61st Issue

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October 2024 – February 2025

Winter Season

Ministry of National Health Services, Regulations and Coordination
Government of Pakistan
Field Epidemiology & Disease Surveillance Division (FE&DSD)
National Institute of Health (NIH) Islamabad, Pakistan

SEASONAL AWARENESS AND ALERT LETTER (SAAL)

National Focal Point for International Health Regulations (IHR)

For Epidemic-prone infectious diseases in Pakistan

Objectives of SAAL:

- To alert concerned health authorities and professionals at all levels about the epidemic-prone infectious diseases in the summer 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 Resources:

- The available national data collected during 2015 to 2024 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 infectious diseases.
- The description of all priority diseases is arranged in an alphabetical order. Additionally, under the section of International Potential Public Health Event, technical details on Mpox are included.

Outbreak - Prone Diseases	Alerts
Coronavirus Disease 2019 (COVID-19)	
Crimean Congo Hemorrhagic Fever (CCHF)	
Dengue Fever	
Gastroenteritis (Acute)	
Leishmaniasis	
Malaria	
Measles	
Meningococcal Meningitis	
Pertussis	
Poliomyelitis	
Probable Diphtheria	
Seasonal Influenza	
Typhoid Fever (XDR)	

High Alert- Peak occurrence in the Summer/Monsoon season

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

CORONA VIRUS DISEASE (COVID-19)

Introduction: A novel coronavirus disease (COVID-19) is caused by a member of the coronavirus family that has never been identified or encountered before. These are a large family of viruses that cause illness in humans as well as in animals such as camels, cats, and bats. Coronaviruses are named for the crown-like spikes on their surfaces and both MERS-CoV and SARS-CoV-1 belong to the same family. SARS-CoV-2 has continued to evolve since it first emerged; 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 etiology (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 declared this outbreak as Public Health Emergency of International Concern (PHEIC) on January 30, 2020 (2) and later on declared it as a pandemic.

COVID-19 cases from 26th February 2020 to 31st May 2024 in Pakistan:

COVID-19 Lab. confirmed cases	COVID-19 cases recovered/Discharged	Deaths due to COVID-19
1,582,408	1,551,741	30,667

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

RNA genome.

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 late 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 OR MORE of the following signs or symptoms: Fever, dry cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, and altered mentalstatus. **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 contactof 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:

- Face-to-face contact with a probable or confirmed casewithin 1 meter and for more than 15 minutes.
- Direct physical contact with a probable or confirmed

case.

- Direct care for a patient with probable or confirmed COVID- 19 disease without using proper personal protective equipment(PPE); OR
- Other situations as indicated by local risk assessments.

Note: For confirmed asymptomatic cases, the period of contact is measured as the 2 days before through the 14 days after the 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, broncho alveolar 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: COVID-19 Specimen collection and transportation:

Specimen	Transport At	Storage till Testing	Comments
Nasopharyngeal and oropharyngeal Swab	4°C	=48 hours: 4 °C >48 hours: -70 °C	The nasal and oral 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
Endotracheal 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 spread more easily and quickly than other variants. In January 2021, experts in the UK reported that this variant maybe 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, experts 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 smallproportion 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:

The case management of COVID-19 involves a comprehensive approach that includes screening, diagnosis, treatment, and follow-up care. This encompasses infection prevention and control measures, supportive care, therapeutics, and supplemental oxygen and mechanical ventilator support when indicated, according to the severity or risk of progression to severe COVID-19. The U.S. Food and Drug Administration (FDA) has approved several treatments for COVID-19, including remdesivir, which is administered intravenously for hospitalized patients aged 12 years and older. Tocilizumab is approved for hospitalized patients (2 years and older) who are on systemic corticosteroids and require oxygen or mechanical ventilation.

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 ofPakistan (DRAP):

- CanSinoAd5-nCoV (Non-replicating viral vector)
- Pfizer BNT16b2 (mRNA)
- Gamaleya Sputnik (Non-replicating viral vector)
- Oxford/AstraZeneca AZD1222(Non-replicating viral vector)
- Sinopharm (Beijing) BBIBP-CoV (Whole vaccine; In activated)
- Sinovac CoronaVac (Whole vaccine; Inactivated)

References and Guideline links: *References and guideline linksare 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 indifferent parts of Africa, Middle East, Asia, and Europe. Occurrence ofvirus is correlated with the distribution of *Hyalomma* tick species (Principle vector) (4). In Pakistan, CCHF is endemic with sporadic outbreaks since the diagnosis of first human case in 1976 (3).

Clinical Picture: Sudden onset with initial signs and symptoms including headache, high grade fever, backache, diarrhea, joint pain, upperabdominal 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 which may be replaced by drowsiness and lethargy after two to four days. 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). In patients who recover, improvement generally begins on the ninth or tenth day after the onset of illness.

Infectious Agent: Crimean-Congo Hemorrhagic 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 except for 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/ secretions/ aerosol of infected patients. Nosocomial infections are common source of transmission (7).

Incubation Period:

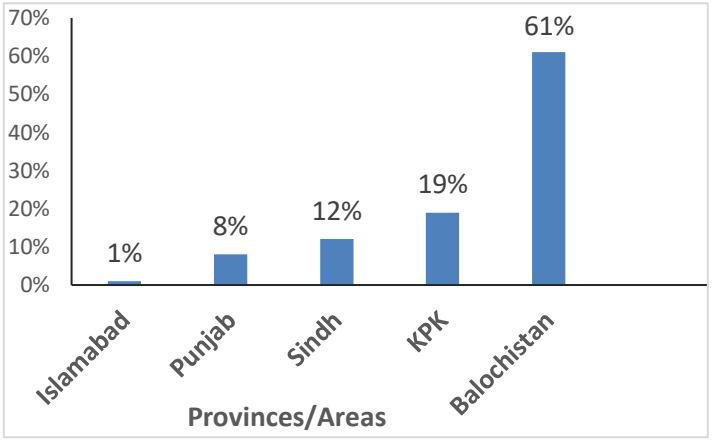
- 1-3 days after tick bite, maximum 9 days.
- 5–6 days after exposure to infected blood or tissues with a (documented) maximum of 13 days (8).

Seasonality:

Peak of cases occur during hot and humid season associated with life cycle of ticks, exposure of newborn 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.

Lab Confirmed CCHF Cases by Province/Area from January 2019 to September 2024 (n=351)



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

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

Case Definitions

SuspectedCase:

Any person with sudden onset of fever over 38^0C for more than 3 days 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 to CCHF endemic areas 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:

A Suspected/Probable case confirmed through:

- Detection of viral nucleic acid by PCR and/or,
- Presence of IgM antibodies in serum by ELISA (11).

Laboratory Confirmation: Blood for PCR test and ELISA test

Specimen Collection and T ransportation:

Collect 3-5ml of blood in vacutainer or serum separator vial observing strict biosafety precautions. Keep in upright position to prevent hemolysis. Transport to the laboratory in triple packaging with ice packs along with a prominent Bio-Hazard label and complete laboratory 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 transmission-based precautions. Use additional precautions, (droplet/aerosol) in case of any extensive contact/ procedure.

Only designated medical / para-medical staff and attendants should attend to the patient.

- All medical, paramedical staff and attendants should wear

recommended Personal Protective Equipment (PPE) before entering the isolation room and must dispose of it properly after use.

- All secretions of the patient and hospital clothing in use by 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 before incinerating.
- After the patient is discharged from the hospital, room surfaces should be wiped down with disinfectants like 0.5% Chlorine concentration, 0.1% Chlorine concentration or 0.05% Chlorine concentration depending upon the surfaces. The room should be fumigated in case of risk for tick infestation (12).

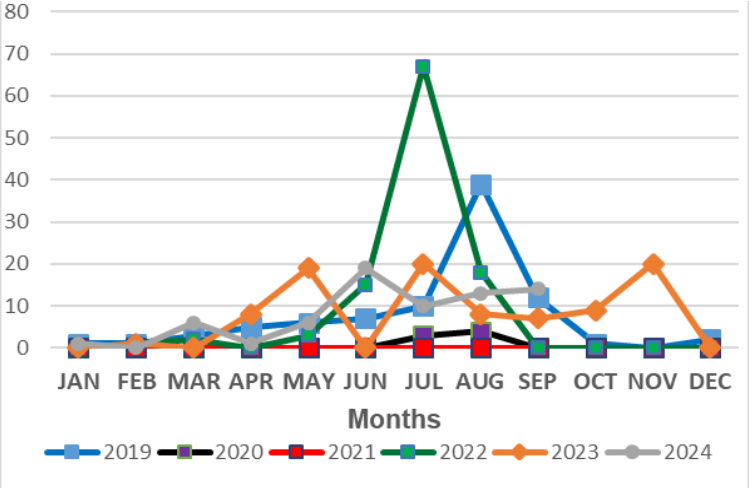
Treatment: General supportive therapy is the mainstay of CCHF management. Intensive monitoring to guide volume and blood component replacement is recommended. If the patient meets the case definition for probable CCHF, oral Ribavirin needs to be initiated immediately in consultation with the attending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

Lab Confirmed CCHF Cases by Months from January 2019 to September 2024 (n=351)



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 provinces hasbeen observed multiple times there after [2].

Clinical Picture:

Dengue fever: Dengue fever is defined by fever (for >3 days and < 10 days) as reported by the patient or healthcare provider and thepresence of one or more of the following signs and symptom 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 virus 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,
- 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].

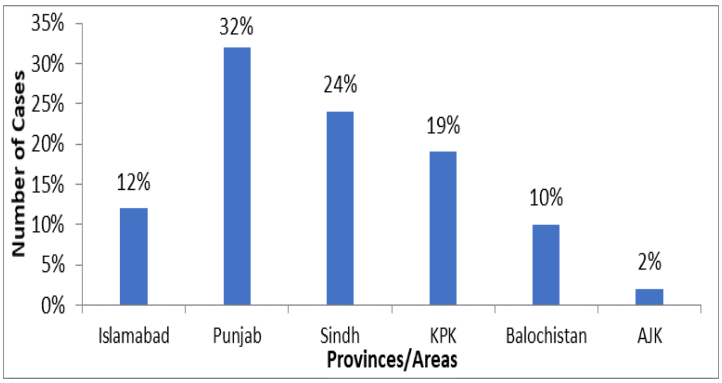
Mode of Transmission: Bite of infected mosquitoes, Aedes Aegypti and Aedes Albopictus [6].

Incubation period: 3-14 days (average 4–7 days) after 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 2019 - September 2024 (n=225,756)



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 ofillness (acute).
- IgG is used for the detection of past Dengue infection andusually can be detected during second week of illness [11].

Specimen Collection and Transportation:

Collect 5 ml of blood, centrifuge, and separate serum for analysis, observingstrict safety precautions. Transport serum specimens to the lab in triple container packing with ice packs or frozen with dryice (for long distance) along with a prominent biohazard labeland 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 recommendations.
- 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 doesnot 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 education campaigns.
- Indoor residual spray in areas with high mosquito density and thermal fogging in case of outbreaks
- 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, use of insecticide treated nets and repellents [10].

Vaccination: First Dengue vaccine, Dengvaxia (CYD-TDV) was registered in several countries for the prevention of 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/.

PROBABLE DIPHTHERIA

Introduction: An acute, toxin-mediated vaccine preventable upper respiratory tract illness that affects the throat and sometimes tonsils. Diphtheria causes a thick covering (pseudo-membrane) in the back of the throat and can involve any mucous membrane. Classification based on sites of disease are anterior nasal, pharyngeal & tonsillar, laryngeal, cutaneous, ocular, and genital [1]. Diphtheria affects people of all, but most often it strikes unimmunized children younger than 5 years of age.

Clinical Picture: Sore throat, low grade fever and an adherent pseudo-membrane on the tonsils, pharynx and/or nasal cavity. Symptoms range from sore throat to toxic life-threatening diphtheria of the larynx or of the lower and upper respiratory tracts. The toxin produced by bacteria may also get into the blood stream and can cause damage to the heart, kidneys, and nerves [1].

Infectious Agent: *Corynebacterium diphtheriae*, an aerobic toxin producing gram positive bacillus. *C. diphtheriae* has 4 biotypes i.e. *gravis, intermedius, mitis* and *belfanti* [1].

Reservoir: Humans are the reservoir for *C. diphtheriae* and are usually asymptomatic [2]

Mode of Transmission: Transmitted from person to person, usually through respiratory droplets (coughing or sneezing). Infection may come by contact/touching open sore (skin lesions) and material objects (cloths, fomites) used by the patient of Diphtheria. Raw milk may also serve as a vehicle [2].

Incubation Period: Usually 2-5 days, occasionally longer [2].

Infectivity/Communicability: Organisms usually persist 2 weeks or less and seldom more than 4 weeks. Chronic carriers may shed infectious agent for 6 months or more [2].

Seasonality: Throughout the year; higher incidence is in winter and spring [3].

Alert Threshold: One probable case is an alert [3]

Outbreak Threshold: One lab confirmed case is an outbreak [3]

Case Definition:

Probable Case: In the absence of a more likely diagnosis, an upper respiratory tract illness with each of the following:

- An adherent "membrane" on the nose, pharynx, tonsils, or larynx;
- Absence of lab confirmation; AND
- Lack of epidemiological linkage to a lab confirmed case of
- Diphtheria [4].

Confirmed Case: Any probable case that has been laboratory confirmed or linked epidemiologically to a laboratory confirmed case [4].

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

Discarded: Any probable case in whom other compatible organisms are isolated or if *C. diphtheriae/ C. ulcerans/ C. pseudotuberculosis* is isolated but is confirmed to be a non-toxigenic strain [3]

Lab Confirmation:

- Conventional culture method (bacteriological culture testing)

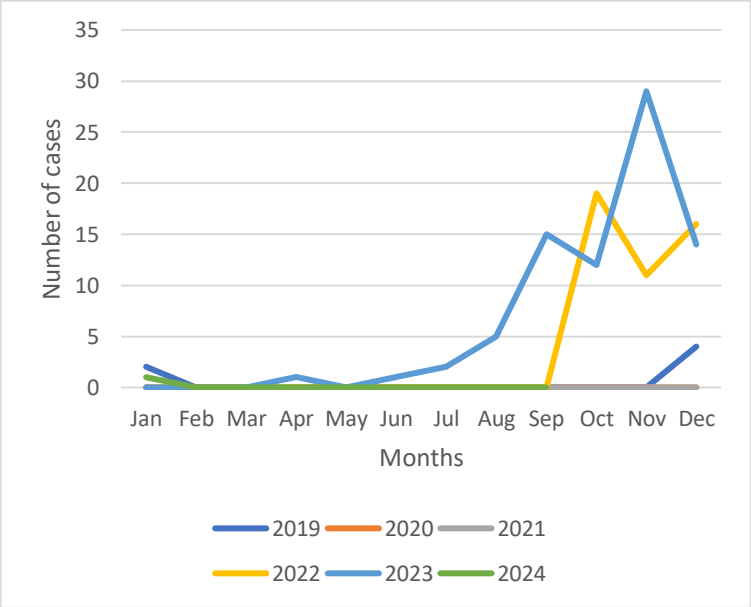
Specimen Collection and Transportation:

- Collect nasopharyngeal and throat swabs by using polyester, or nylon swabs.
- Pieces of pseudo-membrane may also be submitted in sterile saline [not formalin] for culture.
- The swabs should be placed in transport media such as Amies or Stuart respectively at ambient temperature [3].

Timings:

Specimens for culture should be obtained as soon as diphtheria [involving any site] is suspected, even if treatment with antibiotics has already begun [1].

Month Wise Lab Confirmed Diphtheria Cases in Pakistan from January 2019 to September 2024 (n=132)



Case Management:

For Patients:

- Do not wait for laboratory results before starting treatment/ control activities. All cases must receive diphtheria antitoxin (DAT).
  - For mild pharyngeal or laryngeal disease, the dose: 20,000 – 40,000 units
  - For moderate nasopharyngeal disease, the

dose: 40,000 - 60,000 units
    - For severe, extensive or late [3 or more days] the dose: 80,000 – 100,000 units
- Removal of membrane by direct laryngoscopy or bronchoscopy may be necessary to prevent or improve airway obstruction.
- Either penicillin 250 mg orally 6 hourly daily or erythromycin 500 mg orally 6 hourly is effective therapy, although erythromycin is slightly more effective in eliminating the carrier stage, should be continued for 14 days.
- Other macrolides are probably as effective as erythromycin.
- The patient should be isolated until three consecutive cultures at the completion of therapy have documented elimination of the organism from oropharynx.

Preventive measures:

- Standard plus droplet transmission-based 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 proper treatment.
- Tertiary prevention of complications and deaths by early diagnosis and proper management [1].

Vaccination:

- Routine immunization consists of 3 doses of 0.5 ml DPT-Hep- BHib (Pentavalent Vaccine) administered IM to all the children less than one year of age with the schedule of:
    - 1st dose at the age of 6 weeks.
    - 2nd at 10 weeks.
    - 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 [1]

References:

References are available at online version at www.nih.org.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. The geographical distribution of the disease depends on sand fly species acting as vectors, their ecology, and the conditions of internal development of the parasite. 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:

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

Mode of Transmission: Spread by the bite of the sand fly on theskin. 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].

Seasonality: May and October with a usual peak in June.

Clinical Picture:

Cutaneous Leishmaniasis: 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 the 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 Leishmaniasis:

Affects several internal organs (usually, spleen, liver, 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, popular 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).

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.

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

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 person showing clinical signs (skin or mucosal lesions) without parasitological confirmation of the diagnosis (positive smear or culture) [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 specimens. 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 ina 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:

- Most of the recommended precautionary measures are aimed at reducing contact with Phlebotominae (sandfly).
- 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 leishmaniasis, 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) cumulative for all the districts/agencies of Pakistan in 2023 at 11.03 (1). The two parasites which account for malaria in Pakistan are Plasmodium vivax and P falciparum. 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.

Uncomplicated: 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) 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, and abnormalities in blood coagulation.
- Hyper parasitemia where more than 5% of Rbcs are infected with malarial parasite.
- Can be characterized by cardiovascular collapse, acute kidney injury and acute respiratory distress syndrome.

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 post monsoon i.e. from August to November.

Alert Threshold: Number of cases reaches two times the meannumber of confirmed 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 Definitions:

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 and neighborhood.

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) with sensitivity of 95% is recommended for use.
- PCR
- Serology (Indirect immunofluorescence and ELISA)

Specimen Collection and Transportation:

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

Storage: Blood in EDTA tube may be refrigerated up to two to three 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:

Artemisinin-based combination therapies (ACTs) are 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
- 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 reported cases by month in Pakistan, predefined weight bands (5–14 kg: 1 tablet; 15–24kg: 2 tablets; 25-35 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 thistreatment fails).

Therapy for uncomplicated vivax infection:

Chloroquine combined with primaquine is the treatment of choice for chloroquine sensitive infection, dosage as below:

- Chloroquine phosphate 4 tablets stat, 2 after 6 hours, then 12 hourly for two days
- Primaquine base 30 mg once daily for 14 days. For G6Pd Deficiency 45mg base weekly for 8 weeks
- Pediatric dose 0.5mg/kg for 14 days

Preventive Measures: Travelers and their advisers should adopt the four principles of malaria protection:

- Beware of the risk, incubation period, possibility of delayed onset and main symptoms
- 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-sleeved trousers outside the house in the evening. Use repellent creams and sprays. Avoid nighttime outside activities.
- Use mosquito's coils or vaporizing mat containing a Pyrethrin.
- Use of 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) Recommended Chemoprophylaxis: Atovaquone-P proguanil, Doxycycline or Mefloquine

References and guideline links: *References and guideline links are available at online version at www.nih.org.pkandh1p://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 after measles infection is life long,although there are few reports of measles reinfection. The case-fatality rate may be as high as 25% [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 after the rash erupts [6].

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

Alert Threshold: One suspected case is an alert [7].

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

Case Definitions:

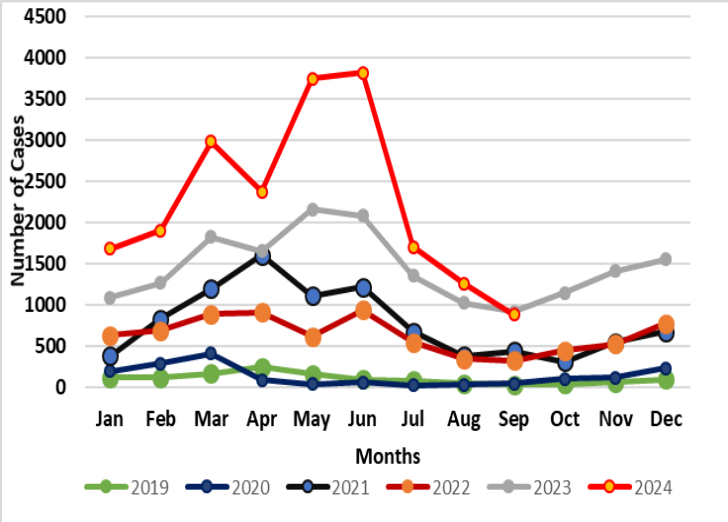
Suspected case: Any person in whom a clinician suspects measles infection, **OR** Any person with fever, maculopapular rash (i.e. non-vesicular) and 3C's; cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes) [8].

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 or PCR for measles RNA virus) [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 2019 - September 2024 (n=57,536)



Laboratory Confirmation:

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

Timings:

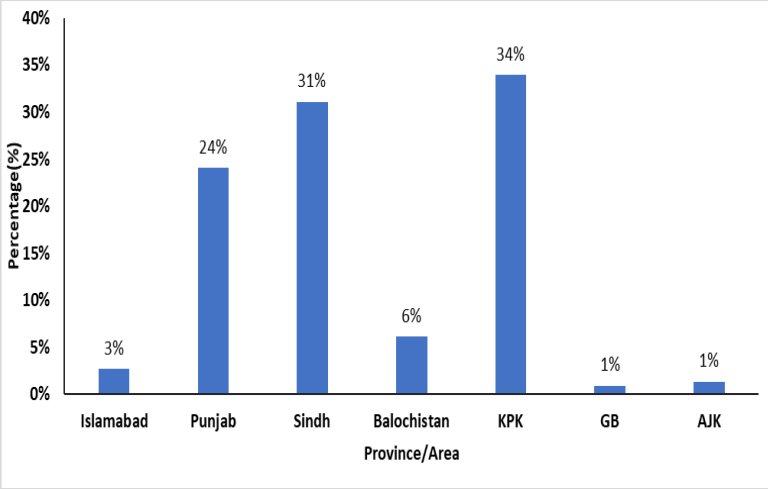
- RT PCR: 1 to 3 days after appearance of rash
- Measles specific IgM: 3 days after appearance of rash.

Specimen Collection and 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 2019 - September 2024 (n=57,536)



Case Management:

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].

Preventive Measures:

- Measles is transmitted through aerosols; thus contact, droplet and aerosol precautions are recommended along with standard precautions.
- Health care providers should follow respiratory etiquette and airborne precautions should be adopted in healthcare settings.
- Regardless of prior immunity status, all healthcare staff entering the room should use respiratory protection consistent with airborne infection control precautions.

Vaccinations:

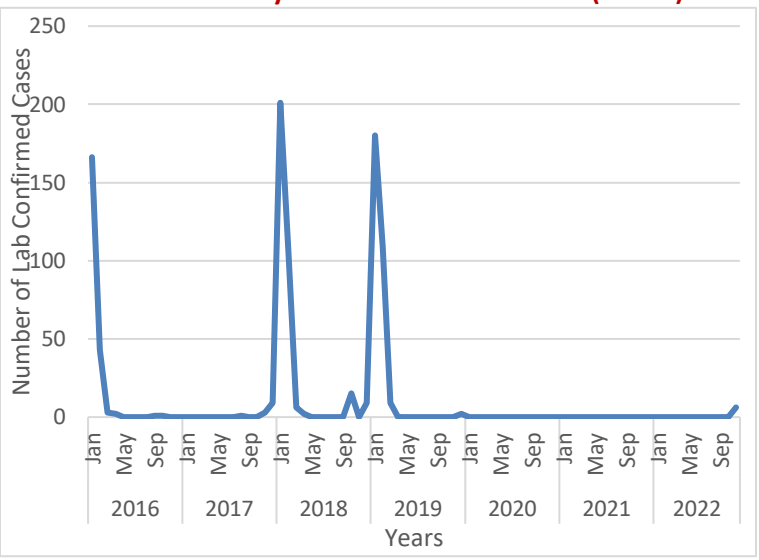
- Measles can be easily prevented through 2 doses of the measles-containing vaccine. Measles routine immunization first dose is given at 9 months and second at 15 months of age.
  - During a measles campaign the priority is to immunize children 6 months to 5 years old, regardless of vaccination status or history of disease.
  - Post-exposure prophylaxis with live measles vaccine if given within 72 hours of exposure provides permanent protection.

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

SEASONAL INFLUENZA

Influenza is a contagious respiratory illness caused by *influenza virus.* It can cause mild to severe illness. Older people, young children and people with co morbidities are at high risk for having serious complications. There are 4 types of seasonal influenza viruses, types A, B, C and D. Influenza type A viruses are further classified into subtypes and currently circulating among humans are influenza-A(H1N1) and A(H3N2) subtypes. In Pakistan, the influenza activity typically starts increasing from September and reaches peak during the winter months. Clinicians to remain vigilant and treat all suspected cases of severe influenza appropriately [3].

Month wise Lab Confirmed Seasonal Influenza H1N1 Cases in Pakistan from January 2016 to November 2022 (n=871)



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 two weeks or more. Most people recover from fever and other mild symptoms within a week without seeking medical attention. But influenza can cause severe illness or death especially in high risk groups [4].

Case definitions for influenza surveillance: As of January 2014, the WHO global influenza surveillance standards define the surveillance case definitions for influenza-like illness (ILI) and severe acute respiratory infections (SARI) [5]

Influenza Like illness (ILI): An acute respiratory infection with measured fever of ≥ 38°C with cough **AND** onset within the last 10 days [5].

Severe Acute Respiratory Illness (SARI): An acute respiratory infection with history of fever or measured fever of ≥ 38°C and cough with onset within the last 10 days **AND** requires hospitalization [5].

Sample Collection & Transportation: Respiratory specimens including throat or nasopharyngeal swabs and nasopharyngeal aspirates/ Broncho-alveolar lavage fluid from intubated patients may be collected and placed immediately in Viral Transport Medium (VTM). The samples may be transported to lab at 4 °C within 4 days, or frozen at -70 °C in case of prolonged storage.

Management: The symptoms in mild illness are relieved by providing warm fluids and taking rest along with analgesics and antipyretics. Analgesics such as Paracetamol 500mg-1G every 4-6 hours usually relieves headache and generalized pains and cough suppressants such as pholcodine 5-10 mg, 3-4 times daily are generally sufficient. Antimicrobial agents are not effective against viruses, treatment with antibiotics for superadded bacterial infection such as bronchitis and pneumonia may be necessary [7].

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* [7].

Difference between Flu and COVID-19;

- Influenza (Flu) and COVID-19 are both contagious respiratory illnesses, however COVID-19 is caused by infection with a new coronavirus (called SARS-CoV-2), andflu is caused by infection with influenza viruses.
- COVID-19 seems to spread more easily than flu and causes more serious illnesses in some people. Incubation period ofCOVID-19 is 2 to 14 days, while flu has incubation period of 1to 4 days.
- Because some of the symptoms and modes of transmissionof flu and COVID-19 are similar, it may be hard to tell the difference between them based on symptoms alone, thus COVID-19 specific lab testing, may be required to help confirm a differential diagnosis.

Prevention and Public Health Measures: Annual winter vaccination (seasonal anti-influenza vaccine) is recommended for health care workers, pregnant women, young children and immuno-compromised patients specially patients with pulmonary, cardiac or renal diseases. About two weeks after vaccination, antibodies develop that protect against influenza virus infection. General precautions include improved ventilation in living places; avoiding close contact with ill people and crowded settings, avoiding touching mouth and nose and regular hand washing with soap. Patients should be encouraged to cover their faces with a mask or handkerchief when coughing and sneezing [8].

Advisory link: https://www.nih.org.pk/wp-content/uploads/2019/10/Advisory-for-the-Prevention-and-Control-of-Seasonal-Influenza.pdf

References:

References are available at online version at www.nih.org.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 World Health 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 takingon 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 (4-8%), and paralytic (<1%). 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 withthe 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	2018	2019	2020	2021	2022	2023	2024
Islamabad	0	0	0	0	0	0	1
Punjab	0	12	14	0	0	0	1
Sindh	1	30	22	0	0	2	12
Khyber Pakhtunkhwa	2	93	22	0	20	4	5
KPTDS	6						
Balochistan	3	12	26	1	0	0	20
GB	0	0	0	0	0	0	0
AJK	0	0	0	0	0	0	0
Total	**12**	**147**	**84**	**1**	**20**	**6**	**39**

Infectious Agent: Polioviruses belong to genus Enterovirus subgroup, family Picornaviridae, having three serotypes of Poliovirus, labelled P1, P2, and P3 (7).

Reservoir: 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 feces for several weeks.

Period of communicability:

Soil: summer: 1.5 days, winter: 20 days

Sewerage: 26 days at 23^0C

Seasonality:

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

Incubation Period: 7 -14 days for paralytic cases (range 3 - 35 days) (7)

Alert Threshold: One suspected case of polio is analert requires an immediate notification and stools sample collection for confirmation (8)

Outbreak Threshold: One lab confirmed case is an outbreak.

Case Definitions: 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 person of <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).

Probable case: AFP clinically compatible with Poliomyelitis in the absence of adequate virological evidence.

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).

Vaccinated associated Poliomyelitis case: A casewith acute paralytic illness in which vaccine-like poliovirus isisolated from stool samples, and the vaccine derived virus isbelieved 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 2weeks after onset of paralysis and was negative for poliovirus (9).

Case Management:

The treatment of polio focuses on supportive care, as there is no cure for the virus. Management includes immediate and adequate diagnosis, followed by symptomatic treatment with pain relievers and antipyretics like ibuprofen. Antibiotics may be prescribed for secondary infections. Physical therapy and moderate exercises are crucial for maintaining muscle strength and function. A balanced diet aids recovery, while bed rest during the acute phase helps alleviate symptoms. In severe cases, hospitalization may be necessary for respiratory support and close monitoring. Preventive measures, particularly vaccination, remain the cornerstone of polio control.

Specimen Collection and 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 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 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 inroutine.
2. Providing supplementary doses of OPV to all children < 5 years old during NIDs and SNIDs, as well as the case

response planned by the Polio Eradication Program.

3. Active and Passive Surveillance for all cases of acute
4. flaccid paralysis
5. House-to-house OPV campaigns, targeting areas in which transmission of wild Poliovirus persists, based on National Emergency Action Plan (NEAP 2019-2020) (11).
6. Along with the above-mentioned measures, improving sanitation and maintaining proper hygiene also play a vital role in preventing the spread of the virus.

References and Guideline 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-XDR)

Introduction:

Typhoid fever, caused by Salmonella Typhi and Paratyphi, poses a significant health threat, particularly in Pakistan, where it ranks among the most affected countries. Contributing factors include poor water quality, inadequate sanitation, low vaccination rates, and insufficient disease monitoring. Since 2016, Pakistan has seen outbreaks of Extensively Drug-Resistant (XDR) S. Typhi, resistant to multiple antibiotics, including first-line treatments and Fluoroquinolones. This resistance is linked to the H58 haplotype and has been exacerbated by the misuse of antibiotics. The emergence of an XDR S. Typhi strain in Sindh, resistant to a broad range of antibiotics, underscores the urgency for improved public health measures.

Infectious Agent: Anti-microbial resistant (AMR) strains of *Salmonella enterica serovar typhi.*

Clinical picture: Typhoid fever typically begins with a low-grade fever and general malaise, progressing to more severe symptoms like persistent high fever, headaches, muscle pain, and fatigue. Gastrointestinal issues such as abdominal pain and alternating constipation and diarrhea are common, along with loss of appetite and subsequent weight loss. Some patients may exhibit a rash or rose spots. If untreated, typhoid can result in grave complications like intestinal hemorrhage and systemic infection. Prompt medical treatment is crucial to prevent these serious outcomes.

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. The contamination of food and water usually occurs due to poor sanitation and mixing of sewerage water with drinking water.

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 for S.Typhi and 1 to 10 days for Paratyphoid.

Seasonality: Annual endemicity with a peak in April to August (Monsoon season)

Alert Threshold: One case of typhoid

Outbreak Threshold: 5 suspected/confirmed cases per 50,000 population.

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

Case definitions:

Suspected Case: Suspected Case: Any person with a history of fever of at least 38°C for 3 or more days with abdominal symptoms like diarrhea or constipation, abdominal tenderness, and prostration.

Confirmed Case: A suspected/ probable case that is laboratory confirmed by isolation of S. Typhi from blood/ stool or urine.

Chronic Carrier: An individual excreting S.Typhi in the stool or urine for longer than one year after onset of acute typhoid fever. (1-5% of the patients, depending on age, become chronic carriers harboring S.typhi)

Laboratory Confirmation: Blood and bone marrow culture is gold standard. Blood culture before initiating antimicrobial therapy remains the diagnostic method of choice.

Classification of Typhoid Fever Cases by Drug Resistance in Pakistan:

- **Non-Resistant typhoid fever:** Typhoid fever caused by Salmonella Typhi and/or Salmonella Para-typhi A, B or C strains which are sensitive to first line- drugs and third generation cephalosporin, with or without resistance to second line drugs.
- **Multi-drug resistance (MDR)Typhoid fever:** Typhoid fever caused by *Salmonella Typhi* and/or Salmonella Para-typhi 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.

Treatment: Suspected cases having history compatible with the case definition(s) should immediately seek medical advice from health care facilities. Samples should be collected for culture & sensitivity before starting the empirical therapy from all the suspected cases. Unnecessary use of antimicrobial agents should be discouraged to treat the patients presenting with fever. To limit the antimicrobial resistance (AMR), antibiotics should be prescribed based on the results of culture and sensitivity tests.

COVID-19 Situation and Antibiotics Prescribing 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 including vaccination: It is suggested that withthe treatment options for typhoid becoming more limited, following preventive measures are urgently needed, including improved sanitation and vaccination campaigns:

- 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 fruitsand vegetables 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 people and those who are exposed to the disease. Typhoid fever vaccines do not provide 100% protection; however, they will 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.

Reported XDR Typhoid Fever Cases in Sindh by Years (November 2016 to August 2021)

(No data received after 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

(Source: FDSRU-NIH weekly Report Volume 3-- Issue 33, August 08-14, 2021Date: August 18, 2021)

References and guideline links: *References and guideline links are available at online version at www.nih.org.pkandh1p://dmc.gov.pk/*

Advisory link: *https://www.nih.org.pk/wp-content/uploads/2019/02/Advisory-for-Typhoid-5-oct.pdf*

Potential International Public Health Event

Mpox Disease

Mpox is a viral zoonotic disease very first observed among monkeys kept for research in 1958 in Copenhagen, later on the disease was observed first in 9 months old child from Democratic Republic of Congo in 1970. Since then, the disease is endemic in Central and West African countries. Mpox virus is part of the same family of viruses as variola virus, the virus that causes smallpox. Mpox symptoms are similar to smallpox symptoms, but milder, and is rarely fatal. Mpox is not related to chickenpox. In 2003, the first Mpox outbreak outside of Africa was 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 May 2022, multiple cases of Mpox were identified in several non-endemic countries. Currently, the disease is being reported from 118 countries mostly from US, followed by Spain, Brazil, France and UK. It is less severe with case-fatality less than 1%. The World Health Organization declared Mpox as Public Health Emergency of International Concern (PHEIC) on 25th June 2022 for the first time and with the resurgence of Clade-I virus in several African countries it was declared a PHEIC for a second time on August 14, 2024. Since 2022, Pakistan has reported 16 Mpox cases, including one death. In 2024 alone, seven cases have been confirmed with six identified after the WHO's PHEIC declaration. All cases in Pakistan are the Clade-IIb strain, with no evidence of local transmission.

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, laterwith 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 ismore reliable to diagnose the virus.

Clinical Management: Clinical care for Mpox should be fully optimized to alleviate symptoms, manage complications andprevent 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, policiesto 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 workersmay have received a more recent smallpox vaccine to protect them in the event of exposure to orthopox viruses in the workplace. A still newer vaccine based on a modified attenuated vaccinia virus (Ankara strain) was approved for the prevention of Mpoxin 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 orthopox viruses

Guidelines link:

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

Produced by the Center of Disease Control (CDC) (Ex-FE&DSD)

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