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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 about 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 2013 to 2018 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 Extensively drug resistant typhoid has been included. Zika Virus, Ebola Virus disease, Middle East Respiratory Syndrome Corona virus (MERS CoV) infection, and Yellow Fever have been shared as International Potential Public Health Events.

CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF)

Introduction: A tick-borne 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 (Principle 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, 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 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 Hemorrhagic Fever (CCHF) Virus belongs to Bunyaviridae family [1].

Reservoir: Hyalomma tick, domestic animals, such as cattle, goats, sheep, rodents such as hedgehog, rats, hares and birds are generally resistant with the 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

Outb	Alerts				
Crimean Cor					
C hikungunya					
Dengue Feve					
D iphtheria					
Gastroenteri					
L eishmanias					
M alaria					
Measeles					
Meningococ					
P ertussis					
Poliomyelitis					
Seasonal Inf					
Typhoid Feve					
Viral Hepatit					
	High Alert- peak occourrence in the Winter season				
	Medium Alert - cases will be encountered and any show up as an outbreak				

 5-6 days after exposure to infected blood or tissues with a maximum of 13 days [8].

Seasonality: Surge 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 months in Pakistan, 2013-August 2018 (n=391) [10]



Geographical Distribution in Pakistan: Since the diagnosis of first human case of CCHF in 1976, the sporadic cases have continued to occur all over Pakistan and predominantly in Baluchistan [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 [1] Case Definitions:

Suspected Case: Any person with sudden onset of fever over 38.5oC for more than 72 hours and less than 10 days, especially in CCHF endemic areas 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/mm [3], 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 ELISA [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: storage and transportation: Collect 3-5 ml of blood in vacutainer observing strict biosafety precautions: Keep in upright position to prevent haemolysis. Sample storage at 2-80C.Transport to the laboratory in triple package with ice packs or frozen with dry ice along with complete lab request form.

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, paramedical staff and attendants should attend the patient and limit unnecessary visits.
- All medical, paramedical staff and attendants should wear recommended Personal Protective Equipment (PPEs) before entering the isolation room and dispose the PPEs 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, clothing 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 and discarded in proper safety disposal box.
- All used material e.g. syringes, gloves, cannula, tubing etc. should be collected in autoclavable bag and autoclave before incineration.
- All re-useable instruments should be decontaminated (5% bleach solution) and autoclaved before reuse.
- All surfaces should be decontaminated with 5% bleach solution.
- After the patient is discharged, room surfaces should be wiped down with 5% bleach solution to kill the virus and the room should be fumigated if risk of tick infestation [12], [13]

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 [13]. 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 (e.g. 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 38.5oC 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-colored clothing covering legs and arms and using repellents on the skin.
- Other measures, such as wearing gloves or other protective clothing to prevent skin contact with infected 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 and emergency rooms. Ensure injection safety measures and maintain stock of Ribavirin and 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 positive patient, family should be advised to follow safe burial practices.
- 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].

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CHIKUNGUNYA

Introduction: Chikungunya is a mosquito-borne viral disease which was first reported from southern Tanzania in 1952. In Pakistan, cases were reported from different areas especially from Karachi and travel associated cases were reported from Islamabad and Rawalpindi [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: Non-human 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 4-8 days but can range from 2 to 12 days [3].

Communicability: CHIKV infections cause high level of viraemia, which typically lasts 4-6 days, but can persist for up to 12 days after the onset of illness [4].

Seasonality: Chikungunya virus can spread all year round. Warm humid weather and stagnant water breeds the mosquitoes that carry the virus, which is why an epidemic is most likely to occur during postmonsoon periods [5].



Geographic Distribution in Pakistan: From Dec-2016 to September 2018, Chikungunya cases are being reported from all over Pakistan and predominantly in Sindh [6].



Case Definitions:

Suspected Case: Any person with an acute onset of fever >102°F (38.50 C) 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:

- RT-PCR within one week after onset of illness
- Serological detection by IgM ELISA after 4 days of the onset of illness
- Four-fold rising of IgG titers in samples collected at least three weeks apart [7].

Specimen Collection and Transportation: Collect 3-5 ml venous blood/ serum of 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 laboratory along with complete history form [8]. Transport the sample to the Virology Department of PHLD at National Institute of Health, Islamabad if the diagnostic facility not available in the particular area.

Case Management: There is no specific antiviral drug for Chikungunya. It is a self-limiting disease and treatment is directed primarily at relieving the symptoms, including the joint pain by using anti-pyretic, optimal analgesics and rest [9].

Preventive measures & vaccination:

- No vaccine 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].

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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 rise in cases and the annual epidemic trend first occurred in Karachi in November 2005 [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).

Any warning sign for Dengue hemorrhagic fever i.e. abdominal pain, persistent vomiting, extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites), mucosal bleeding at any site, liver enlargement >2 centimeters and increasing hematocrit concurrent with rapid decrease in platelet count (a total white blood cell count of <50,000/mm3, Platelets <100,000)

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, excrement), 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

Severe Dengue defined as Dengue fever 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].

In 1-3% of cases, the disease develops into the life-threatening Dengue hemorrhagic fever (DHF), sometimes progressing into Dengue shock syndrome (DSS) [4].

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. Surge of cases occurred during September to October [8].



Geographical distribution: During 2013-2018, KP followed by Sindh and Punjab remained most affected areas with Dengue in Pakistan [9].



Alert threshold for Dengue fever: Cluster of 3 suspected cases with at least one confirmed [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 outbreak10.

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 infection11

Confirmed Case: A clinically compatible case of dengue fever, or Dengue hemorrhagic fever with confirmatory laboratory results11.

Lab confirmation: Probable; Detection of IgM anti-DENV by validated immunoassay in a serum specimen

Confirmatory:

- Detection of DENV nucleic acid in serum, plasma, blood by Reverse Transcriptase-Polymerase Chain Reaction (PCR),
- Detection in serum or plasma of DENV Non Structural Protein 1 (NS1) antigen by a validated immunoassay

Timings:

- 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
 - 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 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.
- Extra amounts of fluids 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.
- All Dengue patients must be carefully observed for signs of shock for at least 24 hours after recovery from fever.
- The patient who does not have any evidence of circulatory disturbance and who has been afebrile for > 24 hours does not need further observation and may be discharged [10].

Protocol for management according to Phases of DHF

a. Dengue hemorrhagic fever (DHF) Grades I and II:

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

b. DHF Grades III and IV (DSS):

- Common manifestations observed during the afebrile phase of DHF Grade III are circulatory failure manifested by rapid and weak pulse, narrowing of the pulse pressure characterized by high diastolic pressure relative to systolic pressure, e.g. 90/80 mm of Hg (this is usually due to plasma leakage) or hypotension (possibly due to bleeding), 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.
- Community mobilization should be conducted through schools, religious leaders, to promote health education campaigns.
- Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg-laying female mosquitoes.
- Protection against day biting mosquitoes including use of screening, protective clothing and repellents [10].

Vaccination: In late 2015 and early 2016, the first Dengue vaccine, Dengvaxia (CYD-TDV) was registered in several countries for use in Individuals aged 9-45 years 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 though 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:
 - a. 1stdose at the age of 6 weeks;
 - b. 2nd at 10 weeks;
 - c. 3rd at 14 weeks, a booster DTP at 18 months to 4 years.

If children or adults have not been immunized with three-dose series, children < 5 years should receive DT vaccine, and children \ge 5 years and adults should receive Td vaccine to complete a series of three doses [1]

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MEASLES

Introduction: Measles is a highly contagious viral disease mostly affecting children caused by measles virus of genus Morbillivirus which belongs to Paramyxoviridae family. Despite community vaccination coverage, Measles outbreaks can occur among undervaccinated children and remains an important cause of death among young children globally. The virus spreads via droplets from nose, mouth or throat of the infected person [1]. Women infected while pregnant are also at risk of severe complications and the pregnancy may end in miscarriage or preterm delivery. Immunity after measles infection is life long, although there are few reports of measles re infection. The case-fatality rate may be as high as 25% [2].

Clinical Picture: Cough, coryza, conjunctivitis, fever, rash, photophobia, muscle pain, sore throat, tiny white spots inside the mouth (Koplik's spots) etc. [3]. The occurrence of fever beyond the 3rd - 4th day of rash 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 days6.

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

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

Outbreak threshold: Five or more clinical cases in a single location over a 30 days 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 has been reported usually during April to May.



Geographical Distribution in Pakistan: During 2012-2018, Sindh remained the most effected province and has reported 33% (16365) followed by KPK 26% (12169) and Punjab 24% 10970 cases.



Specimen Collection & Transportation: Collect throat swab for virus isolation, 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 by maintaining cold chain at 4-8°C [8].

Laboratory diagnosis: WHO recommends ELISA method as the gold standard for measles diagnosis. Anti-measles IgM is detectable in 3 - 30 days after the appearance of rashes. Anti-measles IgG is undetectable up to 7 days after rash onset and subsequently peaks about 14 days after the appearance of skin rashes8.

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. Antibiotics should be prescribed to treat eye and ear infections and pneumonia complicated cases should be referred to the health facility after Vitamin- A supplementation10.

Prevention and Control Measures:

Immunize the population as soon as possible; which is at risk. 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 at 15 months. All children aged 6 months-5 years should also be administered prophylactic Vitamin- A supplementation6. **References:**

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PERTUSSIS (WHOOPING 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].



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-Sulfamethoxozole, 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: The word Polio (grey) and myelin (marrow, indicated spinal cord) are derived from the Greek. It is a potentially fatal viral infectious disease that can affect nerves and can lead to partial or full paralysis [1]. It is caused by Polio virus which belongs from subgroup Enterovirus and Picornaviridae family. Poliovirus have three

serotypes P1, P2 and P3 and each is capable of causing paralysis [2]. Humans are the only known reservoir and the disease is transmitted person to person mostly through the oro-fecal route [1]. Cases are most infectious from 7 to 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].

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 20146.

Government of Pakistan has also declared Polio as an Emergency Program as Pakistan is one of only three countries in the world with ongoing wild Polio virus transmission, alongside Afghanistan and Nigeria. The year 2018 showed the lowest ever annual number of Polio cases in the country but Polio virus continues to be isolated through environmental surveillance over a significant geographical range [7].

Province/Area wise distribution of Polio cases in Pakistan, October 2018

Province/Area	2012	2013	2014	2015	2016	2017	2018
Islamabad	0	0	0	0	0	0	0
Punjab	2	7	5	2	0	1	0
Sindh	4	10	30	12	4	2	1
КРК	27	11	68	17	7	1	2
Balochistan	4	0	25	7	1	3	3
GB	1	0	0	0	0	1	0
AJK	0	0	0	0	0	0	0
FATA	20	65	179	16	2	0	0
Total	58	93	307	54	14	8	6

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 and requires an immediate notification and sampling for confirmation [10].

Outbreak threshold: One lab confirmed case is an outbreak [10].

Case Definitions: This sensitive case definition will capture acute Poliomyelitis but also other diseases, including Guillain-Barre syndrome, transverse myelitis and traumatic neuritis, such that each case must be investigated carefully.

Suspected Case: Sudden onset of weakness and floppiness in a child aged <15 years, including Guillain-Barre Syndrome; OR Any paralytic illness in a person of any age whom Polio is suspected by a physician [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 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 [12]. **Prevention and Control:**

Four pillars of polio eradication

- Achieving a high level of coverage with at least 4 doses of the oral poliovirus vaccine (OPV) and one dose of IPV
- Providing supplementary doses of OPV to all children<5years old during NIDs and SNIDs
- Active and passive surveillance for all cases of acute flaccid paralysis

House-to-house OPV campaigns, targeting areas in which transmission of wild poliovirus persists, based on surveillance data [13].

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SEASONAL INFLUENZA - A (H1N1, H2N3)

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].

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

Lab Confirmed Seasonal Influenza H1N1 cases by month in Pakistan, 2012-Sep-2018 (n=2194) [3]



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°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°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. Antimicrobial 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 (seasonalanti-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 equipment (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].

Vaccination: Vaccination is the most effective way to prevent infection and severe outcomes caused by influenza viruses particularly in high risk groups. WHO recommends seasonal influenza vaccination for pregnant women (highest priority), children aged 6-59 months, elderly people, individuals with chronic medical conditions and health-care workers. WHO recommends trivalent/ quadrivalent seasonal vaccines for use during 2017-18 in northern hemisphere influenza season with the following composition:

- A. Quadrivalent Vaccine:
- an A/Michigan/45/2015 (H1N1) pdm09-like virus;
- an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;
- B. Trivalent vaccine:
- Containing two influenza B virus component of trivalent vaccines B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage
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AVIAN 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 OC 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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Potential National Public Health Events

SALMONELLA ENTERICA SEROVAR TYPHI (EXTENSIVELY DRUG RESISTANT STRAIN)

Introduction: Salmonella enterica serovar typhi causes typhoid fever, a life-threatening illness that affects more than 21 million people in the developing world. The bacterium is transmitted by contaminated water and food and tends to spread in areas with poor sanitation.

Antibiotic resistance is a major problem in Salmonella typhi. 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 Cephalosporins or Azithromycin have also been reported.

In Pakistan the first large-scale emergence and spread of a novel S. typhi clone harboring 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). From November 2016 to October 2018 there are more than 4000 confirmed XDR Typhoid cases have been reported from the Sindh region, primarily in the cities of Karachi and Hyderabad. Additionally, a single case of travel-associated XDR typhoid have been identified abroad as well.

Clinical manifestations: Patient presents with high grade fever (103 F to 104 F), Weakness, Stomach pains, headache, loss of appetite, in some cases, patients have a rash of flat, rose-colored spots. Blood complete picture and Blood/ stool/ urine cultures are performed to confirm the diagnosis of typhoid fever.

Preventive measures and control:

- Along with the appropriate treatment, preventive measures are urgently needed, including improved sanitation, food safety and vaccination.
- The antibiotic resistance strains have been treated with Azithromycin and Meropenem.
- Typbar-TCV vaccine, a trivalent conjugate vaccine that was recently prequalified by the World Health Organization is recommended. The vaccine has long-lasting immunity, requires only one dose, and can be given to children as young as 6 months.

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Potential International Public Health Events

Zika Virus

Introduction: A mosquito-borne Flavivirus, first identified in Uganda in 1947 in monkeys. It was later identified in humans during 1952 in Uganda and Tanzania. From the 1960s to 1980s, human infections were found across Africa and Asia, typically accompanied by mild illness. The first large outbreak was reported from the Island of Yap in 2007 [1]. In July 2015 Brazil reported an association of Zika virus infection with Guillain-Barré syndrome and microcephaly. Presently an sever outbreak has been occurred in Rajistan, India which has estimated suspected 125 cases 94 confirmed, including 22 pregnant women has been infected cases with Zika Virus as of October, 2018 [2].

Clinical manifestations: Approximately 80% of the infections remain asymptomatic. The disease is clinically classified as congenital and noncongenital. The incubation period of Zika virus disease is estimated to be 3–14 days.

Congenital: Affected infants usually born with birth defects like microcephaly and stillbirth.

Non-Congenital: The most common symptoms are Maculopapular rash, Fever, Arthralgia, Fatigue, Conjunctivitis, Myalgia and Headache. Guillain-Barre syndrome has also been reported in some cases [1]. Zika virus infection during pregnancy can cause infants to be born with microcephaly and other congenital malformations, known as congenital Zika syndrome. Further, infection with Zika virus is also associated with other complications of pregnancy including preterm birth and miscarriage. An increased risk of neurologic complications is associated with Zika virus infection in adults and children, including Guillain-Barré syndrome, neuropathy and myelitis [3].

Control: Government along with public should perform tasks to control larvae and adult mosquitoes and evaluate the effectiveness of actions taken. Steps should be taken to reduce mosquitoes around your area and prevent form mosquito bites.

Prevention: No vaccine available for the prevention from Zika virus infection [3]. Protection against mosquito bites during the day and early evening is a key measure. Special attention should be given to prevention of mosquito bites among pregnant women, women of reproductive age, and young children. Personal protection measures include wearing clothing (preferably light-coloured) that covers as much of the body as possible; using physical barriers such as window screens and closed doors and windows; and applying insect repellent to skin or clothing that contains DEET, or lcaridin according to the product label instructions.

Note: The Zika Birth Defects Surveillance is monitoring infants with birth defects that might be associated with Zika virus infection, regardless of their laboratory tests. Through this we recommend to monitor and collect information on infants with birth defects like microcephaly and other birth defects. Such information may please be shared with respective District Health Departments and NIH for further evaluation and investigations if needed.

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- 2. CNN. Zika spreads rapidly in India, with 94 cases confirmed. CNN News of Health, October 17, 2018
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EBOLA VIRUS DISEASE (EVD)

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 cannot spread through the 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. 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.

On 8 May 2018, the Ministry of Health (MOH) of the Democratic Republic of the Congo officially declared an outbreak of Ebola virus disease in Bikoro Health Zone, Equateur Province. This is the ninth outbreak of Ebola virus disease over the last four decades in the Democratic Republic of Congo, with the most recent occurring in May 2017. During this outbreak a total of 194 cases of hemorrhagic fever were reported in the region, of which 159 confirmed and 35 probable. Out of 159 confirmed cases, 87 died and 53 have been cured.

Risk assessment: The risk is low at global level due to the remoteness and inaccessibility of the area as well as the rapid response launched by the Democratic Republic of Congo MoH, WHO, and all the other coordinating partners.

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 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. Guidelines link: hp://nih.org.pk/files/Guidelines/Recommended%20Standard.pdf

Middle East Respiratory Syndrome Coronavirus (MERS - CoV)

Introduction: First reported case was from Saudi Arabia in 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 which caused outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003. 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 2,260 cases of MERS, including 803 deaths have been reported from 27 countries worldwide (Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Islamic Republic of Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, Philippines, Qatar, Republic of Korea, Kingdom of Saudi Arabia, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States, and Yemen).

Sample Collection and Transportation: Collection of lower respiratory specimens (sputum or broncho-alveolar lavage) is strongly recommended however, nasopharyngeal swab, oropharyngeal swab, sputum, serum, and stool/rectal swab may be collected. Repeat sequential sampling for PCR testing is strongly encouraged in the respiratory tract (upper and lower) and multiple other body compartments. 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.

Guidelines link: http://nih.org.pk/wp-content/uploads/2018/01/Guidelines-for-the-Prevention-Control-and-Management-of-Middle-East-Respiratory-Syndrome-Coronavirus-MERS-CoV-updated-MAY-2014.pdf

Yellow Fever

Introduction: Yellow fever is caused by a virus (Flavivirus) which is transmitted to humans by the bites of infected Aedes and haemogogus mosquitoes. Occasionally, infected travelers from areas where yellow fever occurs have exported cases to other countries.

Sign & Symptoms: The first symptoms of the disease usually appear 3–6 days after infection. The first, or "acute", phase is characterized by fever, muscle pain, headache, shivers, and loss of appetite, nausea and vomiting. After 3–4 days, most patients improve and symptoms disappear. However, in a few cases, the disease enters a "toxic" phase: fever reappears, and the patient develops jaundice and sometimes bleeding, with blood appearing in the vomit. About 50% of patients who enter the toxic phase die within 10–14 days.

Disease Burden: According to the recent analysis, there are an estimated 84,000-170,000 cases and up to 60,000 deaths due to yellow fever per year. The virus is endemic in tropical areas of Africa and Latin America. Between January 2016 and January 2018, seven countries and territories of the Region of the Americas reported confirmed cases of yellow fever: the State of Bolivia, Brazil, Colombia, Ecuador, French Guiana, Peru, and Suriname. Since the 12 January 2018 Epidemiological Update on Yellow Fever published by the Pan American Health Organization / World Health Organization (PAHO/WHO), Brazil and Peru had reported new yellow fever cases. In Brazil, between 1 July 2017 and 30 March 2018, there were 920 confirmed human cases of yellow fever, including 300 deaths. In Peru, between epidemiological week 1 and 4 of 2018, three probable cases of yellow fever were reported, one of which was confirmed by laboratory. All three cases had no history of yellow fever vaccination.

Yellow fever has never been reported from Pakistan but there are vulnerabilities for importation and its transmission through presence of vector mosquito (Aedes Aegypti), warm humid environment, susceptible hosts and movements of ships, containers, aircrafts and international travelers. Unvaccinated travelers heading to areas with active yellow fever outbreaks pose a risk of introducing the virus into areas where yellow fever risk factors (human susceptibility, prevalence of competent vector, and animal reservoirs) are present.

Recommendations:

- Strengthening the surveillance, vaccination for travelers, risk communications, community mobilization, vector control, quickly developing diagnostic capacity and case management measures must be in place. Blood tests to detect yellow fever-specific IgM antibodies or virus genome by PCR must be conducted by a highly trained laboratory staff with specialized equipment and materials.
- There is no specific treatment for yellow fever except supportive care. Yellow fever can be prevented through vaccination and mosquito control. WHO recommends vaccination for all travelers older than 9 months of age in areas where there is evidence of persistent or periodic yellow fever virus transmission
- Centers for Disease Control and Prevention (CDC) updated their travel notice for Brazil. Travelers to Brazil should protect themselves from yellow fever by getting yellow fever vaccine at least 10 days before travel, and preventing mosquito bites.



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