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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, 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 Human Immunodeficiency Virus (HIV)/ Acquired Immunodeficiency Syndrome (AIDS) is included, while Ebola Virus Disease (EVD) has been shared as an International Public Health Event.

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

High Alert- peak occurrence in the winter season

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

Coronavirus Disease 2019 (COVID-19)

Introduction: A Novel Coronavirus Disease (COVID-19) is a member of the coronavirus family that has never been identified or encountered before. Coronaviruses are large family of viruses causing illness in humans as well as among animals i.e. camels, cats and bats. MERS-COV 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 8th October 2021 in Pakistan:

Number of COVID-19 Lab. confirmed cases	Number of COVID-19 cases recovered	Number of deaths due to COVID-19
1,256,233	1,184,527	28,058

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

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

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

Moderate Symptoms: Respiratory symptoms include cough and shortness of breath (or tachypnea in children) with or without fever may present, coupled with headache, muscle pain, or malaise and later loss of smell and taste in some cases. 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 forms of the disease, it can be moderate or even absent. Cyanosis can occur in children. In this definition, the diagnosis is clinical, and radiologic imaging is used for excluding complications. Chest imaging utilized includes chest radiograph, CT scan, or lung ultrasound demonstrating bilateral opacities (lung infiltrates > 50%) (4).

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

Reservoir: Its origin is not entirely understood, the genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats and 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.

Period of Communicability: 02 days before the onset of symptoms and up to 10 days after the onset of illness in mild disease and up to 02 weeks or more in case of severe disease.

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/vomiting, 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 14 days prior to symptom onset ;or
- Residing or travel to an area with community transmission anytime within the 14 days prior 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.

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 Covid-19 virus variants: 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. An increase in the number of cases will put more strain on healthcare resources, lead to more hospitalizations, and potentially more deaths:

- The United Kingdom (UK), identified a variant called B.1.1.7 (WHO label; Alpha) with a large number of mutations in the fall of 2020. This variant spreads more easily and quickly than other variants. Currently authorized vaccines do work against this variant. These vaccines are particularly effective against severe illness, hospitalization, and death.
- In South Africa, another variant called B.1.351 emerged independently of B.1.1.7 (WHO label; Beta). Originally detected in early October 2020, B.1.351 shares some mutations with B.1.1.7.Currently authorized vaccines do work against this variant.
- In Brazil, a variant called P.1 (WHO label; Gamma) emerged that was first identified in travelers from Brazil, who were tested during routine screening at an airport in Japan, in early January 2021.Certain monoclonal antibody treatments are less effective against this variant however currently authorized vaccines do work and effective.
- In India, a new variant named B.1.617 (WHO label; Delta) 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. Infections happen with this variant in only a small proportion of people who are fully vaccinated. Preliminary evidence suggests that fully vaccinated people who do become infected with the Delta variant can spread the viral infection to others.

Case Management:

- Current clinical management includes infection prevention & control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. There is no role of prophylactic chloroquine or hydroxychloroquine at this time.
- *The WHO COVID-19 Clinical management: living guidance* contains the Organization's most up-to-date recommendations for the clinical management of people with COVID-19 and is accessible at https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1
- For the treatment of COVID-19 in Pakistan, list of available drugs and medical devices approved by Drug Regulatory Authority of Pakistan (DRAP), is available at the website and can be accessed at https://www.dra.gov.pk/Home/covid/drug.

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

Vaccination: Vaccines save millions of lives each year. 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).

Types of 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: To date, following 7 vaccines procured and administered are being approved by DRAP:

- *CanSino-Bio Ad5-nCoV (Non replicating viral vector)*
- *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)*
- *Moderna: Spikevax (mRNA-1273)*
- *Pfizer/BioNTech: BNT162b2 (mRNA)*

The 2 vaccines with clinical trials conducted in Pakistan are *CanSino: Ad5-nCoV* (Non replicating viral vector) and *Anhui Zhifei Longcom: ZF2001* (Protein subunit).

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, clinical management and other pertinent features.*

Guideline Links:

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

References:

References are available at online version at www.nih.org.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).

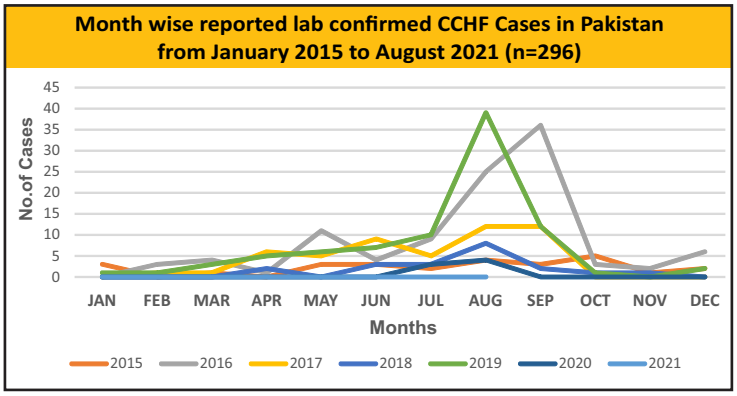
Reservoir: *Hyalomma* tick, domestic animals, such as cattle, goats, sheep, rodents, such as hedgehogs, rats, hares and birds are generally resistant with the exception of Ostrich (6).

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).

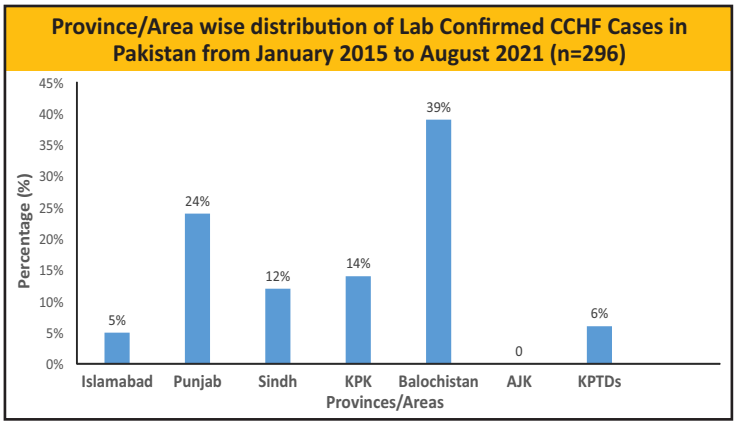
Incubation Period:

- 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:

Preventive measures: 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).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.

Hospitals in endemic areas should ensure standard plus contact precautions in OPD and emergency rooms. There is no approved vaccine available till date.

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).

Guideline Link: https://www.nih.org.pk/wp-content/uploads/ 2019/07/Advisory-CCHF-July-2019.pdf

References:

References are available at online version at www.nih.org.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 < 10 days) as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms i.e. nausea/vomiting, rash, aches and pains (e.g. headache, retro-orbital pain, joint pain, myalgia, arthralgia), tourniquet test positive, Leukopenia (Platelets count <150,000).

Dengue Hemorrhagic Fever: Defined as Dengue fever with any

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

OR

Dengue shock syndrome (DSS): Defined as a syndrome due to dengue virus with any one or more of the following scenarios: Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g. pleural or pericardial effusion, ascites) with respiratory distress, Severe bleeding from the gastrointestinal tract; and Vital organs involvement [3].

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].

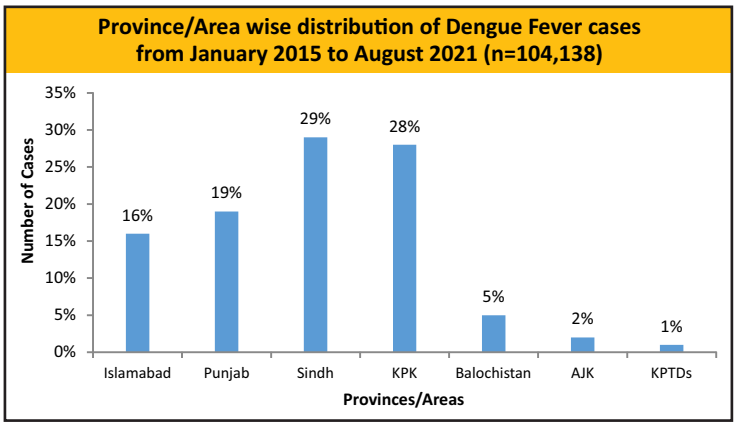
Mode of transmission: Bite of infected mosquitoes, Aedes Aegypti and Aedes Albopictus [6].

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 August 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:**
  - IgM antibodies are detectable after 4th day of onset of illness (acute).
  - 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].

Guideline Link: https://www.nih.org.pk/wp-content/uploads/2020/04/Advisory-on-Dengue-Fever.pdf

References:

References are available at online version at www.nih.org.pk

LEISHMANIASIS

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

Leishmaniasis is one of the prevailing public health issues in Pakistan and is endemic in some areas of Khyber Pakhtunkhwa and Balochistan province from where, disease is continuously reported through DHIS. Since 2011, KP has reported more than 10,000 cases where Karak, Peshawar, Lower Dir and Malakand are the most affected districts. 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].

Clinical Features:

(A) Visceral Leishmaniasis (VL): Also known as kala-azar, is fatal if left untreated in over 95% of cases. It is characterized by irregular bouts of fever, weight loss, with anemia and enlargement of spleen and liver.

(B) Cutaneous Leishmaniasis (CL)-Oriental sore: It is the most common form of Leishmaniasis and causes skin lesions without involvement of the mucosa, mainly ulcers, on exposed parts of the body, leaving life-long scars and serious disability [4].

(C) Mucocutaneous Leishmaniasis (MCL): MCL is due *to L. braziliensis and L. Panamensis*. It has two stages: During the first stage, there is development of a primary cutaneous lesion, which eventually is followed by nasal mucosal involvement, later on destroying the nasal septum. During the second stage, disease can progress to lips, palate and larynx [4].

(D) Post Kala-Azar Dermal Leishmaniasis (PKDL): After a latent period of one year following kala-azar cure, skin lesions can appear in around 20% of cases [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. [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 are available at online version at www.nih.org.pk

MALARIA

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

It contributes 22% of total disease burden in the Eastern Mediterranean Region (EMR).With an estimated burden of 1.6 million cases annually, malaria is considered among major

public health problems in Pakistan. 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 recommended ACTs are: Artesunate plus Sulfadoxine, Pyrimethamine Artemether plus lumefantrine. In case of pregnant women, during first trimester Quinine plus Clindamycin to be given for 7 days, (Artesunate plus Clindamycin for 7 days is indicated if this treatment fails).

Preventive Measures: Travelers and their advisers should note be aware of the risk, the incubation period, and the main symptoms. Avoid being bitten by mosquitoes, especially between dusk and dawn. Use anti-malarial dugs (chemoprophylaxis) when appropriate, to prevent infection from developing into clinical disease. Immediately seek diagnosis and treatment if a fever develops 1week or more after entering an area where there is a Malaria risk and up to 3 months (or, rarely, later) after departure from a risk area.

a) Personal protection

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

b) Vector control

Indoor spraying with residual insecticides (IRS).Reduce mosquito breeding sites. Improve vector surveillance. Optimize the use of resources for vector control through Integrated Vector Management (IVM).

c) Chemoprophylaxis Malaria control Program:

Recommended chemoprophylaxis: Atovaquone-proguanil, Doxycycline or Mefloquine

References and Guideline links:

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

PERTUSSIS (WHOOPING COUGH)

Introduction: A toxin-mediated disease that can affect people of all ages but can be very serious even deadly among infants. [1].Despite generally high coverage with childhood vaccines for pertussis, it is one of the leading causes of vaccine-preventable deaths worldwide [2].

Clinical Picture: The clinical course of the illness is divided into three stages: Catarrhal, Paroxysmal and Convalescent. 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. Coughing fits due to pertussis infection can last for up to 10 weeks or more. Some people know this disease as the “100 days cough". 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*; Gram *negative aerobic bacteria [*3]

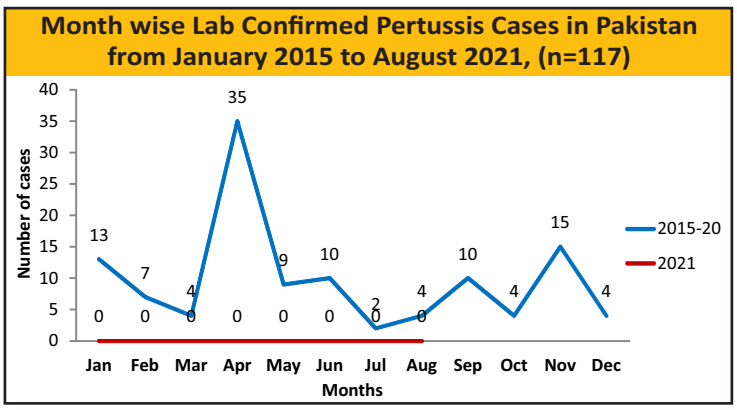
Reservoir: Humans are the only known reservoir [3]

Mode of transmission: By direct contact with discharges from respiratory mucous membranes of infected persons. Airborne/aerosols transmission [3]

Incubation period: 9 -10 days (range 6-20 days) [3]

Communicability: Highly communicable in the early catarrhal stage and gradually decreases after paroxysmal cough. Untreated patients may be contagious for up to 3 weeks after the onset of paroxysmal cough or up to 5 days after onset of treatment [3]

Seasonality: Pertussis has no distinct seasonal pattern [3]



Alert Threshold: One suspected case [5]

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

Case Definition:

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

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

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

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

Specimen Collection:

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

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

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

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

Case Management: Antibiotic treatment should be initiated in all suspected cases.

Treatment options include:

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

Preventive measures & vaccination:

- Timely treatment of the cases decreases the risk of transmission
- Immunization: Active primary immunization against *B. pertussis* infection with the whole-cell vaccine (WP) is recommended. Children who have received at least 3 doses are estimated to be protected especially against severe disease. However, protection begins to wane after about 3 years [5].

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

References:

References are available at online version at www.nih.org.pk

POLIOMYELITIS

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

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

Polio was declared as a Public Health Emergency of International Concern (PHEIC) by WHO on 5th May, 2014 and continues to stay as such till date. Pakistan is classified by the International Health Regulations (IHR-2005) as a state, currently being infected with wild poliovirus type 1 (WPV1) and circulating vaccine-derived poliovirus type 2 (cVDPV2) 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 wild poliovirus type 1 cases by province/area in Pakistan, January 2012-August 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

The number of cVDPV2 cases in 2021 remains at eight. There were 135 cVDPV2 cases reported in 2020

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 2020-2021) (11).

References:

References are available at online version at www.nih.org.pk

PROBABALE DIPHTHERIA

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

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

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

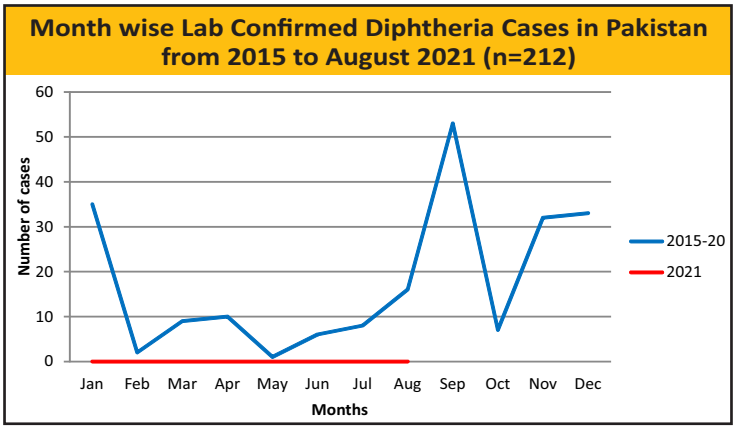
Reservoir: Humans are the reservoir for *C. diphtheriae* and are usually asymptomatic [2]

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

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

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

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



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

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

Case Definition:

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

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

Confirmed Case: Any probable case that has been laboratory

confirmed or linked epidemiologically to a laboratory confirmed case [4].

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

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

Lab Confirmation:

- Conventional culture method (bacteriological culture testing)

Specimen Collection and Transportation:

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

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

Case Management:

For Patients:

- Do not wait for laboratory results before starting treatment/ control activities. All cases must receive diphtheria antitoxin (DAT)
  - For mild pharyngeal or laryngeal disease, the dose: 20,000 – 40,000 units
  - For moderate nasopharyngeal disease, the dose: 40,000 - 60,000 units
  - For severe, extensive or late [3 or more days] the dose: 80,000 – 100,000 units
- Removal of membrane by direct laryngoscopy or bronchoscopy may be necessary to prevent or improve airway obstruction.
- Either penicillin 250 mg orally 6 hourly daily or erythromycin 500 mg orally 6 hourly is effective therapy, although erythromycin is slightly more effective in eliminating the carrier stage, should be continued for 14 days.
- Other microlides are probably as effective as erythromycin.
- The patient should be isolated until three consecutive cultures at the completion of therapy have documented elimination of the organism from oropharynx.

Preventive measures:

- Standard plus droplet 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:

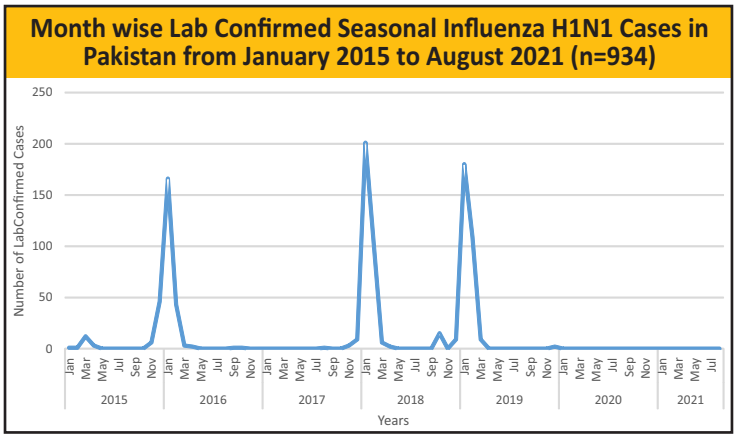
- Routine immunization consists of 3 doses of 0.5 ml DPT-Hep-B-Hib (Pentavalent Vaccine) administered IM to all the children less than one year of age with the schedule of:
  a. 1stdose at the age of 6 weeks;
  b. 2nd at 10 weeks;
  c. 3rd at 14 weeks, a booster DTP at 18 months to 4 years.
- If children or adults have not been immunized with three-dose series, children < 5 years should receive DT vaccine, and children ≥ 5 years and adults should receive Td vaccine to complete a series of three doses [1]

References:

References are available at online version at www.nih.org.pk

SEASONAL INFLUENZA

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



Clinical Picture: Seasonal influenza is characterized by a sudden onset of fever, cough (usually dry), headache, muscle and joint pain, severe malaise (feeling unwell), sore throat and a runny nose. The cough can be severe and can last two weeks or more. Most people recover from fever and other mild symptoms within a week without seeking medical attention. But influenza can cause severe illness or death especially in high risk groups [4].

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

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

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

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

Management: The symptoms in mild illness are relieved by providing warm fluids and taking rest along with analgesics and antipyretics. Analgesics such as Paracetamol 500mg-1G every 4-6 hours usually relieves headache and generalized pains and cough suppressants such as pholcodine 5-10 mg, 3-4 times

daily are generally sufficient. Antimicrobial agents are not effective against viruses, treatment with antibiotics for superadded bacterial infection such as bronchitis and pneumonia may be necessary [7].

Note: *Patients not considered being at higher risk of developing severe or complicated illness and who have uncomplicated illness due to confirmed or strongly suspected influenza virus infection need not be treated with antivirals* [7].

Difference between Flu and COVID-19;

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

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

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

References:

References are available at online version at www.nih.org.pk

SALMONELLA ENTERICA SEROVAR TYPHI

(Extensively drug resistant strain)

Introduction: 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.

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

Years	Karachi	Hyderabad	Other Districts	Sindh Total
2016	0	12	0	12
2017	175	485	4	664
2018	3712	891	207	4810
2019	7088	1645	998	9731
2020	2510	708	415	3633
2021	1739	360	175	2274
Total	15224	4101	1799	21124

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

Lab Diagnosis:

The only way to confirm Typhoid fever is blood or stool sample tested for the presence of *S. Typhi*. *S. Typhi* can be isolated from blood during the first week of illness or from stool and urine after the first week of illness. Widal and 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.

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.
- Raising community awareness for 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.

- 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.

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

References:

References are available at online version at www.nih.org.pk

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

Potential National Public Health Events

Human Immunodeficiency Virus (HIV)/ Acquired Immunodeficiency Syndrome (AIDS):

The human immunodeficiency virus (HIV) infects cells (CD4 cell a type of T cell) of the immune system, destroying or impairing their function. Infection with the virus results in progressive deterioration of the immune system, leading to "immune deficiency." The immune system is considered deficient when it can no longer fulfill its role of fighting infection and disease. Infections associated with severe immunodeficiency are known as "opportunistic infections", because they take advantage of a weakened immune system. Acquired immunodeficiency syndrome (AIDS) is a term which applies to the most advanced stages of HIV infection and is often characterized by the presence of any of the more than 20 associated opportunistic infections, complications or cancers.

Present situation in Pakistan: HIV is endemic in many parts of the country. According to Pakistan National AIDS Control Program data December 2020, there are 0.18 million estimated people with HIV, 42,563 registered people living with HIV who know their status in 45 Antiretroviral Therapy (ART) centers and 24,606 people are currently receiving ARV therapy.

Preventive measures and control: Promote Injection safety practices which includes, safe phlebotomy practices, safe disposal of sharps and healthcare waste. Reduce sexual transmission of HIV including uptake of appropriate HIV preventive measures including safe sex practices and promotion of the use of condoms. Modify the risk behavior of people in the community through “behavior change communication” (BCC). Sexually transmitted infections (STIs) control practices especially for sex workers, using the syndromic STIs management approach with partner notification and promotion of safer sex. Preventing the transmission of HIV through infected pregnant women to infants by the use of antiretroviral therapy (ART) i.e. Teneforvir, Emtricitabine and Raltegravir throughout pregnancy.

Occupational exposure: If a person has had occupational exposure to HIV, the following regimen is preferred; Emtricibine plus Tenofovir along with Raltegravir or Dolutegravir for a duration of 4 weeks depending on the type of exposure.

Guideline links:

- https://www.nih.org.pk/wp-content/uploads/2019/05/Advisory-for-the-Prevention-and-Control-of-HIVAIDS.pdf
- https://www.nacp.gov.pk/

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

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