective means of prevention among communities and educational institutions.
- General cleanliness including body washing and washing of clothes and bed linens is recommended.
- Bedding including mattresses, bed linens, blankets and clothing should be kept in sun (from 10:00 a.m. to 1:00 p.m.) to kill the parasites.
- Personal hygiene plays an important part in the prevention and control of scabies and depends on access to adequate water-supply.
- There is no use of environmental disinfection using pesticides, sprays or fogs.

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35. Severe Acute Respiratory Syndrome (SARS)

Introduction

A viral respiratory illness first reported in Asia in February 2003. The illness spread to more than two dozen countries in North America, South America, Europe and Asia. Since 2004, there haven't been any known cases of SARS reported anywhere in the world.

Clinical Picture

- Early illness
  - o Presence of two or more of the following features: fever (might be subjective), chills, rigors, myalgia, headache, diarrhoea, sore throat, rhinorrhea
- Mild-to-moderate respiratory illness
  - o Temperature of >100.4°F (>38°C) and
  - o One or more clinical findings of lower respiratory illness (e.g., cough, shortness of breath, difficulty breathing)
- Severe respiratory illness
  - o Meets clinical criteria of mild-to-moderate respiratory illness, and
  - o One or more of the following findings:
    - Radiographic evidence of pneumonia, or
    - Acute respiratory distress syndrome, or
    - Autopsy findings consistent with pneumonia or acute respiratory distress syndrome without an identifiable cause
- Epidemiologic Criteria
  - o One or more of the following exposures in the 10 days before onset of symptoms:

- Travel to a foreign or domestic location with documented or suspected recent transmission of SARS-CoV
- Close contact with a person with mild-to-moderate or severe respiratory illness and with travel history

Infectious Agent—Severe Acute Respiratory Syndrome (SARS) coronavirus

Host/Reservoir—SARS-CoV is thought to be an animal virus from an as-yet-uncertain animal reservoir, perhaps bats, that spread to other animals (civet cats)

Period of Communicability—Peak of virus excretion in respiratory secretions and stool occurred mainly during the second week of illness.

Mode of Transmission—Aerosol and/or droplet infection of an affected individual

Direct contact through contaminated hands, surfaces and body fluids.

Incubation period—5–6 days, (Range: 2–10 days)

Alert Threshold—01 SARS suspected case

Outbreak threshold—Cluster of suspected cases with clear epidemiological linkage or one confirmed case

Reporting Time—Within 24 hours

Case Definition

Suspected Case—A person with an unexplained acute respiratory illness resulting in death or any person with a fever (temperature >38°C), lower respiratory tract symptoms without an identifiable cause.

Probable Case—A suspected case with history of contact with a person believed to have had SARS or a history of travel to a geographic area where there has been documented transmission of the illness.

Confirmed Case—Any person who has a clinically compatible illness (i.e., early, mild-to-moderate, or severe) that is laboratory confirmed

Lab confirmation—

- Detection of the SARS-CoV antibody by indirect fluorescent antibody (IFA) or enzyme-linked immunosorbent assay (ELISA)
- Isolation of SARS-CoV in tissue culture
- Detection of SARS-CoV RNA by reverse transcriptase- polymerase chain reaction (RT-PCR), which must be confirmed by a second PCR test

Note: *Negative laboratory results for PCR, viral culture, or antibody tests obtained within 21 days of illness do not rule out coronavirus infection. In these cases, an antibody test of a specimen obtained more than 21 days after the onset of illness is needed to determine infection.*

Specimen Collection—Throat and/or nasopharyngeal swab, bronchial lavage, blood culture, urine specimen, blood for complete examination and serology, stool specimen (added)

Packaging—Triple Packaging

Storage—2-8°C for short duration 24-48 hours
Frozen at –20°C (for antibody detection)
Frozen at –70°C (antigen detection)

Transportation—Transport specimens to the lab in triple container packing with ice packs or frozen with dry ice (for long distance) along with a prominent BioHazard label and complete lab request form with brief history of the patient.

Case Management

Management of suspected case

- Isolation and barrier-nursing techniques/adopting extended isolation precautions
- If chest x-ray is normal, discharge the patient with advice to seek medical care
- If respiratory symptoms worsen, use best personal hygiene and restrict mobility.

Management of Probable/Confirmed case

- If CXR demonstrates unilateral or bilateral infiltrates with or without interstitial infiltrations Hospitalize under isolation with other SARS patients.
- Lab investigation to exclude known cause of atypical pneumonia.
- symptomatic treatment
- Broad-spectrum antibiotics have not appeared to be proven effective in halting SARS progression to date.
- Ribavirin is ineffective.
- Potential therapies are in development but none available currently.

Management of contacts

- Record name and contact in detail.
- Advise to seek medical assistance in the event fever or respiratory symptoms worsen, and immediately report to the health authority.
- Do not report to work until advised by the physician.
- Minimize contact with family members and friends.
- Avoid public places

Preventive Measures

- Public awareness about infection prevention and control is recommended including;
  - o Standard precautions (e.g. hand hygiene) of hygiene.
  - o Contact precautions like use of personal protective equipments (PPES).
- Antibiotics attribute no clinical improvement. However, good supportive care including intensive therapy has been shown to improve the prognosis.
- Children should not be allowed to visit the hospitalsas the disease may affect them more adversely.
- Quarantine stations help prevent exposure at the points of entry (POE).

- International travelers: The health professionals should be aware of the main symptoms of SARS. People who have fever or who appear acutely ill should be assessed by a healthcare physician and shouldbe advised to postpone their trip until they have recovered completely.
- No vaccine or chemoprophylaxis is available as yet.

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36. Syphilis

Introduction

An infectious venereal disease and common STD that can cause long-term complications if not treated. Syphilis is divided into stages (primary, secondary, latent, and tertiary), and there are different signs and symptoms associated with each stage. Mortality rate in Pakistan 1.8 per 100,000 people

Clinical Picture

Primary syphilis (Chancre): painless ulcer with clean base and firm indurated borders

Regional lymphadenopathy

Secondary syphilis

- Mainly involves skin and mucous membranes; manefist as skin rashes, mucosal ulceration and generalized lymphadenopathy.
- Constitutional symptoms includes fever, malaise, anorexia, arthralgia and myalgia.
- Central nervous system: headache, meningitis, cranial neuropathies (II-VIII)
- Ocular involvement
- Renal: Glomerulonephritis, Nephrotic syndrome
- Liver: hepatitis
- Bone and joint: arthritis, periostitis

Late syphilis Late benign (gummatous): cardiovascular: aortic regurgitation, coronary ostial stenosis, aortic aneurysm and neurosyphilis

Infectious Agent—*Treponema pallidum* (Spirochete)

Host/Reservoir—Human are the only known reservoir

Period of Communicability—A person with syphilis can easily pass the infection (is contagious) to physically intimate partners when primary or secondary stage sores are present. But the person may be contagious for years, off and on, and is always contagious whenever an open sore or skin rash from syphilis is present.

Mode of Transmission—

- Sexual transmission
- Vertical transmission
- Blood transfusion
- Direct skin contact

Incubation period—10 to 90 days (three weeks on average)

Case Definition

Suspected Case—A case with one or more ulcerative lesions (e.g. chancre)

OR localized or diffuse mucocutaneous lesions (e.g., rash — such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalized lymphadenopathy with or without other symptoms like mucous patches, condyloma lata, and alopecia.

Probable Case—A case that meets the clinical description of syphilis with a reactive serologic test (nontreponemal and treponemal test)

Confirmed Case—A suspected/probable case of syphilis with demonstration of treponema pallidum in clinical specimens.

Note: *Suspected, Probable and Confirmed Cases of Syphilis are classified into primary, secondary and tertiary stages depending on clinical manifestation*

Latent Syphilis

Suspected Case—A person with no clinical signs or symptoms of syphilis who has one of the following:

- No past diagnosis of syphilis and a reactive nontreponemal test and a reactive treponemal test or equivalent serologic methods OR
- A current nontreponemal test titer demonstrating fourfold or greater increase from the last nontreponemal test titer.

Note: *Early Latent syphilis is distinguished from late latent syphilis on the basis of demonstration of infection within previous 12 months based on one or more of the following:*

- Documented seroconversion or fourfold or greater increase in titer of a nontreponemal test during the previous 12 months
- Documented seroconversion of a treponemal test during the previous 12 months
- A history of symptoms consistent with primary or secondary syphilis during the previous 12 months
- A history of sexual exposure to a partner within the previous 12 months who had primary, secondary, or early latent syphilis (documented independently as duration <12 months)
- Only sexual contact was within the last 12 months (sexual debut)

Confirmed case: There is no confirmed case classification for early latent syphilis

Lab confirmation—Direct Method for demonstration of treponema pallidum:

- Dark field microscopy of exudates or fluids from lesion (most simplest and reliable especially early syphilis when antibodies are not detectable
- Direct fluorescent antibody test for *T. Pallidum* (most specific test)
- Direct test for *T. Pallidum* in tissue sections
- PCR (method of choice in congenital syphilis, neurosyphilis and in early primary syphilis)

Serological testing (Indirect):

- Nontreponemal: Venereal Disease Research Laboratory (VDRL), Rapid plasma reagin [RPR]
- Treponemal: fluorescent treponemal antibody absorbed [FTA-ABS], T. pallidum particle agglutination [TP-PA], enzyme immunoassay [EIA], chemiluminescence immunoassay [CIA], or equivalent serologic methods.

Specimen Collection—

- Exudates from lesion of primary, secondary and early congenital syphilis for direct examination
- Serum for serological testing

Packaging—Triple Packaging

Storage—4-8°C (for serological testing)

Transportation—Triple Packaging with reverse cold chain

Case Management

Syphilis can be cured with the right antibiotics. However, treatment will not undo any damage that the infection has already caused. Primary and secondary syphilis are easy to treat with a penicillin injection. Penicillin is one of the most widely used antibiotics. People who are allergic to penicillin will likely be treated with a different antibiotic, such as Doxycycline, Azithromycin and ceftriaxone

A single intramuscular injection of long acting **Benzathine penicillin G** (2.4 million units administered intramuscularly) will cure the primary, secondary or early latent syphilis. Three doses of long acting Benzathine penicillin G (2.4 million units administered intramuscularly) at weekly intervals is recommended for individuals with late latent syphilis or latent syphilis of unknown duration.

Contact Tracing Period

Syphilis stage	**Trace-back period****
Primary	3 months
Secondary	6 months
Early latent	12 months
Late latent/Tertiary	Assess marital or other long-term partners and children as appropriate; the decision to test these contacts depends on estimated duration of infection in the source case. Although the late latent stage is not considered infectious, it is important to find the source of infections to ensure all contacts receive follow up.

Syphilis stage	Trace-back period**
Congenital	Assess mother and her sexual partner(s).
Undetermined	Assess/consult
**Trace-back period refers to the time period prior to symptom onset or date of specimen collection (if asymptomatic).	

Preventive Measures

Public awareness through;

- Provision of information on safe sex practices using condoms.
- Improving service access and instigating comprehensive communications plans.
- Treating the mother early in pregnancy to prevent vertical transmission.
- Infants should be screened by testing the mother's serum because infants' serum may notcome out to be positive if the mothers' serological tests are of low titer or if the mothers were infected late in pregnancy.
- Screening of partners for syphilis and other STIs is recommended.

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37. Trachoma

Introduction

Trachoma is the world's leading cause of preventable blindness of infectious origin. It is known to be a public health problem and is responsible for the blindness or visual impairment of, at present, for approximately 3% of the world's blindness. Nearly 182 million people live in trachoma endemic areas and are at risk of trachoma blindness. With repeated episodes of infection over many years, the eyelashes may be drawn in so that they rub on the surface of the eye, with pain and discomfort and permanent damage to the cornea. Blindness from trachoma is irreversible. In areas where trachoma is endemic, active (inflammatory) trachoma is common among preschool-aged children, with prevalence rate which can be as high as 60–90%. Africa is the worst affected continent. The risk of blinding trachoma is greater in women than in men.

Clinical Picture

It develops redness and irritation of the eyes with tearing, which can progress through repeated new infection to scarring and visual loss. Repeated episodes of re-infection within the family cause chronic follicular or intense conjunctival inflammation (active trachoma), which leads to tarsal conjunctival scarring. The scarring distorts the upper tarsal plate and, in some individuals, leads to entropion and trichiasis (cicatricial trachoma). The end result includes corneal abrasions, corneal scarring, opacification, and ultimately blindness.

Infectious Agent—*Chlamydia trachomatis*, a gram-negative, obligate intracellular bacteria

Host/Reservoir—No non-human reservoir of infection has been found, with flies only acting as passive vectors

Mode of Transmission—

- Direct spread from eye to eye during close contact such as during play or sleep.

- Spread of infected ocular or nasal secretions on fingers.
- Indirect spread by Fomites such as infected face-cloths.
- Transmission by eye-seeking flies(Synanthropic flies).
- Possible spread from nasopharyngeal infection by aerosol.

Infection usually first occurs in childhood and through the discharge from an infected child's eyes, trachoma is passed on by hands, on clothing, or by flies that land on the face of the infected child.

Incubation period—Ranges from 5 to 12 days

Seasonality—Hot, dry climates, dust and water scarcity are thought to be associated with the distribution of trachoma but the evidence is unclear. Temperature and rainfall appear to play a role in the transmission of acute trachoma, possibly mediated through reduced activity of flies at lower temperatures.

Outbreak threshold—Cluster of cases OR unusual increase in the number of cases.

Case Definition

Active Trachoma—Trachomatous inflammation – Follicular (TF) and Trachomatous inflammation Intense (TI) are indications of active trachoma and are usually found in children and teenagers, but may occasionally occur in older persons. Each sign is individually graded as being absent or present. One or more signs can, and often do, occur together

Chronic sequelae of trachoma—Trachomatous conjunctival Scarring (TS) is sequelae of trachoma and a sign of severe damage which signals the risk of developing trichiasis. Trachomatous Trichiasis (TT) is a result of severe distortion and scarring in the upper eyelid and the rubbing lashes lead to corneal scarring and corneal opacity (CO) which represents late stages; both are usually found in older adults

Individual contacts—A contact is anyone who is living and/or sleeping in the same household as a person with trachoma. If the active case lives or sleeps in multiple households, then members of all households in which the active case stays are considered contact.

Community contacts—In communities in which trachoma is endemic, contact management refers to the treatment of household and other community members, depending on the prevalence of active trachoma among the target group, 5 – 9 year old.

WHO simplified grading system for trachoma

Infectious	TF	Trachomatous inflammation-Follicular	Presence of 5 or more follicles of >0.5mm in diameter on the upper tarsal conjunctiva
	TI	Trachomatous inflammation – Intense	Presence of pronounced inflammatory thickening of the upper tarsal conjunctiva obscuring more than half of the normal deep tarsal vessels
Non-infectious	TS	Trachomatous conjunctival Scarring	Presence of easily visible scars on the upper tarsal conjunctiva
	TT	Trachomatous Trichiasis	Presence of at least one ingrown eyelash touching the eyeball, or evidence of recent removal of inturned lashes

Lab confirmation—Lab confirmation

- The diagnosis is almost always based on the clinical appearance.
- Laboratory assays are principally used in research.
- To confirm that the clinical diagnosis of active trachoma is the result of ocular *C trachomatis* infection, the best laboratory techniques are the nucleic acid amplification tests (NAATs), of which the polymerase chain reaction (PCR) is one example.
- Giemsa cytology is microscopic examination of stained conjunctival scrapings for intracytoplasmic inclusions.
- Immunofluorescence(IF) is a technique for detecting cellular molecules.
- Enzyme-linked immunosorbent assays

Case Management

- It is important to remember that treatment of cases of active trachoma found during screening programs should not be managed separately from the treatment of households and communities.
- Antibiotic treatment (Tetracycline/Doxycycline, Azithromycin)
- Facial cleanliness
- Surgery (in chronic cases)
- Environmental changes

Safe Strategy:

S: Surgery for people at immediate risk of blindness

A: Antibiotic therapy to treat individual active cases and reduce the community reservoir of infection

F: Facial cleanliness and improved hygiene to reduce transmission

E: Environmental improvements to make living conditions better so that the environment no longer facilitates the maintenance and transmission of trachoma

Preventive Measures

- **Education**: Health education should be provided to children, community members, and clinic and school staff about the disease and its transmission. The importance of maintaining good personal hygiene, especially of the face and hands should be emphasized.
- Primary interventions advocated for preventing trachoma infection include improved sanitation, reduction of fly breeding sites and increased facial cleanliness (with clean water) among children at risk of disease. The scarring and visual change for trachoma can be prevented by a simple lid surgery.
- Good personal and environment hygiene has been proven to be successful in curtailing infection due to trachoma. Encouraging the washing of children's face, improved access to water, and proper disposal of human and animal waste has been shown to decrease the number of trachoma infections in communities.
- Separation of animal quarters from human living space, as well as safe handling of food and drinking water is recommended.

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38. Tuberculosis

Introduction

Tuberculosis is an infectious, systemic, chronic granulomatous disease caused by a bacterium called Mycobacterium tuberculosis (tubercle bacilli). Which is transmitted to other persons by infected droplet generated by coughing or sneezing of patient having pulmonary Tuberculosis. It is an important public health problem that is preventable and curable. One fourth of the world's population is infected with TB. Pakistan ranks 5th among 30 high burden tuberculosis countries in the world.The prevalence, incidence and mortality per 100,000 population per year of TB in Pakistan are 341, 268 and 44 respectively (National TB Control Program)

Latent Tuberculosis Infection (LTBI): Latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB. Someone has latent TB if they are infected with the TB bacteria but do not have signs of active TB disease and do not feel ill. However, they can develop active TB disease in the future

TB disease: If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply rapidly. The tubercle bacilli overcome the immune system and multiply, resulting in progression from LTBI to TB disease. This process can occur in different areas in the body, such as the lungs, abdomen, brain, bone, and genitourinary system.

Drug-resistant TB: Drug resistance tuberculosis (DR-TB) is caused by mycobacterium organisms that are resistant to a first-line or second-line anti-TB drugs. Drug-resistant TB is transmitted in the same way as drug-susceptible TB and is equally infectious. However, delay in the recognition of drug resistance or prolonged periods of infectiousness may facilitate increased transmission and further development of drug resistance.

Multidrug-resistant TB (MDR TB): is caused by organism resistant to both Isoniazid (H) and Rifampicin (R) with or without resistance to any other drug.

Extensively drug-resistant TB (XDR TB): is a relatively rare type of drug-resistant TB. XDR TB is resistant to Isoniazid and Rifampicin, plus any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin). Because XDR TB is resistant to first-line and second-line drugs, patients are left with treatment options that are more toxic, more expensive, and much less effective.

Clinical Picture

Pulmonary Tuberculosis: The most common symptom of pulmonary TB is a productive cough for more than 2 weeks, which may be accompanied by other respiratory symptoms (shortness of breath, chest pain, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue).

Extra Pulmonary Tuberculosis: In case of Extra pulmonary TB, symptoms depend on the organs involved, for example: swollen lymph nodes, pleural effusion, pain and swelling in joints, meningeal involvement (TB meningitis) etc.

Infectious Agent—*Mycobacterium tuberculosis* (MTB is a non-motile, acid-fast, obligate aerobe). This includes M. tuberculosis and M. Africanum primarily cause disease in humans, and M. Bovis cause disease in cattle

Host/Reservoir—Humans are the only known reservoir for M. tuberculosis.

Period of Communicability—Patients having active tuberculosis are contagious. Infectiousness of the person with TB is directly related to the number of tubercle bacilli that he or she expels into the air.

Mode of Transmission—Human Source:

- Pulmonary Tuberculosis—airborne/droplet transmission
- Extra-pulmonary tuberculosis—non-infectious

Bovine Source:

- Usually by ingestion of unpasteurized milk or dairy products of infected cattle
- Airborne spread to farmers and animal handlers

Incubation period—Ranges from 2-10 weeks, but latent infections may persist for whole life. Progression to active disease can take from weeks to years

Seasonality—A seasonal pattern of tuberculosis with a mostly predominant peak is seen during the spring and summer seasons.

Case Definition

Presumptive—Refers to a patient who presents with symptoms or signs suggestive of TB (previously known as a TB suspect).

Bacteriologically confirmed TB case—(One which is conferm by smear microscopy, culture) such asGene Xpert MTB/RIF. All such cases should be notified, regardless of whether TB treatment has started.

Clinically diagnosed TB case—One who does not fulfill the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed based on X-ray abnormalities or suggestive histology and extra-pulmonary cases without laboratory confirmation.

Classification based on anatomical site of disease

Pulmonary tuberculosis (PTB)—Refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree.

Miliary TB is characterized by wide spread dissemination in body. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of PTB.

Extra-pulmonary tuberculosis (EPTB)—Refers to any Bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, and meninges.

Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of extra-pulmonary TB.

Classification based on history of previous TB treatment (patient registration group)

New patients—Have never been treated for TB or have taken anti-TB drugs for less than 1 month

Previously treated patients—Have received 1 month or more of anti-TB drugs in the past. They are further classified by the outcome of their most recent course of treatment as follows:

Relapse patients—Have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection)

Treatment after failure patients—Are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.

Treatment after lost to follow-up patients—Are previously been treated for TB and were declared lost to follow-up at the end of their most recent course of treatment. (These were previously known as treatment after default patients.)

Other previously treated patients—Are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented

Patients with unknown previous TB treatment history—Patients who do not fit into any of the categories listed above

Diagnostic Tools for Tuberculosis			
Bacteriological Diagnosis	**Clinical Diagnosis**	**TB infection**	**Non Specific/Not recommended**
AFB Smear Microscopy 2. X-PERT MTB/ RIF ASSAY (Rapid Molecular Test) 3. Culture & Species Identification (DST)	1. Chest X-rays 2. Histopathology	Tuberculin Test 2. TB interferon Gamma Release Assays (Not recommended by WHO for Low and middle income countries)	Serological Test (Not Recommended) 2. Other tests Blood examination e.g. Hb, CBC, ESR,

Specimen collection, storage and transportation			
Disease Type	**Specimen Type**	**Recommended Quality/Volume**	**Special Instruction Preservative**
Pulmonary Specimen	Sputum (Purulent/ Mucopurulent)	2-5 ml-	Nil
	Bronchial alveolar lavage (BAL)	20-40 ml	Nil
	Bronchial aspirates	2-5 ml	Nil
	Trans-bronchial Biopsy		Taken under sterile condition, should be kept in sterile container with few drops of sterile 0.9% saline to keep tissue wet
	Gastric Aspirate		Neutralize by adding 100 mg sodium bicarbonate
Extra-pulmonary Specimen	CSF	2-3 ml	Nil
	Body fluids (Pleural, Pericardial, Asciticetc)	20-50 ml	Collect aseptically in sterile container without using any preservative
	Tissue biopsy		Add few drops of sterile 0.9% saline to keep tissue wet
	Pus		NIL
	Urine	Min 200 ml	Single, early morning, midstream sample, collected in a wide mouthed sterile vessel

Case Management

Case management of TB should follow Pakistan's national guidelines for the management of TB.

The most common chemotherapeutic agents used in treatment of TB include Rifampicin (R), Isoniazid (H), Pyrazinamide (P), Ethambutol (E). The detailed description of duration and regimens for treatment of TB is beyond scope of this document.

Preventive Measures

Immunization:

BCG is strongly recommended for all newborn children and children up to the age of 5 years who have not already received it. It has shown to be effective in preventing complications of TB such as meningitis in children.

Re-vaccination is not recommended.

Complementary control strategies:

- Health education to improve awareness i.e. mode of spread, symptoms, methods of control, importance of early diagnosis and continued adherence to treatment.
- Maintaining good ventilation and reducing overcrowding in health clinics and ensuring hospitalized patients with pulmonary TB are kept in a separate ward for the first two weeks of treatment.
- Isoniazid prophylaxis is not recommended in refugee situations except for children being breast-fed by smear positive mothers. If the child is well, BCG vaccination should be postponed and isoniazid should be given to the child for 6 months. In the event of a sudden disruption to the programme, isoniazid may be stopped and BCG should be given before the child leaves the area. (Preferably after a one week interval).

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39. Typhoid and Paratyphoid Fever

Introduction

Typhoid fever also known as enteric fever (Difference between Typhoid and Enteric Fever: Typhoid caused by Salmonella typhi, Enteric fever caused by both) is a potentially severe and occasionally life-threatening febrile illness, which predominantly occurs in association with poor sanitation and lack of clean drinking water. According to the most recent estimates (2017) approximately 21 million cases and 222000 typhoid-related deaths occur annually worldwide. Pakistan is located in a highly endemic region with incidence rate of 451.7 per 100,000 persons per year of typhoid fever. More than 80-90% reported typhoid and paratyphoid fever cases in non–endemic countries are due to travelers coming from South east Asia.

Clinical Picture

The acute illness is characterized by prolonged high grade (> 100 ^{0}F) fever, headache, nausea, loss of appetite, and constipation or diarrhea. Symptoms are often non-specific and clinically non-distinguishable from other febrile illnesses. Complications include intestinal ulceration and perforation in 3rd week of illness.

Infectious Agent—Typhoid fever: *Salmonella Typhi.*

Paratyphoid fever: *Salmonella paratyphi* A, B or C, with A being most common in Pakistan.

Host/Reservoir—Humans are the only reservoir for *Salmonella Typhi*, whereas Salmonella *paratyphi* can also have animal reservoirs.

Period of Communicability—The disease is communicable for as long as the infected person excretes *S.Typhi* in their excreta, usually after the 1st week of illness through convalescence. Approximately 10% of untreated cases will excrete *S. typhi* for 3 months and between 2-5% of all cases become chronic carriers.

Mode of Transmission—Faeco-oral route, particularly ingestion of water and food contaminated by faeces and urine of patients and carriers.

Incubation period—8-14 days but may be from 3 days up to two months

Risk factors—Lack of availability of safe drinking water, food and poor sanitation (poor socio-economic conditions).

Seasonality—Annual endemicity with peak in April to August (Monsoon season).

Alert Threshold—The alert threshold for typhoid is 1 case.

Outbreak threshold—5 suspected/confirmed cases per 50,000 population.

Case Definition

Suspected Case—Any person with acute illness and fever of at least 38^0 C for 3 or more days with abdominal symptoms; diarrhoea, constipation, abdominal tenderness and prostration

Probable Case—A suspected case with a positive sero-diagnosis but no S. typhi isolation

OR

A clinical compatible case that is epidemiologically linked to a confirmed case in an outbreak

Confirmed Case—A suspected/probable case that is laboratory confirmed by: isolation of Salmonella typhi/paratyphi from blood, or/and stool, urine or bone marrow specimen.

Chronic Carrier—An individual excreting S. typhi in the stool or urine for longer than one year after the onset of acute typhoid fever.

(1-5% of patients, depending on age, become chronic carriers harbouringS. typhi in the gallbladder/kidneys).

Lab confirmation—Confirmatory Tests/Gold Standard: Blood & Bone Marrow Culture. Blood culture before initiating antimicrobial therapy remains the diagnostic method of choice.

Serological Tests: Serum (Typhidot/Widal) can be done but discouraged due to low specificity and sensitivity in endemic regions and a risk of developing a practice for unwarranted antibiotic use if not followed by confirmatory tests leading to antibiotic resistance.

Timings—Serology: First sample should be collected at the time of presentation for baseline titres and a second sample, if possible, should be collected 7-10 days after the onset of fever.

Specimen Collection—Blood for Culture and Sensetivity: Blood should be drawn using aseptic technique to reduce the possibility of contaminating the blood culture with skin organisms

Serum: Collect 1-3 ml of blood inoculated in a tube without anticoagulant for serological purposes.

Stool/ Rectal and Urine: Carriers: Collect samples on three consecutive days for diagnosing typhoid carriers.

Packaging—Rectal swabs inoculated into Carry Blair transport medium, properly packed (Triple Packaging) and should be transported to the lab in a cool box.

Storage—Blood: Culture bottles should be kept at 37°C/room temperature in tropical countries.

Serum: Separate serum after clotting and store in aliquots of 200 microliters at +4°C. Testing can take place immediately or storage can continue for a week without affecting the antibody titre at refrigerated temperatures of 2-10° C. For longer storage the serum may be frozen at –20°C.

Stool/Rectal for culture: Specimens should preferably be processed within two hours after collection. In case of delay, store at 4°C or in a cool box with freezer packs

Transportation—Blood culture bottles should be transported to the referral laboratory at 22-30°C temperature.

Case Management

Uncomplicated: The total treatment duration is 14 days. Recommended empirical therapy is injectable Ceftriaxone (50-75 mg/kg) in OD doses for 7-10 days as the drug of choice. Switch to oral third generation cephalosporins like Cefixime after 7 days (10 mg/kg). Second line of treatment should be based on antibiogram of Ampicillin, Chloramphenicol, Co-trimoxazole and Azithromycin.

Do not use Ciprofloxacin/Quinolones as majority of the isolates are now resistant.

XDR Salmonella: Due to the inadvertent use of antibiotics in the community there is an increase in the number of isolates of S Typhi that are resistant to all the first line drugs and requires second line line drugs like azithromycin and carbapenems hence making it mandatory to collect cultures in time in all patients to avoid failures.

Supportive Care: Oral or intravenous rehydration, antipyretics and appropriate nutrition also play an important role.

Preventive Measures

General preventive measures: Avoid contaminated food and water, half cooked food, raw vegetables and fruits which cannot bepeeled off.

Typhoid vaccination: Vaccine is not recommended in children under 2 years of age. Two vaccines are currently available: TAB for all antigens (I/M Injection) and oral vaccine for S. typhi only.

A new conjugate vaccine TCV is recently approved and is used as ring vaccination in the regions with XDR salmonella outbreaks, it will be available soon and efforts are underway to make it a component of EPI.

Preventive Measures during outbreaks:

Outbreak may occur via person-to-person contamination (faeco-oral transmission via contaminated hands or instruments) and direct faecal contamination of untreated water.

Note: Investigations must pinpoint the source (acute case & carrier) and mode of infection to identify corrective measures for application (chlorination/boiling of water, selective elimination of suspected food; carriers and food handlers).

- Inform the Health Authorities if one or more suspected cases are identified.
- Confirm the outbreak.
- Confirm the diagnosis and ensure prompt treatment.
- Encourage immunization during sustained, high incidence epidemics.
- Identify the carriers through surveillance, treat them and ensure follow up.
- All food handlers (domestic or commercial) to be screened for carrier state.

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40. Varicella (Chickenpox)/Zoster

Introduction

An acute, viral, highly contagious disease, which occurs worldwide. The identification of a single case should trigger appropriate intervention measures as it can be a source of potential outbreaks. In temperate climates most cases occur before the age of 10 years

Clinical Picture

- Characterized by an itchy, vesicular rash, initially accompanied by the prodromal phase of fever and malaise.
- Blisters usually appear in crops, starting on the scalp and face and can spread over the entire body causing between 250 and 500 itchy blisters. As the rash gradually spreads to the trunk and extremities, the first vesicles dry out. It usually takes about one week for all the blisters to become scabs.
- While mostly mild and self-limiting in childhood, it can be serious, especially in infants, adults, and people with weakened immune systems.
- Chicken pox illness usually lasts about 5 to 7 days. It normally takes about 7–10 days for all crusts to disappear.
- Vaccinated persons can still get the disease in modified form.
- Complications include VZV-induced pneumonitis or encephalitis and invasive group-A streptococcal infections.
- Pregnant women who get Varicella are at increased risk of developing serious complications like pneumonia, pneumonitis and encepalitis leading to death in some rare cases. If a pregnant woman gets Varicella in her 1st or early 2nd trimester, her baby has a small risk of being born with congenital Varicella syndrome. If a woman develops Varicella rash from 5 days before to 2 days after delivery (perinatal period), the newborn will be at enhanced risk for neonatal Varicella.

Zoster (Shingles)

Painful vesicular rash over sensory dermatome (zoster) is the common presentation, a dessiminated variant also exist that usually occurs in severly immunocompromised.

Infectious Agent—*Varicella-zoster* (HSV-3) virus of herpes virus family

Host/Reservoir—Humans are the only reservoir

Period of Communicability—The period of contagiousness of infected persons is estimated to begin 1–2 days before the onset of rash and to end when all lesions are crusted, typically 4–7 days after onset of rash

Mode of Transmission—The virus enters the host through the upper-respiratory tract or the conjunctiva

Incubation period—14–16 days (range: 10–21 days).

Seasonality—May occur any time during the year but usually peaks during spring & summer

Alert Threshold—One case (clinically suspected)

Outbreak threshold—One case (clinically suspected)

Case Definition

Suspected Case—A child with prodromal symptoms (without rash) with positive cases in the environment/community.

Probable Case—An illness with acute onset of diffuse (generalized) maculopapulovesicular rash without other apparent cause, not laboratory confirmed and is not epidemiologically linked to another probable or confirmed case.

Confirmed Case—A probable case and epidemiologically linked to another probable or confirmed case and confirmed by lab tests.

Note: *Two probable cases that are epidemiologically linked are considered confirmed, even in the absence of laboratory confirmation.*

Lab confirmation—Lab confirmation is done by multinucleate giant cells on Tzanck smear of skin lesions eosinophilic Cowdry intranuclear inclusion bodies on skin biopsy testing serum IgM through ELISA

Direct fluorescend antibody (DFA)

PCR from a clinical specimen like blister fluid or swab from the base of the blister.

Specimen Collection—Ideally scabs, vesicular fluid, or cells from the base of a lesion for lab confirmation

Packaging—All above samples should be kept in separate label screw capped tubes to prevent from splashes and breakage. The samples collected in the tubes are shipped dry at ambient temperatures.

Storage—Specimens may be kept indefinitely at –20°C

Transportation—In triple packaging maintaining cold chain

Case Management

Varicella (chickenpox)

- Management is mainly supportive.
- Use non-aspirin analgesics, such as Acetaminophen/Paracetamol to relieve fever.
- Calamine lotion and baking soda may help relieve some of the itching.
- Keeping fingernails trimmed may help prevent skin infections caused by scratching blisters.
- Oral Acyclovir therapy is not recommended for use in otherwise healthy children experiencing typical Varicella without complications. Certain groups at increased risk for moderate to severe Varicella may be considered for oral acyclovir treatment. These cases include healthy persons:
  - o older than 12 years of age;
  - o chronic cutaneous or pulmonary disorders; long term salicylate therapy;

- o short, intermittent or aerosolized courses of corticosteroids;
- o secondary cases within a household

- Some recommend oral Acyclovir during pregnancy especially in 2nd and 3rd trimester and IV Acylovir in pregnant women experiencing complications e.g pneumonia
- In severe or disseminated Varicella Disease IV Acyclovir is recommended
- For maximum benefit, oral Acyclovir therapy should be given within the first 24 hours after the Varicella rash starts.

Zoster (shingles)

- Anti viral therapy can speed up healing and reduces the risk of complications if initiated earlier
- Antiviral therapy is indicated for about 50 yrs, moderate to severe rash or pain, involvement of face/eyes, immunocompromised.
- Antivirals that can be used are Valacyclovir, Famciclovir and acyclovir

Preventive Measures

- In residential and healthcare settings, airborne infection isolation rooms should be established, and standard and contact precautions should be followed.
- Keep children out of school and day care to prevent spread of the virus to others. Infected adults should also stay at home.
- Strategies for controlling varicella outbreaks include confirming the outbreak, identifying the cases, conducting case investigations, implementing control measures and establishing surveillance for additional cases.

Vaccination

- Chickenpox vaccination is recommended for preventing and controlling outbreaks.
- Persons without evidence of immunity to varicella and who do not have a contraindication to vaccination should be vaccinated.

- Two doses of chickenpox vaccine are recommended for children aged 1-4 years for best protection. The first dose is given at 12-15 months of age and the second dose at 4-6 years.
- School-aged children, adolescents and adults are vaccinated with 2 doses 4–8 weeks apart.

Post Exposure Prophylaxis (PEP)

Vaccine administered within 3 days of exposure to rash is most effective in preventing disease (≥90%); however, vaccine administered within 5 days of exposure to rash is about 70% effective in preventing disease and 100% effective in modifying disease.

Vericella Zoster Immune Globulin (VZIG) 125 units/10kg IM is recommended for PEP in susceptible persons at greater risk for complications as soon as possible after exposure (<96 hrs)

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41. Viral Hemorrhagic Fever

Introduction

Viral hemorrhagic fever (VHF) is a general term for a severe illness, sometimes associated with bleeding, that may be caused by a number of viruses. VHFs include Crimean Congo Haemorrhagic Fever (CCHF), Ebola Virus Disease, Marburg fever, Lassa Fever, Yellow Fever, Dengue etc. VHFs can be severe and life-threatening with particular public health importance because they can spread within a community and hospital setting, with a high case-fatality rate and are difficult to recognize and detect rapidly.

Principles of VHF management

- **Case identification/detection**

The diagnosis of VHF is based on 3 components:

- o History of exposure/epidemiological link
- o Detailed clinical assessment/compatible symptoms
- o Laboratory investigations/thrombocytopenia

Notification: Once VHF is suspected, immediate notification to the next level and district should be done using the appropriate and quickest available means. All subsequent suspected cases should be reported and recorded on a line list for further action.

Isolation: Single room isolation. This room should have an adjoining toilet or latrine, good ventilation, screened windows and restricted access.

Contact tracing: All close contacts must be enlisted and followed up for 14 days for any development (symptoms, hematologic changes, bleeding manifestations)

Prevention & control: Livestock department must be taken on board for tick's identification & elimination.

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41.1 Crimean Congo Hemorrhagic Fever

Introduction

A tick-borne zoonotic viral disease that is asymptomatic in infected animals, but a serious threat to humans. Human infections begin with nonspecific febrile symptoms, but progress to a serious hemorrhagic syndrome with a high case fatality rate (10 – 40%). It is one of the most widely distributed viral hemorrhagic fevers occurring in parts of Africa, Middle-east, Asia and Europe. The occurrence of this virus is correlated with the distribution of Hyalomma tick species (Principal vector). CCHF is endemic in Pakistan with sporadic outbreaks. Since the diagnosis of first human case of CCHF in 1976, the sporadic cases have continued to occur across Pakistan. Balochistan has reported with the maximum number of cases during last 5 years

Clinical Picture

Sudden onset with initial signs and symptoms including headache, high fever, back pain, joint pain, abdominal pain and vomiting, red eyes, a flushed face, a red throat, and petechiae (red spots) on the palate are common. Symptoms may also include jaundice and in severe cases, changes in mood and sensory perception.

With illness progression, large areas of severe bruising, severe nosebleeds, and uncontrolled bleeding at injection sites can be seen, beginning on the fourth day of illness and lasting for about two weeks

Infectious Agent—Crimean-Congo Haemorrhagic Fever (CCHF) Virus belonging to *Bunyaviridae* family

Host/Reservoir—

- Hyalomma tick
- Domestic animals, such as cattle, goats, sheep
- Wild animals/rodents, such as hedgehog, rats, hares. Birds are generally resistant with exception of Ostrich

Mode of Transmission—Bite of infected Hyalomma tick (Vector), handling of tick infested animals, direct contact with blood/tissue of infected domestic animals (slaughtering); or direct contact with blood/tissue of infected patients. Nosocomial infections are also common

Incubation period—

- 1–3 days after a tick bite
- 5–6 days after exposure to infected blood or tissues with a documented maximum of 13 days

Seasonality—Cases peak during fall and spring seasons, associated with life-cycle of ticks and, exposure of migrating animals

Alert Threshold—One probable case is an alert and requires an immediate investigation.

Outbreak threshold—One lab confirmed case of CCHF is an outbreak.

Case Definition

Suspected Case—Any person with sudden onset of fever over 38.5°C for more than 3 days and less than 10 days, especially in CCHF endemic area and in contact with livestock such as shepherds, butchers, and animal handlers.

Probable Case—Suspected case with history of febrile illness of 10 days or less with epidemiological link AND any two of the following: thrombocytopenia less than 50,000/mm^3, petechial or purpuric rash, epistaxis, haematemesis, haemoptysis, blood in urine and/or stools, ecchymosis and gum bleeding.

Confirmed Case—Suspected/ probable case with laboratory diagnosis of CCHF i.e. PCR and/or serology

Lab confirmation—

- Confirmation of presence of IgM antibodies in serum by ELISA (enzyme-linked immunoassay assay)
- Detection of viral nucleic acid by PCR in blood specimen

Timings—

- Specimens should be taken at time of presentation

Specimen Collection—

- Collect 5 ml of blood in Vacutainer tube observing strict biosafety precautions to avoid contact with blood or needle stick injury.

Packaging—Transport in triple packaging

Storage—2–8°C, or Frozen at –20°C

Transportation—Transport serum specimen to the lab with ice packs or frozen with dry ice along with a prominent Biohazard label and completely filled lab request form with brief history and provisional diagnosis of the patient.

Case Management

- Patients with probable or confirmed CCHF should be isolated and cared for using strict barrier-nursing techniques using PPE like masks, goggles, gloves, gowns with proper removal and disposal of contaminated articles through autoclave and/or incineration.
- In case of non-availability of above facilities burn and bury the waste.
- Only designated and trained medical/para-medical staff should attend the patient.
- All medical, Para-medical staff and attendants should wear disposable gloves, disposable masks and gowns on entering room, remove on exiting, and disposed articles completely incinerated/burned.
- All secretions of the patient and hospital clothing in use of the patient and attendants should be treated as infectious and where possible, should be autoclaved before incinerating or burning.
- Every effort should be made to avoid spills, pricks, injury and accidents during the management of patients. Needles should not be re-capped but discarded in proper safety disposal box.
- All used material e.g. syringes, gloves, cannula, tubing etc, should be collected in autoclave-able bag and autoclaved before incinerating/ burning.
- All instruments should be decontaminated and autoclaved before reuse.

- All blood specimen should be clearly labelled and lab staff should ensure safe handling and proper specimen disposal through autoclaving and incineration.
- All surfaces should be decontaminated with 5% liquid bleach.
- After the patient is discharged, room surfaces should be wiped down with 5% liquid bleach to kill the virus and the room should be fumigated if risk of tick infestation.

Treatment

General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to maintain adequate volume and blood component replacement is recommended.

If the patient meets the case definition for probable CCHF, oral Ribavirin treatment protocol needs to be initiated immediately in consultation with the attending physician. Studies suggest that Ribavirin is most effective if given in the first 6 days of illness. Oral Ribavirin: 30 mg/kg as loading dose, followed by 16 mg/kg every 6 hours for 4 days and then 8 mg/kg every 8 hours for 3 days.

Prophylaxis Protocol

- The efficacy for post exposure Ribavirin in the management of hospital-associated CCHF, remains anecdotal.
- It may be given in a high loading dose (35 mg/kg orally followed by 15 mg/kg three times daily for 10 days) and only for high-risk settings (e.g. needle stick injury, mucous membrane contamination, emergency resuscitative contact, or prolonged intimate exposure during transport) after baseline blood studies.

Household or other contacts of the case who may have been exposed to infected ticks or animals, or who recall indirect contact with case body fluids should be monitored for 14 days from the date of last contact with the patient or other source of infection by taking the temperature twice daily. If the patient develops a temperature of 38.5°C or greater, headache and muscle pains, he/she would be considered a probable case and should be admitted to hospital and started on Ribavirin treatment as mentioned above

Preventive Measures

- Mass education about the mode of transmission of the disease and the means for personal protection is recommended.
- Peopleliving in endemic areas should use personal protective measures including:
  - o Avoidance of areas where tick vectors are abundant, especially when they are active (Spring to fall).
  - o Regular examination of clothing and skin for ticks and their removal (without crushing them).
  - o Wearing light-coloured clothing covering legs and arms and using repellents.
  - o Other measures, such as wearing gloves or other protective clothing to prevent skin contact with infected tissue or blood, shoulld be adopted by people who work with livestock or animals in endemic areas.
- For tick control animal dipping and spraying in an insecticide solution i.e. Cypermethrin and Tricloroform is recommended. Injectable insecticide i.e. Ivermectin is also recommended.
- Butchers should wear gloves and other protective clothing to prevent skin contact with freshly slaughtered meat, blood and other tissues. Meat should drain 30 minutes, before distribution to the public.
- Hospitals in endemic areas should ensure universal precautions in OPD. Emergency Rooms should be stocked with supply of disposable gloves and other PPE, Injection safety measures should be ensured, and a stock of ribavirin maintained.
- Biosafety is the key to avoid nosocomial infection. Patients with suspected or confirmed CCHF should be isolated and cared for using barrier-nursing techniques to prevent transmission of infection to health workers.
- In case of death of a CCHF patient, family should be informed to follow safe burial practices.
- Exposed HCWs, family members and contacts, specially those with high risk exposures such asneedle stick, sharps, blood or body fluids contact should be observed for fever for 14 days. If fever develops then high dose ribavirin should be started immediately.

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41.2 Dengue Fever

Introduction

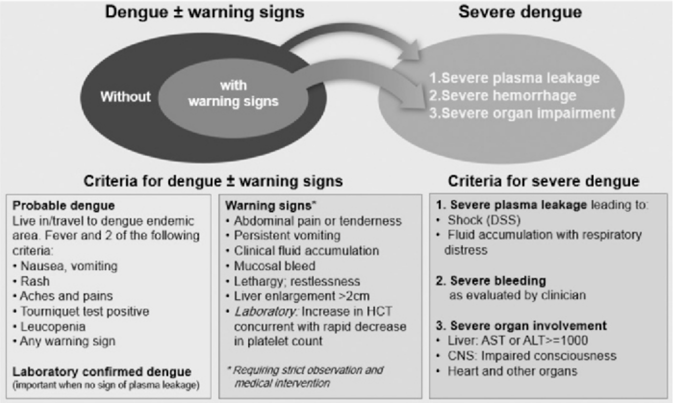
A mosquito-borne viral disease (Also known as break bone fever), causes flu-like illness, and occasionally develops into a potentially lethal complication called severe Dengue. The global incidence of Dengue has grown dramatically in recent decades and about half of the world's population is now at risk. The first confirmed outbreak of Dengue fever in Pakistan was reported in 1994.

Clinical Picture

After the incubation period, the illness begins abruptly and will be followed by 3 phases:

- Febrile phase
- Critical phase
- Recovery phase

Dengue is characterized by fever (for >3 days and <10 days) and the presence of one or more of the following signs and symptoms; i.e. nausea/vomiting,



rash, aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia).

Warning signs for Dengue Hemorrhagic Fever are abdominal pain or tenderness, persistent vomiting, extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites), mucosal bleeding at any site, liver enlargement >2 centimetres.

Causes of Death in Dengue

- Unrecognized disease → patient sent home with diagnosis of gastroenteritis at onset of the critical period
- Unrecognized shock or prolonged shock
- Unrecognized occult hemorrhage
- Fluid overload
- Nosocomial sepsis especially in elderly

Infectious Agent—Belonging to *Flavivirus* group; Four different Dengue serotypes are known: DEN1, DEN2, DEN3, and DEN4.

Host/Reservoir—Humans are the only vertebrate host.

Period of Communicability—2–7 days.

Mode of Transmission—Bite of infected mosquitoes, Aedes aegypti and Aedesalbopictus.

Incubation period—3–14 days (average 4–7 days) after the infective bite.

Seasonality—Peak of cases during September to October (Monsoon and Rainy Season).

Alert Threshold—Dengue Fever: Cluster of 3 suspected cases with at least one confirmed.

Dengue Haemorrhagic Fever: One probable case is an alert and requires an immediate investigation to assess differential diagnosis to rule CCHF.

Outbreak threshold—Cluster of 6 suspected cases and one lab confirmed case is an outbreak.

Case Definition

Suspected Case—An acute febrile illness of 2–7 days duration with 2 or more of the following: Headache, Retro-orbital pain, Myalgia, Arthralgia or Haemorrhagic Rash.

Probable Case—A suspected case of Dengue fever, or Dengue hemorrhagic fever with laboratory results indicative of probable infection.

Confirmed Case—A clinically compatible case of Dengue fever, or Dengue hemorrhagic fever with confirmatory laboratory results.

Dengue Hemorrhagic Fever—Defined as Dengue with any one or more of warning signs i.e. severe abdominal pain or persistent vomiting, red spots or patches on the skin, bleeding from nose or gums, vomiting blood, black, tarry stools (faeces, excrement), drowsiness or irritability, pale, cold, or clammy skin, difficulty breathing and blood picture showing a total white blood cell count of <50,000/mm^3 and Platelets <100,000.

Dengue Shock Syndrome—Dengue with any one or more of the following scenarios: Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress.

Signs of Shock: Low BP, feeble pulse, cold and clammy skin and vital organs involvement.

Note: *In 1–3% of cases, the disease develops into the life-threatening Denguehaemorrhagic fever (DHF), sometimes progressing into Dengue shock syndrome (DSS).*

Lab confirmation—Probable: Detection of IgM anti-DENV by validated immunoassay in a serum specimen.

Confirmatory:

- Detection of DENV antigen in serum, plasma, blood, by reverse transcriptase-polymerase chain reaction (PCR),
- Detection in serum or plasma of DENV Non-Structural Protein 1 (NS1) antigen by a validated immunoassay.

Timings—NS1: one Day Post Onset of symptoms (DPO) up to 8 DPO

PCR: Initial 4–5 days of onset of illness

Serology:

- IgM antibodies are detectable after 4th day of onset of illness (acute)
- IgG is used for the detection of past Dengue infection and usually can be detected during 2nd week of illness.

Specimen Collection—Observing standard precautions and collect 5 ml of blood, centrifuge, and separate serum for analysis, observing strict safety precautions.

Packaging—Triple packaging

Storage—2–8°C for short duration

Frozen at –20°C

Transportation—Transport serum specimens to the lab in triple container packing with ice packs or frozen with dry ice (For long distance) along with a prominent Biohazard label and complete lab request form with brief history of the patient.

Case Management

****Refer to Dengue Case Management brucher by CDC.**

In the early febrile phase, it is not possible to distinguish DF from DHF/DSS. The treatment during febrile phase is symptomatic and largely supportive, as follows:

- Rest and give extra amounts of fluids.
- Paracetamol 10 mg/kg/dose in children and 500–1,000 mg/dose in adult. Maximum adult dose is 4 grams/day.
- Do not give Aspirin or other NSAID like Ibuprofen.
- Oral rehydration therapy (ORT/ORS) is recommended for patients with moderate dehydration.

Complete blood count (CBC/CP) with follow up is an important tool in management of suspected Dengue patients and Increasing hematocrit (10–15% per day) is sign of impending Dengue SS and rapid decrease concurrent rapid decrease in platelet count (a total white blood cell count of <50,00/mm^3, Platelets <100,00 but specially below 50,000) is an impending sign of DHF.

- Provide brochure for families about the "warning signs" together with other recommendation.
- All Dengue patients must be carefully observed for signs of shock for at least 24 hours after recovery from fever.
- The patient who does not have any evidence of circulatory disturbance and who has been afebrile for >24 hours does not need further observation and may be discharged.

Protocol for Management According to Phases of DHF

(1) Dengue Hemorrhagic Fever (DHF) Grades I and II.

As in DF, during the afebrile phase of DHF Grades I and II, the patient has the same symptoms as during the febrile phase. The clinical signs plus thrombocytopenia and hemoconcentration or rise in hematocrit are sufficient to establish a clinical diagnosis of DHF. During this situation hospitalized the patient and treat accordingly.

(2) DHF Grades III and IV (DSS):

- Common manifestations observed during the afebrile phase of DHF Grade III are circulatory failure manifested by rapid and weak pulse, narrowing of the pulse pressure characterized by high diastolic pressure relative to systolic pressure, e.g. 90/80 mm of Hg (this is usually due to plasma leakage) or hypotension (possibly due to bleeding), and the presence of cold clammy skin and restlessness or lethargy.
- Immediately shift the patient to Intensive Care Unit (ICU) and treat accordingly.
- The mortality is up to 30% without treatment but less than 1% with adequate treatment by experienced physician in dedicated facility.

Preventive Measures

Preventive measures:

- Community survey to determine density of vector mosquitoes.
- Identify and destroy mosquito breeding sites in nearby outdoor/indoor premises.

- Indoor residual spray in areas with high mosquito density and thermal fogging in case of outbreaks.
- Conduct community mobilization through schools and religious leaders to promote:
    - o Proper solid waste management and larval habitats may be destroyed by filling depressions that collect water, by draining swamps or by ditching marshy areas to remove standing water. Container-breeding mosquitoes are particularly susceptible to source reduction as people can remove or cover standing water in cans, cups, and rain barrels around houses.
    - o Protection against day biting mosquitoes including use of screening, protective clothing and repellents.
    - o Sleeping or resting in screened or air-conditioned rooms.
    - o Use of insecticide-treated mosquito nets.
    - o Community based environmental management and health education campaigns.

Vaccination: In late 2015 and early 2016, the first dengue vaccine, Dengvaxia (CYD-TDV) was registered in several countries for use in individuals 9–45 years of age living in endemic areas. WHO recommends that countries should consider introduction of the dengue vaccine CYD-TDV only in geographic settings where epidemiological data indicate a high burden of disease.

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41.3 Ebola Virus Disease (EVD)

Introduction

A fatal viral hemorrhagic fever with reported case fatality rate around 50% (25% to 90%). First appeared in 1976 in a village near the Ebola River, from which the disease takes its name. The outbreak in West Africa in 2014 (first cases notified in March 2014), was the largest and most complex Ebola outbreak in the recent past.

Clinical Picture

Fever, fatigue, muscle pain, headache and sore throat followed by vomiting, Diarrhea, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding (e.g. oozing from the gums, blood in the stools).

Epidemiological Criteria

Having travel history to endemic areas or contact with probable/confirmed case within 21 days before the onset of symptoms

High-risk exposure criteria

Any of the following:

- Close face-to-face contact without appropriate personal protective equipment with a probable or confirmed case or had unprotected sexual contact with a case up to three months after recovery
- Direct contact with any soiled material with bodily fluids from a probable or confirmed case
- Percutaneous injury (e.g. with needle) or mucosal exposure to bodily fluids, tissues or laboratory specimens of a probable or confirmed case;
- Participation in funeral rites with direct exposure to human remains in or from an affected area without appropriate personal protective equipment
- Direct contact with bats, rodents, primates, living or dead, in or from affected areas

Infectious Agent—Ebola virus belons to family *Filoviridae*.

Host/Reservoir—The natural reservoir is unknown however Guinea pigs, wild rodents, fruit bats of the Pteropodidae family are thought to be the natural hosts.

Period of Communicability—Humans are not infectious until they develop symptoms. Infectivity remains until the virus persists in blood. Ebola virus has been isolated from semen 61-82 days post illness and sexual transmission can occur seven weeks even after recovery.

Mode of Transmission—

- Close contact with the blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.
- Ebola spreads through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids.
- Sexual transmission

Incubation period—2-21 days.

Alert Threshold—One suspected case is an alert

Outbreak threshold—One confirmed case is an outbreak

Case Definition

Suspected Case—Any person with onset of fever and no response to treatment for usual causes of fever in the endemic area, and having any haemorrhagic signs.

OR

Any person, alive or dead, suffering or having suffered from a sudden onset of high fever and having had contact with:

– a suspected, probable or confirmed Ebola or Marburg case;

– a dead or sick animal (for Ebola)

OR

Any person with sudden onset of high fever and at least three of the following symptoms: – headaches – lethargy – anorexia/loss of appetite – aching muscles or joints – stomach pain – difficulty swallowing – vomiting – difficulty breathing – diarrhea – hiccups

Probable Case—Any person meeting the clinical and exposure criteria

Any suspected case evaluated by a clinician; OR

Any deceased suspected case (where it has not been possible to collect specimens for laboratory confirmation) having an epidemiological link with a confirmed case

Confirmed Case—Laboratory-confirmed diagnostic evidence of Ebola virus infection.

Any suspected or probably cases with a positive laboratory result. Laboratory confirmed cases must test positive for the virus antigen, either by detection of virus RNA by reverse transcriptase-polymerase chain reaction (RT–PCR), or by detection of IgM antibodies directed against Marburg or Ebola.

Lab confirmation—

- ELISA (IgM) within 3 days after appearance of symptoms (positive between 10-29 days and can persist for 168 days in some cases)
- PCR for Virus isolation: (3-10 days)
- After recovery for prognostic criteria: IgM, IgG Antibodies
- Antigen capture detection tests

Specimen Collection—Full PPE is required to collect samples.

Minimum 4 ml whole blood preserved with EDTA is preferred or serum from Sodium Polyanethol Sulfonate, Citrate or from clot activator is also acceptable

Packaging—Tripple packaging

Storage—2–8°C for short duration

Frozen at –20°C

Transportation—Transport serum specimens in triple packaging to the lab with ice packs or frozen with dry ice (for long distance) along with a prominent Biohazard label and complete lab request form with provisional diagnosis of the patient

Case Management

- Recovery from EVD depends on good supportive clinical care and the patient's immune response.
- Supportive care with rehydration with oral or intravenous fluids and treatment of specific symptoms, improves survival.
- There is no specific treatment available for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated.

Preventive Measures

- Follow standard recommended precautionsalong with extended infection prevention control precautions(Standard plus Contact plus airborne plus droplet) to:
- Reduce the risk of Human-to-human transmission.
- Reduce the risk of possible sexual transmission.
- Ensure proper waste disposal to implement strict environmental IPC.
- Control infection in health-care settings.
- Outbreak containment measures (refer to standard guidelines/docs) should be adopted.
- Burial should not be delayed, and dead bodies should be handled with strict PPE measures.

- WHO recommends that male survivors of Ebola virus disease practice safe sex and hygiene for 12 months from onset of symptoms or until their semen tests are negative twice for Ebola virus.
- Reduce the risk of wildlife-to-human transmission in endemic areas.

Vaccination: No licensed vaccines are available yet.

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41.4 Yellow Fever

Introduction

Yellow fever is a mosquito born acute viral haemorrhagic disease. The "Yellow" in the name refers to jaundice, its main symptom. There are an estimated 84,000–170,000 cases and up to 60 000 deaths due to yellow fever per year. The virus is endemic in tropical areas of Africa and Latin America. No case of Yellow fever has been reported in Pakistan so far but keeping in view the presence of its vector and travel risk, it is imperative to be vigilant.

Clinical Picture

Symptoms in first phase include fever, headache, muscle pain, nausea, vomiting, and fatigue. A small percentage of infected people experience a second more severe phase of illness which includes high fever, jaundice and internal bleeding. At least half of severely affected patients who don't receive treatment die within 10 to 14 days.

Infectious Agent—Yellow fever virus belongs to *Flavivirus*

Host/Reservoir—Infected primates (human or non-human)

Period of Communicability—Human blood is infective for mosquitoes shortly before the onset of fever and for 3–5 days after. Mosquitoes require 9–12 days after a blood meal to become infectious and remain so for life.

Mode of Transmission—By the bites of infected Aedes aegypti and Haemagogus mosquitoes.

Incubation period—3 to 6 days

Alert Threshold—One suspected case

Outbreak threshold—One laboratory confirmed case of yellow fever in an unvaccinated population could be considered an outbreak

Case Definition

Suspected Case—Any person with disease characterized by fever of abrupt onset followed by jaundice two weeks after the onset of symptoms, and one of the following symptoms:

- Bleeding from the nose, gums, skin, or digestive tract; or
- Death within three weeks of the onset of symptoms.

Probable Case—Any suspected case with one of the following

- Presence of yellow fever IgM antibody in the absence of yellow fever immunization with in thirty days before onset of illness; or
- Positive post mortem liver histopathology or epidemiological link to a confirmed case or in an outbreak

Confirmed Case—Any suspected/probable case in absence of yellow fever immunization with in thirty days before onset of illness and one of the following

- Detection of yellow fever specific IgM or
- Detection of fourfold increase in yellow fever specific IgM or IgG antibody titer between acute and convalescent serum sample or both
- Detection of yellow fever specific neutralizing antibody
- Detection of yellow fever virus genome in blood sample by PCR

Lab confirmation

- Nucleic Acid amplification tests (RT-PCR)
- Serological Testing (IgM and IgG)
- Immunohistochemical method for detection of yellow fever virus antigen in liver histopathology samples

Timings—PCR and virus isolation testing during first 3-4 days

Specimen Collection—

- Serum for serological testing
- Blood/serum for PCR

Packaging—Tripple packaging

Storage—4–8°C, or Frozen

Transportation—Transport serum specimens in triple packaging to the lab with ice packs or frozen with dry ice (for long distance) along with a prominent Biohazard label and complete lab request form with provisional diagnosis of the patient

Case Management

There is no specific treatment for yellow fever. Only supportive care to treat dehydration, respiratory failure, and fever. Associated bacterial infections can be treated with antibiotics.

Preventive Measures

Vaccination:

It is recommended that the yellow fever vaccine be administered at 12 months of age. In case of outbreaks, it can be administered as early as 6 months of age. The International Health Regulations recommends re-vaccinating travelers to enzootic areas every 10 years (validating the International Yellow Fever Vaccination Certificate) including pregnant and immunocompromised patients. However, routine revaccination of residents is not necessary in enzootic areas.

Vector Control:

Mosquito control can also help to prevent yellow fever and is vital in situations where vaccination coverage is low, or the vaccine is not immediately available. Mosquito control includes:

- Community survey to determine density of vector mosquitoes.
- Identify and destroy mosquito breeding sites in nearby outdoor/indoor premises.
- Indoor residual spray in areas with high mosquito density and thermal fogging in case of outbreaks.
- Conduct community mobilization through schools and religious leaders to promote:

- o Proper solid waste management.Larval habitats may be destroyed by filling depressions that collect water, by draining swamps or by ditching marshy areas to remove standing water. Container-breeding mosquitoes are particularly susceptible to source reduction as people can remove or cover standing water in cans, cups and rain barrels around houses.
- o Protection against day biting mosquitoes including use of screening, protective clothing and repellents.
  - Sleeping or resting in screened or air-conditioned rooms.
  - Use of insecticide-treated mosquito nets.

Community based environmental management and health education campaigns.

Epidemic preparedness and response:

Prompt detection of yellow fever and rapid response through emergency vaccination campaigns is essential for controlling outbreaks.

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42. Viral Meningitis/Aseptic Meningitis

Introduction

The term 'aseptic meningitis' refers to meningitis for which an etiological agent is not apparent after Gram stain and bacterial culture of cerebrospinal fluid (CSF). A syndrome characterized by acute onset of meningeal symptoms, fever, and cerebrospinal fluid pleocytosis with Bacteriologically sterile cultures. Viral meningitis is the most common type of meningitis, often less severe than bacterial meningitis with self-recovery. However, it's very important for anyone with symptoms of meningitis to see a healthcare provider right away because some types of meningitis can be very serious. Younger than 1 month old and people with compromised immunity are more likely to have severe illness from viral meningitis.

Clinical Picture

Initial symptoms of viral meningitis are similar to those for bacterial meningitis. Small babies may present with fever, irritability, poor feeding, sleepiness or trouble waking up from sleep and lethargy.

Adults may present with fever, headache, stiff neck stiffness, sensitivity to bright light, sleepiness or trouble waking up from sleep, nausea, vomiting, lack of appetite and lethargy.

Most patients usually get better on their own within 7 to 10 days. Long-term neurologic sequelae from uncomplicated viral meningitis are rare. Concomitant encephalitis adds significant potential for adverse outcomes. Concurrent systemic manifestations, such as pericarditis and hepatitis are other poor prognostic indicators.

Infectious Agent—Non Polio *Enteroviruses* account for more than 85% of all cases of viral meningitis. Other viruses that can cause meningitis are Mumps virus (causing 10-20% of meningitis and meningoencephalitis cases), *Herpes viruses,* including, *Herpes Simplex viruses, and Varicella-zoster virus, Measles virus, Influenza virus, Arboviruses,* such as *West Nile virus* and *Lymphocytic Choriomeningitis virus.*

Mode of Transmission—Depending on the etiology, viruses can spread in different ways:

- Enteroviruses – Usually through the oral-fecal route, but also sometimes through the respiratory route
- Arboviruses – Via blood-sucking arthropods, usually mosquitoes
- Lymphocytic choriomeningitis virus – Through contact with rodents (e.g., hamster, rats, mice) or their excreta;
- With close contact with a viral meningitis patient one can get infected with the virus, however, the probability of developing viral meningitis is very low.

Incubation period—Depends on the causative agent, with *Enteroviruses*it is 17-20 days.

Seasonality—No established seasonal pattern, however more cases occur in winter season.

Case Definition

Suspected Case—Fever of acute onset with one or more of the following signs of meningeal irritation/inflammation: neck stiffness, poor sucking (in infants), bulging fontanelles (in infants), altered consciousness, irritability, seizures, other signs of meningeal irritation/inflammation

Probable Case—A suspected case with CSF findings including pleocytosis(usually mononuclear, occasionally polymorphonuclear in the early stage), increased protein, normal sugar and absence of other causative organisms.

Confirmed Case—A suspected or probable case which is laboratory confirmed by isolation of a causal organism by CSF and/or blood culture and/or antigen detection.

Lab confirmation—

- Routine Chemistry and Hematology tests should be performed.
- The serum amylase level may be elevated in cases of viral meningitis that are caused by mumps, even in the absence of parotitis (parotid glands).

- Cerebrospinal fluid (CSF) analysis:
  - o An increase in lymphocytes with a viral infection
  - o Detection of viruses by molecular tests (PCR) – detection of viral genetic material (DNA, RNA) such as West Nile virus, herpes, and Enteroviruses

Timing—Ideally samples should be processed immediately or within 12-24 hours of collection.

Specimen Collection—Blood, feces and throat swabs may be sent for viral serology and cultures. Acid-fast staining of CSF should be performed and the remaining fluid should be sent for testing, using the polymerase chain reaction (PCR).

Packaging—Samples should be packed in sterile tubes.

Storage—Up to 5 days at 4°C

For 6 or more days should be at −20°C or preferably at −70°C. Specimens for freezing should first be diluted or emulsified in Viral transport media.

Transportation—Specimens for bacterial culture should not be refrigerated or exposed to extreme cold, excessive heat, or sunlight. They should be transported at temperatures between 20°C and 35°C. For proper culture results, CSF specimens must be plated within 1 hour.

Case Management

There is no specific treatment for viral meningitis. Most people who get viral meningitis completely recover on their own within 7 to 10 days. However, meningitis caused by certain viruses such as herpes virus and influenza, will usually need treatment such as an antiviral medicine. People who develop severe illness, or at risk for developing severe illness, such as babies, and people with weakened immune systems may need to be hospitalized. Treatment includes Acyclovir (an antiviral drug) for HSV infection

Preventive Measures

- No vaccines are available for majority of viruses; however effective vaccines are available for measles, mumps & influenza.
- Wash hands with soap and water, especially after changing diapers, using the toilet and coughing or blowing your nose.
- Avoid touching face with unwashed hands.
- Avoid close contact such as kissing, hugging, or sharing utensils with people who are sick.
- Cover your mouth during coughing and sneezing with a tissue paper or your shirt sleeve but not your hands.
- Clean and disinfect frequently touched surfaces such as toys and doorknobs, especially if someone is sick.
- Avoidance of exposure to rodents can decrease the incidence of lymphocytic choriomeningitis virus (LCMV) meningoencephalitis.
- Infected pets, house mice and rats pose a risk to pregnant women.
- Pregnant women should avoid exposure to rodents, rats and house micewhich carry LCMV.
- Neonates should be kept away from exposure to mosquitoes for the prevention of arboviral infection.

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43. West Nile virus Disease (WNVD)

Introduction

It is a zoonotic disease and outbreaks occur in humans, birds and horses. West Nile virus can cause a fatal neurological disease in humans. However, approximately 80% of people who are infected will not show any symptoms. The virus can cause severe disease and death in horses.

Clinical Picture

About 20% of infected people will develop West Nile fever. Patients usually present with flu-like symptoms such as fever, headache and body aches. Occasionally patients present with a skin rash on the neck, trunk, arms or legs. Symptoms include fever, headache, tiredness, bodyaches, nausea, vomiting, occasionally with a skin rash (on the trunk of the body) and swollen lymph nodes.

Severe cases include signs of encephalitis, meningoencephalitis or meningitis. Symptoms include high fever, headache, neck stiffness, stupor, tremors, convulsions, flaccid paralysis and coma. The case fatality rate in patients with neurological involvement ranges from 4% to 14% and as high as 29% in elderly patients. Serious illness can occur in people of any age; however, people over the age of 50 and some immunocompromised persons are at the highest risk for getting severely ill when infected with WNV.

Infectious Agent—West Nile Virus (WNV) is a member of the *flavivirus* genus and belongs to the Japanese encephalitis antigenic complex of the family *Flaviviridae*.

Host/Reservoir—Birds are the natural hosts of West Nile virus.

Mode of Transmission—

- Mainly by the bite of an infected mosquito (mainly Culex species)
- Mosquitoes become infected when they feed on infected birds
- Exposure in a laboratory setting
- Blood transfusion and organ donation

- Mother to baby, during pregnancy, delivery, or breast feeding
- Humans, horses and other mammals are 'dead end' hosts. This means that they do not develop high levels of virus in their bloodstream and cannot pass the virus on to other biting mosquitoes.

Incubation period—3 to 14 days.

Seasonality—WNVD occur during mosquito breeding season, which starts in the summer and continues through fall.

Case Definition

Suspected Case—Clinical illness in the absence or pending diagnostic test criteria AND in the absence of any other obvious cause

Probable Case—Clinical illness AND at least one of the probable case diagnostic test criteria (serology)

Confirmed Case—Clinical illness AND at least one of the confirmed case diagnostic test criteria (PCR/Cell culture etc)

Lab confirmation—

- Presence of IgM antibodies against West Nile Fever
- IgM antibody capture enzyme-linked immunosorbent assay (ELISA) neutralisation assays; Serum IgM antibody may persist for more than a year.
- Viral detection by reverse transcription polymerase chain reaction (RT-PCR) assay, and virus isolation by cell culture.

Timings—2 serial specimens at 1 week interval

Specimen Collection—For ELISA: Whole blood, serum or plasma
For PCR: Whole blood or blood clot, serum/plasma or tissue
For immunohistochemistry: Skin or tissue specimens from fatal cases.
Acute: 3 to 10 days after onset of symptoms
Convalescent: 2-3 weeks after acute symptoms

Packaging—Triple packaging

Storage—At least 0.5 mL of serum and/or 1.0 mL of CSF is required for serology testing.

Whole blood will not be accepted for serology testing.

Refrigerate serum or clot

Freeze (–20°C or colder) tissue specimens for virus isolation

Fix skin snip specimen in Formalin. Specimen can be stored up to 6 weeks. The specimen is not infectious once it is in Formalin. Store at room temperature. Formalin-fixed specimens may be transported at room temperature.

Transportation—Transfer serum or CSF in a plastic tube with screw cap maintaining cold chain

Case Management

Treatment is supportive for patients with neuroinvasive West Nile virus, often involving hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections.

Preventive Measures

- No vaccine is available for humans.
- West Nile Fever can be prevented by avoiding mosquito bites especially at dusk when the mosquitoes are most active. Using insect repellents, wearing long sleeves and trousers, staying indoors and draining breeding sites like pools of standing water can reduce exposure to mosquitoes.

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44. Zika Virus Disease

Introduction

A mosquito-borne Flavivirus, first identified in Uganda in 1947 in monkeys. It was later identified in humans during 1952 in Uganda and Tanzania. From the 1960s to 1980s, human infections were found across Africa and Asia, typically accompanied by mild illness. The first large outbreak was reported from the Island of Yap in 2007. In July 2015 Brazil reported an association of Zika virus infection with Guillain-Barré syndrome and microcephaly.

Clinical Picture

Approximately 80% of the infections remain asymptomatic. The disease is clinically classified as congenital and non-congenital.

- Congenital: Affected infants usually born with birth defects like microcephaly and stillbirth.
- Non-Congenital: The most common symptoms are Maculopapular rash, Fever, Arthralgia, Fatigue, Conjunctivitis, Myalgia and Headache. Guillain-Barre syndrome has also been reported in some cases

Infectious Agent—Zika virus belongs to *Flaviviridae* family

Host/Reservoir—Human and Non-Human primates

Communicability—Throughout the pregnancy
Non-pregnant females: 8 weeks
Males: 6 months
Zika virus remains in urine and semen for longer period than saliva and whole blood

Mode of Transmission—

- Bite of an infected mosquito (Aedes. Aegypti and Aedes. Albopictus)
- Vertical (Virus can be passed from a pregnant woman to her fetus)

- Sexual
- Through blood transfusion and organ transplantation

Incubation period—3-5 days after the bite by an infected mosquito

Seasonality—Post monsoon period

Alert Threshold—One suspected case is an alert

Outbreak threshold—One laboratory confirmed case is an outbreak

Case Definition

Suspected Case—A person presenting with rash and/or fever and at least one of the following signs or symptoms: Arthralgia; or Arthritis; or conjunctivitis (non-purulent/hyperaemic) with epidemiological link

Probable Case—A suspected case with presence of IgM antibody against Zika virus and an epidemiological link.

Confirmed Case—A person with laboratory confirmation of recent Zika virus infection:

- Presence of Zika virus RNA or antigen in serum or other samples (e.g. saliva, tissues, urine, whole blood); or
- IgM antibody against ZIKV positive and PRNT90 for ZIKV with titre ≥20 and ZIKV PRNT90 titre ratio ≥4 compared to other flaviviruses; and exclusion of other flaviviruses

Epidemiological link—Contact with a confirmed case, or a history of residing in or travelling to an area with local transmission of Zika virus within 2 weeks prior to onset of symptoms.

OR

- Sexual contact with a male having been confirmed with a Zika virus infection in the past four weeks or
- Sexual contact with a male who had been in an area with Zika virus transmission in the past four weeks

Congenital

Suspected Case—Newborn who presents with:

- Microcephaly: head circumference below –2 standard deviations for gestational age and sex, measured at 24 hours postpartum according to the standardized reference; **OR**
- Other congenital malformation of the central nervous system;
- **AND** whose mother:
- Traveling history to an area where Zika virus vectors were present during her pregnancy; **OR**
- Had unprotected sex during pregnancy with a partner who resided in, or traveled to, an area with the presence of Zika virus vectors.

Probable Case—Live newborn who meets the criteria for a suspected case of congenital syndrome associated with Zika virus **AND**

- Intracranial morphological alterations detected by any imaging method, and not explained by other known causes; **OR**
- Mother had rash during pregnancy

Confirmed Case—A neonate meets the clinical criteria for congenital disease

AND meets laboratory criteria (PCR/Culture)

OR

Live newborn who meets the criteria for a suspected case of congenital syndrome associated with Zika virus

AND

Zika virus infection was detected in specimens of the newborn, regardless of detection of other pathogens.

Zika-virus-associated abortion or stillbirth

Suspected Case—

- Abortion or stillbirth among women, presented with rashes AND

- Resided in or travelled to an area where Zika virus vectors were present; **OR**
- Had unprotected sex during pregnancy with a partner, resided in or travelled to an area where Zika virus vectors were present.

Confirmed Case—Suspected case in which specimens from either the mother (blood or urine) or the abortion/stillbirth are laboratory-positive for Zika virus.

Vertical transmission (without congenital syndrome)

Suspected Case—

- Live newborn of any gestational age who has not met the criteria for a suspected case of congenital syndrome associated with Zika virus **AND**
- The mother had a suspected, probable or confirmed case of Zika infection during pregnancy.

Probable Case—Live newborn meeting the criteria for suspected vertical transmission in whom Zika IgM antibodies are detected by ELISA or virus RNA is detected by RT-PCR in the umbilical cord blood sample.

Confirmed Case—Live newborn meeting the criteria for suspected vertical transmission in whom anti-Zika IgM* is detected by ELISA in a serum sample of the newborn.

- When only PCR is available, and it is positive, follow-up serology is advised because the viral detection could be from perinatal rather than vertical transmission.

Lab confirmation—

- Serological assays (IgM testing): include enzyme immunoassays (EIAs) and Immunofluorescence assays (IFA) detecting IgM antibodies as well as neutralization assays such as Plaque-Reduction Neutralization Tests (PRNT) which has the greatest specificity.
- Nucleic Acid Testing(RT-PCR)
- Preliminary diagnosis is based on the patient's clinical features, places and dates of travel, and activities.

- Laboratory diagnosis is generally accomplished by testing whole blood, serum, or plasma to detect virus, viral nucleic acid, or virus-specific immunoglobulin M and neutralizing antibodies.
- Laboratory testing is recommended for infants born to mothers with laboratory evidence of Zika virus infection during pregnancy, and for infants who have abnormal clinical findings suggestive of congenital Zika virus syndrome and a maternal epidemiologic link, regardless of maternal Zika virus test results.
- Maternal diagnostic testing should be performed and testing of the placenta for Zika virus RNA Nucleic Acid Testing (NAT) should be considered.

Timing—NAAT in patients presenting with onset of symptoms < 7 days.

Serology and/or NAT in patients presenting with onset of symptoms ≥ 7 days (Wherever possible, paired serum specimens should be collected at least 2-3 weeks apart)

Specimen Collection—

- Specimens for nucleic acid testing (NAT) testing: Whole blood, serum and/or urine. Other specimen for NAT testing include saliva, semen, CSF, amniotic fluid, placenta, fetal membranes and umbilical cord
- Serology (IgM detection): Whole blood
- Infant urine for NAT and serum for antibody testing.

Packaging—Triple Packaging

Storage—All types of specimens may be kept frozen at –20°C for up to 7 days. For storage longer than 7 days, specimens should be frozen at –70°C.

Transportation—Triple Packaging for specimens which should be transported maintaining cold chain.

Case Management

The treatment is symptomatic and mainly based on a good hydration, pain relief, and anti-histamines for pruritic rash. Treatment with acetylsalicylic acid and non-steroidal anti-inflammatory drugs is discouraged if the diagnosis of

Dengue is not excluded because of a potential increased risk of haemorrhagic syndrome. Acetylsalicylic acid is also discouraged because of the risk of Reye's syndrome after viral infection in children and teenagers.

Preventive Measures

- No vaccine or prophylactic treatment is available.
- Community survey to determine density of vector mosquitoes.
- Identify and destroy mosquito breeding sites in nearby outdoor/indoor premises.
- Indoor residual spray in areas with high mosquito density and thermal fogging in case of outbreaks is recommended.
- Conduct community mobilization through schools and religious leaders to promote:
    - o Proper solid waste management. Larval habitats may be destroyed by filling depressions that collect water, by draining swamps or by ditching marshy areas to remove standing water. Container-breeding mosquitoes are particularly susceptible to source reduction as people can remove or cover standing water in cans, cups and rain barrels around houses.
    - o Protection against day biting mosquitoes including use of screening, protective clothing and repellents.
    - o Sleeping or resting in screened or air-conditioned rooms.
    - o Use of insecticide-treated mosquito nets.
- Community based environmental management and health education campaigns.
- Symptomatic patients should strictly follow personal protection measures to prevent mosquito bites for at least the first week of illness to decrease the risk of human-to-mosquito-to-human transmission.
- Asymptomatic individuals returning from an area with Zika virus outbreaks should follow personal protection measures against mosquito bites for three weeks after their return.

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Annexures

Annexure I

Infection Prevention & Control

Healthcare-associated infections

Health care-associated infections (HCAIs) are infections that occur while receiving health care, developed in a hospital or other health care facility that first appear 48 hours or more after hospital admission, or within 30 days after having received health care.

HAIs can develop either as a direct result of healthcare intervention (such as medical or surgical treatment) or from being in contact with some infected patient or infected belongings/surroundings in healthcare settings. At any one time, up to 7% of patients in developed and 10% in developing countries will acquire at least one HAI. HAIs include central line-associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia. Infections may also occur at surgery sites, known as surgical site infections.

Steps to design and implement IPC program:

- Design Infection control program as per facility requirements and type of care provided
- Organization of an infection control Team/Committee: Establish a multidisciplinary infection control committee at hospital level and departmental teams (responsible for the day-to-day activities)
- Ensuring availability of adequate resources
- Development of Infection control manual and SOPs
- Education and training of the staff and awareness of the public
- Immunization and Care of Health Care Workers
- Environmental Management services
- Monitoring & Evaluation

Infection control precautions:

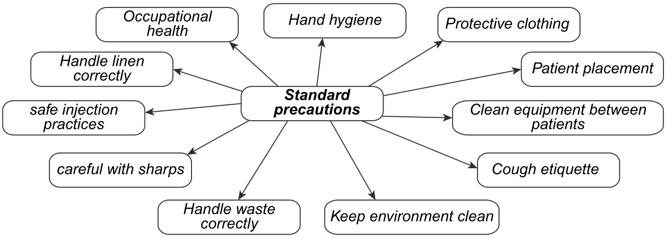
IPC guidelines should include at least the following:

1. Standard precautions:
   - o Hand hygiene
   - o Use of personal protective equipment
   - o Sterilization & Disinfection
   - o Medical devices decontamination
   - o Safe handling of linen and laundry
   - o Health care waste management
   - o Patient placement
   - o Respiratory hygiene and cough etiquette
   - o Environmental cleaning
   - o Principles of asepsis
   - o Prevention of injuries from sharp instruments
   - o Post-exposure prophylaxis
2. Transmission-based precautions
3. Aseptic technique and device management for clinical procedures, according to the scope of care.

A. Standard Precautions

Infection control precautions "Standard precautions" require that health care workers assume that the blood and body substances of all patients are potential sources of infection, regardless of the diagnosis, or presumed infectious status. Standard precautions are meant to reduce the risk of transmission of blood borne and other pathogens from both recognized and unrecognized sources. Standard precautions should be combined with transmission-based precautions for patients with confirmed or suspected infection with highly transmissible pathogens. These are the basic level of infection control precautions which are to be used, as a minimum, in the care of all patients with the following objectives:

- o To reduce the risk of transmission from both recognized and unrecognized sources
- o Basic level
- o Every patients, Every time, Every place, Everyone



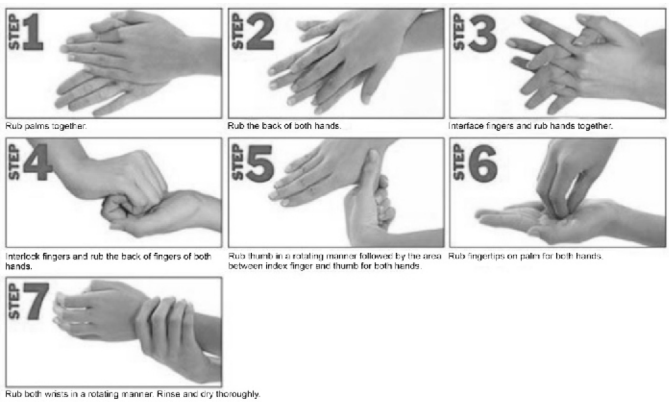
1. Hand hygiene:

Disinfect: Alcohol based Hand Rub (if not visibly soiled) faster, more effective, and less harmful – to your hands.

Wash: with soap and water – if visibly dirty or visibly soiled with blood/ body fluids.

Hand washing: Wash hands after touching blood, secretions, excretions and contaminated items, whether or not gloves are worn. Wash hands immediately after gloves are removed, between patient contacts.

Hand hygiene procedures include the use of alcohol-based hand rubs (containing 60–95% alcohol) and handwashing with soap and water. Alcohol-based hand rub is the preferred method for decontaminating hands, except when hands are visibly soiled (e.g., dirt, blood, body fluids),



or after caring for patients with known or suspected infectious diarrhea (e.g., Clostridium difficile, norovirus), in such situations soap and water should be used. Hand hygiene stations should be strategically placed to ensure easy access.

2. **Gloves:** Wear gloves when touching blood, body fluids, secretions, excretions, and contaminated items. Put on clean gloves just before touching mucous membranes and non-intact skin.
3. **Mask, eye protection, face shield:** Wear a mask and eye protection or a face shield during procedures and patient care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions.
4. **Gown:** Wear a gown during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.
5. **Patient-care equipment:** Ensure that reusable equipment is not used for the care of another patient until it has been cleaned and reprocessed appropriately.
6. **Environmental control:** Ensure that the hospital has adequate procedures for the routine care, cleaning, and disinfection of environmental surfaces.
7. **Linen:** Handle used linen, soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, and that avoids transfer of microorganisms to other patients and environments.

B. Transmission Based Precautions (TBP)/ Additional Precautions

Additional precautions are needed for diseases transmitted by air, droplets and contact. These are termed "additional (transmission-based) precautions".

Transmission-based precautions are used in addition to standard precautions when use of standard precautions alone does not fully prevent communicable disease transmission. There are three types of transmission-based precautions—contact, droplet and airborne, the type used depends on the Mode of Transmission of a specific disease. Some diseases require more than one type of transmission-based precaution (e.g. Ebola, MERS Cov and SARS).

a) **Contact Precautions:** Contact precautions are used to prevent the spread of microorganisms that are spread by direct or indirect contact with the patient or the patient's environment. Effective contact precautions require a single room, if possible, and the use of gloves and gowns by anyone having contact with the patient, the patient's support equipment, or items that have come in contact with the patient or the patient's environment. Dedicate certain reusable equipment (thermometer, stethoscope, blood pressure cuff) for the patient in contact precautions to reduce the risk of transmitting infection to other patients. Proper hand hygiene and handling and disposal of articles that have come in contact with the patient and his environment are essential. All re-usable items should be cleaned and disinfected before removed and dispose all disposable items. Put contact precautions sign at the patient's door to notify anyone entering the room of the situation.

b) **Droplet Precautions:** Diseases include Pneumonias, Pertussis, Diphtheria, Influenza type B, Mumps, and Meningitis. Large particle droplets (>5 microns), are usually generated from the infected person during coughing, sneezing, talking or when health care workers undertake procedures such as suctioning or endotracheal intubation. Wear a surgical mask within 3 feet of patient. When exposure to a highly virulent pathogen is likely, it may be prudent to wear a mask when within 2 to 3 meters of the patient or upon entering the patient's room. Droplet precautions prevent infectious pathogens from traveling from the respiratory tract of an infected person to the mucous membranes of a susceptible host. Put a droplet precautions sign at the patient's door to notify anyone entering the room of the situation.

c) **Airborne Precautions:** Airborne transmission occurs when droplet nuclei (evaporated droplets) <5 micron in size are disseminated in the air. These droplet nuclei can remain suspended in the air for long periods of time. Diseases include open/active Pulmonary Tuberculosis (TB), Measles, Chicken pox, Pulmonary plague, and Hemorrhagic fever with Pneumonia. Use N-95 respirator just before entry to an area of shared air space and wear at all times while in the area of shared air space. Requires an airborne infection isolation room—a single-patient room that's equipped with monitored negative pressure. Isolation room equipped with high efficiency particulate air (HEPA) filtration units may be used. Put a Airborne precautions sign at the patient's door to notify anyone entering the room of the situation.

Transmission based precautions may be necessary in addition to standard precautions, depending on the patient's condition.

Precaution type	Indications	Nursing actions
Airborne	To prevent the spread of infection when a patient is suspected or known to have an infection that is spread by airborne route	• Place the patient in an airborne infection isolation room with monitored negative pressure, if available. • Caution all pressure entering the room to wear a respirator mask.
Contact	To prevent the spread of epidemiologically important infectious organisms through direct or indirect contact with the patient or his environment	• Place the patient in a single patient room if possible. • Wear a gown and gloves for all interactions with the pt or the pts environment. • Follow your facility's infection control plan to determine when to initiate contact precautions. • Designate patient care equipment if possible.
Droplet	To prevent the spread of infectious organisms through close respiratory or mucous membrane contact with respiratory secretions from an infected individual	• Place the patient in a single room patient if possible. • Put on a mask before entering the patients' room if working within 3' feet (0.9 m) of the patient. • Designate patient care equipment if possible.

C. Isolation Garb Donning

Isolation precautions are implemented to prevent the spread of infection from patient to patient, from patients to health care workers or from health care workers to patients.

Equipment

Check the cart or anteroom to make sure an adequate amount of the proper isolation supplies is available for the designated isolation category. Materials required for isolation typically include personal protective equipment, an isolation cart or anteroom for storing equipment, and a door card or sign alerting staff members and others entering the room that isolation precautions are in effect. Personal protective equipment are gown, gloves, and goggles or face shield, mask or respirators and shoe covers or boots. If airborne precautions are required, an N95 or higher level particulate respirator should be worn rather than a surgical mask.

Steps:

1. Remove your watch and rings.
2. Perform hand hygiene.
3. Put on the gown and wrap it around the back of your uniform, making sure that it overlaps and completely covers your uniform to prevent contact with the patient or his environment. Tie the strings or fasten the snaps or pressure-sensitive tabs at the neck. Then tie the waist strings.
4. Place the mask snugly over your nose and mouth. Secure the ear loops around your ears or tie the strings at the middle of the back of your head and neck so that the mask won't slip off. If the mask has a metal strip, squeeze it to fit your nose firmly but comfortably. If you wear eyeglasses, tuck the upper edge of the mask under the lower edge of the glasses.
5. Choose eye protection according to your risk of exposure. Although goggles provide eye protection, they don't protect the rest of the face from splashing of potentially infectious substances. Wear a face shield for any procedures that may involve spraying or splashing of respiratory secretions or other body fluids.
6. Select gloves according to your hand size to make sure they fit properly. Put on the gloves and pull them over the cuffs of your gown to cover the edges of the gown's sleeves.
7. Always perform hand hygiene before putting on gloves to avoid contaminating the gloves with microorganisms from your hands.

D. Isolation Garb Removal (Doffing)

Proper removal techniques are essential for preventing the spread of pathogens from your gloves to your skin surfaces. Follow these steps carefully to properly remove your contaminated gloves.

Steps:

1. Ensure two containers one for re-usable and other for disposable items.
2. Remember that the outside surfaces of your goggles or face shield, mask or respirator, and barrier clothes, such as a gown, are contaminated.
3. Except for a respirator mask, remove all personal protective equipment at the patient's doorway or in the anteroom. Remove a respirator after leaving the patient's room and closing the door.
4. Remove your gloves using the appropriate technique. Grasp the outside of one glove with the opposite gloved hand and peel it off, turning the glove inside out as you pull it off. Hold the removed glove in the remaining gloved hand.
5. Slide the fingers of the ungloved hand under the remaining glove at the wrist, taking care not to touch the outer surface of the glove.
6. Peel off the glove over the first glove, containing the one glove inside the other. Discard the gloves in an appropriate container and perform hand hygiene.
7. To remove your goggles or face shield, grasp the ear pieces or headband and remove carefully. Place the equipment in the appropriate receptacle for reprocessing or discard it in an appropriate container.
8. To remove your gown, untie the neck straps and then the waist ties. Pull your gown away from your neck and shoulders, touching only the inside of the gown. Turn the gown inside out as you remove it, folding it or rolling it into a bundle to ensure containment of pathogens. Discard the gown in the appropriate container.
9. Remove your mask or respirator, grasp the bottom tie or elastic and lift it over your head; then grasp the top tie or elastic, and carefully remove the mask or respirator. Don't touch the front of the mask to prevent contamination. Discard the mask in the appropriate container.
10. Perform hand hygiene immediately.

Injection Safety

Injection safety refers to the proper use and handling of supplies for administering injections and infusions (e.g., syringes needles, finger stick devices, intravenous tubing, medication vials, and parenteral solutions).

These practices are intended to prevent transmission of infectious diseases between one patient and another, or between some patient and healthcare personnel during preparation and administration of parenteral medications.

The following aspects should be considered to prevent needle stick injury…

1. Sharps should not be passed directly hand to hand, and handling should be kept to a minimum and carried out with care.
2. Needles must not be re-sheathed, re-capped, bent, broken or disassembled after use.
3. Never try to manipulate/remove a needle/other sharp from its holding implement with your hands.
4. Used sharps must be discarded into a sharps container.
5. Items should never be removed from sharps containers. The temporary closure mechanism.
6. Sharps containers should be used in between use for safety.

Sharps containers:

- Must be available at point of use
- Conform to international standards; puncture-resistant, leak-proof.
- Sealed when ¾ fulland, be disposed of when the line is reached.
- Stable when on horizontal surfaces, at a height that enables safe disposal by all members of staff
- Easily visible, accessible,
- Be secured to avoid spillage

Safe Burial Practices

Applicable to viral haemorrhagic fevers such as Ebola and CCHF OR Novel Coronavirus infections (MERS and SARS) OR any other highly infectious and fatal disease.

Rationale

Risk of transmission may exist to the health care workers and the community when a patient dies due tohighly infectious disease because body fluids of the deceased may remain contagious for some period afterthe death. Hence specific precautions are recommended when following the burial ritual and practices.

Safe burial practices recommended by WHO and CDC

Prepare the Body Safely

Burial should take place as soon as possible after the body is prepared in the health facility. Health facility staff should:

1. Be aware of the family's cultural practices and religious beliefs
2. Help the family understand why some practices cannot be done because they place the family or others at risk for exposure
3. Counsel the family about why special steps need to be taken to protect the family and community from illness
4. If the body is prepared without giving information and support to the family and the community, they may not want to bring other family members to the health facility in the future. They may think that if the patient dies, the body will not be returned to them
5. Identify a family member who has influence with the rest of the family and who can make sure family members avoid dangerous practices such as washing or touching the body

To Prepare the Body in the Health Facility

1. Wear protective clothing as recommended for staff in the patient isolation area. Use thick rubber gloves as the second pair (or outer layer) of gloves.
2. Spray the body and the area around it with 1:10 bleach solution.
3. Place the body in a "body bag" and close it securely. Spray the body bag with 1:10 bleach solution.
4. If body bags are not available, wrap the body in two thickness of cotton cloth and soak with 1:10 bleach solution. Then wrap the body in plastic sheeting. Seal the wrapping with plastic tape. Spray the body bag as in Step 3. Place the body in a coffin if one is available.
5. Transport the body to the burial site as soon as possible. Assign a health officer or health facility staff person to accompany the body to ensure that the safety precautions remain secure during the journey.

Transport the Body Safely

Isolation precautions should remain in force when the body is being transported to burial site.

1. Plan to take the shortest route possible for security purposes and to limit any possibility of disease transmission through accidental contact.

2. Any health facility staff that must touch or carry the body during transport should wear the same protective clothing as is worn in the isolation area. Note: The driver does not need to wear protective clothing if there is no contact with the body.
3. Take a closed container or sprayer with 1:10 bleach solution in the event of any accidental contact with the body or infectious body fluids. Also use it to clean up spills in the transport vehicle.

Prepare Burial Site

1. The grave should be at least 2 meters deep.
2. Explain to the family that viewing the body is not possible. Help them to understand the reason for limiting the burial ceremony to family only.

Disinfect the Vehicle after Transporting the Body

1. The staff person who disinfects the vehicle must wear protective clothing.
2. Rinse the interior of the vehicle where the body was carried with 1:10 bleach solution.
3. Let it soak for 10 minutes.
4. Rinse well with clean water and let the vehicle air-dry. Be sure to rinse well because the solution is corrosive to the vehicle.

Recommended IPC Precautions Summary

S#	Disease	Recommended IPC precautions	Patient placement	Duration of precautions
	Always use transmission-based precautions in addition to Standard Precautions			
1	MERS CoV	Airborne Precautions	Airborne infection isolation room (AIIR)	For 14 days after the onset of symptoms or until an alternative diagnosis is confirmed
2	Avian influenza (H5N1, H7N9)			
3	Seasonal Influenza (Human)	Droplet precautions	Single room with good ventilation and lighting	For 7 days after the onset of symptoms and for total illness duration in immune-compromised patients
4	Hib influenza disease	Droplet	Single room with good ventilation and lighting	Until 24 hours after initiation of effective therapy

S#	Disease	Recommended IPC precautions	Patient placement	Duration of precautions
5	Neisseria Miningitidis	Droplet	Single room with good ventilation and lighting	Until 24 hours after initiation of effective therapy
6	Severe Acute Respiratory Syndrome (SARS)	Contact plus Airborne plus droplet Precautions	Airborne infection isolation room (AIIR)	Duration of illness and 10 days after resolution of fever
7	Cholera	Contact precautions/Water & food safety	Dedicated ward with standard beds spacing	Duration of illness
8	Dengue	Not transmitted directly from person to person	Apply Screens on bed and use mosquito repellants	Duration of illness
9	Leishmaniasis			
10	Chikungunya			
11	Zika Viral disease			
12	Measles	Airborne Precautions	Airborne infection isolation room (AIIR)	4 days after onset of rash and for illness duration in immuno-compromised patients/ duration of illenss
13	Anthrax	Standard Precautions	NA	
14		Pulmonary: Not transmitted from person to person		
15		Environmental/spores: Wear respirator (N95 mask or PAPRs), protective clothing; decontaminate persons with powder on them		
16	Diphtheria	Droplet precautions	Single room	Until off antibiotics and negative two cultures taken 24 hours apart
17	Congenital Rubella syndrome	Contact precautions	NA	Until infant's age 1 year or Negative urine/NP culture after age 3 months
18	Tuberculosis (pulmonary)	Contact and/ or Airborne Precautions	Single-patient room preferred	Until clinical improvement, with three consecutive AFB negative sputum slides OR 2 weeks of adequate therapy

S#	Disease	Recommended IPC precautions	Patient placement	Duration of precautions
19	Tuberculosis (Extra pulmonary/ draining lesion)	Contact Precautions	Single-patient room preferred	Until clinical improvement
20	Viral hemorrhagic fevers due to Lassa, Ebola, Marburg, Crimean-Congo fever viruses	Contact precautions. Use additional precautions and use N95 or higher respirators when performing aerosol-generating procedures	Single-patient room preferred	Duration of illness
21	Scabies	Contact precautions	Multi-patient rooms, >3 feet spatial separation between beds/ Home isolation	For 24 hours following initiation of effective therapy or Duration of illness/symptoms
22	B. Pertussis	Droplet precautions	Single patient room preferred	Until 5 days after initiation of effective therapy
23	Adenovirus, Rhinovirus	Droplet precautions	Single patient room preferred	Duration of illness
24	Group A streptococcus	Droplet precautions Contact precaution in case of skin lesions	Single patient room preferred	Until 24 hours after initiation of effective therapy
25	Pneumonic plague	Droplet precautions Concurrent disinfection of respiratory secretions, soiled articles and surfaces	Single patient room preferred	Until 48-72 hours after initiation of effective therapy
26	Rubella	Droplet precautions	Single patient room preferred	Until 7 days after onset of rash

S#	Disease	Recommended IPC precautions	Patient placement	Duration of precautions
27	Chickenpox (Varicella)	Contact plus Airborne Precautions	Single patient room isolation	during illness until skin lesions are crusted (usually 5 days from onset of rash)/During prodromal phase and no new lesion appears
28	Herpes Zoster (Disseminated disease or immune-compromised with localized disease)	Contact plus Airborne Precautions	Single patient room preferred	Duration of illness
29	Hepatitis A	Water & food safety/enteric precautions	NA	Two weeks after the onset of symptoms/for the duration of illness
30	Hepatitis E	Water & food safety	NA	Duration of illness
31	Salmonella	Water & food safety	NA	Duration of illness
32	Shigellosis/GE	enteric precautions/ Water & food safety	NA	Duration of illness
33	Rota virus GE	Contact precautions	NA	Duration of illness
34	Brucellosis	Standard precautions	NA	Duration of illness
35	Botulism	Standard Precautions	NA	Duration of illness
	Mumps	Standard plus Droplet and Contact Precautions	Single room or cohort multiple cases	Until 9 days after the onset of swelling (parotitis).
	Cholera	Standard plus contact Concurrent disinfection of soiled articles, faeces etc.	Strict isolation is not indicated	Contact (enteric) precautions for the duration of illness

Annexure II

Principles of Outbreak Management

The principles of outbreak management are to:

1. Detect and investigate outbreaks of public health importance within a time frame appropriate to the situation and as a result, limit secondary cases and/or risk to the community
2. Manage public health outbreaks in accordance with legislation, regulations, standards, and protocols
3. Ensure timely coordination, participation, and communication of relevant stakeholders

The decisions whether and how extensively to investigate a potential outbreak depends on risk assessment that involves a number of factors such as:

1. The severity of the illness
2. The number of cases
3. The source
4. The mode or the ease of transmission
5. The availability of prevention and control measures

The "Outbreak Management" functions include:

1. Investigation management
2. Case investigation
3. Surveillance and epidemiology information
4. Coordination
5. Outbreak communication
6. Resource management
7. Laboratory investigations
8. Logistics management

Rapid Response Team (RRT)

RRT is a multidisciplinary team responsible for the investigation of outbreak or any event of concern to humans and generating an appropriate response in conjunction with appropriate partners (external and internal) and its composition depends on the nature of disease outbreak or event. In case of an outbreak the RRT will vary dependingon the type of infectious agent, the site and the geographical extent of spread. Additional teammembers will be required for the operational requirements to implement public health measures forthe control of transmission.

Outbreak Investigation & Response

Detection: Immediately contact the respective District Health Officer to get available information about the suspected outbreak/alert.

Preparedness:

1. Prepare an outbreak investigation, response and communication plan
2. Ensure to have all necessary protocols, SOPs, guidelines, supplies, stocks of essential material, sampling materials, transport media and contacts details
3. Identify sites for isolation and treatment of infectious patients in advance
4. Have proper travel and security plan

Response:

1. Key components of outbreak response are: coordination, case management, surveillance and epidemiology, laboratory, specific preventive measures depending on disease, risk communication, social mobilization, media relations and information management, logistics and security.
2. District Rapid Response Team (RRT) is activated upon confirmation of an outbreak.

Control: Identification of high-risk individuals and adapted control measures and Implement appropriate control measures that are specific to the disease and context

The terms of reference (TOR) may include:

1. To compose a multidisciplinary team according to outbreak situation and nature.
2. To confirm or deny the existence of an outbreak.
3. To develop strategy to control the outbreak and define role & responsibilities
4. To document the investigations and control measures.
5. To communicate the finding to concerned authorities

Steps in investigating an Outbreak

1. Confirm the existence of an epidemic or an outbreak.
2. Prepare for an outbreak investigation and field work.
3. Verify the diagnosis.
4. Recommend immediate control and prevention measures.
5. Design case definition, identify and enlist cases/contacts.
6. Describe the data in terms of person, place, and time.
7. Develop hypothesis.
8. Evaluate hypothesis (analyze and interpret the data).
9. Refine hypothesis and carry out additional studies.
10. Recommend control and prevention measures.
11. Communicate findings, write a report.

Response to alert and outbreak

Alert: Different priority diseases have different thresholds for notifying as alert or outbreak e.g., a single CCHF case is an outbreak, while 04 cases of the measles are the alert in same geographic area in a given time. In case of any alert, early reporting is mandatory for mentioned diseases in this booklet. To achieve this continuous watch over on disease pattern is mandatory. In case of altered pattern of disease incidence immediate reporting to district health offices for further dissemination to policy makers is required.

Outbreak: The numbers of priority disease cases exceeds the threshold level follow the steps for an outbreak investigation in a scientific way. By opting the systematic way descriptive analysis tell about the time, place and person of the event which further helps in identifying the possible risk factors to be evaluated. The associated risk factors with the occurrence of event or disease can be mitigated by adopting specific control measures.

Annex III

Disease Claasification

S#	Diseases	Classification	Alert Threshold	Outbreak Threshold
1.	AIDS/HIV	STD/blood borne	One case	One lab confirmed case
2.	Ameobiasis			
3.	Anthrax	Zoonotic	One suspected (clinical) case	One lab confirmed case
4.	Bacterial Meningitis (unspecified, not meningococcal)	Air borne/respiratory droplets		
5.	Botulism	Foodborne	NA	NA
6.	Brucellosis	Zoonotic	NA	NA
7.	CCHF	Vector borne VHF	One probable case	One lab confirmed case, if CCHF. 6 or more cases in one location + one lab confirmed case
8.	Chicken pox/ Varicella	Airborne	One clinically confirmed case	NA
9.	Chikungunya	Vector borne	Three or more cases in one location + one lab confirmed case	Cluster of cases: 6 or more cases in one location + one lab confirmed case
10.	Cholera Acute watery diarrhoea	Waterborne	Single case of AWD is an alert, and it must be investigated.	One lab confirmed case, or cluster of 6 or more cases of AWD in one location, is an outbreak.
11.	Congenital Rubella syndrome (CRS)	VPD	NA	NA

S#	Diseases	Classification	Alert Threshold	Outbreak Threshold
12.	Dengue	Vector borne VHF	Three or more cases in one location + one lab confirmed case	Cluster of cases: 6 or more cases in one location + one lab confirmed case
13.	Diphtheria	VPD	One probable case	One lab confirmed case
14.	Ebola	VHF	one suspected case is an alert	One lab confirmed case is an outbreak
15.	Encephalitis (Japanese, Unknown aetiology, arbovirus)	Vector borne	One suspected or travel associated case	One indigenous lab confirmed case
16.	Enteric Fever (Typhoid and Para Typhoid)	Water & Food borne	Two or more linked cases	6 or more cases in one location
17.	Gonorrhoea	STD	NA	NA
18.	Haemophilusinflu-enzae type b (Hib)	Airborne/respi-ratory droplets	NA	NA
19.	Hepatitis A, E Acute viral hepatitis	Water & food-borne	Three or more cases in one location	A cluster of cases: 6 or more cases in one location + Lab confir-mation of type
20.	Hepatitis B and C	Blood borne	NA	NA
21.	Influenza	Respiratory droplets/VPD	3 or more cases in one location	A cluster of 6 or more cases with at least one lab confirmed case
22.	Leishmaniasis Visceral	Vector borne	One suspected case	One lab confirmed case
	cutaneous	Vector borne	One case outside endemic area, 3 cases in endemic areas	6 or more cases in one location
23.	Leprosy	Airborne/respi-ratory droplets	NA	NA

S#	Diseases	Classification	Alert Threshold	Outbreak Threshold
24.	Malaria	Vector borne	Two times the mean number of cases of the previous 3 weeks for a given location	In endemic area: Slide positivity rate above 50% or Falciparum rate above 40%; In non-endemic area, evidence of indigenous transmission of Falciparum.
25.	Measles	VPD	one suspected case	Five or more clinical cases in a single location over a 30-day time period with at least one lab confirmed case
26.	Meningococcal Meningitis	Air borne/respiratory droplets	Three or more suspected case in one location or one confirmed cases of N. meningitides	Two or more lab confirmed meningococcal meningitis cases from a single location
27.	MERS CoV	Zoonotic	One probable case	One lab confirmed case
28.	MERS CoV	Airborne	One probable case	One lab confirmed case
29.	Mumps	VPD	Unusual presentation may require investigation	Three or more cases linked by time and place
30.	Neonatal Tetanus	VPD	One case requires investigation for safe birth practices and immunization.	NA
31.	NIPAH Virus	Zoonotic	One suspected/ probable case	One lab confirmed case
32.	Pertussis	VPD	One suspected case	Five cases in one locality

S#	Diseases	Classification	Alert Threshold	Outbreak Threshold
33.	Plague	Vector borne	One probable case	One lab confirmed case
34.	Polio (AFP)	VPD	One suspected case	One lab confirmed poliomyelitis case
35.	Primary Amoebic meningo-encephalitis (PAM)	Water borne protozoan disease	One suspected/ probable case	One lab confirmed case
36.	Rabies	Zoonotic	One case in a suspected animal/ human species	NA
37.	Rota virus	Food/water borne/VPD	NA	NA
38.	SARS	Airborne	One case	NA
39.	Scabies	Tick borne	Case count greater than 2 times the mean number of cases over the previous 3 weeks for a given locality	Clustering of cases in a single location above the alert threshold
40.	Shigellosis/Bloody Diarrhoea/Dysentery	Water& Food borne	Three or more cases in one location are an alert and require an immediate investigation.	Six (6) or more cases in one location with one lab confirmed case of Shigella
41.	Syphilis	STD	NA	NA
42.	Trachoma	STD		Cluster of cases OR unusual increase in the number of cases.
43.	Tuberculosis	Airborne/respiratory droplets	NA	NA
44.	Viral Meningitis	Air borne/respiratory droplets	NA	NA

S#	Diseases	Classification	Alert Threshold	Outbreak Threshold
45.	West Nile disease	Vectorborne	NA	NA
46.	Yellow fever	VHFs/Vector borne/VPD	One suspected case	One lab confirmed case in an unvaccinated population
47.	Zika	Vector borne	NA	NA

Annex IV

Lab Summary

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
1	AIDS and HIV	Screening test ELISA/CMIA	5 ml of blood/serum	2°C–8°C -20°C	Biohazard Bag Triple packaged
2	Anthrax	Microscopy, Culture Serology (ELIZA, PCR, F1. ab)	Blood, skin lesion exudates, pleural fluid, cerebrospinal fluid (CSF) and stool/ related swab/ biopsy	2°C–8°C	Triple Packaging
3	Bacterial Meningitis (unspecified, not meningococcal)	Gram stain, Blood culture India Ink Preparation C/S, Chemistry	CSF	2°C–8°C	Triple Packaging
4	Bloody Diarrhoea/ Dysentery/ Shigellosis	Culture and sensitivity Serological identification of E cloi 0157/ H7	Stool, Rectal Swab	2°C–8°C	Plastic bags containing with absorbent material

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
5	Botulism	Culture Gram Stain	5-10ml venous blood without anti-coagulant. From infants collect 5 ml blood. 25-50g faeces, 25-50 ml gastric contents 10-50 g suspect food Tissue from suspected wound	2°C–4°C	Triple Packaging
6	Brucellosis	Serology, Culture ELISA , PCR	Whole blood, bone marrow, splenic aspirate, synovial fluid and abscesses. CSF	2°C–8°C	Triple Packaging
7	Chikungunya	Serology, ELISA PCR	5ml blood/ serum	2°C–8°C, –20°C	Triple Packing
8	Cholera/Acute Watery Diarrhoea	Gram Stain/ direct micrscopy, Culture	Stool, Rectal Swab	2°C–8°C,	Cary-Blair transport medium
9	Congenital Rubella Syndrome	Serology ELISA, PCR	Blood/Serum, Nasal/Throat swabs/Saliva/ Urine	2°C–8°C, –20°C	Triple Packing
10	Dengue Fever	ELISA, NS1 ICT, PCR	Blood/serum	2°C–8°C	Triple Packaging

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
11	Diphtheria	Gram stain, Culture, PCR	Nasopharyngeal and throat swabs	2°C–8°C	Triple Packing
12	Ebola Virus Disease	ELISA, PCR After recovery: IgM, IgG Antigen capture detection tests	Blood/serum	2°C–8°C	Triple Packaging
13	Gonorrhea	Gram Stain Culture	urethral/high vaginal/cervical /rectal specimen with rayon/Dacron swab	2°C–8°C	Triple Packing
14	Haemophilus Influenzae Type B (Hib)	Culture, PCR, Serology,	Blood & CSF	2°C–8°C,	Triple Packing
15	Hepatitis A & E	ELISA/ CMIA/PCR	3-5 ml blood/ serum	2°C–8°C, –20°C	Triple Packing
16	Hepatitis B, C & D	ELISA/ CMIA/PCR	3-5 ml blood/ serum	2°C–8°C, –20°C	Triple Packing
17	Hospital Acquired Infections (Nosocomial Infections)	Gram stain C/S PCR	Blood Urine Wound Swab Pus Swab CSF Tissue	2°C–8°C	Plastic bags or pouches containing absorbent material

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
18	Influenza (Seasonal and Pandemic)	PCR	Nasopharyngeal and throat swabs	2°C–8°C -70°C	Triple Packing
19	Japanese Encephalitis (JE)	Smear, Neutralizing antibody testing, ELISA, PCR, MRI	Blood/serum CSF	2°C–8°C	Triple Packing
20	Leishmaniasis	Smear Serology, Culture, ELISA PCR, Biopsy	Cutaneous: Skin biopsy Slit-skin preparation Visceral: 5ml clotted blood/ serum. Splenic or bone marrow aspirate collected.	2°C–8°C	Plastic bags or pouches containing absorbent material
21	Leprosy	ZN Stain culture Biopsy PCR	Skin/Nerve biopsy Skin/nasal smears Blood/Serum	2°C–8°C. Formalin fixation for biopsy.	Triple Packaging
22	Malaria	Peripheral blood smear Rapid Diagnostic Test PCR	3-5 ml blood (EDTA)	2°C–8°C	Blood in EDTA tube
23	Measles	Measles-specific IgM antibodies PCR	Throat swab (Nasal/Nasopharyngeal. Blood/serum	2°C–8°C	Plastic bags or pouches with absorbent material
24	Meningococcal meningitis	Gram Stain C/S Chemistry	CSF Blood	2°C–8°C	Triple Packaging

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
25	Middle East Respiratory Syndrome Corona Virus (MERS-CoV)	Immunofluorescence assay (IFA) Serologic test ELISA PCR	Sputum Broncheo-alveolar lavage, tracheal aspirate, Pleural fluid, Nasopharyngeal swab Oropharyngeal swab Nasopharyngeal wash/ aspirate or nasal aspirate. Blood/Serum	2°C–8°C	Triple Packaging
26	Mumps	Serological testing. PCR	Blood specimen and buccal/oral swab. Throat swabs, urine and cerebrospinal fluid (CSF).	2°C–8°C	Triple Packaging
27	Naegleria fowleri, Primary Amebic Meningo-encephalitis (PAM) (Amoebic Encephalitis)	Direct Visualization Histo-chemistry Indirect immunofluorescence. PCR, Ameba Culture Environmental Detection	CSF, Biopsy, Tissue specimens Spring, well, water tank and pools samples.	Should be stored in leak-proof containers	Properly packaged to avoid leakage and loss of sample

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
28	Neonatal Tetanus	No specific laboratory tests exist for determining the diagnosis of tetanus. The diagnosis is clinically based on the presence of trismus, dysphagia, generalized muscular rigidity, spasm or combination thereof.			
29	Nipah Virus	PCR Serological testing Virus Isolation Histopa-thology and Immunohis-to-chemistry	Throat and nasal swabs, cerebrospinal fluid, urine and blood/ serum	2°C–8°C	Triple Pack-aging
30	Pertussis	Culture, PCR	Throat and nasal swabs	2°C–8°C	Triple Pack-aging
31	Plague (Pestis)	Culture Serological testing by ELISA PCR Fluorescent antibody testing Phytohaem-agglutinin testing	Bubo aspirate Sputum swab Blood/serum CSF	2°C–8°C	Triple Pack-aging
32	Polio	CELL C/S PCR	2 stool samples about 8 grams each Throat swab, CSF	2°C–8°C	Cold box with frozen ice packs.

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
33	Rabies	Direct Fluorescent Antibody Antibody titre Cell C/S PCR	Silva, Brain &Neck Biopsy Blood/serum, CSF Post-mortem samples Fresh tissue samples from the CNS	2°C–8°C	Triple Packaging
34	Rota Virus Diarrhea	EIA, ELISA, PCR. Polyacrylamide gel electrophoresis (PAGE)	5-10 ml of stool Anal sphincter of children aged under 1	2°C–8°C	Clean, screw-top vial bearing. Plastic bags
35	Scabies	Microscopy	Skin scraping.	Room Temp	labeled, packed slides
36	Severe Acute Respiratory Syndrome (SARS)	Indirect fluorescent antibody Tissue culture ELISA PCR	Throat and nasopharyngeal swab, Bronchial lavage Urine specimen, Blood/serum, Stool specimen	2°C–8°C	Triple Packaging
37	Syphilis	ELISA PCR, Dark field microscopy, VDRL, TPHA, FTA ABS.	Blood/serum Exudates from lesion of primary, secondary and early congenital syphilis for direct examination	2°C–8°C	Triple Packaging

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
38	Trachoma	Direct fluorescent antibody Nucleic acid amplification tests (NAATs),ELISA, PCR, Giemsa cytology	Eye swab Dacron swab	2°C–8°C	Biohazard bag.
39	Tuberculosis	Serology Mantoux tuberculin skin test ZN stain, Culture Nucleic-acid amplification tests (NAAT), Gene-Xpert	Sputum Blood/serum Fluids Tissue	2°C–8°C	Biohazard bag.
40	Typhoid and Paratyphoid	Culture	Blood/serum Bone Marrow	2°C–8°C	Triple Packaging
41	Varicella/Chickenpox	ELISA PCR	Scabs, vesicular fluid, or cells from the base of a lesion for lab confirmation.	–20°C	Screw capped tubes Biohazard bag.
42	Viral Haemorrhagic Fevers/ CCHF	ELISA PCR	Blood/serum	2°C–8°C	Triple Packaging

S#	Suspected Disease	Tests required	Sample to be collected	Storage	Transportation
43	Viral Meningitis/ Aseptic Meningitis	Routine Chemistry and Hematology tests ZN stain, Culture, PCR	Blood, feces and throat swabs& CSF	2°C–8°C –20°C –70°C	Biohazard bag.
44	Yellow Fever	PCR, Virus isolation Serological Testing Immuno-histochemical liver histopathology	Blood/serum	2°C–8°C	Biohazard bag.
45	Zika Virus	Serological assays (IgM testing) Plaque-Reduction Neutralization Tests (PRNT) PCR Infant hearing assessment and Ultrasound brain	Specimens for NAT testing: Whole blood, serum and/or urine, saliva, semen, CSF, amniotic fluid, placenta, fetal membranes and umbilical cord Serology (IgM detection): Whole blood Infant urine for NAT and serum for antibody testing.	–20°C–70°C	Triple Packaging

Annex V

Glossary

Active case finding	The process of seeking out cases or health events under surveillance (e.g. house visits by community workers to identify cases of TB, active searching of medical records to identify cases of acute haemorrhagic fever).
Alert threshold	A pre-determined number of reported cases or a reported incidence rate of a disease, above which the situation is defined as an alert. It can be differ depending on the context of the disease burden of the location
Attack rate	The proportion of a group that experiences the outcome under study over a given period
Attributes surveillance	Completeness, timeliness, usefulness, simple, flexible, representative and Hierarchical
Case	A person who has the particular disease, health disorder, or condition which meets the case definition for surveillance and outbreak investigation purposes. The definition of a case for surveillance and outbreak investigation purpose is not necessarily the same as the ordinary clinical definition.
Case definition	A set of criteria (not necessarily diagnostic criteria) that must be fulfilled in order to identify a person as representing a case of a particular disease
Case Definition for AFP	Recent/sudden onset of floppy weakness in a child below 15 years of age due to any cause, including Guillain-Barré Syndrome (GBS) or any paralytic illness in a person of any age when polio is suspected by a physician
Case fatality rate (CFR)	number of deaths from a disease (in a given period)X 100% number of diagnosed cases of that disease (in same period)
Clinically compatible case	A clinical syndrome generally compatible with the disease, as described in the clinical description
Cluster	Aggregation of relatively uncommon events or diseases in space and/or time in amounts that are believed or perceived to be greater than could be expected by chance.

Communicable disease	Infectious disease transmissible (as from person to person) by direct contact with an affected individual or the individual's discharges or by indirect means (as by a vector)
Confirmed case	A case that is classified as confirmed for reporting purposes with positive lab results
Contact (of an infection)	A person or animal that has been in such association with an infected person or animal or acontaminated environment as to have had opportunity to acquire the infection.
Contagious disease	It is a subset category of transmissible diseases, which are transmitted to other persons, either by physical contact with the person suffering the disease, or by casual contact with their secretions or objects touched by them or airborne route among other routes
Endemic disease	The constant presence of a disease or infectious agent within a given geographic area or population group
Enzootic	Regularly affecting animals in a particular district or at a particular season.
Epidemic	The occurrence of an illness or cases, specific health-related behavior, or other health-related events in a community or region of clearly in excess of normal expectancy
Epidemic measures	Describes those procedures of an emergency character designed to limit the spread of a communicable disease that has developed widely in a group or community, or within an area or country.
Epidemiologically linked case	A case in which a) the patient has had contact with one or more persons who either have/had the disease or have been exposed to a point source of infection (i.e., a single source of infection, such as an event leading to a food borne-disease outbreak, to which all confirmed case-patients were exposed) and b) Transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory confirmed case if at least one case in the chain of transmission is laboratory confirmed.

Epidemiology	The study of the occurrence and distribution of health-related states or events in specified populations, including the study of the determinants influencing such states, and the application of this knowledge to control the health problems
Exposure	Proximity and/or contact with a source of an agent in such a manner that effective transmission of the agent, harmful or protective effects of the agent may occur.
Identification	Briefly presents the principle clinical features of the disease and differentiate this disease from others which may have a similar clinical picture. Also noted are appropriate laboratory tests currently used most frequently in diagnostic laboratories for identifying or confirming the etiologic agent.
Immunization	Action of making a person or animal immune to infection, typically by inoculation/administration of vaccines
Incidence	The number of instances of illness commencing, or of persons falling ill, during a given period in a specified population
Incubation period	The time interval between invasion by an infectious agent and appearance of the first sign or symptom of the disease in question
Infection prevention and control (IPC)	Infection control is the discipline concerned with preventing nosocomial or healthcare-associated infection, a practical (rather than academic) sub-discipline of epidemiology. It is an essential, though often under recognized and under supported, part of the infrastructure of health care
Infectious agents	Microbes that Cause Infectious Diseases. There are five major types of infectious agents: bacteria, viruses, fungi, protozoa, and helminthes
Information Education and Communication (IEC)	It is an approach which attempts to change or reinforce a set of behavior in a target audience regarding a specific problem in a predefined period of time
International health regulations (IHR)	IHR scope is basically meant to prevent, protect, and provide a public health response to the international threat and spread of diseases. Also, avoid unnecessary disruption of international travel and trade

Laboratory-confirmed case	A case that is confirmed by one or more of the laboratory methods listed in the case definition under Laboratory Criteria for Diagnosis. Although other laboratory methods can be used in clinical diagnosis, only those listed are accepted as laboratory confirmation for national reporting purposes.
Mode of Transmission	Describes the mechanism by which an infectious agent is spread to humans. Such mechanisms include direct, indirect and airborne.
Morbidity	A measure of a sickness measured by the number of affected person, the illnesses experienced by the persons and the duration of the illness
Mortality	numbers of deaths and/or rates by age, sex, cause, and sometimes other variables
Notifiable diseases	A disease deemed of sufficient importance to the public health to require that its occurrence be reported to health authorities
Occurrence	Provides information on where the disease is known to occur and in which population groups it is most likely to occur. Information on past and current outbreaks may also be included.
Opportunistic infections	The immune system is considered deficient when it can no longer fulfill its role of fighting infection and disease. Infections associated with severe immunodeficiency are known as "opportunistic infections", because they take advantage of a weakened immune system
Outbreak	An epidemic limited to localized increase in the incidence of a disease, e.g. in a village, town, or closed institution.
Outbreak investigation	The investigation procedure undertaken by trained staff to detect the persons, time, place and source of the outbreak in order to implement an effective control mechanism
Outbreak threshold	The outbreak threshold is a pre-determined number of reported measles cases or a reported incidence rate above which the situation is defined as an outbreak
Patient under Investigation (PUI)	A person who has both clinical features and an epidemiologic link should be considered a patient under investigation (PUI).

Period of communicability/ Infectivity period	Is the time (days, weeks, or months) during which an infectious agent may be transmitted, directly or indirectly, from an infected person to another person; form an infected animal to humans; or from an infected person to animals or arthropods
Prevalence	A measure of disease occurrence: the total number of individuals who have an attribute or disease at a particular time (it may be a particular period) divided by the population at risk of having the attribute or disease at that time or midway through the period
Probable case	A case that is classified as probable for reporting purposes OR A clinically compatible case with an epidemiologic link
Public health emergency of International Concern (PHEIC)	PHEIC is an extraordinary eventwhich is determined, as provided in IHR regulations: To constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response
Public health surveillance	It is the ongoing process of systematic, collection, analysis, interpretation and dissemination of information about a selected health event. Health officials use the information to plan, implement and evaluate health programs and activities.
Reservoir	Indicates any person, animal, arthropod, plant, substance—or combination of these—in which an infection agent normally lives and multiplies, on which it depends primarily for survival, and where it reproduces itself in such a manner that it can be transmitted to a susceptible host.
Surveillance	Surveillance is the collection, analyses, interpretation and dissemination of information about a selected health event. Health officials use the information to plan, implement and evaluate health programs and activities
Surveillance Case Definitions	A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

Surveillance types	Routine/active surveillance, passive surveillance, sentinel surveillance, laboratory surveillance, Syndromic surveillance, event base surveillance/indicator base surveillance
Susceptibility	Provides information on human or animal populations at risk of infection, or that are resistant to either infection or disease. Information on subsequent immunity consecutive to infection is also given.
Suspected case	A clinical compatible case that is classified as suspected for reporting purposes.
Viral haemorrhagic fever (VHF)	Viral haemorrhagic fever (VHF) is a general term for a severe illness, sometimes associated with bleeding, that may be caused by a number of viruses. VHFs include Crimean Congo Haemorrhagic Fever (CCHF), Ebola Virus Disease, Marburg Lassa Fever, Yellow Fever and Dengue.

Annexure VI

Sample Packaging, Labelling and Documentation for Transport

Basic triple packaging system:

The system consists of three layers as follows:

1. **Primary receptacle.**
   A labelled primary watertight, leak-proof receptacle containing the specimen. The receptacle is wrapped in enough absorbent material to absorb all fluid in case of breakage. Primary receptacles may contain up to 500 mL each, the total volume in the outer package not to exceed 4L.

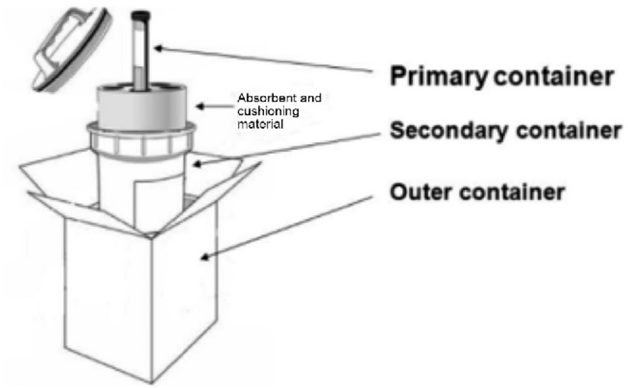
2. **Secondary receptacle.**
   A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.

3. **Outer shipping package.**
   The secondary receptacle is placed in an outer shipping package which protects it and its contents from outside influences such as physical damage and water while in transit.
   Labelling of the outer package for the shipment of diagnostic specimens must include the following:

4. **An address label with the following information:**
   - the receiver's (consignee) name, address and telephone number
   - the shipper's (consignor) name, address and telephone number
   - the statement "Diagnostic Specimen"

Triple Packaging

Triple packaging provides three layers of containment to protect the substances being shipped. These layers are primary, secondary, and outer containers.
The following diagram shows the basic concept of triple packages.



Specimen data forms, letters and other types of information that identify or describe the specimen and also identify the shipper and receiver should be taped to the outside of the secondary receptacle.

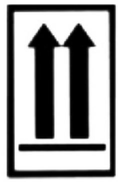
Hazard labels for dangerous goods:

For all dangerous goods to be shipped by airfreight, specific hazard label(s) must be affixed to the outside of each package. The following hazards labels are of importance for culture collections or other institutions shipping biological substances.

Note: The infectious substance label and the shipper's declaration of dangerous goods are not required for diagnostic specimens.

Packages containing liquid cultures of infectious organisms and genetically modified microorganisms must be packed so that the closure(s) of the inner packaging(s) are upward; the upright position of the packaging must be indicated by two "Package Orientation" labels (black or red arrows). The labels must be affixed on opposite sides of the packaging. A label "THIS SIDE UP" or "THIS END UP" may also be displayed on the top cover of the package.

The following practices should be observed:



1. Specimen containers should be watertight and leak-proof
2. If the specimen container is a tube, it must be tightly capped and placed in a rack to maintain it in an upright position
3. Specimen containers and racks should be placed in robust, leak-proof plastic or metal transport boxes with secure, tight fitting covers
4. The transport box should be secured in the transport vehicle
5. Each transport box should be labelled appropriately consistent with its contents
6. Specimen data forms and identification data should accompany each transport box
7. A spill kit containing absorbent material, a chlorine disinfectant, a leak-proof waste disposal container and heavy duty reusable gloves should be kept in the transport vehicle.

Annexure VII

Case Investigation Form

National Institute of Health

Park Road, Chack Shahzad, Islamabad, Pakistan
Tel: +92 (51) 9255090-2   +92 (51) 9255112-4
Fax: +92 (51) 9255099   Email: info@nih.org.pk

Requesting Officer/Department

Report to be returned to:	Public Sector Private Sector Organization Name: Investigation Officer: Contact No:
Phone No:	Email:

Patient/ Source Information

CNIC No: - -	Patient's Present Address:
Name:	
Date of Birth: - - Age: mm yy	Permanent Address:
Gender: Male Female Transgender	

Sample Information

Sample Type: Blood/Serum Faeces Sputum Urine Nasopharyngeal Vaginal smear Others (Specify) ____________	Do you suspect that the sample you are referring could contain a Hazard Group 3 pathogen? Yes No Unknown
Date of Collection: - - Time	Please State the presumptive identification

Travel History

(a) Has the Patient had a recent history of Internal travel   Yes   No   Place:
(b) Has the Patient had a recent history of foreign travel   Yes   No   Country:
(a) Date of return to present area ____________   (b) Date of returned to Pakistan ____________

Clinical Details

Diarrhea	Vomiting	Fever
Respiratory Symptoms	STI	Headache / Stiff neck
Jaundice	Encephalitis / meningitis	Maculopapular rash
Blood in Vomiting	Blood in stool	Others (Specify)__________

Reason for Test

New Diagnostic	Follow-up Case	House Hold Case
Chronic Condition	Prenatal Case	Sporadic Case
Contac	Others (Specify)____________	

For Lab Use (Only)