Ministry of National Health Services, Regulations & Coordination
Government of Pakistan
National Institute of Health, Islamabad, Pakistan
Field Epidemiology & Disease Surveillance Division (FE&DSD)
Tel: 051-9255237, 9255575
National Focal Point for International Health Regulations (IHR)

51st Issue

June 2021 – September 2021

SEASONAL AWARENESS AND ALERT LETTER (SAAL)

For Epidemic-prone infectious diseases in Pakistan

Summer / Monsoon Season

OBJECTIVES OF SAAL

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

DATA SOURCES

- The available national data collected during 2015 to 2021 by FE&DSD, NIH, Provincial Health Departments, Provincial Disease Surveillance & Response Units (PDSRUs), Expanded Program on Immunization (EPI), Directorate of Malaria Control and laboratory based data from NIH has been analyzed to assess the exhibited patterns of high priority communicable infectious diseases.
- The description of all priority diseases has been arranged in an alphabetical order. Additionally, under the section of National Potential Public Health Events, technical detail on the Heat Stroke and Naegleria Fowleri infection is included. Ebola Virus disease, has been shared as International Public Health Event.

Outbreak - Prone Diseases	Alerts
Acute Viral Hepatitis (A&E)	
Cholera (Acute Watery Diarrhea)	
Coronavirus disease 2019 (COVID-19)	
Crimean Congo Hemorrhagic Fever (CCHF)	
Dengue Fever	
Diphtheria	
Leishmaniasis	
Malaria	
Measles	
Meningococcal Meningitis	
Pertussis	
Poliomyelitis	
Typhoid Fever (XDR)	

	High Alert- peak occurrence in the Summer/Monsoon season
	Medium Alert- cases will be encountered and may show up as an outbreak

Acute Viral Hepatitis (A&E)

Introduction: Acute viral hepatitis is a diffuse liver inflammation caused by specific hepatotropic viruses that have diverse modes of transmission.

In Pakistan, epidemics of acute viral hepatitis (AVH) were reported as early as the 1950s and 1960s.Hepatitis A and E infections are highly endemic in Pakistan. Both infections occur in their sporadic form due to poor water/sanitation and sewage systems.

Clinical Picture: Clinical Picture depends upon severity of infection acquired. The common symptoms are acute jaundice, dehydration, dark urine, anorexia, nausea, malaise, extreme fatigue and right upper quadrant tenderness with hepatomegaly. A variable proportion of adult infections are asymptomatic. Lab findings include increased urine urobilinogen and >2.5 times the upper limit of serum alanine aminotransferase.

Infectious Agent: *Hepatitis A virus (HAV), Hepatitis E virus (HEV)*

Host/Reservoir: Humans are the only reservoir of the Hepatitis A virus (HAV).

Humans and non-human primates (pigs, deer, and wild boars) are the reservoirs of Hepatitis E virus (HEV)

Mode of Transmission: Faecal-oral route

Incubation period: Hepatitis A: Ranges from 15 to 50 days. Hepatitis E: Ranges from 15 to 64 days.

Seasonality: Occur regularly during monsoon rains and floods due to major contamination of drinking water with sewage

Alert Threshold: Clustering of 3 or more cases.

Outbreak threshold: A cluster of 6 or more cases in one location with one Lab confirmed case.

Case Definition:

Suspected Case: Any person having acute onset of jaundice less than 1-month duration with acute illness (dark urine, fatigue, nausea, vomiting and abdominal pain) with high serum ALT level and absence of any known precipitating factors.

Confirmed Case: A suspected case that meets the clinical case definition and is laboratory confirmed i.e. IgM anti HAV/HEV antibody positive.

Lab confirmation:

- ELISA: positive for IgM anti-HAV/HEV
- Polymerase Chain reaction (PCR): Antigen detection

Specimen Collection: Collect 5 ml blood during acute phase of illness observing all safety precautions. Separate serum by centrifugation technique in a tube.

Packaging and storage: An insulated box with ice or frozen refrigerant packs. Sample can be stored at 2-8°C for 48-72 hours. Long term storage at -20°C, with complete lab request form.

Case Management:

- There is no specific management for acute hepatitis but general supportive measures are recommended like bed rest, fluid replacement, nutritional support, and avoidance of use of all the hepatotoxic drugs during the illness. If within 2 weeks of exposure, Hepatitis A vaccination is equally effective.
- Hospitalization is required for fulminant hepatitis (a rare syndrome of massive necrosis of liver parenchyma and a decrease in liver size).

Preventive measures: Public health measures for epidemic-

prone diseases, Hepatitis A and E should include;

- Provision of safe & drinking water and proper disposal of sanitary waste.
- Important measures to reduce the risk of disease transmission include good personal hygiene including frequent and proper hand washing after bowel practices and before food preparation, avoiding drinking water of unknown purity, avoiding eating uncooked fruits or vegetables, following high quality standards for public water supplies and proper disposal of sanitary waste.

Vaccination: Hepatitis A vaccine is available both for adults and children aged 2 years or older and is administered I/M with a recommended vaccination schedule of 0, 1, and 6-12 months apart. There is currently no commercially available preventive vaccine or medication against Hepatitis E.

Cholera (Acute Watery Diarrhea)

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

Clinical Picture: Cholera infection is often mild or without symptoms, but can sometimes be severe and life threatening. Approximately 5-10% infected persons in the early stages will have severe disease characterized by profuse watery diarrhea, vomiting, and leg cramps. In these people, rapid loss of body fluids leads to dehydration and shock (1).

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

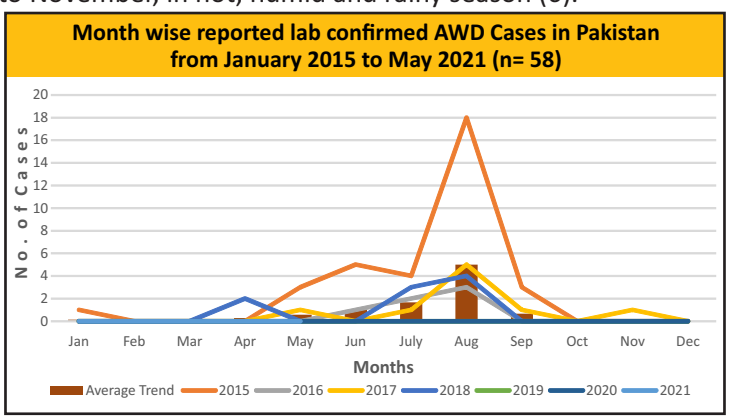
Infectious Agent: *Vibrio cholerae* (1).

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

Incubation period: Few hours to 5 days (4)

Infectivity period: The contagious period for cholera begins as soon as the organism is excreted in the feces. This can occur as early as about 6 to 12 hours after exposure to the bacteria and can last for about 7 to 14 days (5).

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



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

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

Case Definitions:

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

Probable Case: Person aged over 5 years or older with severe dehydration or a death from acute watery diarrhoea with or without vomiting. **OR**

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

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

Specimen Collection and Transportation:

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

Case Management: ORS should be given orally every hour. Even with severe dehydration, intravenous electrolyte solutions should be used only for initial rehydration, including those who are in shock. Severely dehydrated patients require administration of intravenous fluids. Ringer's Lactate Solution (Hartman's Solution) is the preferred fluid for intravenous rehydration. Antibiotics (Doxycycline, Ciprofloxacin, Cefixime, Co-trimaxozole, Erythromycin) reduce the duration of disease and period of excretion of *V.cholerae* in the stool of an infected patient (7).

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

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

Vaccination: A single-dose live oral cholera vaccine called Vaxchora (lyophilized CVD 103-HgR) for adults 18 – 64 years old, who are traveling to an area of active cholera transmission is recommended.

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

References and Guideline links:

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

Coronavirus Disease 2019 (COVID-19)

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

Outbreak of this viral disease started in Wuhan city, capital of central China's Hubei province during late December 2019, when a cluster of patients was admitted to hospitals in Wuhan with an initial diagnosis of pneumonia of unknown aetiology (1). The cluster was epidemiologically linked to a local seafood and wet animal wholesale market, suggestive of zoonotic spill

over. Amid the rising spread of the Novel Coronavirus cases globally, the World Health Organization has declared this infectious disease as Public Health Emergency of International Concern (PHEIC) on January 30, 2020 (2).

COVID-19 cases from 26th February 2020 to 07th June 2021 in Pakistan:

Number of COVID-19 Lab. confirmed cases	Number of COVID-19 cases recovered	Number of deaths due to COVID-19
933,630	864,931	21,323

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

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

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

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

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

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

Reservoir: Its origins are not entirely understood, the genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats and snakes. The potential amplifying mammalian host, intermediate between bats and humans, is, however, not known (5).

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

Incubation Period: It ranges from 02 days to 14 days from the date of last contact to infected person.

Seasonality: Not yet known

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

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

Case Definitions

Suspected Case:

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

Clinical Criteria:

- Acute onset of fever AND cough; OR
- Acute onset of ANY THREE O RMORE of the following signs or symptoms: Fever, cough, generalized weakness / fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting1, diarrhoea, altered mental status **AND**

Epidemiological Criteria:

- Residing or working in an area with high risk of transmission of virus closed residential settings, humanitarian settings such as camp and camp-like settings for displaced persons; anytime within the 14days prior to symptom onset ;or
- Residing or travel to an area with community transmission anytime within the 14daysprior to symptom onset; or
- Working in any health care setting, including within health facilities or within the community ;any time within the 14 days prior of symptom onset

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

C. A symptomatic person not meeting epidemiologic criteria with a positive SARS-CoV-2Antigen-RDT

Note: Clinical and public health judgment should be used to determine the need for further investigation in patients who do not strictly meet the clinical or epidemiological criteria.
Surveillance case definitions should not be used as the sole basis for guiding clinical management.

Probable case:

A) A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or linked to a COVID-19 cluster
B) A suspect case with chest imaging showing findings suggestive of COVID-19 disease
C) A person with recent onset of anosmia (loss of smell) or ageusia (loss of taste) in the absence of any other identified cause
D) Death, not otherwise explained, in an adult with respiratory distress preceding death AND was a contact of a probable or confirmed case or linked to a COVID-19 cluster

Confirmed case:

A) A person with a positive Nucleic Acid Amplification Test (NAAT)
B) A person with a positive SARS-CoV-2 Antigen-RDT AND meeting either the probable case definition or suspect criteria A OR B
C) An asymptomatic person with a positive SARS-CoV-2Antigen-RDT who is a contact of a probable or confirmed case

Note: for confirmed asymptomatic cases, the period of contact

is measured as the 2 days before through the 14 days after the date on which the sample was taken which led to confirmation.(7)

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

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

Table for Covid-19 Specimen Collection and Transportation

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

Laboratory testing for 2020 novel coronavirus in suspected human cases. WHO/2019-nCoV/laboratory/2020.3

New variants of the virus that causes COVID-19: Viruses constantly change through mutation, and new variants of a virus are expected to occur over time. Multiple variants of the virus that causes COVID-19 have been documented and circulating globally during this pandemic. These variants seem to spread more easily and quickly than other variants, which may lead to more cases of COVID-19:

- The United Kingdom (UK), identified a variant called B.1.1.7 with a large number of mutations in the fall of 2020. This variant spreads more easily and quickly than other variants. In January 2021, experts in the UK reported that this variant may be associated with an increased risk of death compared to other variant viruses.
- In South Africa, another variant called B.1.351 emerged independently of B.1.1.7. Originally detected in early October 2020, B.1.351 shares some mutations with B.1.1.7.
- In Brazil, a variant called P.1 emerged that was first identified in travelers from Brazil, who were tested during routine screening at an airport in Japan, in early January 2021.
- In India, a new variant named B.1.617 was first detected in late October 2020. Later on, experts have identified three subtypes, or sub lineages: B.1.617.1, B.1.617.2, and B.1.617.3.

All above mentioned variants are prevalent in Pakistan.

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

Preventive Measures:

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

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

COVID-19 Vaccines: There are four types of vaccines recommended against COVID-19 namely; Whole virus vaccine, RNA or mRNA vaccine, Non replicating viral vector and Protein subunit.

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

- CanSino Ad5-nCoV (Non replicating viral vector)
- Pfizer BNT16b2 (mRNA)
- Gamaleya Sputnik (Non replicating viral vector)
- Oxford/AstraZeneca AZD1222 (Non replicating viral vector)
- Sinopharm (Beijing) BBIBP-CorV (Whole vaccine; In activated)
- Sinovac CoronaVac (Whole vaccine; In activated)

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

Guideline Links:

- https://www.nih.org.pk/novel-coranavirus-2019-ncov/
- http://covid.gov.pk/
- https://covid19.trackvaccines.org/country/pakistan/

References:

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

CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF)

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

species (Principle vector) (4).

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

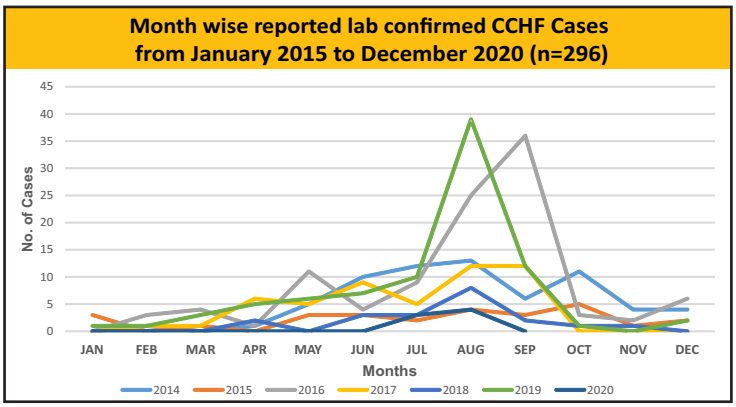
Infectious Agent: Crimean-Congo Haemorrhagic Fever (CCHF) Virus belongs to *Bunyaviridae* family (1).

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

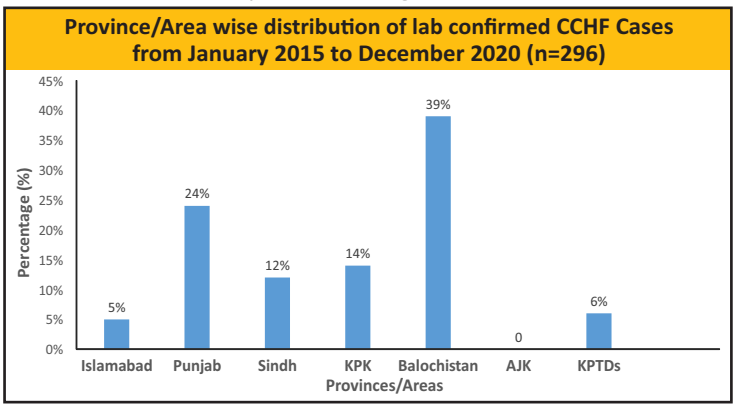
Mode of transmission: Bite of the infected *Hyalomma* tick , handling of tick infested animals, direct contact with blood / tissue of infected domestic animals (slaughtering); or direct contact with blood / tissue of infected patients. Nosocomial infections are common source of transmission (7).

Incubation Period:

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



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



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

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

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

Case definitions:

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

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

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

Laboratory Confirmation: Blood for PCR test and ELISA test

Specimen Collection and Transportation: Collect 3-5ml of blood in vacutainer observing strict biosafety precautions. Keep in upright position to prevent hemolysis. Transport to the laboratory in triple package with ice packs along with a prominent Bio-Hazard label and complete lab request form with brief history of the patient (11).

Case Management

- Patients with probable or confirmed CCHF should be isolated and cared for using strict barrier-nursing techniques with recommended Infection Prevention & Control (IPC) measures i.e. standard plus contact precautions. Use additional precautions, (droplet/aerosol) in 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 Equipment (PPE) before entering the isolation room and must dispose it properly after use.
- All secretions of the patient and hospital clothing in use of the patient and attendants should be treated as infectious and where possible, should be autoclaved before incinerating.
- Every effort should be made to avoid spills, pricks, injury and accidents during the management of patients. Needles should not be re-capped but discarded in proper safety disposal box.
- All used material e.g. syringes, gloves, cannula, tubing etc. should be collected in autoclave-able bags and autoclaved before incinerating.
- After the patient is discharged from the hospital, room surfaces should be wiped down with disinfectant like 0.5% Chlorine concentration, 0.1% Chlorine concentration or 0.05 % Chlorine concentration depending upon the surfaces. The room should be fumigated in case of risk for tick infestation (12).

Treatment: General supportive therapy is the mainstay of CCHF management. Intensive monitoring to guide volume and blood component replacement is recommended. If the patient meets the case definition for probable CCHF, oral Ribavirin needs to be initiated immediately in consultation with the attending physician. Studies suggest that Ribavirin is most effective if given within the first 6 days of illness. Oral Ribavirin: 30 mg/kg as loading dose, followed by 16 mg/kg every 6 hours for 4 days and then 8 mg/kg every 8 hours for net 3 days (12).

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

Avoidance of areas where tick vectors are abundant, especially when they are active (spring to autumn). Regular examination of clothing and skin for ticks, and their removal (without

crushing them). Wearing light colored clothing, covering legs and arms, and using repellents on the skin. Other measures, such as wearing gloves or other protective clothing to prevent skin contact with infected tissues or blood, may be taken by persons who work with livestock or other animals. For tick control, animal dipping/spraying in an insecticide solution of Permethrin/Pyrethrin/DEET is used. Injectable insecticide like Ivermectin is also recommended. Butchers should wear gloves and other protective clothing to prevent skin contact with freshly slaughtered meat, blood and other tissues. Meat should be drained for least 30 minutes, before distribution to public. Hospitals in endemic areas should ensure standard plus contact precautions in OPD and emergency rooms. Ensure injection safety measures and maintain stockpiling of Ribavirin with PPE. Bio-safety is the key element to avoid nosocomial infection. Suspected or confirmed CCHF cases must be isolated and cared by using barrier-nursing techniques to prevent transmission of infection to health workers and others. Exposed contacts: Those with high risk exposure (needle stick, sharps, blood or body fluids) contacts should be observed for fever for 14 days. If fever develops, Ribavirin should be started immediately (12). There is no approved vaccine available till date (13).

References and Guideline links:

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

DENGUE FEVER

Introduction: Dengue is a mosquito-borne viral disease (also known as break bone fever), causes flu-like illness, and may develops into a potentially lethal complication called severe Dengue. The global incidence of Dengue has grown dramatically in recent decades and about half of the world's population is now at risk [1]. The first confirmed outbreak of Dengue fever in Pakistan was in 1994, but a sudden surge in Dengue cases and the annual epidemic trend in the provinces has been observed multiple times there after [2].

Clinical Picture:

Dengue fever: Dengue fever is defined by fever (for >3 days and < 10days) as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms i.e. nausea/vomiting, rash, aches and pains (e.g. headache, retro-orbital pain, joint pain, myalgia, arthralgia), tourniquet test positive, thrombocytopenia (Platelets count <150,000).

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

Dengue shock syndrome (DSS): Defined as a syndrome due to dengue virus with any one or more of the following scenarios:

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

Note: 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].

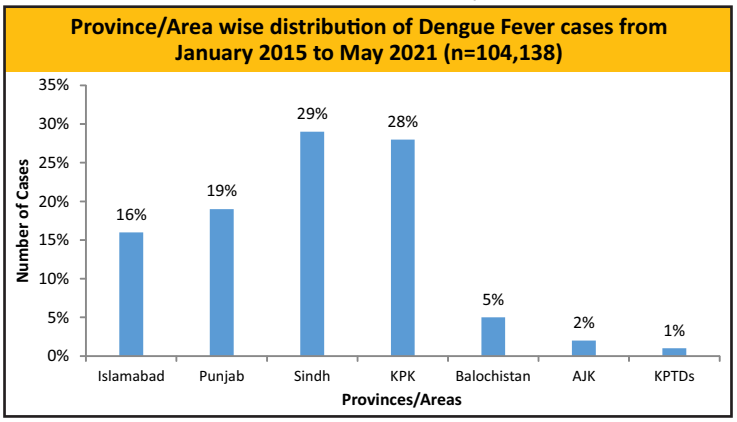
Mode of transmission: Bite of infected mosquitoes, Aedes Aegypti and Aedes Albopictus [6].

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 [8] .

Geographical distribution: From January 2015 to June 2021, Sindh & KPK remained the most affected provinces.



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

Alert threshold for Dengue hemorrhagic fever: One probable case is an alert and requires an immediate investigation to assess differential diagnosis with CCHF.

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

Case Definitions:

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

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

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

Lab confirmation:

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

Confirmatory:

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

Timings:

- PCR: Initial 4–5 days of onset of illness
- NS1: One day post onset of symptoms (DPO) up to 18 DPO
- **Serology:**
  - o IgM antibodies are detectable after 4th day of onset of illness (acute).
  - o IgG is used for the detection of past Dengue infection and usually can be detected during 2nd week of illness [11].

Specimen Collection and Transportation: Collect 5 ml of blood, centrifuge, and separate serum for analysis, observing strict

safety precautions. Transport serum specimens to the lab in triple container packing with ice packs or frozen with dry ice (for long distance) along with a prominent bio hazard label and complete lab request form with brief history of the patient [10].

Case Management:

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

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

Preventive measures: Identify mosquito breeding sites, destroy mosquito larval habitats and indoor breeding sites. Community awareness sessions should be conducted in schools, through religious leaders, aiming to promote health education campaigns. Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg-laying female mosquitoes. Protection against mosquitoes including use of screening, protective clothing and repellents [10].

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

References and Guideline links:

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

LEISHMANIASIS

Introduction: Leishmaniasis is a parasitic vector borne disease and is classified as a Neglected Tropical Disease (NTD). It can present as cutaneous, mucosal and visceral forms but the most common form is cutaneous Leishmaniasis (1).

Leishmaniasis is one of the prevailing public health issues in Pakistan and is endemic in some areas of Khyber Pakhtunkhwa and Balochistan province from where, disease is continuously reported through DHIS. Since 2011, KP has reported more than 10,000 cases where Karak, Peshawar, Lower Dir and Malakand are the most affected districts. There are more than 6,000 cases reported from merged districts of KP, where most affected tribal district is Bajaur. In Balochistan, DHIS has reported more than 68,000 cases from 2007 to 2018 and more than 2,000 cases were reported in 2019-20.The most affected districts are Quetta, Killa Abdullah, Pishin, Sibi, Jhal Magsi and Khuzdar [2].

Infectious agent: Leishmaniasis is caused by a *protozoa parasite* (3).

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

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

Case Definition:

1. Visceral Leishmaniasis (VL)

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

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

2. Cutaneous Leishmaniasis (CL)

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

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

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

Diagnostic criteria:

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

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

Specimen Collection:

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

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

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

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

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

Prevention:

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

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

MALARIA

Introduction: A vector borne parasitic disease transmitted by female Anopheles mosquito species.

With an estimated burden of 1.6 million cases annually, malaria is considered as a major public health problem in Pakistan. It contributes 22% of total disease burden in the Eastern Mediterranean Region (EMR). Epidemiologically, Pakistan is classified as a moderate malaria endemic country with national Annual Parasite Index (API) averaging at 1.69 and important diversity within and between the provinces and districts. The two parasites which account for malaria in Pakistan are *Plasmodium Vivax* and *P falcipaum*. The main vectors are *Anopheles Culicifacies* and *Anopheles Stephensi.* This malariogenic potential of Pakistan has a negative impact on country's socio-economic growth and national productivity. (Malaria Control Program Pakistan, 2015-2020)

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

Un-complicated: The classical (but rarely observed) Malaria attack lasts 6-10 hours.

It consists of: Cold stage (sensation of cold, shivering),Hot stage (fever, headaches, vomiting; seizures in children), and Sweating stage (sweats, return to normal temperature, redness).

Classically (but infrequently observed) the attacks occur every Second day with the "tertian" parasites (*P. falciparum, P. vivax, and P.ovale*) and every third day with the "Quartan" parasite (*P. malariae*)

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

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

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

Reservoir: Humans are the only known reservoir.

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

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

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

Outbreak threshold: In endemic area: Slide positivity rate above 50% or falciparum rate above 40%; while in non-endemic area, evidence of indigenous transmission of falciparum.

Case Definitions:

Suspected Case: A case with clinical manifestations of uncomplicated/complicated Malaria.

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

Confirmed Case: Clinical case with laboratory confirmation.

Lab Confirmation:

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

Specimen Collection & Transportation:

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

Case Management: Artemisinin-based combination therapies (ACTs) are there commended treatments for uncomplicated *P. falciparum* Malaria. However Artemisinin and its derivatives should not be used as monotherapy. The following ACTs are recommended:

- Artesunate plus Sulfadoxine,
- Pyrimethamine Artemether plus lumefantrine,
- Artemether-lumefantrine is currently available as a fixed dose formulation with dispersible or standard tablets containing 20mg of Artemether and 120 mg of lumefantrine. The recommended treatment is a 6-dose regimen twice Daily (BD) over a 3-day period. The dosing is based on the number of tablets per dose according to reported cases by month in Pakistan, predefined weight bands (5–14 kg: 1 tablet; 15–24kg: 2 tablets; 25–34 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).

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

Be Aware of the risk, the incubation period, the possibility of delayed onset, and the main symptoms.

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

a) Personal protection

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

b) Vector control

- Indoor spraying with residual insecticides (IRS)

- Reduce mosquito breeding sites
- Improve vector surveillance
- Optimize the use of resources for vector control through Integrated Vector Management (IVM)

c) Chemoprophylaxis Malaria control Program:

Recommended chemoprophylaxis: Atovaquone-proguanil, Doxycycline or Mefloquine

References and Guideline links:

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

MEASLES (RUBEOLA)

Introduction: Measles is a highly contagious viral disease mostly affecting children. Caused by measles virus of genus *Morbillivirus*. Despite community vaccination coverage, Measles outbreaks can occur among under vaccinated children and remains an important cause of death among young children globally. The virus spreads via droplets from nose, mouth or throat of an infected person [1]. Pregnant women while infected are also at greater risk of having severe complications and the pregnancy may end in miscarriage or preterm delivery. Immunity after measles infection is life long, although there are few reports of measles 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 onset, suggests a measles-associated complication. Severe measles is more likely among poorly nourished young children, especially those with insufficient vitamin A or whose immune systems have been weakened by other infections [5].

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

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

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 period with at least one lab confirmed case is an outbreak. It requires an immediate investigation and prompt response [7].

Case Definitions:

Suspected Case: Any person in whom a clinician suspects measles infection, OR

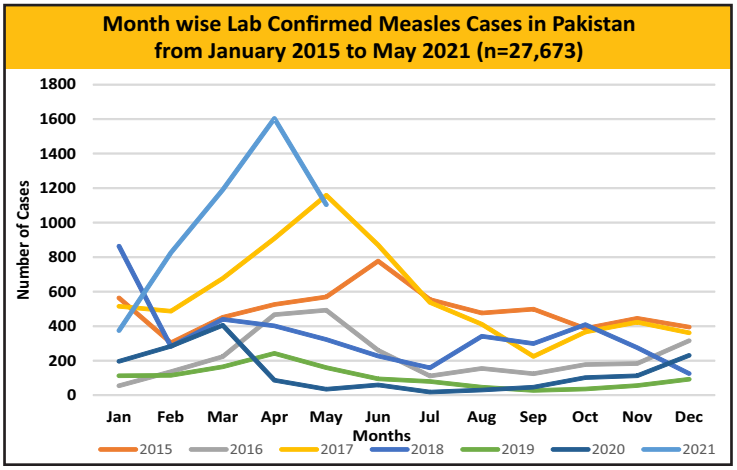
Any person with fever, maculopapular rash (i.e. non-vesicular) and 3C's; cough, coryza (i.e. runny nose) or conjunctivitis (i.e. red eyes)

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

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

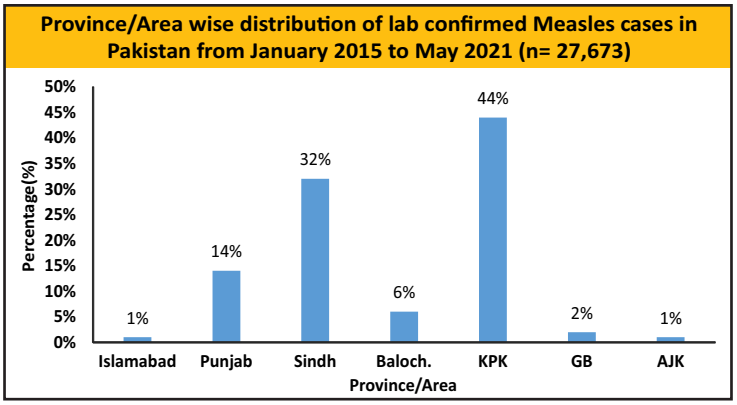
Discarded case: If an activate search in the community does not find evidence of measles transmission and there is no history of travelling to areas where measles virus is known to be circulating, the case should be discarded [8].

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



Geographical Distribution in Pakistan: During 2015-2021, Sindh and KPK remained the most effected provinces in Pakistan [9].

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



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

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

Treatment:

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

Antibiotics should be prescribed to treat eye and ear infections, and pneumonia [10].

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

References and Guideline links:

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

POLIOMYELITIS

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

The disease is marked for global eradication through the World Health Assembly resolution in 1988.The efforts so far reduced endemic countries from 125 to only 2 including Pakistan, and Afghanistan.

Polio was declared as a Public Health Emergency of International Concern (PHEIC) by WHO on 5th May, 2014 and continues to stay as such till date. Pakistan is classified by the International Health Regulations (IHR-2005) as a state being infected with WPV1, cVDPV1 or cVDPV3 with potential risk of international spread. Therefore the Government of Pakistan has also declared Polio as a national public health emergency and an annually updated National Emergency Action Plan (NEAP) is being implemented nationwide under the overall supervision of the National Task Force led by the Prime Minister of Pakistan and taking on board all provincial chief ministers as well as Prime Minister of AJK.

Geographical Distribution in Pakistan:

Year wise lab. Confirmed Polio cases by province/area in Pakistan, January 2012- May 2021

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

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

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

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

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

Note: After initial infection with Poliovirus, the virus is shed intermittently in faeces for several weeks

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

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

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

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

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

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

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

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

Specimen Collection & Transportation: Collect two stool samples about 8 grams each (about the size of the tip of both thumbs) at an interval of 24 to 48 hours for virus isolation as soon as possible or within 14 days of onset of illness in a clean, leak proof, screw-capped container, preferably in a transport medium like Minimal Essential Medium or Eagle's Medium. Seal the container with tape and place samples immediately after collection in refrigerator at 2-8°C or in a cold box with frozen ice packs. Transport specimens to the lab maintaining cold chain with duly filled request form within 72 hours after collection. (10).

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

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

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

TYPHOID FEVER

SALMONELLA ENTERICA SEROVAR TYPHI
(extensively drug resistant strain)

Introduction: A life-threatening illness that affects more than 21 million people in the developing world. Multidrug-resistant (MDR) isolates are prevalent in different parts of Asia and Africa

and are associated with the dominant H58 haplotype. Reduced susceptibility to Fluoroquinolones is also widespread, and sporadic cases of resistance to third-generation Cephalosporin or Azithromycin have also been reported.

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

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

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

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

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

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

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

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

Classification of Typhoid Fever Case Definitions by Drug Resistance Status, Pakistan (WHO-2018-2020)

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

Years	Karachi	Hyderabad	Other Districts	Sindh Total
2016	0	12	0	12
2017	175	485	4	664
2018	3712	891	207	4810
2019	7088	1645	998	9731
2020	2510	708	415	3633
2021	827	237	120	1184
Total	14312	3978	1744	20034

(Source: FDSRU-NIH weekly Report Volume 3-- Issue 22, May 23-29 , 2021 Date: June 02, 2021

Lab Diagnosis:

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

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

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

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

- Use of azithromycin and Meropenem should be restricted and only given to XDR cases of typhoid fever based on prescription by registered medical practitioner.
- In case of other infections such as upper and lower respiratory tract infections, other available drug options should be used instead of oral azithromycin which should be spared/ reserved for lab confirmed XDR Typhoid cases and other serious medical conditions.
- Raising community awareness on the following:
  - Thorough hand washing with soap and water is highly recommended after using toilet, before and after attending patient, before handling, cooking and eating.
  - Drink treated, boiled or bottled water. Use ice, prepared from clean drinking water preferably boiled. Wash fruits and vegetable properly before eating. Eat freshly cooked, hot served and home-made food.
  - Avoid eating raw fruits or vegetables, market prepared or leftover food.
  - Use pasteurized milk.
- Vaccination should be considered especially for those who are travelling to and from endemic areas, high risk group of people and those who are exposed to the disease. Typhoid fever vaccines do not provide 100% protection, however they will reduce the severity of the illness.
- Typhoid conjugate vaccine (Typbar-TCV@) is a new conjugate vaccine with longer immunity. WHO has prequalified the first conjugate vaccine in December 2017 to prevent typhoid fever .

References and Guideline links:

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

Potential National Public Health Events

Primary Amebic Meningoencephalitis (Naegleria fowleri)

In Pakistan, according to the Lancet infectious disease 2020, first case of PAM was reported in 2008. Until year 2021, 153 cases have been reported from Karachi in total. Primary Amebic Meningoencephalitis (PAM) is caused by *parasite Naegleriafowleri*; a rare, with about 99% CFR. *Naegleriafowleri* "brain-eating amoeba" is a unicellular, free-living microscopic organism & grows best at higher temperature up to 46°C.It is naturally found in warm freshwater environments feeding on bacteria and other microbes. Extended summers and prolonged humid conditions due to climate change provide an ideal environment for amoebas to flourish

in bodies of water. 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.

Clinical symptoms: of PAM usually start from 1-7 days after infection which may include headache, fever, nausea or vomiting.

Prevention & 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 concerned health authorities. Awareness and education in the affected areas must also be undertaken to educate and sensitize communities on preventive measures.

Guideline links: https://www.nih.org.pk/wp-content/uploads/2019/05/Advisory-for-Naegleriasis-May-2019.pdf

Heat stroke

Introduction: Heat stroke is a medical emergency and is a form of hyperthermia in which the body temperature elevates drastically and can be fatal if not promptly and properly treated. The body's temperature rises rapidly, the sweating mechanism fails and the body becomes unable to cool down consequently, the body temperature can rise to 104°F or higher within 10 to 15 minutes.

Signs & Symptoms: It include profuse sweating or the absence of sweating, with hot red or flushed dry skin, weakness/ lethargy, chills, throbbing headache, high body temperature, hallucinations, confusion/ dizziness and slurred speech. Infants, elder persons, athletes and outdoor workers are at high risk for heat stroke.

Treatment: The most critical step is the lowering of the temperature of the patients. The patients should be moved to shady area, unnecessary clothing should be removed and cool tepid water should be applied to the skin while soaking remaining clothes with water. Notify the emergency services immediately as severe cases often require hospitalization and Intravenous re-hydration. Promote sweat evaporation by placing the patient before fan and ice packs under the armpits and groin. If the patient is able to drink liquids, he/ she should be given plenty of cool water or other cool beverages that do not contain alcohol or caffeine. Maintain intravenous fluids and hospitalize if required. Monitor body temperature with a thermometer and continue cooling efforts until the body temperature drops to 101°F to 102°F. Antipyretics may be given once the body temperature drops to 101°F or below.

Preventive Measures: Heat/ sun stroke is a preventable condition. Public should be made aware of early signs/ symptoms of dehydration and subsequent evolving signs and symptoms of heat/ sun stroke such as muscle cramps, nausea, vomiting, light-headedness and even heart palpitations. The patients should avoid use of alcohol and caffeine containing soft drinks and/or tea, which may exacerbate dehydration. Public should be encouraged to consume salty foods, ORS, wear hats and light-colored, lightweight and loose clothes during the hot/ humid environmental conditions.

Guidelines link: https://www.nih.org.pk/wp-content/uploads/2018/07/Heat-SunStroke_2.pdf

Potential International Public Health Event

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 02 to 21 days (incubation period) after exposure which typically include fever, headache, joint and muscle aches, weakness, diarrhea, vomiting, stomach pain, lack of appetite and may follow by rash, red eyes, difficulty in breathing, difficulty in swallowing, and 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/secretions of an infected person. No specific drug is available, however early supportive clinical treatment and management are essential and can improve the chances of recovery.
It was declared as Public Health Emergency of International Concern (PHEIC) twice by WHO in 2014 and 2018 respectively.

Public Health Measures: WHO recommends the implementation of proven strategies for the prevention and control of Ebola outbreaks. These strategies include (1) coordination of the response, (2) enhanced surveillance, (3) laboratory confirmation, (4) contact identification/tracing and follow-up, individuals are monitored for up to 21 days in the case of EVD, (5) case management, (6) infection prevention and control, (7) safe and dignified burials, the IFRC has called funerals "super-spreading events" as burial traditions include kissing and generally touching bodies. Safe burial teams formed by health workers are subject to suspicion (8) social mobilization and community engagement, (9) logistics, (10) risk communication, (11) vaccination, (12) partner engagement, (13) research and (14) resource mobilization.

Vaccination: On November 2019, the World Health Organization prequalified an Ebola vaccine, rVSV-ZEBOV, for the first time against EVD. WHO stated that the rVSV-ZEBOV-GP vaccine had been 97.5% effective at stopping Ebola transmission. The ring vaccination strategy was effective at reducing EVD in contacts of contacts (tertiary cases), with only two such cases being reported.

Guidelines link: https://www.nih.org.pk/wp-content/uploads/2018/03/Guidelines-for-Prevention-and-Control-of-Ebola Virus-Disease-EVD-August-2014.pdf

Produced by the Field Epidemiology & Disease Surveillance Division (FE&DSD)
National Institute of Health, Islamabad

This document can also be accessed at NIH Website www.nih.org.pk , Email: eic.nih@gmail.com
Ph: +92-51-9255237, Fax: +92-51-9255575