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SEASONAL AWARENESS AND ALERT LETTER (SAAL)

For Epidemic-prone infectious diseases in Pakistan

Spring Season

OBJECTIVES OF SAAL

- To alert concerned health authorities and professionals at all levels about the epidemic-prone infectious diseases in the spring season.
- To facilitate the preparations for timely, efficient and meaningful response to the encountered alerts/ outbreaks/ epidemics and thus reduce the associated morbidity and mortality.

DATA SOURCES

- The available national data collected during 2015 to 2023 by FE&DSD, NIH, Provincial Health Departments, Provincial Disease Surveillance & Response Units (PDSRUs), Expanded Program on Immunization (EPI), Directorate of Malaria Control and laboratory-based data from NIH has been analyzed to assess the exhibited patterns of high priority communicable infectors diseases.
- The description of all priority diseases is arranged in an alphabetical order. Additionally, under the section of National Potential Public Health Event, technical detail on Human Immunodeficiency Virus / Acquired Immuno-deficiency Syndrome (AIDS) is included. Avian Influenza A has been shared as an International Public Health Event.

Outbreak - Prone Diseases	Alerts
Cholera Disease	
Coronavirus Disease 2019 (COVID-19)	
Crimean Congo Hemorrhagic Fever (CCHF)	
Dengue Fever	
Leishmaniasis	
Malaria	
Measles	
Meningococcal Meningitis	
Primary Amebic	
Meningoencephalitis	
Pertussis	
Poliomyelitis	
Typhoid Fever (XDR)	

High Alert - peak occurrence in the season.

Medium Alert - cases will be encountered and may show up as an outbreak

Cholera (Acute Watery Diarrhea)

Cholera (Acute Watery Diarrhea)

Introduction: Cholera is an acute, diarrheal illness caused by infection of the intestine due to bacterium *Vibrio cholerae*. It remains a global threat to public health and is a global indicator of inequity and lack of social development. It is estimated that every year, there are 1.3 to 4.0 million cases of cholera, and 21,000 to 143,000 deaths worldwide due to the infection (1).

Clinical Picture: Cholera infection is often mild or without symptoms, but can sometimes be severe and life threatening. Approximately 5-10% infected persons in the early stages 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 (1).

Reservoir of Infection: Water environment and humans are reservoirs for *V. cholerae O1* and *O139.* Humans are considered the primary reservoir and can be asymptomatic carriers (2).

Infectious Agent: *Vibrio cholerae* (1)

Mode of transmission: Infection results from ingestion of organisms present in contaminated food and water or directly from person to person by the fecal–oral route (3)

Incubation period: Few hours to 5 days (4)

Infectivity period: The contagious period for cholera begins as soon as the organism is 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 (5).

Seasonality: Throughout the year; higher incidence from May to November, in hot, humid and rainy season (6).

Alert Threshold: One suspected case of AWD is an alert (7).

Outbreak Threshold: One lab confirmed cholera case, or cluster of 6 or more cases of AWD in one location, is an outbreak (7).

Case Definitions:

Suspected case: Any patient of ≥ 2 years of age, presenting with three or more watery, non-bloody stools (rice watery stools) in last 24-hour, and severe dehydration or dying from acute watery diarrhea.

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 above 2 years with acute watery diarrhoea in an area where there is a cholera outbreak.

Confirmed Case: Any suspected case confirmed through isolation of *Vibrio cholerae* 01 or 0139 from the stool (7).

Specimen Collection and Transportation:

- Place specimen in clean container and transport to laboratory within two hours of collection at room temperature with laboratory request form
- If there is a 72 hours delay, place stools soaked swab in a Cary-blair transport medium at room temperature (7).

Case Management: ORS 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. Severely dehydrated patients require administration of intravenous fluids. Ringer's Lactate Solution (Hartman's Solution) is the preferred fluid for intravenous rehydration. Antibiotics (Doxycycline, Ciprofloxacin, Cefixime, Co-trimaxozole, Erythromycin) reduce the duration of disease and period of excretion of *V.cholerae* in the stool of an infected patient (7)

Preventive measures & vaccination: Ensure adequate safe drinking water supply and proper sanitation. To make water safe for drinking, either boil the water or chlorinate it (7). People (visitors or residents) in areas where cholera is occurring or has occurred, should observe the following recommendations:

- Drink only boiled, or chemically treated water and canned carbonated beverages. When using boiled drinks, make sure that the seal has not been broken.
- Avoid drinking tap water.
- Wash hands often with soap and clean water.
- If no water and soap are available, use an alcohol-based hand cleaner (with at least 60% ethyl alcohol).

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 is recommended.

No cholera vaccine is 100% protective and vaccination against cholera is not a substitute or alternate for Standard prevention and control measures (4).

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COVID-19 CASES

Introduction: A Novel Coronavirus Disease (COVID-19) is a member of the coronavirus family that has never been identified or encountered before. Coronaviruses are large family of viruses causing illness in humans as well as among animals i.e. camels, cats and bats. MERS-COV and SARS-CoV-1 belongs to the same family. Coronaviruses are named for the crown-like spikes on their surfaces.

Outbreak of this viral disease started in Wuhan city, capital of central China's Hubei province during late December 2019, when a cluster of patients was admitted to hospitals in Wuhan with an initial diagnosis of pneumonia of unknown aetiology (1). The cluster was epidemiologically linked to a local seafood and wet animal wholesale market, suggestive of zoonotic spill over. Amid the rising spread of the Novel Coronavirus cases globally, the World Health Organization has declared this outbreak as Public Health Emergency of International Concern (PHEIC) on January 30, 2020 (2).

COVID-19 cases from 26 February 2020 to 3 Feburaryr 2024 in Pakistan:

Number of COVID-19 Lab. confirmed cases	Number of COVID-19 cases recovered	Number of deaths due to COVID-19
1,576,998	1,545,780	30,643

Infectious Agent: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) belongs to beta CoV category of coronavirus family. It is a single-stranded RNA genome (3).

Clinical Picture: The clinical course of the COVID-19 is divided into three categories;

Mild Symptoms: It usually presents with symptoms of an upper respiratory tract viral infection, including fever, cough (dry), sore throat, and nasal congestion. Some patients may present with gastrointestinal symptoms like nausea, vomiting and diarrhea.

Moderate Symptoms: Respiratory symptoms include cough and shortness of breath (or tachypnea in children) with or without fever may present, coupled with headache, muscle pain, or malaise, a rash on skin, or discoloration of fingers or toes and later loss of sense of smell & taste as a distinguishing feature of COVID-
19. Most infected people develop mild to moderate illness and recover without hospitalization.

Severe Symptoms: High grade fever is associated with severe dyspnea, respiratory distress, tachypnea (> 30 breaths/min), and hypoxia (SpO2 < 90% on room air). However, the fever symptom must be interpreted carefully as even in severe category of the disease, it can be moderate or even absent. Cyanosis can occur in children. Under this category, the diagnosis is clinical, and radiologic imaging is used for excluding complications. Chest imaging utilized includes chest radiograph, CT scan, or lung ultrasound demonstrating bilateral ground glass opacities (lung infiltrates > 50%) (4).

ASymptomatic/Atypical Presentation: Nasopharyngeal /Oropharyngeal RT- PCR positive for SARS-CoV-2 but having no symptoms.

Reservoir: Its origin is not entirely understood, the genomic

analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats and Pangolins. The potential amplifying mammalian host, intermediate between bats and humans is however, not known (5).

Modes of Transmission: SARS-CoV-2 is primarily transmitted (direct transmission) between people through respiratory droplets via coughing, sneezing, or talking and contact routes. It may be possible that a person can become infected by touching a surface or object (fomites) that has the virus present on it and then touching their own mouth, nose, or possibly their eyes, but this is not considered to be the main way the virus spreads (indirect transmission). Airborne transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed; i.e. endotracheal intubation, bronchoscopy, administration of nebulized treatment, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive- pressure ventilation, tracheostomy, and cardiopulmonary resuscitation(6).

Incubation Period: On average 4-5 days but ranges from 2 days to 14 days from the date of last contact to infected person.

Infectious Period: 2 days before the onset of symptoms and up to 10 days after the onset of illness in mild disease and up to 02 weeks or more in case of disease with severe symptoms.

Seasonality: Not yet known

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

Outbreak Threshold: One laboratory confirmed case is an outbreak (7).

Case Definitions:

A. A person who meets the clinical AND epidemiological criteria:

Clinical Criteria:

- Acute onset of fever AND cough; OR
- Acute onset of ANY THREE ORMORE of the following signs or symptoms: Fever, dry cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhoea, and altered mental status. **AND**

Epidemiological Criteria:

- Residing or working in an area with high risk of transmission of virus: closed residential settings, anytime within the 14 days prior to symptom onset; or
- Residing or travel to an area with community transmission any time within the 14 days prior to symptom onset

B. A patient with severe acute respiratory illness: (SARI: acute respiratory infection with history of fever, or measured fever of ≥38C°; and cough; with onset within the last 10 days; and requires hospitalization). **OR**

C. Asymptomatic person not meeting epidemiologic criteria with a positive SARS-CoV-2 Antigen-Rapid Diagnostic test (RDT) (7).

Probable

A. A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or linked to a COVID-19 cluster.

B. A suspect case with chest imaging showing findings suggestive of COVID-19 disease.

C. A person with recent onset of anosmia (loss of smell) or ageusia (loss of taste) in the absence of any other identified cause.

D: Death, not otherwise explained, in an adult with respiratory distress preceding death AND was a contact of a probable or confirmed case or linked to a COVID-19 cluster.

Confirmed Case:

A. Any person with a positive Nucleic Acid Amplification Test (NAAT) including RT-PCR test

B. Any person with a positive SARS-CoV-2 Antigen-RDT **AND** meeting either the probable case definition or suspect criteria A OR B

C. An asymptomatic person with a positive SARS-CoV-2 Antigen-RDT, who is a contact of a probable or confirmed case (7)

Contact: A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

1. Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes;
2. Direct physical contact with a probable or confirmed case;
3. Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment (PPE); OR
4. Other situations as indicated by local risk assessments.

Note: For confirmed asymptomatic cases, the period of contact ismeasuredasthe2days beforethroughthe14daysafterthe date on which the sample was taken which led to confirmation. (7)

Laboratory Confirmation: Routine confirmation of COVID-19 cases is based on detection of COVID-19 virus nucleic acid (RNA) by real time RT-PCR assays. RNA can be extracted from samples such as oropharyngeal/nasopharyngeal swabs, nasal swabs/secretions, bronchoalveolar lavage fluid/washings or sputum, using any standard extraction protocols or kits.

Specimen collection and transportation: For transport of samples, use viral transport medium (VTM) containing antifungal and antibiotic supplements. Avoid repeated freezing and thawing of specimens.

Table or Covid-19 Specimen Collection and Transportation

Specimen	Transport to laboratory at	Storage till testing	Comments
Nasopharyngeal and oropharyngeal Swab	4°c	≤48 hours: 4 °C >48 hours: -70 °C	The nasopharyngeal and oropharyngeal swabs should be placed in the same tube to increase the viral load
Bronchoalveolar lavage	4°c	≤48 hours: 4 °C >48 hours: -70 °C	
Sputum	4°c	≤48 hours: 4 °C >48 hours: -70 °C	Ensure the material is from the lower respiratory tract
(Endo)tracheal aspirate, nasopharyngeal aspirate or nasal wash	4°c	≤48 hours: 4 °C >48 hours: -70 °C	

Laboratory testing for 2019 novel coronavirus in suspected human cases.
WHO/2019-nCoV/laboratory/2020.3

New Variants of SARS-CoV-2 that causes COVID-19: Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented and circulating globally during this pandemic:

- The United Kingdom (UK), identified a variant called B.1.1.7 with a large number of mutations in the fall of 2020. This variant spreads more easily and quickly than other variants.

In January 2021, experts in the UK reported that this variant may be associated with an increased risk of death compared to other variant viruses.

- In South Africa, another variant called B.1.351 emerged independently of B.1.1.7. Originally detected in early October 2020, B.1.351 shares some mutations with B.1.1.7.
- In Brazil, a variant called P.1 emerged that was first identified in travelers from Brazil, who were tested during routine screening at an airport in Japan, in early January 2021.
- In India, a new variant named B.1.617 was first detected in late October 2020. Later on, experts have identified three subtypes, or sub lineages: B.1.617.1, B.1.617.2, and
- B.1.617.3. Infections happen with this variant in only a small proportion of people who are fully vaccinated. Preliminary evidence suggests that fully vaccinated people who do become infected with the Delta variant can spread the viral infection to others.
- The B.1.1.529 variant (WHO label: Omicron) was first reported to WHO from South Africa on 24 November 2021(10). Infection with this variant causes milder symptoms with a very low hospitalization rate in fully vaccinated people.

Case Management: There is no medication presently approved by the U.S. Food and Drug Administration (FDA) to prevent or treat COVID-19. There is no role of prophylactic chloroquine or hydroxychloroquine at this time. Current case management includes infection prevention & control measures and supportive care, including supplemental oxygen and mechanical ventilator support when indicated.

Preventive Measures:

1. Clean hands regularly with an alcohol-based hand rub, or wash thoroughly with soap and water.
2. Clean surfaces regularly with recommended disinfectants (70% Ethyl Alcohol or 0.5% bleach solution).
3. Avoid touching eyes, nose and mouth with contaminated hands.
4. Practice respiratory hygiene by coughing or sneezing into a bent elbow or tissue and then immediately dispose off.
5. Wear a medical/surgical mask if you have respiratory symptoms and perform hand hygiene after disposing off of the mask.
6. Maintain a minimum of mandatory one meter or three feet distance from individuals with respiratory symptoms.
7. Healthcare workers are required to select and use appropriate PPE.

Vaccination: Vaccination is one of the most effective ways to protect us against COVID-19 and prevent the spread. It is possible that a person could be infected with the virus that causes COVID- 19 just before or just after vaccination and then get sick because the vaccine did not have enough time to provide protection or development of antibodies. Sometimes after vaccination, the process of building immunity can cause symptoms, such as fever or mild body aches (10).

Globally there are four types of vaccines recommended against COVID-19 namely; Whole Virus Vaccine, RNA or mRNA Vaccine, Non-Replicating Viral Vector and Protein Subunit.

COVID-19 vaccines in Pakistan: Till date, following 5 vaccines procured and administered are approved by Drug Regulatory Authority of Pakistan (DRAP):

- CanSinoAd5-nCoV(Non replicating viral vector)
- PfizerBNT16b2 (mRNA)
- Gamaleya Sputnik (Non replicating viral vector)
- Oxford/AstraZenecaAZD1222(Non replicating viral vector)
- Sinopharm(Beijing)BBIBP-CorV (Whole vaccine; In activated)
- Sinovac CoronaVac (Whole vaccine; Inactivated)

References and Guideline links: References and guideline links are available at online version at www.nih.org.pk and h1p://dmc.gov.pk/

CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF)

Introduction: A tick-borne zoonotic viral disease that is asymptomatic in infected animals, but can be a serious threat to humans (1). Human infections begin with nonspecific febrile symptoms, but can progress to a serious hemorrhagic syndrome with a high case fatality rate (10 – 40%) (2). It is one of the most widely distributed viral hemorrhagic fevers occurring in different parts of Africa, Middle-East, Asia and Europe. CCHF is endemic in Pakistan with sporadic outbreaks. (3). Occurrence of virus is correlated with the distribution of *Hyalomma* tick species (Principle vector) (4).

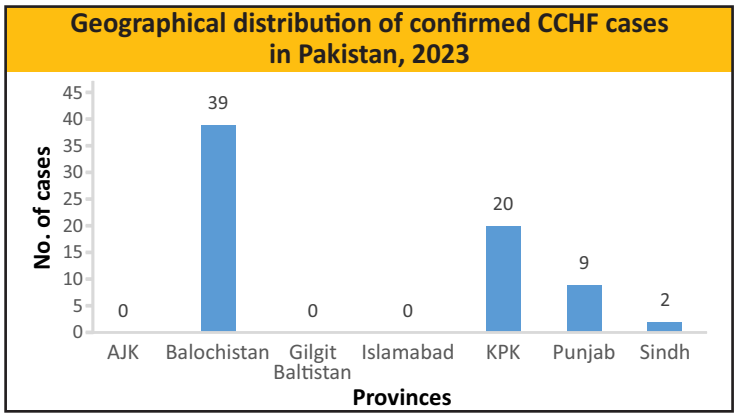
Clinical Picture: Sudden onset with initial signs and symptoms including headache, high grade fever, backache, joint pain, upper abdominal pain, vomiting, redness of eyes, a flushed face, sore throat, and petechiae (red spots) on the palate. Symptoms may also include jaundice along with changes in mood and sensory perception. With progression of the illness, large areas of severe bruising, severe nose bleeds, and uncontrolled bleeding at injection sites can be seen, usually beginning on the fourth day of illness and lasting for about two weeks(5).

Infectious Agent: Crimean-Congo Haemorrhagic Fever (CCHF) Virus belongs to *Bunyaviridae* family (1).

Reservoir: *Hyalomma* tick, domestic animals, such as cattle, goats, sheep, rodents, such as hedgehogs, rats, hares and birds are generally resistant with the exception of Ostrich (6).

Mode of Transmission:

Bite of the infected *Hyalomma* tick, 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 common source of transmission (7).



Incubation Period:

- 1-3 days after tick bite
- 5–6 days after exposure to infected blood or tissues with a

(documented) maximum of 13 days (8).

Peak of cases occur during autumn and spring seasons, associated with life-cycle of ticks, exposure of new born animals, and exposure of migrant animals (9).

Geographical Distribution in Pakistan: Since the diagnosis of first human case of CCHF in 1976, the sporadic cases have continued to occur all over in Pakistan and predominantly from Balochistan.

Alert Threshold: One probable case is an alert and requires immediate investigation (11).

OutbreakThreshold: One lab confirmed case of CCHF is an outbreak (11).

Case Definitions

Suspected Case: Any person with sudden onset of fever over 38.5°C for more than 72 hours and less than 10 days, especially in a CCHF endemic area and those in contact with livestock such as shepherds, butchers, animal handlers and health care personals (11).

Probable Case: Suspected case with history of febrile illness of 10 days or less with an epidemiological link **AND** any two of the following: thrombocytopenia less than 50,000/mm3, petechial or purpuric rash, epistaxis, hematemesis, hemoptysis, blood in urine and/or stools, ecchymosis and gum bleeding (11).

Confirmed Case: Suspected/Probable case confirmed through PCR and/or serology (11).

Laboratory Confirmation: Blood for PCR test and ELISA test

Specimen Collection and Transportation: Collect 3-5ml of blood in vacutainer observing strict biosafety precautions. Keep in upright position to prevent hemolysis. Transport to the laboratory in triple package with ice packs along with a prominent Bio-Hazard label and complete lab request

form with brief history of the patient (11).

Case Management:

- Patients with probable or confirmed CCHF should be isolated and cared for using strict barrier-nursing techniques with recommended Infection Prevention & Control (IPC) measures i.e. standard plus contact precautions. Use additional precautions, (droplet/aerosol) in caseof any extensive contact/ procedure.
- Only designated medical / para-medical staff and attendants should attend the patient.
- All medical, para-medical staff and attendants should wear recommended Personal Protective Equipment (PPE) before entering the isolation room and must dispose it properly after use.
- 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.
- 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 bags and autoclaved beforeincinerating.
- After the patient is discharged from the hospital, room surfaces should be wiped down with disinfectants like 0.5% Chlorine concentration, 0.1% Chlorine concerntration or 0.05% Chlorine concentration depending upon the surfaces. The room should be fumigated in case of risk for tick infestation(12).

Treatment: General supportive therapy is the mainstay of CCHF management. Intensive monitoring to guide volume and blood component replacement is recommended. If the patient meets the case definition for probable CCHF, oral Ribavirin needs to be initiated immediately in consultation with the attending physician. Studies suggest that Ribavirin is most effective if given withinthe 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 net 3 days(12).

Preventive Measures: Educate public about the mode of transmission and personal protection. Persons living in endemic areas must be educated on:

- Avoidance of areas where tick vectors are abundant, especially when they are active (spring to autumn).
- Regular examination of clothing and skin for ticks, and their removal (without crushing them).
- Wearing light colored clothing, covering legs and arms, and using repellents on the skin.
- Other measures, such as wearing gloves or other protective clothing to prevent skin contact with infected tissues or blood, may be taken by persons who work with livestock or other animals.
- For tick control, animal dipping/spraying in an insecticide solution of Permethrin/Pyrethrin/DEET is used. Injectable insecticide like Ivermectin is also recommended.
- Hospitals in endemic areas should ensure standard plus contact precautions in OPD and emergency rooms. Ensure injection safety measures and maintain stockpiling of Ribavirin with PPE.
- Bio-safety is the key element to avoid nosocomial infection. Suspected or confirmed CCHF cases must be isolated and cared by using barrier-nursing techniques to prevent transmission of infection to health workers and others.
- In case of death of patient positive with CCHF, family members should be advised to follow safe burialpractices.
- Exposed contacts: Those with high risk exposure (needle stick, sharps, blood or body fluids) contacts should be observed for fever for 14 days. If fever develops, Ribavirin should be started immediately (12).
- There is no approved vaccine available till date (13).

References and Guideline links: References and guideline links are available at online version at www.nih.org.pk , h1p://dmc.gov.pk/and h1ps://www.nih.org.pk/wp-content/uploads/2019/07/Advisory-CCHF-July-2019.pdf

DENGUE FEVER

Introduction: Dengue is 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 [1]. The first confirmed outbreak of Dengue fever in Pakistan was in 1994, but a sudden surge in Dengue cases and the annual epidemic trend in the provinceshas been observed multipletimes there after [2].

Clinical Picture:

Dengue fever: Dengue fever is defined by fever (for >3 days and< 10days) as reported by the patient or healthcare provider 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), tourniquet test positive, Leukopenia (Platelets count<150,000).

Dengue Hemorrhagic Fever: Defined as Dengue fever with any one or more of the warning signs i.e. severe abdominal pain or persistent vomiting, red spots or patches on the skin, bleeding from the nose or gums, blood in vomiting, black tarry stools/feces, drowsiness or irritability, pale, cold or clammy skin, difficulty in breathing, a total white blood cells count of<50,000/mm3 and Platelets count <100,000.

Dengue Shock Syndrome (DSS): Defined as a syndrome due to dengue viruswith any one or more of the following scenarios:

- Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g. pleural or pericardialeffusion, ascites) with respiratory distress,
- Severe bleeding from the gastrointestinal tract and
- Vital organs involvement [3].

Infectious Agent: Belonging to Flavivirus group; four different Dengue viruses (serotypes) are known: DEN1, DEN2, DEN3, and DEN4 [5].

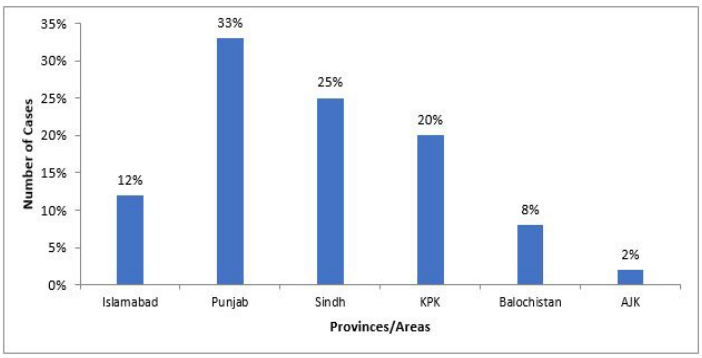
Mode of Transmission: Bite of infected mosquitoes, Aedes Aegypti and Aedes Albopictus [6].

Incubation period: 3-14 days (average 4–7 days) aGer the infective bite [7].

Period of communicability: 2-7 days [7].

Seasonality: Cases are increased during and after rainy season as compared to winter and summer seasons.

Area wise Distribution of Dengue Fever Cases from January 2017 to December 2023 (n=216,899)



Relatively humidity, temperature and rain remained significant Predictors of dengue incidence in Pakistan [8].

Alert Threshold for Dengue Fever: Cluster of 3 suspected cases with at least one confirmed case [10].

Alert Threshold for Dengue Hemorrhagic Fever: One probable case is an alert and requires an immediate investigation to assess differential diagnosis with CCHF.

Outbreak Threshold: Cluster of 6 suspected cases and one lab confirmed case is an outbreak [10].

Case Definitions:

Suspected case: A clinically compatible case of Dengue fever, or Dengue hemorrhagic fever [11]

Probable case: A clinically compatible case of Dengue fever, or Dengue hemorrhagic fever with an epidemiologic linkage and laboratory results indicative of probable infection [11].

Confirmed case: A clinically compatible case of dengue fever, or Dengue hemorrhagic fever with confirmatory laboratory results [11].

Lab confirmation:

Probable: Detection of IgM anti-DENV by validated immunoassay in a serum specimen in those areas where multiple *flaviviruses* are circulating.

Confirmatory:

- Detection of DENV nucleic acid in serum, plasma, blood by Reverse Transcriptase-PCR,
- Detection in serum or plasma of DENV Non Structural Protein 1 (NS1) antigen by a validated immunoassay.
- **Timings:**
- PCR: Initial 4–5 days of onset of illness
- NS1: One day post onset of symptoms (DPO) up to 18 DPO

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 second week of illness [11].

Specimen Collection and Transportation: Collect 5 ml of blood, centrifuge, and separate serum for analysis, observing strict safety precautions. 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 bio hazard label and complete lab request form with brief history of the patient [10].

Case Management:

Febrile Phase: In the early febrile phase, it is not possible to distinguish DF from DHF. The treatment during febrile phase is symptomatic and mainly supportive, as follows:

- 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.
- Extra amounts of fluids Oral rehydration therapy/salt (ORT/ ORS) is recommended for patients with moderate dehydration.
- Complete blood count (CBC/CP) with follow up is an important tool in the management of suspected Dengue patients.
- Provide brochure for families about the “warning signs”
- Together with other recommendation.
- All Dengue patients must be carefully observed for the signs of shock at least for 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 can be discharged [10].

Preventive Measures:

- Identify mosquito breeding sites, destroy mosquito larval habitats and indoor breeding sites.
- Community awareness sessions should be conducted in schools, through religious leaders, aiming to promote health educationcampaigns.
- Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg-laying female mosquitoes.
- Protection against mosquitoes including use of screening,

protective clothing and repellents [10].

Vaccination: First Dengue vaccine, Dengvaxia (CYD-TDV) was registered in several countries for the prevention of the all four Dengue virus serotypes [12]. Moreover, WHO recommends that countries should consider introduction of the CYD-TDV only in geographic settings, where epidemiological data indicate a high burden of disease [13].

References and Guideline links: References and guideline links are available at online version at www.nih.org.pk and h1p://dmc.gov.pk/

LEISHMANIASIS

Introduction: Leishmaniasis is a parasitic vector borne disease and is classified as a Neglected Tropical Disease (NTD).It can present as cutaneous, mucosal and visceral forms but the most common form is cutaneous Leishmaniasis (1). Leishmaniasis is one of the prevailing public health issues in Pakistan and is endemic in some areas of Khyber Pakhtunkhwa and Balochistan province from where, disease is continuously reported through DHIS. Since 2011, KP has reported more than 10,000 cases where Karak, Peshawar, Lower Dir and Malakand are the most affected districts. There are more than 6,000 cases reported from merged districts of KP, where most affected tribal district is Bajaur. In Balochistan, DHIS has reported more than 68,000 cases from 2007 to 2018 and more than 2,000 cases were reported in 2019- 20.The most affected districts are Quetta, Killa Abdullah, Pishin, Sibi, Jhal Magsi and Khuzdar [3].

Infectious Agent: Leishmaniasis is caused by a protozoa parasite from over 20 Leishmania species (1).

Mode of Transmission: Spread by the bite of the sand fly on the skin. If animals are the primary host reservoirs, it is called Zoonotic Leishmaniasis, if humans are the primary host reservoirs is called Anthroponotic Leishmaniasis. (Human-sand fly-human) (1).

Incubation period: Considered to be at least a week but may extend up to several months [4].

Case Definitions:

1. VISCERAL LEISHMANIASIS

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

Confirmed case: A suspected / probable case of Visceral Leishmaniasis with serological/parasitological confirmation [5].

2. CUTANEOUS LEISHMANIASIS

Suspected case: A person presenting with one or more lesions (skin or mucosal), skin lesions typically present on uncovered parts of the body; the face, neck, arms and legs which are the most common sites. The site of inoculation may present with a nodular appearance followed by indolent ulcer [5].

Probable case: A suspected case of VL with serological evidence of infection [5].

Confirmed case: A suspected/probable case confirmed by a positive smear or culture [5].

Diagnostic criteria:

1) History of residence and travel to Leishmaniasis endemic areas,
2) Clinically compatible findings,
3) Laboratory confirmation.

Specimen Collection:

Cutaneous Leishmaniasis: Skin biopsy is the standard dermatologic technique for obtaining specimen. No preservatives are required for examining LD bodies or for Leishmanial culture [5].

Visceral Leishmaniasis: Collect 5ml of clotted blood or serum for serologic studies. Splenic or bone marrow aspirate collected in a tube with anticoagulant is required for the demonstration of amastigote. Specimen may be transported at room temperature without delay [5].

Laboratory: Examination of slides (e.g. of biopsy specimens, impression smears, and dermal scrapings). Serologic testing for detection of antibodies against organisms useful primarily for visceral Leishmaniasis.

Culture: Aspirates of pertinent tissue/fluid (e.g., skin lesion, bone marrow, lymph node, blood/Buffy coat) [6].

Case Management: The treatment of Leishmaniasis depends on several factors including type of disease, concomitant pathologies, parasite species and geographic location. Leishmaniasis is a treatable and curable disease which requires an immunocompetent system because medicines will not help rid parasites from the body, thus risk of relapse may occurs with immunosuppression of the patient. All patients diagnosed with visceral Leishmaniasis require prompt and complete treatment. Detailed information on treatment of the various forms of the disease by geographic location is available in the WHO technical report series 949,''Control of Leishmaniasis'' [7].

Prevention:

- The majority of the recommended precautionary measures are aimed at reducing the contact with Phlebotominae (sand fly).
- Prevention of ACL is very similar to Malaria, as sand flies bite at night and indoors.
- Permethrin treated bed nets, should be used in endemic areas. Sand flies are generally more sensitive than mosquitoes to insecticide, i.e. residual spraying of indoor rooms for vector control.
- Use of insecticide is unlikely to work in prevention of zoonotic cutaneous, as the sand fly vector tends to bite outdoors, so the most effective strategy is to poison or dig up the burrows of reservoir rodents [6].

References and guideline links: References and guideline links are available at online version at www.nih.org.pk and h1p://dmc.gov.pk/

MALARIA

Introduction: A vector borne parasitic disease transmitted by female Anopheles mosquito species. With an estimated burden of 1.6 million cases annually, malaria is considered as a major public health problem in Pakistan. It contributes 22% of total disease burden in the Eastern Mediterranean Region (EMR). Epidemiologically, Pakistan is classified as a moderate malaria endemic country with national Annual Parasite Index (API) averaging at 1.69 and important diversity within and between the provinces and districts. The two parasites which account for malaria in Pakistan are *Plasmodium Vivax* and *P falcipaum*. The main vectors are *Anopheles Culicifacies* and *Anopheles Stephensi.* This malariogenic potential of Pakistan

has a negative impact on country's socio-economic growth and national productivity. (Malaria Control Program Pakistan, 2015-2020)

Clinical Picture: Fever, chills, sweats, headache, nausea, vomiting, body aches and malaise.

Un-complicated: The classical (but rarely observed) Malaria attack lasts 6-10 hours. It consists of, Cold stage (sensation of cold, shivering), Hot stage (fever, headaches, vomiting; seizures in children), Sweating stage (sweats, return to normal temperature, redness), classically (but infrequently observed)attacks occur every Second day with the "tertian" parasites (*P. falciparum,P.vivax, andP.ovale*) and every third day with the "Quartan" parasite (*P. malariae*)

Infectious Agent: *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium knowlesi* (rarely infect humans)

Mode of Transmission: Bite of an infective female Anopheles mosquito and rarely through blood transfusion from infected person.

Incubation period: *P.falciparum* 9-14 days, P.malarie 18-40 days*, P.ovale* and *P. vivax*12-18 days.

Reservoir: Humans are the only known reservoir.

Infectivity: Humans may infect mosquitoes as long as infective gametocytes are present in the blood. Anopheles mosquitoes remain infective for life.

Seasonality: Malaria in Pakistan is typically unstable and major transmission period is postmonsoon i.e. from August to November.

Alert threshold: Number of cases reaches two times the mean number of suspected cases of the previous 3 weeks for 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: A case with clinical manifestations of uncomplicated/complicated Malaria.

Probable Case: A suspected case with history of similar manifestations among other household members

Confirmed Case: Clinical case with laboratory confirmation.

Lab Confirmation:

- Peripheral blood smear (gold standard for identification of
- Malarial parasite, trophozoites and gametocytes, within RBCs)
- Rapid Diagnostic Test(Immunochromatography)
- PCR
- Serology (Indirect immunofluorescence and ELISA)

Specimen Collection & Transportation

Peripheral Blood Film: Collect 3-5ml blood in a tube with anti-coagulant (EDTA).

Case Management: Artemisinin-based combination therapies (ACTs) are there commended 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 Artemetherplus lumefantrine,

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 reported cases by month in Pakistan, predefined weight bands (5–14 kg: 1 tablet; 15–24kg: 2 tablets;

- 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 treatmentfails).

Preventive Measures: Travelers and their advisers should adopt the following public health measure:

- Avoid being bitten by mosquitoes, especially between dusk and dawn.
- Use anti-malarial dugs (chemoprophylaxis) when appropriate, to prevent infection from developing into clinical disease.
- Immediately seek diagnosis and treatment if a fever develops 1week or more after entering an area where there is a Malaria risk and up to 3 months (or, rarely, later) after departure from a risk area.

a) Personal protection:

- Wear long sleeves and trousers outside the houses in the evening. Use repellent creams and sprays. Avoid night time outside activities
- Use mosquito's coils or vaporizing mat containing a Pyrethrin.
- Useof Insecticide-treated mosquito nets (ITNs)

b) Vector control:

- Indoor spraying with residual insecticides (IRS)
- Reduce mosquito breeding sites
- Improve vector surveillance
- Optimize the use of resources for vector control through Integrated Vector Management (IVM)

c) Chemoprophylaxis Malaria control Program:

Recommended chemoprophylaxis: Atovaquone-proguanil, Doxycycline or Mefloquine

Reference and Guideline link: *References and guideline links are available at online version at* www.nih.org.pk *and h1p://dmc.gov.pk/*

MEASLES (RUBEOLA)

Introduction: Measles is a highly contagious viral disease mostly affecting children, caused by measles virus of genus *Morbillivirus*. Despite community vaccination coverage, Measles outbreaks can occur among under vaccinated children and remains an important cause of death among young children globally. The virus spreads via droplets from nose, mouth or throat of an infected person [1]. Pregnant women while infected are also at greater risk of having severe complications and the pregnancy may end in miscarriage or preterm delivery. Immunity against measles infection is life long, although there are few reports of measles reinfection. Case-fatality rate may be as high as 25% if complicated [2].

Clinical Picture: Cough, coryza, conjunctivitis, fever, rash, photophobia, muscle pain, sore throat, tiny white spots inside

the mouth (Koplik's spots) etc. [3]. The occurrence of fever beyond the 3rd - 4th day of rash onset, suggests a measles-associated complication. Severe measles is more likely among poorly nourished young children, especially those with insufficient vitamin A or whose immune systems have been weakened by other infections [5].

Incubation period: Averages 14 days with a maximum range of 7-21 days [6].

Infectivity period: It can be transmitted by an infected person from 4 days prior to the onset of the rash to 4 days aGer the rash erupts [6].

Alert Threshold: One suspected case is an alert [7]. **Percentage (%)**

Outbreak threshold: Five or more clinical cases in a single location over a 30 days' time period with at least one lab confirmed case is an outbreak. It requires an immediate investigation and prompt response [7].

Case Definition:

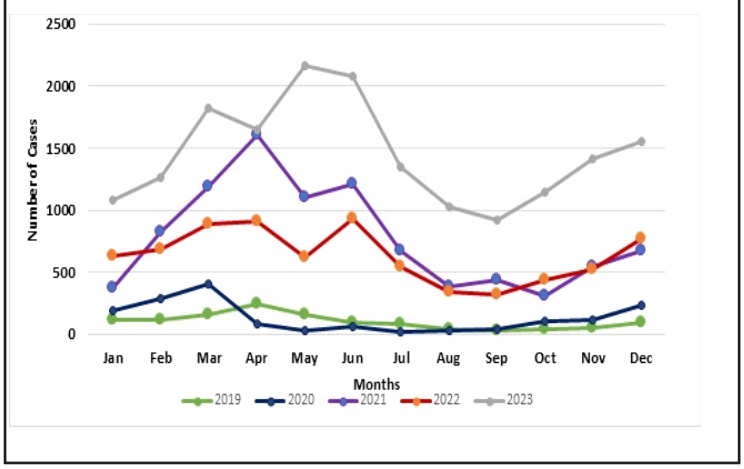
Suspected Case: Any person in whom a clinician suspects measles infection, **OR** Any person with fever, maculopapular rash (i.e. non-vesicular) and 3C's;cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes)[8].

Probable Case: Any person with history of fever, rash and linked epidemiologically to a laboratory confirmed case of measles.

Confirmed Case: A suspected case, which is laboratory-confirmed (positive IgM antibodies; 3 days after appearance of rash) [8].

Discarded Case: If an activate search in the community doesn't find evidence of measles transmission and there is no history of travelling to areas where measles virus is known to be circulating, the case should be discarded [8].

Lab Confirmed Measles Cases by Months in Pakistan
January 2017 - December 2023 (n=32,920)



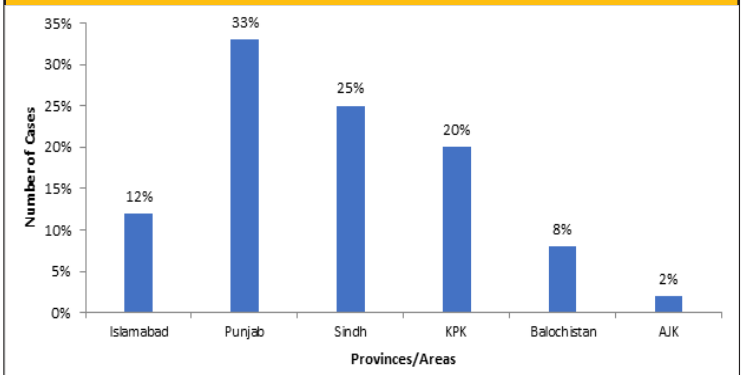
*Note: **Adequate blood specimen:** While IgM ELISA tests are more sensitive between days 4 and 28 after the onset of rash, a single serum sample obtained at the first contact with the health care system within 28 days after onset is considered adequate for measles surveillance [8].*

Seasonality: Peak incidence in Pakistan is usually during April and May.

Specimen Collection & Transportation: Collect throat / nasal / nasopharyngeal swabs for virus isolation, very early in the rash phase and preserve in Viral Transport Medium (VTM). Collect 5ml blood for serology. Do not freeze the whole blood. Transport the specimens in triple packaged with complete request form by maintaining cold chain at 4-8°C [8].

Geographical Distribution in Pakistan:

Lab. Confirmed Measles Cases by Province/ Area
January 2017 - December 2023 (n=32,920



Laboratory Diagnosis WHO recommends ELISA as the gold standard for Measles diagnosis. Anti-measles IgM is detectable in 3 - 30 days after the appearance of the rashes. Anti-measles IgG is undetectable up to 7 days after rash onset and subsequently peaks about 14 days after the appearance of skin rashes [8].

Prevention and Control measures: Immunize population at risk as soon as possible. Priority is to immunize children of age 6 months to 5 years, regardless of vaccination status or history of disease. Children who are vaccinated against measles before 9 months of age must receive a 2nd dose of measles vaccination at 15 months of age [6].

Treatment:

Uncomplicated Cases: The treatment is mainly supportive which includes antipyretics, fluids and antibiotics for only bacterial super infection(s). The WHO recommend Vitamin- A supplementation for 2 days with the dose of 50,000IU in <6 months, 100,000 IU in 6-11 months, 200,000IU in >12 months and for children with ophthalmologic evidence of Vitamin- A deficiency, doses should be repeated on day 2 and 28. Antibiotics should be prescribed to treat eye and ear infections, and pneumonia [10].

Complicated Cases: Pneumonia complicated cases should be referred to the health care facility immediately after Vitamin- A supplementation [10].

References and Guidelines link: *References and guideline links are available at online version at* www.nih.org.pk *and h1p://dmc.gov.pk/*

POLIOMYELITIS

Introduction: A potentially disabling and life threatening viral infectious disease that can affect nerves and can lead to partial or full paralysis among a proportion of infected children; mainly under 5 years of age. Once affected, the paralysis has no cure, but it can be easily prevented through safe and effective vaccines administered orally (OPV) as well as through injections (IPV).

The disease is marked for global eradication through the WorldHealth Assembly resolution in 1988.The efforts so far reduced endemic countries from 125 to only 2 including Pakistan, and Afghanistan. Polio was declared as a Public Health Emergency of International Concern (PHEIC) by WHO on 5th

May, 2014 and continues to stay as such till date. Pakistan is classified by the International Health Regulations (IHR-2005) as a state being infected with WPV1, cVDPV1 or cVDPV3 with potential risk of international spread. Therefore the Government of Pakistan has also declared Polio as a national public health emergency and an annually updated National Emergency Action Plan (NEAP) is being implemented nationwide under the overall supervision of the National Task Force led by the Prime Minister of Pakistan and taking on board all provincial chief ministers as well as Prime Minister of AJK.

Clinical Picture: There are three basic phases of Polio virus infection: subclinical, non-paralytic, and paralytic. Mostly infection remains asymptomatic but Poliovirus may cause Acute Flaccid Paralysis (AFP); one in 200 infections. The onset of asymmetric paralysis is usually sudden coupled with fever. The severity of weakness also varies with the level of immunity among the affected child rendered through immunization. Weakness is ascending and may vary from one muscles or group of muscles, to quadriplegia, and respiratory failure. Proximal muscles usually are affected more than distal muscles and lower limbs more than the upper limbs. Reflexes are decreased or absent while sensory examination may be normal. (6).

Lab. Confirmed Polio Cases By Province/Area In Pakistan

Province/Area	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Islamabad	0	0	0	0	0	0	0	0	0	0	0	0
Punjab	2	7	5	2	0	1	0	12	14	0	0	0
Sindh	4	10	30	12	8	2	1	30	22	0	0	0
Khyber Pakhtunkhwa	27	11	68	17	8	1	2	93	22	0	20	0
KPTDS	20	65	179	16	2	0	6					
Balochistan	4	0	25	7	2	3	3	12	26	1	0	0
GB	1	0	0	0	0	1	0	0	0	0	0	0
AJK	0	0	0	0	0	0	0	0	0	0	0	0
Total	58	93	307	54	20	8	12	147	84	1	20	0

Infectious agent: Poliovirus belong togenus *Enterovirus* subgroup, family *Picornaviridae*, having three serotypes of Poliovirus, labelled P1, P2, and P3 (7).

Reservior: Humans are the only known reservoir (7).

Mode of transmission: Primarily person to person spread through the fecal-oral route. After initial infection with the poliovirus, the virus is shed intermittently in faeces for several weeks

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 days) (7)

Alert & outbreak threshold: One suspected case of polio is an alert/outbreak and requires an immediate notification an notification and stools sample collection for confirmation (8)

Case Definition: This sensitive case definition will capture Poliomyelitis but also other diseases, including Guillain-Barre syndrome (GBS), Transverse Myelitis and Traumatic Neuritis, such that each case with limping must be investigated carefully (9).

Suspected Case: Recent/Sudden onset of floppy/flaccid weakness in a child below 15 years of age due to any cause including GBS **OR** any illness in a person of any age if clinically polio is suspected by a medical doctor (9).

Polio-compatible AFP: A case in which one adequate stool specimen was not collected from a probable case within 2 weeks of the onset of paralysis, and there is either an acute paralytic illness with polio-compatible residual paralysis at 60 days, or death takes place within 60 days, or the case is lost to follow-up (9).

Vaccine Associated Poliomyelitis: A case with acute paralytic illness in which vaccine-like poliovirus is isolated from stool samples, and the vaccine derived virus is believed to be the cause of the paralysis(9).

Confirmed Polio case: A case with acute paralytic illness, with or without residual paralysis, and isolation of wild poliovirus from the stools of either the case or its contacts (9).

Discarded case: A case with acute paralytic illness for which one adequate stool specimen was obtained within 2 weeks after onset of paralysis and was negative for poliovirus (9).

Specimen Collection & Transportation: Collect two stool samples about 8 grams each (about the size of the tip of both thumbs) at an interval of 24 to 48 hours for virus isolation as soon as possible or within 14 days of onset of illness in a clean, leak proof, screw-capped container, preferably in a transport medium like Minimal Essential Medium or Eagle's Medium. Seal the container with tape and place samples immediately after collection in refrigerator at 2-8°C or in a cold box with frozen ice packs. Transport specimens to the lab maintaining cold chain with duly filled request form within 72 hours after collection.

Public Health Measures: Four pillars of polio eradication as public health measures include:

1. Achieving a high level of coverage with at least 4 doses of the oral poliovirus vaccine (OPV) and one dose of IPV in routine.
2. Providing supplementary doses of OPV to all children <5years old during NIDs and SNIDs, as well as the case response planned by the Polio Eradication Programme.
3. Active and Passive Surveillance for all cases of acute flaccid paralysis
4. House-to-house OPV campaigns, targeting areas in which transmission of wild Poliovirus persists, based on National Emergency Action Plan (NEAP 2019-2020)(11).

References and Guidelines link: *References and guideline links are available at online version at* www.nih.org.pk *and h1p://dmc.gov.pk/*

TYPHOID FEVER

SALMONELLA ENTERICA SEROVAR TYPHI (EXTENSIVELY DRUG RESISTANT STRAIN)

Introduction: A life-threatening illness that affects more than 21 million people in the developing world. Multidrug-resistant (MDR) isolates are prevalent in different parts of Asia and Africa and are associated with the dominant H58 haplotype. Reduced susceptibility to Fluoroquinolones is also widespread, and sporadic cases of resistance to third-generation Cephalosporin or Azithromycin have also been reported.

Since 2016, the first large-scale emergence and spread of a novel *S. typhi* clone harbouring resistance to three first-line drugs (Chloramphenicol, Ampicillin, and Trimethoprim Sulfamethoxazole) as well as Fluoroquinolones and third generation Cephalosporin has been identified in Sindh, which was classified as extensively drug resistant (XDR).

Infectious agent: Anti-microbial resistant (AMR) strains of

Reported XDR Typhoid Fever Cases in Sindh by Years (November 2016 to August 2021)	
Classification	**Case Definition**
Non-resistant Typhoid Fever	Typhoid fever caused by Salmonella Typhi and/or Salmonella Paratyphi A,B or C strains which are sensitive to first line- drugs and third generation cephalosporin, with or without resistance to second-line drugs
Mutli-drug resistance (MDR) Typhoid fever	Typhoid fever caused by Salmonella Typhi and/or Salmonella Paratyphi A,B or C strains which are resistant to the first-line recommended drugs for treatment, with or without resistance to second-line drugs
Extensive Drug Resistant (XDR) Typhoid fever	Typhoid fever caused by Salmonella Typhi strain which are resistant to all the recommended antibiotics to the typhoid fever

Salmonella enterica serovar typhi

Clinical picture: Patient presents with high grade fever (>38°C), weakness, abdominal pain, headache and loss of appetite. In some cases, patients have a rash of rose-colored spots.

Mode of transmission: Typhoid infection occurs through feco-oral route and infection spreads through contaminated food, milk, frozen fruits and water or through close contact with already infected persons.

Incubation period: Depends on the inoculum size and host factors; 3 days to more than 60 days with a usual range of 8 to 14 days.

High Risk groups: Preschool children are at greater risk of developing disease and usually have milder symptoms than the adults do. Travelers to, or workers in endemic areas and care givers of the patient infected with *S. Typhi* are also at higher risk.

Treatment: Suspected cases having history compatible with the case definition(s) should immediately seek medical advice from health care facilities.

COVID-19 Situation and Antibiotic Perscribing Practices In Pakistan: Since the emergence of COVID-19, it has been observed that health care professionals are frequently prescribing Azithromycin for the treatment of suspected and confirmed COVID-19 infections. The increased use of Azithromycin for the COVID-19 patients may develop resistance against the Azithromycin through selective pressure due to overuse of Azithromycin leading to resistance strains, and consequently their spread which will further limit out the treatment options in the XDR typhoid cases. This practice should therefore immediately be addressed and Azithromycin must carefully be prescribed for COVID-19 cases based on local and international recommendations.

Preventive measures and Vaccination: It is suggested that with the treatment options for typhoid becoming more limited, following preventive measures are urgently needed, including improved sanitation and vaccination campaigns:

Reported XDR Typhoid Fever Cases in Sindh by Years (November 2016 to August 2021)				
Years	**Karachi**	**Hyderabad**	**Other Districts**	**Sindh Total**
2016	0	12	0	12
2017	175	485	4	664
2018	3712	891	207	4810
2019	7088	1645	998	9731
2020	2510	708	415	3633
2021	1739	360	175	2274
Total	15224	4101	1799	21124

- In case of other infections such as upper and lower respiratory tract infections, other available drug options should be used instead of oral azithromycin which should be spared/ reserved for lab confirmed XDR Typhoid cases and other serious medical conditions.
- Raising community awareness on the following:
- Thorough hand washing with soap and water is highly recommended after using toilet, before and after attending patient, before handling, cooking and eating.
- Drink treated, boiled or bottled water. Use ice, prepared from clean drinking water preferably boiled. Wash fruits and vegetable properly before eating. Eat freshly cooked, hot served and home-made food.
- Avoid eating raw fruits or vegetables, market prepared or left over food.
- Use pasteurized milk.
- Vaccination should be considered especially for those who are travelling to and from endemic areas, high risk group of peopl e and those who are exposed to the disease. Typhoid fever vaccines do not provide 100% protection, however theywill reduce the severity of the illness.
- Typhoid conjugate vaccine (Typbar-TCV@) is a new conjugate vaccine with longer immunity. WHO has pre-qualified the first conjugate vaccine in December 2017 to prevent typhoid fever.
- **References and Guidelines links:** *References and guideline links are available at online version at* www.nih.org.pk *and h1p://dmc.gov.pk/*
- **Advisory link:** https://www.nih.org.pk/wp-content/uploads/2019/02/Advisory-for-Typhoid-5-oct.pdf

Potential National Public Health Event

Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS)

The 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.

Present situation in Pakistan: HIV is endemic in many parts of the country. According to Pakistan National AIDS Control Program data December 2020, there are 0.18 million estimated people with HIV, 42,563 registered people living with HIV who know their status in 45 Antiretroviral Therapy (ART) centers and 24,606 people are currently receiving ARV therapy.

Preventive measures and control: Promote Injection safety practices which includes, safe phlebotomy practices, safe disposal of

sharps and healthcare waste. Reduce sexual transmission of HIV including 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). Sexually transmitted infections (STIs) control practices especially for sex workers, using the syndromic STIs management approach with partner notification and promotion of safer sex. Preventing the transmission of HIV through infected pregnant women to infants by the use of antiretroviral therapy (ART) i.e. Teneforvir, Emtricitabine and Raltegravir throughout pregnancy.

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

Guideline links: https://www.nih.org.pk/wp-content/uploads/2019/05/Advisory-for-the-Prevention-and-Control-of-HIVAIDS.pdf

Potential International Public Health Event

Monkeypox Disease (Mpox)

Mpox is a viral zoonotic disease very first observed among monkeys kept for research in 1958 in Copenhagen. The first case in humans was reported in 9 months old child form Democratic Republic of Congo in 1970. Since then, the disease is endemic in Central and West African countries. The Mpox virus belongs to same family of viruses as variola virus, the virus that causes smallpox. Mpox symptoms are similar to smallpox symptoms, but milder, and Mpox is rarely fatal. Mpox is not related to chickenpox. In 2003, the first Mpox outbreak outside of Africa was reported in the United States of America and was linked to contact with infected pet prairie dogs. These pets had been housed with Gambian pouched rats and dormice that had been imported into the country from Ghana. This outbreak led to over 70 cases of Mpox in the U.S. In early 2022, many non-endemic countries reported clustering of Mpox cases which obligated World Health Organization to declare Mpox as Public Health Emergency of International Concern (PHEIC) on 25th June 2022. The disease is being reported from 113 countries mostly from US, followed by Spain, Brazil, France and UK with less severity and case-fatality less than 1%. Decreased morbidity and mortality associated with Mpox along with decreased case burden led the WHO declared Mpox as no more PHEIC in May 2023 citing steady progress in controlling the spread of the disease. However, Pakistan reported a total of 07 travel associated confirmed cases of Mpox till from April 2023 till date.

Transmission: Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person or recently contaminated objects. Transmission via droplet respiratory particles usually requires prolonged face-to-face contact, which puts health workers, household members and other close contacts of active cases at greater risk. The disease is observed to be more common among immune-compromised people, men sex with men (MSM)

Clinical presentation: Mpox typically presents with fever, itching, rash and generalized lymphadenopathy. The presentation of rash is different from Small pox and chickenpox. It starts to appear 2-3 days after the onset of fever in the form of macules, later with interval of 2-3 days it changes into papules, vesicles and pustules. After 21-24 days, it can heal spontaneously leaving a depressed scar.

Laboratory confirmation: swabs taken from vesicular fluid or lesion crust can be processed for Real-time PCR confirmation which is more reliable to diagnose the virus.

Clinical Management: Clinical care for Mpox should be fully optimized to alleviate symptoms, manage complications and prevent long-term sequelae. Patients should be offered fluids and food to maintain adequate nutritional status. Secondary bacterial infections should be treated as indicated.

Preventive Measures: Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for Mpox. Scientific studies are now underway to assess the feasibility and appropriateness of vaccination for the prevention and control of Mpox. Some countries have, or are developing, policies to offer vaccine to persons who may be at risk such as laboratory personnel, rapid response teams and health workers.

Vaccination: Vaccination against smallpox was demonstrated through several observational studies to be about 85% effective in preventing Mpox. Thus, prior smallpox vaccination may result in milder illness. Some laboratory personnel or health workers may have received a more recent smallpox vaccine to protect them in the event of exposure to orthopoxviruses in the workplace. A still newer vaccine based on a modified attenuated vaccinia virus (Ankara strain) was approved for the prevention of Mpox in 2019. This is a two-dose vaccine for which availability remains limited. Smallpox and Mpox vaccines are developed in formulations based on the vaccinia virus due to cross-protection afforded for the immune response to orthopoxviruses.

Guidelines link: https://www.nih.org.pk/wp-content/uploads/2022/05/Alert-Multi-Country-Monkey-Pox-outbreak-in-Non-endemic-Countries.pdf

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