



SEASONAL AWARENESS AND ALERT LETTER (SAAL)

For Epidemic-prone infectious diseases in Pakistan
Winter Season

OBJECTIVES OF SAAL

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

DATA SOURCES

The available national data collected during 2012 to September 2017 by FE&DSD from Disease Early Warning System (DEWS), Provincial Health Departments, Provincial Disease Surveillance & Response Units (PDSRUs), Expanded Program on Immunization (EPI), Acute Viral Hepatitis Sentinel Surveillance Program, Directorate of Malaria Control and laboratory based data from NIH has been analyzed to see the exhibited patterns of high priority communicable diseases.

The description of all priority diseases has been arranged in alphabetical order. Additionally, under the section of National Potential Public Health Events, technical details on *Naegleria fowleri* infection are included because of fatal cases encountered in Karachi since 2013. Ebola Virus disease, Zika Virus, Middle East Respiratory Syndrome Corona virus (MERS CoV) infection and Influenza (H7N9) has been shared as International Potential Public Health Events.

Outbreak - prone Diseases	Alerts
Crimean Congo Hemorrhagic Fever (CCHF)	
Chikungunya	
Dengue Fever	
Diphtheria	
Gastroenteritis (Acute)	
Leishmaniasis	
Malaria	
Measles	
Meningococcal Meningitis	
Poliomyelitis	
Pertussis	
Seasonal Influenza - A(H1N1, H5N1)	
Typhoid Fever	
Viral Hepatitis (Acute)	
	High Alert- peak occurrence in the winter season
	Medium Alert - cases will be encountered and any show up as an outbreak

CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF)

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

Clinical Picture: Sudden onset with initial signs and symptoms including headache, high fever, back pain, joint pain, stomach pain, vomiting. Red eyes, a flushed face, red throat, and petechiae (red spots) on the palate are common. Symptoms may also include jaundice and in severe cases, changes in mood and sensory perception. With illness progression, large areas of severe bruising, severe nosebleeds, and uncontrolled bleeding at injection sites can be seen, 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, wild animals/rodents, such as hedgehog, rats, hares and birds are generally resistant with exception of Ostrich⁽⁶⁾.

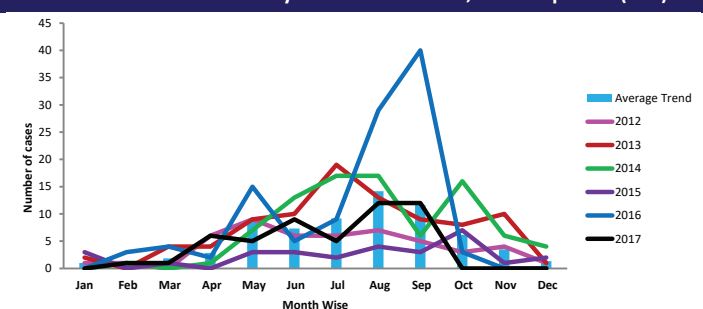
Mode of transmission: Bite of infected *Hyalomma* tick (Vector), handling of tick infested animals, direct contact with blood / tissue of infected domestic animals (slaughtering); or direct contact with blood / tissue of infected patients. Nosocomial infections are common⁽⁷⁾

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⁾.

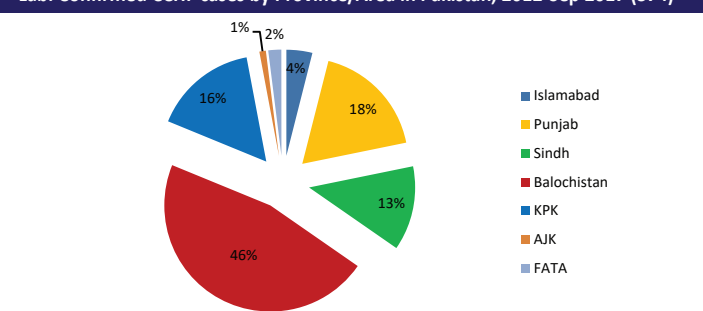
Seasonality: Peak of cases occur during Fall and Spring seasons, associated with life-cycle of ticks, exposure of new born animals, exposure of migrating animals⁽⁹⁾.

Lab. Confirmed CCHF cases by month in Pakistan, 2012-Sep 2017 (374)⁽¹⁰⁾



Geographical Distribution in Pakistan: Since the diagnosis of first human case of CCHF in 1976, the sporadic cases have continued to occur, mostly from Balochistan province⁽¹⁰⁾.

Lab. Confirmed CCHF cases by Province/Area in Pakistan, 2012-Sep 2017 (374)⁽¹⁰⁾



Alert Threshold: One probable/ case is an alert and requires an 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 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 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 with laboratory diagnosis of CCHF i.e. PCR and/or serology⁽¹¹⁾.

Laboratory Confirmation:

- Detection of viral nucleic acid by PCR in blood specimen
- Confirmation of presence of IgM antibodies in serum by ELISA (enzyme-linked immunoassay)⁽¹¹⁾.

Specimen Collection and Transportation: Collect 5ml of blood in vacutainer observing strict biosafety precautions. Keep in upright position to prevent haemolysis. Transport to the laboratory with ice packs or frozen with dry ice 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 Precautions (IPC) i.e. standard plus contact precautions. Use additional precautions, (droplet/aerosol) in case of any extensive contact/ procedure.
- Only designated medical / para-medical staff and attendants should attend the patient.
- All medical, para-medical staff and attendants should wear recommended Personal Protective Equipments (PPEs) before entering the isolation room and dispose it properly after use.
- All secretions of the patient and hospital clothing in use of the patient and attendants should be treated as infectious and where possible, should be autoclaved before incinerating.
- Every effort should be made to avoid spills, pricks, injury and accidents during the management of patients. Needles should not be re-capped but discarded in proper safety disposal box.
- All used material e.g. syringes, gloves, cannula, tubing etc, should be collected in autoclave-able bag and autoclaved before incinerating.
- All re-useable instruments should be de-contaminated and autoclaved before re-use.
- All surfaces should be decontaminated with liquid bleach.
- After the patient is discharged, room surfaces should be wiped down with liquid bleach to kill the virus and the room should be fumigated if risk of tick infestation⁽¹²⁾.

Treatment

General supportive therapy is the mainstay of patient management in CCHF. 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 in the first 6 days of illness. Oral Ribavirin: 30 mg/kg as loading dose, followed by 16 mg/kg every 6 hours for 4 days and then 8 mg/kg every 8 hours for 3 days.

Prophylaxis Protocol

- The efficacy for post exposure Ribavirin in the management of hospital-associated CCHF, remain 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 (eg, needle stick injury, mucous membrane contamination, emergency resuscitative contact, or prolonged intimate exposure during transport) after baseline blood tests.
- Household or other contacts of the case who may have been exposed to infected ticks or animals, or who recall indirect contact with case

body fluids should be monitored for 14 days from the date of last contact with the patient or other source of infection by taking the temperature twice daily. If the patient develops temperature of 38.5°C or greater, headache and muscle pains, he/she would be considered a probable case and should be admitted to hospital and started on Ribavirin treatment as mentioned above⁽¹²⁾.

Preventive measures & vaccination

- Educate public about the mode of transmission and about the means for 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 fall)
 - Regular examination of clothing and skin for ticks, and their removal (without crushing them)
 - Wearing light-coloured 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 tissue or blood, may be taken by persons who work with livestock or other animals.
- For tick control animal dipping/spraying in an insecticide solution. Injectable insecticide i.e. Ivermectin is also recommended
- Butchers should wear gloves and other protective clothing to prevent skin contact with freshly slaughtered meat, blood and other tissues.
- Meat should drain 30 minutes, before distribution to public.
- Hospitals in endemic areas should ensure universal precautions in OPD, Emergency Rooms, ensure injection safety measures and maintain stock of Ribavirin with PPEs.
- Bio-safety is the key element to avoid nosocomial infection. Patients with suspected or confirmed CCHF 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 CCHF patient, family should be informed to follow safe burial practices.
- Exposed house wives, family and contacts - those with high risk exposures (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⁾.

Guidlines Link:

<http://nih.org.pk/files/Guidelines/CCHF%20guidelines%20September%202016.pdf>

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CHIKUNGUNYA

Introduction: Chikungunya is a mosquito-borne viral disease. Its first case was report in southern Tanzania in 1952. The name "Chikungunya" derives from a word in the Kimakonde language, meaning "to become contorted", and describes the stooped appearance of sufferers. Initially a cluster of cases reported from Malir area of Karachi in 2017 followed by cases from other areas of Gawadar and Turbat. Travel associated cases reported from Islamabad and Rawalpindi recently⁽¹⁾.

Clinical Picture: Fever, arthralgia, myalgia, headache, nausea, fatigue and rash. Serious complications are not common with occasional cases of ocular, neurological and cardiovascular complications. There are rare reports of spontaneous abortions and mother-to-child transmission in perinatal period⁽¹⁾.

Infectious Agent: Chikungunya belongs to an *alpha virus* genus *Togaviridae* family, and is a heat-sensitive RNA virus⁽¹⁾.

Reservoir: Nonhuman and human primates are likely the main reservoirs⁽²⁾.

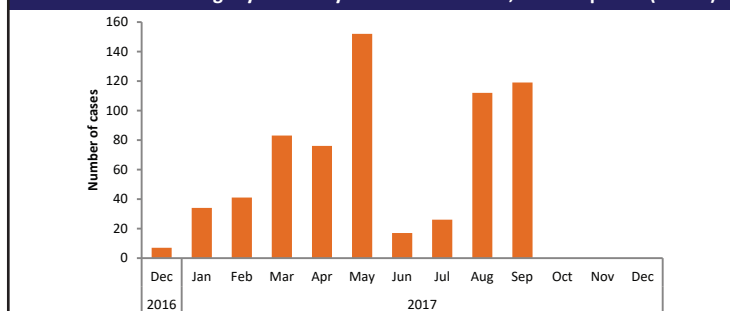
Mode of transmission: Transmit through bite of infected female *Aedes aegypti* and *Aedes albopictus* mosquitoes⁽¹⁾.

Incubation period: Onset of illness occurs usually between 4 and 8 days but can range from 2 to 12 days⁽³⁾.

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

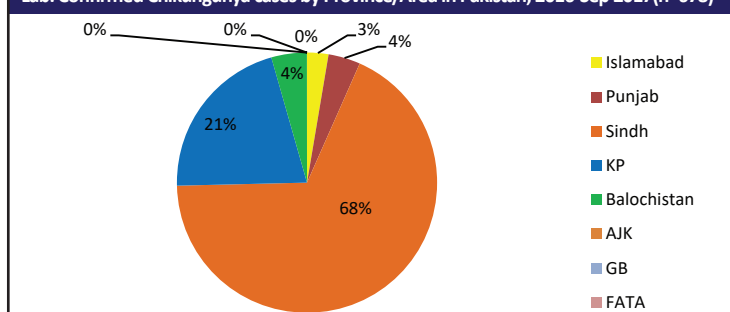
Seasonality: Chikungunya fever epidemics display secular, cyclical, and seasonal trends⁽⁵⁾.

Lab. Confirmed Chikungunya cases by Month in Pakistan, 2016-Sep 2017(n=678)⁽⁶⁾



Geographic Distribution in Pakistan: During Dec-2016 to date maximum cases (90%) were reported from Sindh, the most affected province in Pakistan.

Lab. Confirmed Chikungunya cases by Province/Area in Pakistan, 2016-Sep 2017(n=678)⁽⁶⁾



Case Definitions:

Suspected Case: Any person with an acute onset of fever >102°F and severe arthralgia/arthritis not explained by other medical conditions⁽⁷⁾.

Probable Case: Any suspected case residing or visited endemic areas within 15 days prior to the development of symptoms⁽⁷⁾.

Confirmed case: Suspected/ probable case confirmed by any of the following laboratory tests:

- Molecular detection using Real-time polymerase chain reaction (RT-PCR) test within one week after onset of illness
- Serological detection by IgM ELISA after 4 days of the onset of illness
- Dengue cases must be ruled out by laboratory testing before referral⁽⁷⁾.

Specimen Collection and Transportation: Collect 3-5 ml venous blood/serum of any suspected patient in sterile venoject tubes. Tight and seal it with full biosafety precautions. Label and pack it properly in triple packing with ice packs and transport to lab along-with complete history form⁽⁸⁾. Transport the sample to the Virology Department of PHLD at National Institute of Health, Islamabad.

Case Management: There is no specific antiviral drug for chikungunya. It is self limiting disease and treatment is directed primarily at relieving the symptoms, including the joint pain using anti-pyretics, optimal analgesics and fluids⁽⁹⁾.

Preventive measures & vaccination

- No vaccination available
- **Minimizing vector population:** Intensifying efforts to reduce larval habitats in and around the houses
- **Minimizing vector-patient contact:**
 - Using bed-nets (preferably permethrin-impregnated nets)
 - Wearing full-sleeved clothes to cover extremities
 - Using Wire-mesh/ nets on doors and windows⁽¹⁰⁾

Guidelines Link:

<http://www.nih.org.pk/files/Advisory%20for%20the%20Prevention%20and%20Control%20of%20Chikungunya%20Viral%20Infection,%202017.pdf>

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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 reported in 1994, but a sudden rise in cases and the

annual epidemic trend first occurred in Karachi in November 2005⁽²⁾.

Clinical Picture:

Dengue Fever: Dengue is defined by fever (for >3 days and <10 days) 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 and Leukopenia.

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

OR

Severe dengue is defined as dengue with any one or more of the following scenarios or dengue shock syndrome:

- Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress
- Severe bleeding
- Vital organs involvement⁽³⁾

The disease may develop into the life-threatening dengue haemorrhagic fever (DHF), sometimes progressing into dengue shock syndrome (DSS)⁽⁴⁾.

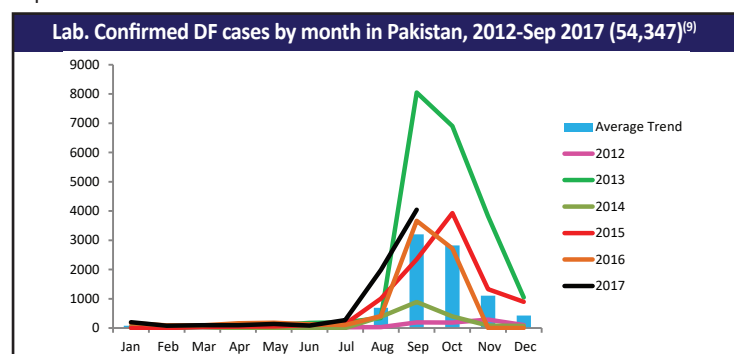
Infectious Agent: Belonging to *Flavivirus group*; Four different Dengue serotypes are known: DEN1, DEN2, DEN3, and DEN4⁽⁵⁾.

Mode of transmission: Bite of infected mosquitoes, *Aedes aegypti* and *Aedes albopictus*⁽⁶⁾.

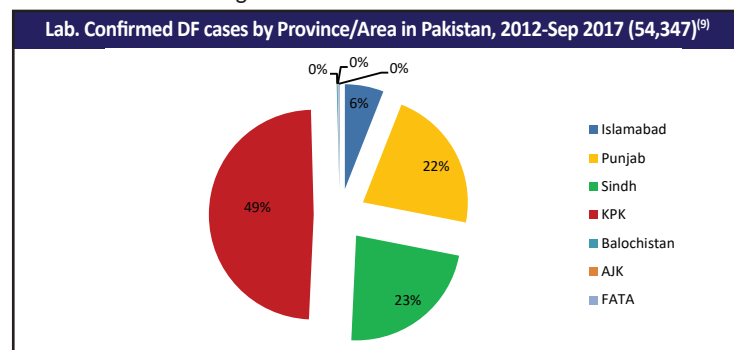
Incubation period: 3-14 days (average 4-7 days) after the infective bite⁽⁷⁾

Infectivity: 2-7 days⁽⁷⁾.

Seasonality: Cases increased during and after rainy seasons as compared to winter and summer. Hot, humid and rainy seasons remained significant predictors of dengue incidence in Pakistan. Peak of cases occurs during September to October⁽⁸⁾.



Geographical distribution: During 2012-2017, KPK remained most affected area with Dengue Fever in Pakistan.



Alert Threshold: Dengue Fever

Cluster of 3 suspected cases with at least one confirmed⁽¹⁰⁾.

Alert Threshold; Dengue Haemorrhagic Fever:

One probable case is an alert and requires an immediate investigation to assess differential diagnosis with other Viral Hemorrhagic Fevers (VHFs).

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 with an epidemiologic linkage⁽¹¹⁾.

Probable Case: A clinically compatible case of dengue fever, or dengue hemorrhagic fever with 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 Methods:

Probable; Detection of IgM anti-DENV by validated immunoassay in a serum specimen.

Confirmatory:

- Detection of DENV nucleic acid in serum, plasma and blood by reverse transcriptase-polymerase chain reaction (PCR),
- Detection in serum or plasma of DENV Non Structural Protein 1 (NS1) antigen by a validated immunoassay⁽¹¹⁾

Timings

- **PCR:** Initial 4-5 days of onset of illness.
- **NS1:** one day post onset of symptoms (DPO) up to 18 DPO
- **Serology:**
 - IgM antibodies are detectable after 4th day of onset of illness & may remain elevated up to 2-3 month after illness.
 - IgG is used for the detection of past dengue infection and usually can be detected during 2nd week of illness (detectable up to an year or more)⁽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 largely supportive, as follows:

- Take rest and extra amount of fluids
- Paracetamol 10 mg/kg/dose in children and 500-1,000 mg/dose in adult. Maximum adult dose is 4 grams/day
- Do not give Aspirin or other NSAID like Ibuprofen.
- Oral rehydration therapy (ORT/ ORS) is recommended for patients with moderate dehydration
- Complete blood count (CBC/CP) with follow up is an important tool in management of suspected dengue patients
- Provide brochure for families about the "warning signs" together with other recommendation
- After febrile recovery, all dengue patients must be carefully observed for signs of shock for at least 24 hours.
- The patient who does not have any evidence of circulatory disturbance and who has been afebrile for > 24 hours does not need further observation and may be discharged⁽¹⁰⁾.

Protocol for management according to Phase of DHF

(1) Dengue Hemorrhagic Fever (DHF) Grade I and II.

As in DF, during the afebrile phase of DHF Grades I and II, the patient has the same symptoms as during the febrile phase. The clinical signs plus thrombocytopenia and hemoconcentration or rise in hematocrit are sufficient to establish a clinical diagnosis of DHF.

During this situation hospitalize the patient and treat accordingly

(2) DHF Grades III and IV (DSS):

- Common manifestations observed during the afebrile phase of DHF Grade III are circulatory failure manifested by rapid and weak pulse, narrowing of the pulse pressure characterized by low systolic pressure relative to diastolic pressure e.g. 90/80 mm of Hg (this is usually due to plasma leakage) or hypotension (possibly due to bleeding), and the presence of cold clammy skin and restlessness or lethargy.
- Immediately shift the patient to Intensive Care Unit (ICU) and treat accordingly.
- The mortality is up to 30% without treatment but less than 1% with adequate treatment by experienced physician in dedicated facility⁽¹⁰⁾.

Preventive measures:

- Community survey to determine density of vector mosquitoes
- Identify and destroy mosquito larval habitats and breeding sites
- Indoor residual spray in urban and peri-urban high-risk areas at least one month before transmission period in case of outbreak.
- Conduct community mobilization through schools, religious leaders, to promote:
 - Source Reduction: Proper solid waste disposal and removing whatever practicable, water from tyers and containers.
 - Protection against day biting mosquitoes including use of screening, protective clothing and repellents.
 - Community based environmental management and health education campaigns⁽¹⁰⁾.

Vaccination: In late 2015 and early 2016, the first dengue vaccine, Dengvaxia (CYD-TDV) was registered in several countries for use in individuals 9-45 years of age living in endemic areas⁽¹²⁾. WHO recommends that countries should consider introduction of the dengue vaccine CYD-TDV only in geographic settings (national or subnational) where epidemiological data indicate a high burden of disease⁽¹³⁾.

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DIPHTHERIA

Introduction: An acute, toxin-mediated Vaccine Preventable (VPD) upper respiratory illness that affects the throat and sometimes tonsils. Diphtheria causes a thick covering in the back of the throat and can involve almost any mucous membrane. Classification based on site of disease are anterior nasal, pharyngeal and tonsillar, laryngeal, cutaneous, ocular and genital⁽¹⁾.

Clinical Picture: Sore throat, low 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 *belfant*⁽¹⁾.

Reservoir:

Humans are the reservoir for *C. diphtheriae* and are usually asymptomatic⁽²⁾

Mode of Transmission:

Contact (usually directly, rarely indirectly) with respiratory droplets of a case or carrier; or rarely through food stuffs (raw milk has served as a vehicle)⁽²⁾.

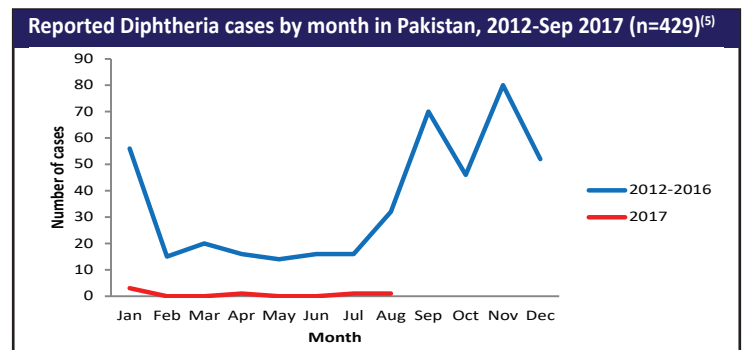
Incubation Period:

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 organisms for 6 months or more⁽²⁾.

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



Alert Threshold: One probable case is an alert⁽³⁾

Outbreak Threshold: One lab Confirmed case is an outbreak⁽³⁾

Case Definition:

Suspected Case: Any person who meets the clinical case definition for respiratory diphtheria⁽³⁾.

Probable Case: Any person who meets the clinical case definition for respiratory diphtheria and a visible adherent "membrane" on the tonsils, pharynx and/or nose and without epidemiological linkage and laboratory confirmation⁽³⁾.

Confirmed Case: Any confirmed case is a probable case that has been laboratory confirmed or linked epidemiologically to a laboratory confirmed case⁽³⁾.

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

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

Lab Confirmation:

- Conventional culture method
- PCR⁽¹⁾

Specimen Collection

- Collect nasopharyngeal and throat swabs by using polyester, rayon or nylon swabs.
- Pieces of pseudo-membrane may also be submitted in sterile saline (not formalin) for culture.
- Collect 5ml blood or serum (acute and convalescent phase) for serological diagnosis⁽¹⁾

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
- 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.
- Azithromycin or Clarithromycin is 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.

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:
 - 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⁾

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MALARIA

Introduction: A vector borne parasitic disease transmitted by female Anopheles mosquitoes species⁽¹⁾. An estimated 98% of Pakistan population (177 million) is at varying risk for malaria while population at high risk is around 29% (54.6 million). The highest endemic districts/agencies are located in bordering regions with Iran and Afghanistan. Every year >3.6 million malaria suspects are treated as malaria cases in health facilities without confirmatory tests⁽²⁾.

Clinical Picture: Fever, chills, sweats, headache, nausea and vomiting, body aches and general malaise⁽³⁾.

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 young children)
- Sweating stage (sweats, return to normal temperature, tiredness).

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*)⁽³⁾.

Complicated:

- Cerebral malaria, with abnormal behavior, impairment of

consciousness, seizures, coma, or other neurologic abnormalities
Severe anemia due to hemolysis

- Hemoglobinuria
- Acute respiratory distress syndrome (ARDS)
- Abnormalities in blood coagulation
- Low blood pressure caused by cardiovascular collapse
- Acute kidney failure
- Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites
- Metabolic acidosis
- Hypoglycemia⁽³⁾

Infectious Agent:

Plasmodium falciparum, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae* and *Plasmodium knowlesi* (rarely infect humans)⁽⁴⁾

Reservoir: Humans are the only known reservoir⁽⁴⁾

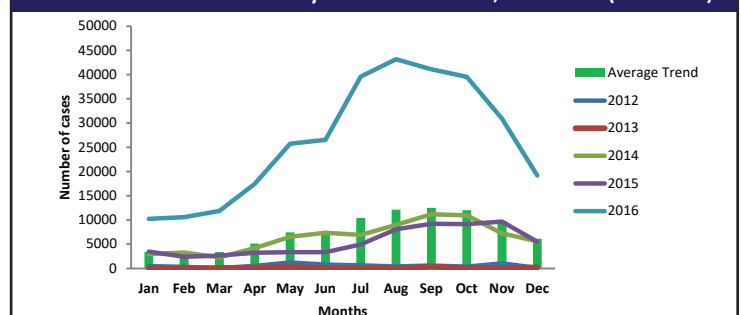
Mode of transmission: Bite of an infective female Anopheles mosquito and rarely through blood transfusion from infected person⁽⁴⁾

Incubation period: *P. falciparum* 9-14 days, *P. malariae* 18-40 days, *P. ovale* and *P. vivax* 12-18 days⁽⁴⁾.

Infectivity: Humans may infect mosquitoes as long as infective gametocytes are present in the blood. Anopheles mosquitoes remain infective for life⁽⁴⁾.

Seasonality: Peak occur during rainy season (August-September)⁽⁵⁾

Lab. confirmed Malaria cases by month in Pakistan, 2012-2016 (n=466108)⁽⁵⁾



Alert Threshold: Number of cases reaches two times the mean number of suspected cases of the previous 3 weeks for a given location⁽⁶⁾.

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⁽⁶⁾.

Case Definitions:

Suspected Case: A case with clinical manifestations of uncomplicated/complicated malaria⁽⁶⁾.

Probable Case: A suspected case with history of similar manifestations among other household members⁽⁶⁾

Confirmed Case: Clinical case with laboratory confirmation⁽⁶⁾

Lab confirmation:

- **Peripheral blood smear**
- **ICT** (Immunochromatography)
- **PCR** (Polymerase Chain reaction)
- **Serology**(Indirect immunofluorescence and ELISA)⁽⁶⁾:

Note: Not for diagnosis of current infection; screening of blood donors, previously treated with questionable diagnosis and testing the patient from endemic area having recurrent / chronic malaria infection

Specimen Collection & Transportation:

Collect 3-5ml blood in a tube with anticoagulant (EDTA). Sample may also be used to demonstrate parasite antigen. Transport the specimen at room temperature preventing sample spillage or damage to the tubes⁽⁶⁾

Case Management

Warning:

- Do not give primaquine to pregnant women and children <2 years of age and it is advisable to do a glucose-6-phosphate dehydrogenase (G6PD) test before giving this drug.
- Do not give undiluted chloroquine or quinine by I/M or I/V route, as it can cause sudden cardiac arrest, especially in children
- Do not give Sulfadoxine/ pyrimethamine to children <2 months of age or during first trimester of pregnancy

- Suspected/Probable case of severe Malaria and high risk groups should be treated immediately⁽⁶⁾

Treatment of uncomplicated Falciparum Malaria

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

The following ACTs are recommended:

- Artesunate plus sulfadoxine-pyrimethamine.
- Artemether plus lumefantrine,
- 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 pre-defined weight bands (5–14 kg: 1 tablet; 15–24 kg: 2 tablets; 25–34 kg: 3 tablets; and > 34 kg: 4 tablets)
- In case of pregnant women, during first trimester quinine plus clindamycin to be given for 7 days (artesunate plus clindamycin for 7 days) is indicated if this treatment fails⁽⁶⁾.

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 02 days.
- **Primaquin:** 0.25mg/kg body weight daily for 14 days treatment is prescribed for radical treatment of Vivax⁽⁷⁾.

Preventive measures

Travellers 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.
- Take antimalarial dugs (Chemoprophylaxis) when appropriate, to prevent infection from developing into clinical disease.
- Immediately seek Diagnosis and treatment if a fever develops 1 week or more after entering an area where there is a malaria risk and up to 3 months (or, rarely, later) after departure from a risk area⁽⁸⁾.

a) Personal protection

- Wear long sleeves and trousers outside the houses in the evening. Use repellent creams and sprays. Avoidance of 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⁽⁶⁾

c) Chemoprophylaxis Malaria control Program

Recommended chemoprophylaxis: Atovaquone-proguanil, Doxycycline or Mefloquine⁽⁸⁾

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MEASLES (RUBEOLA)

Introduction: Measles is a highly contagious viral disease mostly affecting children caused by *Paramyxoviridae*, genus *Morbillivirus*. Despite high community vaccination coverage, measles outbreaks can occur among under- vaccinated children and remains an important cause of death among young children globally. Its virus spreads via droplets from the nose, mouth or throat of the infected person⁽¹⁾. Immunity after measles infection is life long, although there are rare reports of measles re infection⁽²⁾.

Clinical Picture: Bloodshot eyes, cough, fever, rash, photophobia, muscle pain, conjunctivitis, runny nose, sore throat, tiny white spots inside the mouth (Koplik's spots) etc⁽³⁾. The occurrence of fever beyond the 3rd - 4th day of rash suggests a measles-associated complication. Measles can cause variety of clinical syndrome such as post measles infection(s) like pneumonia, lifelong brain damage/neurologic syndromes i.e. acute disseminated encephalomyelitis (ADEM) and Sub acute Sclerosing Pan Encephalitis (SSPE), deafness and death⁽⁴⁾. 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 diseases⁽⁵⁾.

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

Alert threshold: One suspected case is an alert⁽⁷⁾.

Outbreak threshold: Five or more clinical cases in a single location over a 30 day time with at least one lab confirmed case is an outbreak and requires investigation and response⁽⁷⁾.

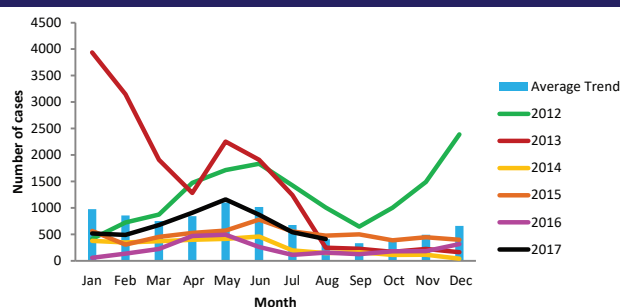
Case Definitions:

Suspected Case: A patient presenting with fever, generalized maculopapular rash with one of these: cough, coryza and conjunctivitis (3Cs)⁽⁸⁾.

Confirmed Case: A suspected case, which is laboratory-confirmed or linked epidemiologically to a laboratory- confirmed case (positive IgM antibodies)⁽⁸⁾.

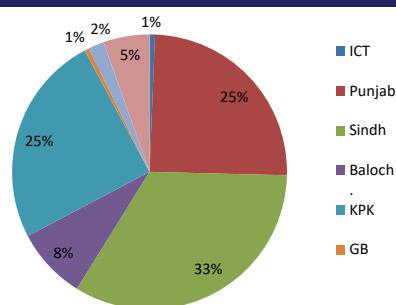
Seasonality: Peak incidence in Pakistan is usually during April and May.

Lab. confirmed Measles cases by month in Pakistan, 2012-Sep 2017 (48,998)⁽⁹⁾



Geographical Distribution in Pakistan: During 2012-2017, Sindh remained the most effected province in Pakistan.

Lab. confirmed Measles cases by Province/Area in Pakistan, 2012-Sep 2017 (48,998)⁽⁹⁾



Specimen Collection & Transportation: Collect throat swab for virus isolation and genotyping, very early in the rash phase and preserve in Viral Transport Medium (VTM). Five samples should be taken from fresh cases, less than five days from rash onset, in documented outbreaks. Collect 5ml blood for serology. Store serum at 4-8°C and not for more than 48 hours. Do not freeze the whole blood. Transport the specimens in triple packaged with complete request form along with the cold chain 4-8°C⁽⁸⁾.

Laboratory diagnosis: WHO recommends serum IgM as the standard confirmatory test for Measles diagnosis. Anti-measles IgM is detectable in 3 - 30 days after the appearance of the rashes. Anti-measles IgG is undetectable up to 7 days after rash onset and subsequently peaks about 14 days after the appearance of skin rashes⁽⁸⁾.

Management:

Uncomplicated cases: The treatment is mainly supportive includes antipyretics, fluids and antibiotics for only bacterial super infection(s). The WHO and UNICEF 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.

Complicated cases should be referred to the health facility after Vitamin- A supplementation⁽¹⁰⁾.

Prevention and Control Measures: Immunize population at risk as soon as possible. Priority is to immunize children of 6 months to 5 years old, regardless of vaccination status or history of disease. Children who are vaccinated against measles before 9 months of age must receive a 2nd measles vaccination. All children aged 6 months-5 years should also be administered prophylactic Vitamin- A supplementation⁽⁶⁾.

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PERTUSSIS (WHOOING COUGH)

Introduction: A toxin-mediated disease that can affect people of all ages, but can be very serious even deadly among infants. In 2015, the World Health Organization reported 142,512 pertussis cases globally, and estimated that there were 89,000 deaths. However, a recent publication modeling pertussis cases and deaths estimates that there were 24.1 million pertussis cases and 160,700 deaths in children younger than 5 years worldwide. Despite generally high coverage with childhood Pertussis vaccines, Pertussis is one of the leading causes of vaccine-preventable deaths worldwide⁽¹⁾.

Clinical Picture

The clinical course of the illness is divided into three stages: Catarrhal, Paroxysmal and Convalescent. Characterized by uncontrollable, violent coughing which often makes it hard to breathe. The disease usually starts with cold-like symptoms and maybe a mild cough or fever. Infants may have a symptom known as "apnea." Pneumonia is the most common complication in all age groups; seizures and encephalopathy generally occur only among young infants⁽²⁾.

Infectious agent: *Bordetella pertussis*⁽³⁾

Reservoir: Humans are the only known reservoir⁽³⁾

Mode of transmission

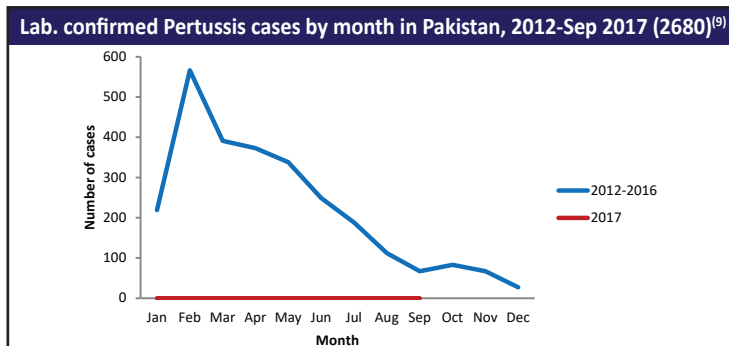
- By direct contact with discharges from respiratory mucous membranes of infected persons
- Airborne⁽³⁾

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⁾



Alert Threshold: One suspected case⁽⁴⁾

Outbreak threshold: Five suspected with one lab confirmed case⁽⁴⁾

Case Definition

Suspected: A person with a cough lasting at least 2 weeks with at least one of the symptoms i.e. Paroxysms/ fits of coughing, Inspiratory "whooping", Post-tussive vomiting and apnoea in infants with or without cyanosis⁽⁵⁾

Probable case: A clinical suspected case with an epidemiological linkage⁽⁵⁾

Confirmed case: Suspected/Probable case with laboratory confirmation⁽⁵⁾

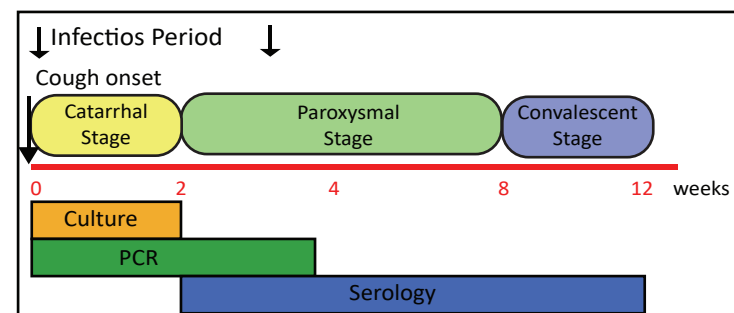
Lab confirmation:

- 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.
- Direct plating at bedside of the patients on a freshly prepared Bordet Gengou (BG) medium is the most reliable method for culturing Bordetella⁽⁶⁾.

Timing



Storage: 4-8°C⁽⁶⁾

Packaging: Triple packaging⁽⁶⁾

Transportation: Reagan Lowe (RL) transport medium⁽⁶⁾

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
- Azithromycin 500mg orally for 3 days OR Clarithromycin

500mg orally twice daily for 7 days

- 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⁽⁷⁾.

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⁽⁸⁾.

Vaccination during pregnancies

- It is important for women to get the whooping cough vaccine during 27th week through 36th week of pregnancy⁽⁸⁾.
- 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⁽⁸⁾.

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POLIOMYELITIS

Introduction: Potentially fatal viral infectious disease that can affect nerves and can lead to partial or full paralysis⁽¹⁾. It is an infection with an Enterovirus subgroup, family *Picornaviridae*, having three serotypes P1, P2 and P3, each capable of causing paralysis and infection with one does not confer protection against the other two strains⁽²⁾. Humans are the only known reservoir and the disease is transmitted person-to-person mostly through the Orofecal route^[1]. Cases are most infectious from 7-10 days before and after paralysis onset⁽³⁾. There are three basic patterns of polio infection: sub clinical infections, non-paralytic, and paralytic. Clinical poliomyelitis affects the CNS and is divided into non paralytic and paralytic forms⁽⁴⁾.

Lab. confirmed Polio cases by Province/Area in Pakistan, 2012- Sep 2017

Area/Provinces	2012	2013	2014	2015	2016	2017
Punjab	2	7	5	2	0	1
Sindh	4	10	30	12	4	1
KPK	27	11	68	17	7	1
FATA	20	65	179	16	2	0
Balochistan	4	0	25	7	1	1
GB	1	0	0	0	0	1
AJK	0	0	0	0	0	0
Total	58	93	306	54	14	05

There is no cure, but there are safe and effective vaccines. The strategy to eradicate polio is therefore based on preventing infection by immunizing every child until transmission stops and the world is polio-free. Global public health efforts are ongoing to eradicate polio by immunizing every child and focusing on pockets of missed children until transmission stops and the world is polio-free⁽⁵⁾. Polio was declared a Public Health Emergency of International Concern (PHEIC) by WHO on 5th May 2014⁽⁶⁾.

Government of Pakistan has also declared Polio as an Emergency Program. The year 2017 showed the lowest ever annual number of polio cases in the country but poliovirus continues to be isolated through environmental surveillance over a significant geographical range⁽⁷⁾.

Incubation Period: 7 -14 days for paralytic cases (range 3 - 35 days)⁽⁸⁾.

Seasonality: The ability of the polio virus to infect children increases in high temperature due to which most of the cases are reported from May to September. The period is called the High Transmission Season (HTS). In low temperature, from October to April, the virus remains less active⁽⁹⁾.

Alert Threshold: One case is an alert requires an immediate notification and sample for confirmation⁽¹⁰⁾.

Outbreak threshold: one lab confirmed case is an outbreak⁽¹⁰⁾.

Case Definitions:

Suspected Case: Acute flaccid paralysis (AFP) in a child aged <15 years, including Guillain-Barré Syndrome; OR Any paralytic illness in a person of any age when polio is suspected⁽¹¹⁾.

Polio-compatible AFP: Clinically compatible with poliomyelitis, but without adequate virological investigation⁽¹¹⁾.

Confirmed AFP: Laboratory-confirmed wild poliovirus in stool sample⁽¹¹⁾.

Discarded case: Discarded case is an AFP case, which is neither diagnosed as confirmed nor compatible with a polio case definition⁽¹¹⁾.

Specimen Collection & Transportation:

Collect 2 stool samples about 8 grams each (about the size of the tip of thumb) 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⁽¹²⁾.

Prevention and Control:

Four pillars of polio eradication

1. Achieving a high level of coverage with at least 4 doses of the oral poliovirus vaccine (OPV) and one dose of IPV
2. Providing supplementary doses of OPV to all children <5 years old during NIDs
3. 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 surveillance studies⁽¹³⁾.

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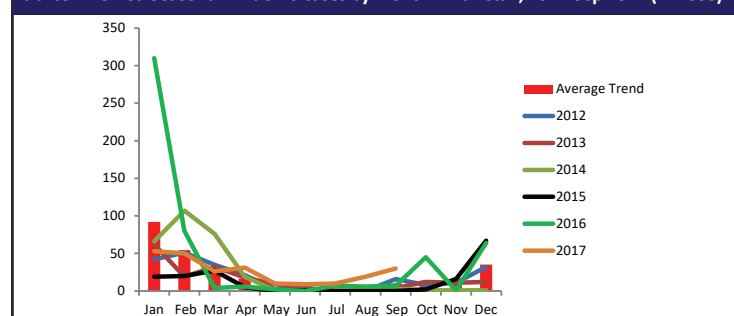
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SEASONAL INFLUENZA –A (H1N1,H5N1)

Influenza is a contagious respiratory illness caused by influenza A and B, RNA viruses and may cause mild to severe illness; at times leading to death. Older people, young children and people with certain health conditions are at high risk for serious complications. A novel influenza-A H1N1 virus emerging in 2009 caused global influenza pandemic with low mortality rate (0.45%)⁽¹⁾. The virus caused serious disease in children and certain risk groups such as diabetes, obesity and pregnant women. During 2010, WHO announced the end of the pandemic period, but recommended clinicians to remain vigilant and treat all suspected cases of H1N1 appropriately⁽²⁾. 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 H1N1 appropriately⁽³⁾.

Lab. confirmed Seasonal Influenza cases by month in Pakistan, 2012-Sep 2017 (n=1608)⁽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 2 or more weeks. Most people recover from fever and other symptoms within a week without requiring medical attention. But influenza can cause severe illness or death especially in people at high risk⁽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 $\geq 38^{\circ}\text{C}$ 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 $\geq 38^{\circ}\text{C}$ and cough with onset within the last 10 days AND requires hospitalization⁽⁵⁾.

Sample Collection & Transportation: Respiratory specimens including throat or nasal/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. Specimens for influenza virus isolation should not be stored or transported in dry ice unless they are sealed, taped with triple packaging as dry ice can rapidly inactivate the virus⁽⁶⁾.

Management:

- The symptoms in mild illness are relieved with warm fluids and 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. Anti microbial agents are not effective against viruses, treatment with antibiotics for complications such as bronchitis and pneumonia may be necessary⁽⁷⁾.
- Currently, most seasonal Influenza A/H3N2 and A/H1N1Pdm09 viruses are sensitive to Neuraminidase Inhibitors, Oseltamivir (Tamiflu) and Zanamivir. Anti-viral treatment should be initiated within the first 2 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, such as pregnant women, young children, people 65 and older and people with certain chronic health conditions. Patients not considered being at higher risk of developing severe or complicated illness need not be treated with anti-viral agents⁽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 Control Measures: Annual winter vaccination (seasonal anti-influenza vaccine) is recommended for health care workers, pregnant women, young children and immuno-compromised patients with pulmonary, cardiac or renal disease. 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.

Procedures should be developed to ensure proper implementation of administrative controls, environmental controls, and use of personal protective equipments (PPEs). Administrative policies that address adequate staffing and supplies, training of staff, education of patients and visitors, and a strategy for risk communication are particularly needed⁽⁸⁾.

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AVIAN/HUMAN INFLUENZA –A (H5N1)

Avian (bird) flu, caused by influenza-A viruses that occur naturally amongst birds. Human infections are primarily acquired through direct contact with infected animals or contaminated environments, but do not result in efficient transmission of these viruses between people though Human infections carry high mortality rates⁽¹⁾. Since 2003 to September 2017, a total of 860 confirmed cases of human infection from subtype influenza-A H5N1 infection have been confirmed globally, including 454 deaths (CFR 53.1%)⁽²⁾. Since reporting of 3 cases and one death in 2007, there has been no reported human H5N1 infection in Pakistan⁽³⁾.

Case Definition

Possible Case: Any person presenting with severe pneumonia, characterized by fever >38 °C AND one or more of these cough, sore throat, shortness of breath AND who can answer “Yes” to any of the following questions: In the 7 days before first symptoms started

- Have you been in contact with a person who was suspected or confirmed case of Influenza-A H5N1 during the infectious period?
- Have you been in contact with live or dead birds, pigeons including chickens, ducks, fancy/backyard birds or crows?
- Have you lived in or have you visited a place where poultry deaths have occurred in the last 2 weeks?
- Have you worked in a laboratory where there is processing of samples from persons or animals that are suspected of having Highly Pathogenic Avian Influenza (HPAI) infection⁽⁴⁾.

Probable Case: Any possible case AND limited laboratory evidence for influenza-A H5N1 such as IFA + using HF5 monoclonal antibodies OR no other disease⁽⁴⁾.

Confirmed Case: Confirmed case of influenza-A H5N1 infection is any probable case with detection of viral nucleic acid by PCR⁽⁴⁾.

Prevention and Control Measures: The primary risk factor for human infection by H5N1 appears to be direct or indirect exposure to infected live or dead poultry or contaminated environments. Humans become infected with avian influenza through close contact with live, sick or dead infected birds, e.g. breathing in particles from their droppings, plucking or handling poultry, playing in an area where carcasses were buried. The public may accordingly be educated on the following preventive measures: a) Report sick or dying poultry to local authorities b) Wash hands after contact with poultry or other birds c) Cook poultry and eggs thoroughly before eating. If you must go to a bazaar where live poultry is sold, protect your eyes, nose and mouth from dust⁽⁵⁾.

Treatment: Suspected H5N1 case should be hospitalized in isolation strictly observing the recommended precautions. Treatment with antiviral medication such as Oseltamivir or Zanamivir should be started as soon as possible, ideally within 48 hours following symptoms onset, to maximize its therapeutic benefits. However, given the significant mortality associated with H5N1 infection and evidence of prolonged viral replication in this disease, administration of the drug should also be considered in patients presenting later in the course of illness⁽⁶⁾.

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National Potential Public Health Events

Primary Amebic Meningoencephalitis (PAM)

Introduction: Since detection of first case in Australia during 1965; about 300 cases have so far been reported from 16 countries. In Pakistan since 2012, a total of 42 fatal cases are reported from different tertiary care hospitals of Karachi (1 fatal case during 2015) and during 2017 three cases have been reported from Karachi. Primary Amebic Meningoencephalitis (PAM) is caused by parasite *Naegleria fowleri*; a rare, with about 99% CFR. *Naegleria fowleri* "brain-eating amoeba" is a unicellular, free-living microscopic & grows best at higher temp. Up to 46°C & is naturally found in warm freshwater environments feeding on bacteria and other microbes. Transmission occurs primarily through inhalation of infested water during swimming or putting contaminated water in to the nose during ablution. Symptoms start 1-9 days (median 5 days) after nasal exposure to *Naegleria*-containing water. People may die 1-18 days (median 5 days) after symptoms begin. Transmission does not occur by drinking contaminated water or by swimming in sea. Initial symptoms of PAM usually start from 1-7 days after infection which may include headache, fever, nausea or vomiting.

Clinical manifestations are similar to bacterial meningitis (severe frontal headache, fever, vomiting, meningeal signs, stiff neck, seizures and focal neurologic deficits) that increases chances of misdiagnoses. After the start of symptoms, the disease progresses rapidly and while death may occur in 1-12 days of illness. Because of rapid progression, the diagnosis is usually made after death.

Control: Both trophozoites and cysts forms are sensitive to adequate levels of chlorination. The municipality public health authorities therefore, must ensure that adequate levels of disinfectants like chlorine are maintained in the supplied tap water along with strict monitoring arrangements. Any of the suspected cases should immediately be reported to health authorities. Awareness and education in the affected areas must also be undertaken to educate people on requisite preventive measures.

Prevention:

- One cannot get infected from drinking water contaminated with *Naegleria*. He or she could only be infected when contaminated water goes up into the nose.
- Potentially contaminated water should not be used for any form of nasal irrigation or nasal lavage
- Ensure swimming pools and spas are adequately chlorinated and well maintained

Advisory link: Advisory is available on NIH website at:

[http://nih.org.pk/files/Newsletter/Advisory%20on%20Detection%20Prevention%20and%20Control%20of%20Amebic%20Meningoencephalitis%20\(PAM\)%202016.pdf](http://nih.org.pk/files/Newsletter/Advisory%20on%20Detection%20Prevention%20and%20Control%20of%20Amebic%20Meningoencephalitis%20(PAM)%202016.pdf)

International Potential Public Health Events

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 and 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 is not spread through the air or by food or water. The virus can spread through direct contact with the bodily fluids of an infected person, or with contaminated objects. No specific drug available however early supportive clinical treatment and management are essential and can improve the chances of recovery. The outbreak of Ebola virus disease began in West Africa mainly affecting Guinea, Liberia and Sierra Leone in December 2013 and declared as Public Health Emergency of International Concern (PHEIC) by WHO. The outbreak has now ended but small additional outbreaks or sporadic cases remain a risk an EVD outbreak has been notified to WHO in Congo.

Public Health Measures: Ensure preparedness, contact tracing, raising awareness and sensitizing healthcare workers, supporting them with resources, information and communication to travelers and surveillance. Ensure implementation of infection control measures, Isolation rooms with dedicated bathroom, availability of personal protective equipment and trained Personnel.

Guidelines link: <http://nih.org.pk/files/Guidelines/Recommended%20Standard.pdf>

Zika Virus Disease (ZVD)

Introduction: Zika virus disease (Zika) is a disease caused by the Zika virus, which spreads to people primarily through the bite of an infected *Aedes* species mosquito. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes). The illness is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. WHO declared ZVD as Public Health Emergency of International Concern (PHEIC) on 01 February 2016 and in November 2016, the Zika declaration as no more a public health emergency of international concern. WHO updated its Interim guidance regarding the possible sexual transmission and more common than previously assumed and advised to couples to adopt safer sex practices or consider abstinence for at least 8 weeks upon return from endemic areas and in case of disease, men should use condoms or consider abstinence for at least 6 months.

Diagnosis: Preliminary diagnosis is based on the patient's clinical features, places and dates of travel, and activities. Laboratory diagnosis by testing serum or plasma to detect virus, viral nucleic acid, or virus-specific immunoglobulin-M and neutralizing antibodies. Patients with suspected Zika virus infections also should be evaluated for possible dengue, Yellow fever or Chikungunya virus infection.

Treatment: No specific antiviral treatment is available. Treatment is generally supportive. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out.

Middle East Respiratory Syndrome Coronavirus (MERS - CoV)

Introduction: First reported case was from Saudi Arabia, September 2012. So far, all cases of MERS have been linked through travel to or residence in countries in and near the Arabian Peninsula. MERS is viral respiratory illness caused by corona virus from the same family as 2003 outbreak of Severe Acute Respiratory Syndrome (SARS). The source of the virus remains unknown but virological studies point towards dromedary camels. MERS-CoV has spread from ill people to others through close contact, such as caring for or living with an infected person. Incubation period is 1-2 weeks. The clinical presentation of MERS ranges from asymptomatic to very severe pneumonia with acute respiratory distress syndrome, septic shock and multi-organ failure resulting in death. The clinical course is more severe in immune-compromised patients and persons with underlying chronic co-morbidities. Human-to-human transmission has occurred mainly in health care settings. Since April 2012, a total of 2081 cases of MERS, including 722 deaths have been reported by health authorities worldwide (27 countries).

Sample Collection and Transportation: Collection of lower respiratory specimens (sputum or bronchoalveolar lavage) is strongly recommended however, nasopharyngeal swab, oropharyngeal swab, sputum, serum, and stool/rectal swab may be collected. Wear personal protective equipment and adhere to infection control precautions. and Notify to district health departments if suspect MERS-CoV infection in a person.

Treatment and Prevention: No specific treatment/drugs and vaccines are currently available. Treatment is mainly supportive and based on the clinical condition of the patient. Preventive measures include standard plus aerosol, droplet precautions and practicing good hand hygiene.

Travel Recommendations: There are currently no travel restrictions in place however travelers are advised to avoid unnecessary contact with camels, consumption of raw milk and should practice good general hygiene especially regular hand washing. Returning travelers must report to health department in case of severe respiratory symptoms.

Guidelines link: <http://nih.org.pk/files/Newsletter/Advisory%20on%20MERS-CoV%20during%20upcoming%20Umrah%20Hajj%202016.pdf>

Influenza-A(H7N9)

Introduction: In February 2017, a new A (H7N9) virus - indicating high pathogenicity in poultry - was detected in three patients connected to Guangdong, China, as well as in environmental and poultry samples. This new virus has been detected in only three out of 460 human cases confirmed in the current epidemic wave and in one province only. It is unclear at the moment if the newly-emerged, highly-pathogenic avian influenza (HPAI) virus A (H7N9) will replace the low pathogenic virus or if both will co-circulate in the bird population. This is an important development to be monitored; however, there is no evidence of sustained human-to-human transmission. To date, there is no evidence of increased transmissibility to humans or sustainable human-to-human transmission.

Since the notification of novel re-assortant influenza A (H7N9) virus on 31 March 2013, 1589 laboratory confirmed cases of human infection with avian influenza A (H7N9) virus have been reported as of Sep 2017. This is the fifth winter season in the northern hemisphere with human cases caused by A (H7N9) infections. During this wave, the number of human cases has been higher than in previous waves and accounts for 37% of the human cases reported so far. This is most likely due to greater environmental contamination in live bird markets and increased circulation of the virus among poultry. The continued transmission of A (H7N9) to humans in China poses the risk that sporadic imported cases may be detected in other countries. The following options for prevention and control of the infection should be considered:

- People travelling to China should avoid direct exposure to poultry and refrain from visiting live poultry markets or backyard farms
- Travelers who have visited affected areas and develop respiratory symptoms and fever upon their return should consult a physician and mention their recent travel history to enable early diagnosis and treatment.

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