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SEASONAL AWARENESS AND ALERT LETTER (SAAL)

For Epidemic-prone infectious diseases in Pakistan

Winter Season

OBJECTIVES OF SAAL

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

DATA SOURCES

- The available national data collected during 2014 to 2020, 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 diseases.
- The description of all priority infectious diseases has been arranged in an alphabetical order. Additionally, under the section of National Potential Public Health Event, technical details on, Human Immunodeficiency Virus (HIV) & Acquired Immunodeficiency Syndrome (AIDS) is included. Ebola Virus disease (EVD) has been shared as International Potential Public Health Event.

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

High Alert- peak occurrence in the winter season

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

Coronavirus Disease 2019 (COVID-19)

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, SARS-CoV-1 and SARS-CoV-2 belongs to the same family.

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 in hospitals of 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 and pandemic as Public Health Emergency of International Concern (PHEIC) on January 30, 2020 (2).

Number of COVID-19 suspected cases till 25 Sept, 2020	Number of COVID-19 Lab. confirmed cases till 25 Sept, 2020	Number of deaths due to COVID-19 till 25 Sept, 2020
3,344,019	309,015	6,444

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 and later loss of sense of smell & taste as a distinguishing feature of COVID-19.

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 and cyanosis can occur in children. In this definition, 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 opacities (lung infiltrates > 50%) (4).

Asymptomatic: Most of the cases may have no symptoms at all.

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: COVID-19 virus is primarily transmitted (direct transmission) between people through respiratory droplets via coughing, sneezing, 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 thought 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, (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 2 weeks or more in case of disease with severe symptoms.

Note: *COVID-19 is an emerging disease and with the day to day evolving situation, there is more to learn about its transmissibility, severity, management and other features*.

Seasonality: Not known

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

Outbreak Threshold: One lab confirmed case of COVID-19 is an outbreak (7).

Case Definitions

Suspected Case: A. Patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g. cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset;

OR

B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset;

OR

C. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation (7).

Probable Case: A. Suspected case for whom testing for the COVID-19 virus is inconclusive.

OR

B. A suspect case for whom testing could not be performed for any reason.

Confirmed Case: A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms. (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; OR
4. 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, bronchoalveolar lavage fluid/washings or sputum, using any standard extraction protocols or kits.

Specimen Collection and Transportation: For transport of samples for viral detection, use viral transport medium (VTM). Avoid repeated freezing and thawing of specimens. If VTM is not available sterile saline may be used instead (in which case, duration of sample storage at 4 °C may be different from what is indicated below).

Aside from specific collection materials, also assure other materials and equipment are available: e.g. transport containers, specimen collection bags/packaging, coolers, and cold packs or dry ice, sterile blood-drawing equipment (e.g. needles, syringes and tubes), labels, permanent markers, PPE, materials for decontamination of surfaces and etc(8).

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.

Case Management: There is no specific therapeutic presently approved by the U.S. Food and Drug Administration (FDA) to treat COVID-19. There is no proven role of prophylactic chloroquine or hydroxychloroquine at this time. Current clinical management includes infection prevention & control measures and supportive care, including supplemental oxygen and mechanical ventilatory 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 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: No vaccine is currently available. Trials are in process for COVID-19 vaccine. **References and guideline links:**

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

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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). 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)

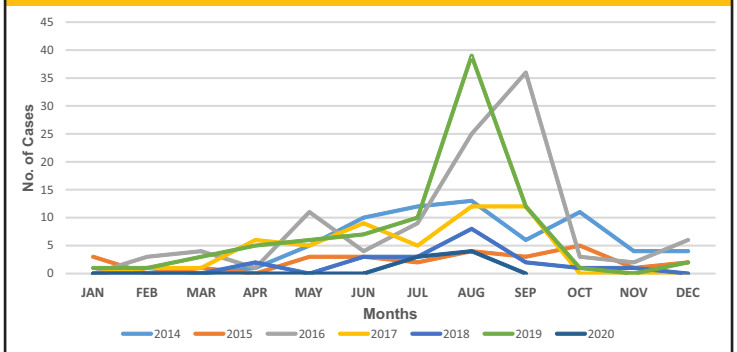
Reservoir: *Hyalomma* tick, domestic animals, such as cattle, goats, sheep, rodents, such as hedgehogs, rats, hares and birds are generally resistant with the exception of Ostrich (6).

Mode of transmission: Bite of the infected *Hyalomma* tick (vector), handling of tick infested animals, direct contact with blood / tissue of infected domestic animals (slaughtering); or direct contact with blood / tissue of infected patients. Nosocomial infections are common sources of transmission (7).

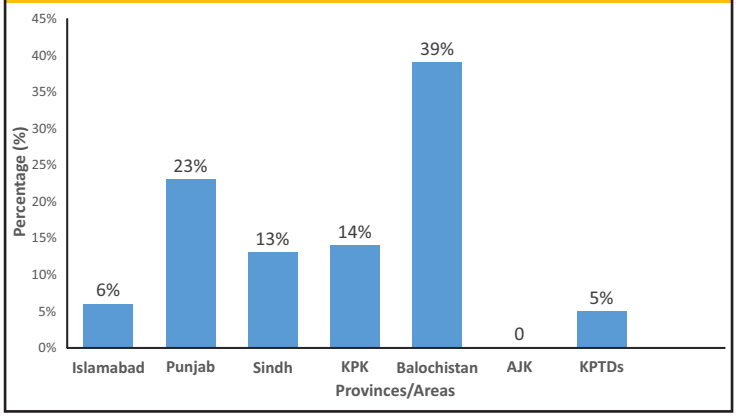
Incubation Period:

- 1-3 days after tick bite
- 5–6 days after exposure to infected blood or tissues with a (documented) maximum of 13 days (8).
- **Seasonality:** Peak of cases occur during Fall and Spring seasons, associated with life-cycle of ticks, exposure of new born animals and exposure of migrant animals (9).

Reported Lab Confirmed CCHF Cases in Pakistan by Months from January 2014 to September 2020 (n=363)



Reported Lab Confirmed CCHF Cases in Pakistan by Provinces/Areas from January 2014 to September 2020 (n=363)



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).

Outbreak Threshold: 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, haematemesis, haemoptysis, 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

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 case of any close 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 should be autoclaved before incinerating.
- After the patient is discharged from the hospital, room surfaces should be wiped down with disinfectant like sodium hypochlorite (Naocl) 10% solution and 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 net 3 days (12).
- **Prophylaxis Protocol:**
- The efficacy for post exposure Ribavirin in the management of hospital-associated CCHF, remains anecdotal.
- It may be given in a high loading dose (35 mg/kg orally followed by 15 mg/kg three times daily for 10 days) and only for high-risk settings e.g. needle stick injury, mucous membrane contamination, emergency resuscitative contact, or prolonged intimate exposure during transport after baseline blood tests.
- **Preventive measures:** Educate public about the mode of transmission and personal protection.
- For tick control, animal dipping/spraying in an insecticide solution of Permethrin/Pyrethrin/DEET is used. Injectable insecticide like Ivermectin is also recommended.
- Butchers should wear gloves and other protective clothing to prevent skin contact with freshly slaughtered meat, blood and other tissues. Meat should be drained for least 30 minutes, before distribution to public.
- 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 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).
- **References and guideline links:**
- *References and guideline links are available at online version at www.nih.org.pk and http://dmc.gov.pk/*

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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 has been observed multiple times there after [2].

Clinical Picture:

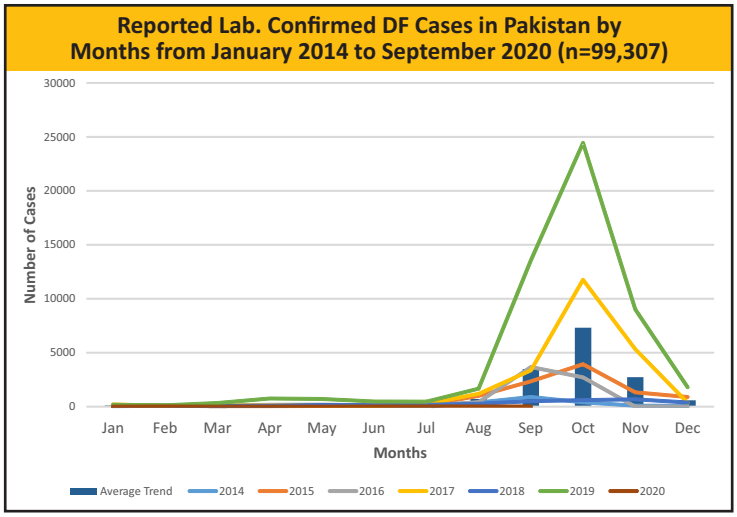
Dengue fever: Dengue fever is defined by fever (for >3 days and < 10days) as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms i.e. nausea/vomiting, rash, aches and pains (e.g. headache, retro-orbital pain, joint pain, myalgia, arthralgia), 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.

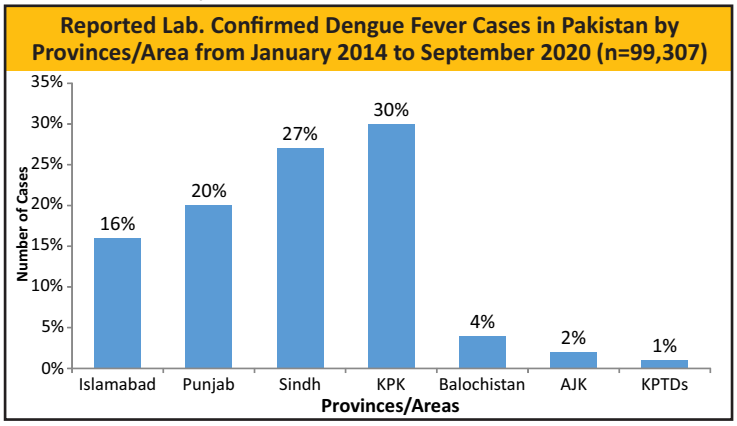
OR

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 seasons as compared to winter and summer seasons. Relatively humidity, temperature and rain remained significant predictors of dengue incidence in Pakistan [8].



Geographical distribution: From January 2015 to December 2020, KPK remained the most affected province with 30% of cases followed by Sindh with 27% Cases.



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:**
- o IgM antibodies are detectable after 4th day of onset of illness (acute).
- o IgG is used for the detection of past Dengue infection and usually can be detected during 2nd 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.
- **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.
- Proper solid waste disposal and improved water storage practices should be in place, 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 (national or subnational) 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 http://dmc.gov.pk/*

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DIPHTHERIA

Introduction: An acute, toxin-mediated vaccine preventable upper respiratory tract illness that affects the throat and sometimes tonsils. Diphtheria causes a thick covering in the back of the throat and may involve any mucous membrane. Classification based on sites of infection are anterior nasal, pharyngeal & tonsillar, laryngeal, cutaneous, ocular and genital [1].

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 as late complications [1].

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

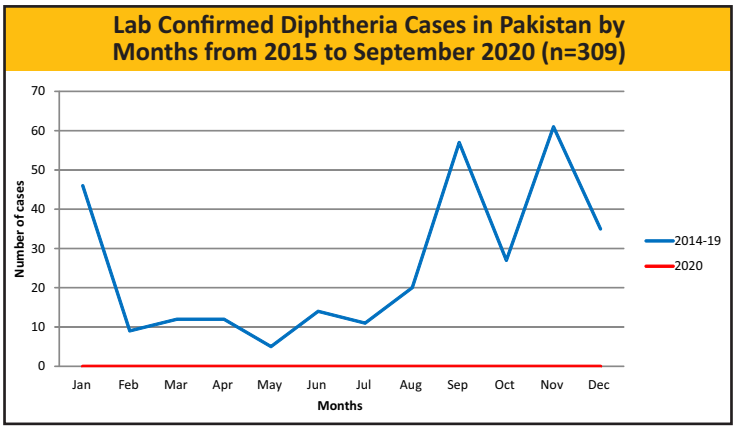
Reservoir: Humans are the reservoir for *C. diphtheriae* and are usually asymptomatic [2].

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 of 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 medium and keep at an 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].
- **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
- ***Note:*** Clinical diphtheria does not necessarily confer natural immunity, and patients should thus be vaccinated before discharge from a health facility with either primary or booster doses. Unless immunized, children and adults may repeatedly be infected with the disease. All close contacts should remain under surveillance for 7 days [1]
- **Preventive measures:**
- Standard plus droplet precautions are recommended with single room isolation.
- Primary prevention of disease by ensuring high population immunity through immunization.
- Secondary prevention of spread by the rapid investigation of close contacts to ensure their 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-B-Hib (Pentavalent Vaccine) administered IM to all the children less than one year of age with the schedule of:
- a. 1st dose at the age of 6 weeks;
- b. 2nd dose at 10 weeks;
- c. 3rd at 14 weeks, a booster DTP at 18 months to 4 years.
- If children or adults have not been immunized with three-dose series, children < 5 years should receive DT vaccine, and children ≥ 5 years and adults should receive Td vaccine to complete a series of three doses [1]
- **References and guideline links:**
- *References and guideline links are available at online version at www.nih.org.pk and http://dmc.gov.pk/*

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LEISHMANIASIS

Introduction: Leishmaniasis is a parasitic vector borne disease and is classified as 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, Sindh 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 Definition:

1. Visceral Leishmaniasis (VL)

Suspected case: A 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 (CL):

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

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

Specimen Collection:

Cutaneous Leishmaniasis: Skin biopsy is the standard dermatologic technique for obtaining specimen. No preservatives are required for examining LD bodies or for Leishmania 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 diagnosis: 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.

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 http://dmc.gov.pk/*

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MALARIA

Introduction: A vector borne parasitic disease transmitted by female Anopheles mosquito species. Epidemiologically, Pakistan is classified as a moderate Malaria endemic country with a National Annual parasite index (API) averaging at 1.08 (MIS, 2015) and wide diversity within and between the provinces and districts. Plasmodium Vivax and Plasmodium Falciparum are the only prevalent species of parasites detected so far with P.vivax being the major parasite species responsible for > 80% reported confirmed cases in the country with 3.5 million presumed and confirmed malaria cases annually. This malariogenic potential of Pakistan has a negative impact on its socio-economic growth and productivity.

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)
- 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)

Infectious Agent:

- *Plasmodium falciparum*
- *Plasmodium vivax*
- *Plasmodium ovale*
- *Plasmodium malariae*
- *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 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 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

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). Immunodiagnostic test kit: Sample may also be used to demonstrate parasite antigen. Transport the specimen at room temperature preventing sample spillage or damage to the tubes.

Case Management:

- **Warning:** Do not give Primaquine to pregnant women and children < 2years of age and it is advisable to do a Glucose-6- phosphatedehydrogenase (G6PD) test before giving this drug. Give Primaquine preferably after the patient has recovered from the acute illness.
- Do not give undiluted Chloroquine or Quinine by I/M or I/V route, as it can cause sudden cardiac arrest, especially in children
- Do not give Sulfadoxine/ Pyrimethamine to children <2 months of age or during first trimester of pregnancy
- Suspected/probable case of severe Malaria and high risk groups should be treated immediately.
- 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 Artemether plus lumefantrine,
- Artemether-lumefantrine is currently available as a fixed dose formulation with dispersible or standard tablets containing 20mg of Artemether and 120 mg of lumefantrine.
- In case of pregnant women, during first trimester Quinine plus Clindamycin to be given for 7 days, (Artesunate plus Clindamycin for 7 days is indicated if this treatment fails).

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

- **Chloroquine:** 04 STAT, 02 after 6 hours, then 12 hourly for 02days.
- **Primaquine:** 0.25mg/kg body weight daily for 14 days treatment is prescribed for radical treatment of Vivax.

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

- Be Aware of the risk, the incubation period, the possibility of delayed onset, and the 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 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.
- 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) Chemoprophylaxis Malaria control Program:

- Recommended chemoprophylaxis: Atovaquone-proguanil,Doxycycline or Mefloquine

References and guideline links:

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

PERTUSSIS (WHOOPING COUGH)

Introduction: A toxin-mediated disease that can affect people of all ages but can be very serious even deadly among infants. According to a study published in Lancet 2017, it was estimated that globally there were 24.1 million pertussis cases and 160,700 deaths in 2014 from pertussis in children younger than 5 years, with the African region contributing the largest proportions [1].Despite generally high coverage with childhood Pertussis vaccines, Pertussis is one of the leading causes of vaccine-preventable deaths worldwide [2].

Clinical Picture: The clinical course of the illness is divided into three stages: Catarrhal, Paroxysmal and Convalescent.

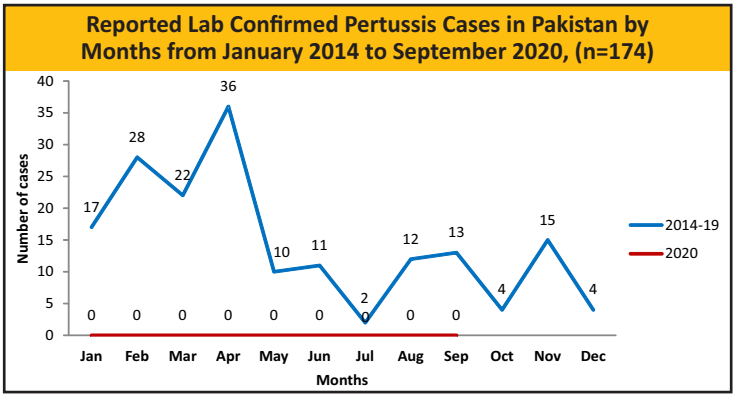
Infectious agent: Bordetella pertussis; Gram *negative aerobic bacteria [*3]

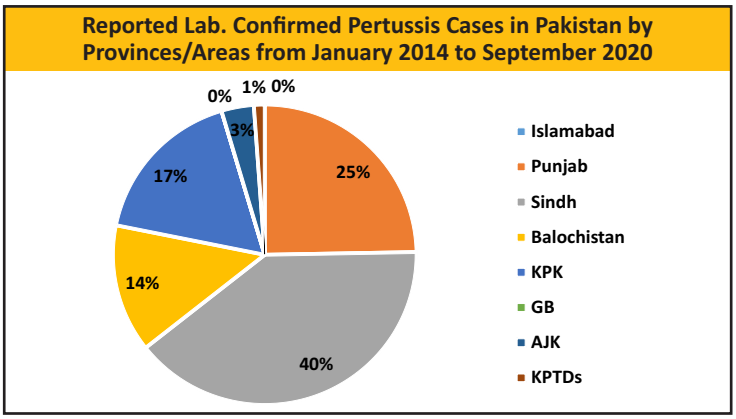
Reservoir: Humans are the only known reservoir [3]

Mode of transmission:

- By direct contact with discharges from respiratory mucous membranes of infected persons
- Airborne/aerosols transmission [3]
- **Incubation period:** 9 -10 days (range 6-20 days) [3]
- **Communicability:**
- Highly communicable in the early catarrhal stage and gradually decreases after paroxysmal cough.
- Untreated patients may be contagious for up to 3 weeks after the onset of paroxysmal cough or up to 5 days after onset of treatment [3]
- **Seasonality:** Pertussis has no distinct seasonal pattern [3]

Geographical distribution: During 2014-2020, Sindh province remained most affected with 40% cases from a total of 174 cases of Pakistan.





Alert Threshold: One suspected case [5]

Outbreak threshold: Five suspected with one lab confirmed case [5]

Case Definition

Suspected: A person with cough lasting at least 2 weeks with at least one of the symptoms i.e. Paroxysms/ fits of coughing, Inspiratory "whooping", Post-tussive vomiting and apnea in infants with or without cyanosis [6]

Probable case: A clinical suspected case with an epidemiological linkage [5]

Confirmed case: Suspected/Probable case confirmed with positive laboratory result [5]

Lab confirmation:

- Culture is the gold standard
- Detection of genomic sequences by polymerase chain reaction (PCR)
- Positive paired serology [5]

Specimen Collection:

- Collect two nasopharyngeal specimen using calcium alginate swabs on fine flexible wire.
- Bronchial or nasopharyngeal secretions/aspirates may provide superior specimens for culture.
- Collect throat swabs in addition to the nasopharyngeal swabs for isolation of organism on culture.

Storage: Can be stored at room temperature for 48 hours, refrigerated for 7 days and frozen for 30 days [5]

Packaging: Triple packaging seal in a biohazard bag [5]

Transportation: Reagan Lowe (RL) transport medium [5]

Case Management:

- Antimicrobial treatment is more effective in the catarrhal phase, prior to paroxysmal coughing.
- Antibiotic treatment should be initiated in all suspected cases.

Treatment options include:

- Erythromycin 500mg, 6 hourly for 7 days
- Clarithromycin 500mg orally twice daily for 7 days
- Other macrolides as prescribed by the physician
- Trimethoprim-Sulfamethoxazole, 160-800 mg orally twice a day for 7 days
- Young infants particularly those younger than 6 months of age should be hospitalized
- Supportive case management including cough suppressant and good nursing care
- Maintenance of proper water and electrolyte balance, adequate nutrition and sufficient oxygenation [6].

Preventive measures & vaccination

- Timely treatment of the cases decreases the risk of transmission
- Chemoprophylaxis: Erythromycin 40-50 mg/kg per day in four divided doses for 14 days
- Immunization:
  - Active primary immunization against *B. pertussis* infection with the whole-cell vaccine (WP) is recommended
  - Children who have received at least 3 doses are estimated to be protected especially against severe disease. However, protection begins to wane after about 3 years [5].

Vaccination during pregnancies

- It is important for women to get the whooping cough vaccine during 27th week through 36th week of pregnancy [5].
- Return to school: Infected child should avoid school / day care until they have completed 5 days course of therapy or if not treated 21 days after the onset of symptoms [5].

References and guideline links:

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

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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. Until poliovirus transmission is interrupted in these 2 countries, all countries remain at risk of importation of polio, especially vulnerable countries with weak public health and immunization services and travel or trade links to endemic countries. The annual case count during the time has been reduced from over 350,000 to only 33 in 2018.

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) 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.

Reported Lab. Confirmed Polio Cases Year Wise Breakdown by Province/Area in Pakistan, 2012-2020

Province/Area	2012	2013	2014	2015	2016	2017	2018	2019	2020
Islamabad	0	0	0	0	0	0	0	0	0
Punjab	2	7	5	2	0	1	0	12	8
Sindh	4	10	30	12	8	2	1	30	22
Khyber Pakhtunkhwa	27	11	68	17	8	1	2	93	22
KPTDS	20	65	179	16	2	0	6		
Balochistan	4	0	25	7	2	3	3	12	18
GB	1	0	0	0	0	1	0	0	0
AJK	0	0	0	0	0	0	0	0	0
Total	58	93	307	54	20	8	12	147	70

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).

Infectious agent: Poliovirus 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 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 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, Traumatic Neuritis, such that each case with limping must be investigated carefully (9).

Suspected Case: Acute/ Sudden onset of weakness and floppiness in a child aged ≤15 years; **OR** Paralytic illness in a person of any age whom Polio is suspected (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 Paralytic Poliomyelitis case: 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 2 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. The set of specimens from a single patient should be placed in a single plastic bag just large enough to hold both the containers (10).

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 guideline links:

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

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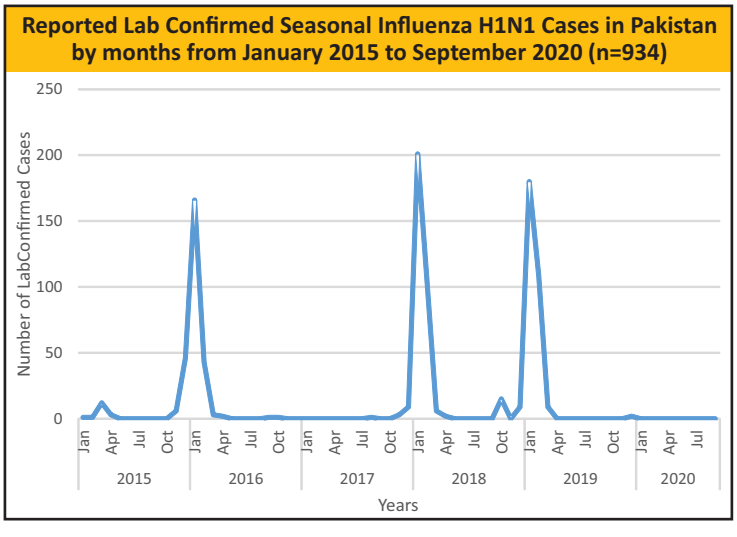
SEASONAL INFLUENZA

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 strains 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].

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].
- Currently, most seasonal Influenza A/H1N1 viruses are sensitive to Neuraminidase Inhibitors, Oseltamivir (Tamiflu) and Zanamivir. Anti-viral treatment should be initiated within the first two days of symptoms to ensure positive clinical outcome and to treat people who are sick with flu symptoms and who are at increased risk of severe flu illness [7].
- Recommended antiviral medications are not licensed for treatment of children (restrictions are for under 1 year of age for Oseltamivir and under 7 years of age for Zanamivir) [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].
- 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].
- Standard operating procedures (SOPs) should be developed to ensure proper implementation of administrative controls, environmental controls, and use of personal

protective equipment (PPE). Administrative policies that address adequate staffing and supplies, training of staff, awareness sessions of communities, and a risk communication strategy is particularly needed [8].

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

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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 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: Antimicrobial resistant (AMR) strains of *Salmonella enterica serovar typhi*

Clinical picture: Patient presents with high grade fever (>100°F), 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.

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

Suspected Case: Any person with history of fever of at-least 38°C for 3 or more days with abdominal symptoms like diarrhea, 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

Classification of Typhoid Fever Case Definitions by Drug Resistance Status, Pakistan (WHO-2018)

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 typhoid fever

Reported Lab Confirmed XDR Typhoid Fever Cases in Sindh by Years (November 2016 to 05 September, 2020)

Years	Karachi	Hyderabad	Other Districts	Sindh Total
2016	0	12	0	12
2017	175	485	4	664
2018	3,712	891	207	4,810
2019	7,088	1,645	998	9,731
2020	1,977	529	331	2,837
Total	12,952	3,562	1,540	18,054

(Source: FDSRU-NIH weekly Report Volume 2-- Issue 01 Dec 30, 2019– Jan 05, 2020 Date: January 15, 2020)

Now cases are being reported from other parts of the country as well. Additionally, travel associated XDR typhoid cases have been identified abroad as well.

Lab Diagnosis:

- **Only way to confirm Typhoid fever is blood or stool sample tested for the presence of** *S. Typhi*
- *S. Typhi* can be isolated from blood during the first week of illness or from stool and urine after the first week of illness.
- Widal and Typhidot have *NO diagnostic value* due to limited sensitivity, specificity and cross reactivity and must be stopped immediately by all labs.
- The XDR Typhoid cases information and lab culture report must be notified to the concerned district health authorities, DG Offices of the respective province and the NIH.

- **Treatment:** Suspected patients having history compatible with case definition(s) should immediately seek medical advice from health care facilities.
- **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 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:
- Use of azithromycin and Meropenem should be restricted and only given to XDR cases of typhoid fever based on prescription by registered medical practitioner.
- 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 leftover 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 prequalified the first conjugate vaccine in December 2017 to prevent typhoid fever

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Advisory link: *https://www.nih.org.pk/wp-content/uploads/2020/07/Advisory-for-Prevention-and-Treatment-of-Typhoid-Fever-including-XDR-Typhoid.pdf*

Potential National Public Health Events

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 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).

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.

Potential International Public Health Event

Ebola Virus Disease (EVD)

Introduction: Ebola Virus Disease (EVD) or Ebola hemorrhagic fever (EHF), is the most virulent human viral hemorrhagic disease caused by the *Ebola virus*; with the average case fatality rate is around 50%. Symptoms may appear from 2 to 21 days after exposure which typically include fever, headache, joint and muscle aches, weakness, diarrhea, vomiting, stomach pain, lack of appetite and may be followed by rash, red eyes, difficulty breathing, difficulty swallowing, bleeding from different sites of the body. A person infected with Ebola virus is not contagious until symptoms appear. Ebola Virus cannot transmit through air, food and water. The virus can spread through direct contact with the body fluids of an infected person. No specific drug available however early supportive clinical treatment and management are essential and can improve the chances of recovery.

On 17 July 2019, the Director-General of the World Health Organization declared the Ebola outbreak in the Democratic Republic of

the Congo (DRC) a Public Health Emergency of International Concern (PHEIC) under the International Health Regulations (IHR 2005). This is the tenth outbreak of Ebola virus disease over the last four decades in the DRC.

Public Health Measures: WHO recommends the implementation of proven strategies for the prevention and control of Ebola outbreaks. These strategies include (i) coordination of the response, (ii) enhanced active surveillance, (iii) laboratory confirmation, (iv) contact identification and follow-up, (v) case management, (vi) infection prevention and control, (vii) safe and dignified burials, (viii) social mobilization and community engagement, (ix) logistics, (x) risk communication, (xi) vaccination, (xii) partner engagement, (xiii) research and (xiv) resource mobilization.

Mosquito Alert Pakistan ماسکیٹو الرٹ پاکستان

GET IT ON Google Play

The National Institute of Health (NIH) has launched its first-ever android-based application named “Mosquitoes Alert Pakistan”. The app will help to collect information on different mosquito species present in different areas which will ultimately help in mapping out the magnitude of burden related to different mosquito species.

Through this Mosquito Alert app, anyone can send photo of mosquitoes or breeding places. These photos will be part of a common database and will be used for investigation, monitoring and control of mosquitoes.

This information is key for generating a participatory alert system to improve the management of mosquito’s species, minimize the risk of disease transmission and raise awareness among general public.

7 Easy Steps

Link of app: https://maa.nih.org.pk/

Produced by the Field Epidemiology & Disease Surveillance Division (FE&DSD)
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