Infectious Disease Control Guideline

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Epidemiology and Disease Control Division

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Infectious Disease Control Guideline

Contributors

Dr. Baburam Marasini, EDCD

Dr. Basudev Pandey, LCD

Dr. Guna Nidhi Sharma, EDCD

Dr. Ram Raj Panthi, EDCD

Mr. Bhim Prasad Sapkota, EDCD

Mr. Resham Lal Lamichhane, EDCD

Clinical Experts

Prof. Dr. Buddha Basnyat, PAHS/OUCRU

Prof. Dr. Subesh Raj Kayastha, NAMS

Prof. Dr. Sudhamshu KC, NAMS

Prof. Dr. Shital Adhikari, CMC

Dr. Jitendra Man Shrestha

Dr. Vivek Kattel, BPKIHS

Dr. Anup Bastola, STIDM

Technical Support

Mr. Pranaya Kumar Upadhyaya, MOH

Dr. Prakash Ghimire, WHO

Dr. Keshav Kumar Yogi, WHO

Dr. Vivek Dhungana, WHO

Dr. Neeta Pokhrel Regmi, WHO

Preface

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Acronyms

AES	Acute Encephalitis Syndrome
AIDS	Acquired Immunodeficiency Syndrome
ARDS	Acute Respiratory Distress Syndrome
CCHF	Crimean-Congo Haemorrhagic Fever
CDC	Center for Disease Control
DHO	District Health Office
DoHS	Department of Health Services
DPT	Diphtheria Polio and Tetanus (Vaccine)
EDCD	Epidemiology and Disease Control Division
EWARS	Early Warning and Reporting System
HAV	Hepatitis A virus
HEV	Hepatitis E Virus
HIV	Human Immune deficiency Virus
HP	Health Post
ICU	Intensive Care Unit
IP	Incubation Period
IPD	Immunization Preventable Diseases
IVDU	Intra-Venous Drug Users
MOHP	Ministry of Health and Population
MOT	Mode of Transmission

NA	Not Applicable/Not Available
NiV	Nipah Virus
NT/NNT	Neonatal Tetanus
PHCC	Primary Health care center
HO	Public Health Officer
RRT	Rapid Response Team
SLTHP	Second Long Term Health Plan
SMO	Surveillance Medical Officer
TB	Tuberculosis
TT	Tetanus Toxoid (vaccine)
VL	Visceral leishmaniasis
VTM	Viral Transport Media
WHO	World Health Organization

Chapter I: Introduction

1. Background

1.1 Health in Constitution of Nepal

The constitution of Nepal has established health as fundamental right of people. In this regard following rights to health have been recognized.

- Every citizen shall have the right to basic health services free of cost and no one shall be deprived of emergency health services.
- Every citizen shall have the right to be informed about the treatment of his or her health.
- Every citizen shall have the right to equal access to health services.
- Every citizen shall have the right to access to clean drinking water and sanitation.

Increasing State's investment in public health, ensuring easy and accessible access for all to quality health service, increasing the number of health organizations and personnel, ensuring health insurance for citizens and developing health as a service sector by regulating and managing the investment of private sector in health are the policies related to elementary needs of citizen which are mentioned in the constitution.

1.2 National Health policy-2071

The National Health Policy envisions, "All Nepali citizens to have the physical, mental, social and spiritual health to lead productive and quality lives".

The following strategies will be adopted in infectious disease control:

a. Along with the addition of necessary immunization services, the current state of management to the communicable diseases will be made up-to-date and implemented as per the action plan.

b. There will be a special provision under Infectious Disease Control Act, 2020 so that when there is occurrence of diseases which are prone for epidemics, concerned authorities will be timely informed.

c. In order to manage the diseases transmitted from animals and insects to human, a mechanism will be developed for effective coordination and collaboration among the stakeholders.

These have been foreseen as major challenges in infectious disease control as per National Health Policy 2071.

- Efforts are needed for pre-planning and to retrofit hospitals and health facilities in case of highly contagious diseases like bird-flu or newly emerging diseases, epidemic management, earthquake and other natural disasters to minimize the loss of human lives.
- The initiative to control diarrhea, respiratory diseases, malaria, kala-azar, leprosy encephalitis, filariasis, dengue, TB, HIV and vaccine preventable diseases need to be more effective.
- Controlling the cross border transmission of communicable diseases is a challenge because of open border.

1.3 SLTHP 1997-2017

As per the Second Long Term Health Plan (1997-2017), Addressing the changing trends of communicable and non-communicable diseases and emerging health issues has been regarded as one of the key issues in Essential Health Care Services. The high burden due to preventable communicable diseases like TB, Kala-azar and HIV requires that emphasis be placed on improving the operational efficiency of ongoing intervention programs and enhancement of community awareness through effective IEC strategies.

For the prevention and control of the communicable diseases, GoN has adopted and implemented the following strategies:

- **Malaria** – Early diagnosis and prompt treatment; affordable and sustainable vector control; prevention and control of epidemics; and continuous program assessment through strengthening HMIS, program management and operational research.

- **Kala-azar** – Reduction of Kala-azar mortality through improved and strengthened disease management in hospitals, reduction in transmission by means of early referral through peripheral health institutions, timely diagnosis and treatment, and a reduction in transmission through vector control and provision of free Kala-azar drugs to patients.

- **Japanese Encephalitis** – Identification of epidemic prone areas and preparedness by early recognition and identification of JE in peripheral health services; early diagnosis and timely management of the disease, anti-vector measures (fogging/ULV spraying) in epidemic foci; developing the necessary nursing care in hospitals.

- **Tuberculosis** – Directly Observed Short Course Therapy (DOTS) for all patients taking Short Course Chemotherapy (SCC). All activities and services are to be implemented through the existing infrastructure of the Ministry of Health; training and supervision of basic staff at all levels is to be gradually expanded to cover all districts. NGOs and bilateral aid agencies will work as "counterparts" to the regional health directorates, achievement of the short term objective of 70% case finding and 85% cure rate by 1999.

- **HIV/AIDS –** IEC, further strengthening of STD clinical management, ensuring safe blood transfusion, strengthening STD/HIV and AIDS surveillance, caring for and supporting people living with HIV/AIDS;

supporting NGOs that provide care to HIV/AIDS patients; and establishment of a national focal point for HIV/AIDS (National Center for AIDS and STD Control, MOH).

The policy implications in addressing burden of disease in SLTHP states that, "The high burden due to preventable communicable diseases like TB, Kala-azar and HIV requires that emphasis be placed on improving the operational efficiency of ongoing intervention programs and enhancement of community awareness through effective IEC strategies".

1.4 Three years plan (2069-72)

In the three years plan (2069-2072) it has been addressed in the strategy that the communicable disease control programs will be continued with added emphasis to the problems of drug addicts, and control of HIV/AIDS. Necessary preparedness will be put in place to cope with the possible outbreak of dangerous diseases like dengue, bird-flu, etc. Also in the policy on Essential and Basic Health services it is mentioned that under the basic health services principles, preventive, diagnostic, promotive and curative health services will be continued, with additional emphasis on surgery, safe motherhood and communicable disease control.

The quality of diarrhea and respiratory diseases treatment services will be enhanced with the increasing of access.

For Newly Emerging Infectious Disease Control Program following measures will be adopted:

- As Dengue has started to appear in Nepal also, sanitation, mosquito control and health education programs will be conducted with the help of municipalities.
- Measures will be adopted to prevent Avian influenza, which is highly communicable and fatal, from entering Nepal, in coordination with the Ministry of Agriculture and Cooperatives.
- A well-equipped laboratory will be established for disease investigation. Intensive care units will be strengthened for the treatment of patients, and appropriate preventive measures will be taken.

Communicable Disease Control Program

- **Tuberculosis Control:** DOTS program coverage will be extended to all the 75 districts with the joint initiatives of the government, the private sector and NGOs. People's participation will be mobilized to establish clinics and to search the patients. Integrated and coordinated programs for HIV/AIDS and tuberculosis control will be conducted.
- **Sexually Transmitted Infection and HIV/AIDS Control Program:** AIDS control requires a multi-dimensional approach. Programs will be conducted through the engagement of Regional Health Directorates, District Public Health Office, and District AIDS Coordination Committees Primary Health Care Centers, health posts, sub-health posts down to Female Community Health Volunteers. A semi-

autonomous body will be established for the wider and effective coverage through monitoring and evaluation works in coordination with the concerned ministries, other government agencies, donor communities and NGOs. Existing antiretroviral drug treatment centers will be extended and necessary medicines will be distributed free of cost to HIV/AIDS infected and patients of sexually transmitted diseases. The national coordination system will be further strengthened and made participatory.

- **Leprosy Control Program**: For the eradication of leprosy, the current program will be conducted more effectively. Mobilizing NGOs for an early identification of such patients will be emphasized, along with the rehabilitation and multiple drug treatment of the patients.

- **Malaria Control Program**: Emphasis will be given to the programs such as the strengthening of the laboratory, spraying of insecticides in the most affected areas, promoting the use of insecticide-treated mosquito nets (Supanet), and treatment after the testing of doubtful cases. Research will be continued to reduce the drug resistance. Community participation will be mobilized for the behavioral change program.

- **Yellow Fever Control**: Medical treatment of patients and routine and focal spray programs will be continued. Community help in patient identification and management will be mobilized. A social awareness campaign about the preventive measures and health education will be launched. Study of new drugs and disease transmitting parasites will be conducted.

- **Japanese Encephalitis Control:** Programs such as behavioral change communications (BCC), surveillance, supply of necessary drugs, diagnosis and treatment, disease infection risks minimization, mapping of risk-prone areas and the people, and strengthening of the drugs procurement system will be launched. Effective control measures will also be included in the routine district vaccination program.

- **Disease Surveillance Program**: Surveillance network for the polio and vaccination resistant diseases is well established now. This network will therefore, be activated to save the people from other kinds of communicable diseases and epidemics.

1.5 Global burden of Infectious Disease

Globally, there are various infectious diseases that pose serious threat to the population. The diseases which have high potentiality for outbreak are more challenging and needs immediate response.

- Pneumonia is the single largest infectious cause of death in children worldwide. Pneumonia accounts for 15% of all deaths of children under 5 years old, killing an estimated 922,000 children in 2015.
- Diarrhoeal disease is the second leading cause of death and one of the leading cause of malnutrition in children under five years old. Each year diarrhoea kills around 760,000 children under five years of age. Globally, there are nearly 1.7 billion cases of diarrhoeal disease every year.

- Cholera is an extremely virulent disease which affects both children and adults and can kill within hours if untreated. It is estimated that there are 1.4 to 4.3 million cases, and 28 000 to 142 000 deaths worldwide due to cholera every year.
- Measles is a highly contagious disease and one of the leading causes of death among young children. In 2014, there were 114,900 measles deaths globally which is about 314 deaths every day or 13 deaths every hour.
- About 3.2 billion people – almost half of the world's population are at risk of malaria. In 2015, 95 countries and territories had ongoing malaria transmission. According to the latest WHO estimates, released in December 2015, there were 214 million cases of malaria in 2015 and 438 000 deaths.
- Chikungunya occurred only in Africa, Asia and the Indian subcontinent but now outbreaks have been reported from USA, Canada and also in European countries. Since 2005, India, Indonesia, Maldives, Myanmar and Thailand have reported over 1.9 million cases of Chikungunya.
- Epidemics of Hepatitis A can be explosive and cause substantial economic loss. In developing countries with poor sanitary conditions and hygienic practices, most children (90%) have been infected with the hepatitis A virus before the age of 10 years. An estimated 1.4 million people are infected with Hepatitis A every year.
- Hepatitis E is found worldwide, but the prevalence is highest in East and South Asia. Every year, there are an estimated 20 million Hepatitis E Virus (HEV) infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E, and 56,600 hepatitis E-related deaths.

- Seasonal influenza is a serious public health problem that causes severe illness and death in high risk populations. Influenza occurs globally with an annual attack rate estimated at 5%–10% in adults and 20%–30% in children. Worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 250 000 to 500,000 deaths.
- In 2015, the WHO Foodborne Disease Burden Epidemiology Reference Group identified T. solium as a leading cause of deaths from food-borne diseases, resulting in a considerable total of 2.8 million disability-adjusted life-years (DALYs). T. solium is the cause of 30% of epilepsy cases in many endemic areas where people and roaming pigs live in close proximity.
- An estimated 900,000–1.3 million new cases and 20 000 to 30 000 deaths occur annually due to Kala-azar. The disease affects some of the poorest people on earth, and is associated with malnutrition, population displacement, poor housing, a weak immune system and lack of financial resources.
- 1.10 billion People in 55 countries worldwide remain threatened by lymphatic filariasis and require preventive chemotherapy to stop the spread of this parasitic infection. In 2000 over 120 million people were infected, with about 40 million disfigured and incapacitated by the disease.
- Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. The global incidence of dengue has grown dramatically in recent decades. About half of the world's population is now at risk. One recent estimate indicates 390 million dengue infections per year of which 96 million manifest clinically (with any severity of disease).

1.6 Regional Burden of Infectious Diseases

- Nipah Virus Infection (NiV) is an emerging infectious disease of public health importance in the South-East Asia Region. So far, NiV has infected 477 people and killed 252 since 1998. Case fatality rate of NiV ranges from 40-70% although it has been as high as 100% in some outbreaks.
- From 2003 to 2013, of the 649 laboratory-confirmed human cases of Avian Influenza A (H5N1) officially reported to WHO from 15 countries, 385 died. Of these, 228 cases (35%) and 181 deaths (47%) were from South-East Asia.
- In Asia, virus strains were isolated in parts of India, Sri Lanka and Thailand in the 1960s, Myanmar and Viet Nam in 1975, and Indonesia in 1982.10 After more than 20 years, chikungunya is being reported again in India, Indonesia, Maldives and Thailand, and in 2012 cases were reported for the first time from Bhutan. Chikungunya is thus considered as a re-emerging disease.
- Crimean-Congo haemorrhagic fever (CCHF) is a viral haemorrhagic fever transmitted by ticks. It can cause severe outbreaks in humans, with high mortality rates. The tick responsible for transmission of CCHF is found in countries of the South-East Asia Region but human infection with the virus is rare and has been reported from only one country, India, where an outbreak was reported for the first time in Ahmedabad in January 2011.

- Dengue has shown a 30-fold increase globally over the past five decades. Bhutan and Nepal are the most recent countries in South-East Asia to report outbreaks of dengue.

- Out of 56,600 estimated hepatitis E-related deaths more than 50% of global deaths from viral hepatitis E occur in South East Asia Region.

- Scrub typhus is endemic to a part of the world known as the “tsutsugamushi triangle”, extending from northern Japan and the far-eastern Russian Federation to northern Australia and Pakistan. This includes Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka and Thailand.

1.7 National Burden of infectious Disease

- In FY 2071/72, a total of 1,413,111 diarrhoeal cases were reported. The reported number of new diarrhoeal cases has slightly decreased in FY 2071/72 compared to FY 2069/70 and FY 2070/71. At the national level, percentage of severe dehydration has decreased to 0.2 in FY 2071/72 compared to FY 2069/70 and FY 2070/71. Similarly, the national incidence of diarrhoea per 1,000 under five years' children has considerably decreased to 501/1,000 under 5 year children in FY 2071/72 from 528/1,000 in 2069/70 and 629/1,000 in 2070/71.

- Regarding to ARI cases, in FY 2071/72, a total of 2,208,221 ARI cases has been reported. At the national level, reported ARI cases per 1,000 under-five population has decreased to 783 in FY 2071/72 compared to FY 2069/70 and 2070/71. Percentage of severe pneumonia remained constant in FY 2071/72 at National level (0.4%) compared to FY 2069/70 and FY 2070/71.

- The proportion of P. falciparum infections has sharply increases and reached 20.26%. There is a decreasing trend of confirmed case and case severity with sustaining zero deaths due to malaria.

- Kala-azar is a major public health problem in 12 districts in Eastern and Central Terai. Out of 220 cases reported in FY 2071/72, 148 were reported from the 12 programme districts. The incidence of Kala-azar in 12 programme districts is 0.25 per 10,000 with highest in Morang (0.47) and lowest in Bara (0.01).
- In the fiscal year 2071/72 total number of dengue case reported from 12 districts were 302. Among them, 119 cases were reported from Chitwan and 114 cases from Parsa where outbreak was recorded.

2. Objectives

Chapter II: Syndromic Approach to Infectious Disease

1. How to approach the patients with fever

Fever in Nepal is a common problem seen by the health care worker at all levels, from the health post to the referral hospital. Arbitrarily we can divide fever (>37.7C (>99.9F) into acute (< 2 weeks) and prolonged fever (> 2 weeks). In prolonged fever in Nepal, it is always important to keep in mind tuberculosis which may present in many different ways. Being the great "imitator" tuberculosis should be considered in almost all causes of fever, especially prolonged fever. In the context of Nepal, post-earthquake, brucellosis (which may also be an important cause of prolonged fever) outbreaks have taken place in rural areas as perhaps people and cattle may have had to live in closer proximity. Clearly, in the diagnosis of fever what is important to keep in mind is the epidemiological aspects of fever. For example, in London or New York City it would be unlikely that tuberculosis, brucellosis or typhoid would be common causes of fever unlike in Nepal and the rest of South Asia.

It is also important to understand that not all causes of fever are related to infections. Malignancies such as lymphomas may present with fever especially of prolonged nature. Connective tissue diseases like rheumatoid arthritis may also present with fever and bilateral pain and inflammation in the joints. Finally, what should not be forgotten is that when there is persistent fever, we have to rule out drug fever too. The very medicines we are using for the benefit of the patient may be the cause of fever.

Fever of acute origin in Nepal often presents in an undifferentiated manner (i.e. no focus of infection). If a patient presents with fever and burning micturition (possible urinary tract infections or pyelonephritis), or fever, headache, and neck stiffness (possible meningitis) or fever with a pocket of abscess in the muscles (pyomyositis), treatment can be directed accordingly. Viral fevers are common but in an immune competent host usually, they may subside after 2 to 3 days. But what is to be done when there is high fever for 3 or more days with no focus of infections as cited in the above examples? Importantly it is of vital importance to try to recognize in the beginning, the life-threatening causes of fever like meningitis, falciparum malaria, typhoid perforation, staphylococcal septicaemia with hypotension so that therapy can be rapidly instituted to avoid death.

Comprehensive History and Physical Examination

In the first place, a proper and thorough history has to be taken. Many health care workers are in a hurry and inadequate history taking can lead to an incorrect diagnosis which may prove to be fatal. For example, a Nepali coming from a peace- keeping mission from the Sub-Saharan Africa

complained of fever with “flu like” symptoms. But the health care worker did not take a travel history. He just gave the patient some cough medicine. Unfortunately, the patient who had just returned died in 2 days as he was suffering from falciparum malaria due to transmission of the deadly falciparum malaria through mosquito bites in the Congo. A proper history could have alerted the health care worker (if he had the proper knowledge base) of the possibility of deadly malaria in a returning Nepali worker from Africa. He may have been saved if prescribed anti - malarial treatment like the artemisinin compound, coartem, available in Nepal. As Nepalese are now traveling in great numbers, it is absolutely important to obtain a travel history because the patient may not think it is vital to give this history unless asked for.

Likewise many migrant workers who are engaged in different metro cities of India returning back with fever should be searched for malaria and dengue. As in recent days majority of Pf malaria are imported mostly from India. If the Pf malaria is of endogenous origin without any travel history must initiate an urgent and intensive surveillance and monitoring of surrounding foci of VDC in order to prevent outbreak, morbidity and mortality in time.

Proper history taking will also help with ascertaining the incubation period of certain common diseases. For example, it is very unusual to suffer from dengue fever if the patient has left the ‘dengue’ area 2 weeks ago. Information obtained this way to firmly exclude a potential diagnosis like dengue can be very useful especially in our part of the world where diagnostic tests are limited. Making a diagnosis of certain causes of fever like schistosomiasis and trypanosomiasis which are not seen here (but are common in the African continent), are almost completely dependent on proper history taking skills and knowledge about the area travelled by the patient.

Finally, a vaccination history may also be important. For example, if a patient has taken typhoid fever vaccine, he or she has lesser likelihood of suffering from typhoid fever. But what has to be kept in mind is that paratyphoid fever for which there is no vaccination mimics typhoid fever. Furthermore, the efficacy of the typhoid vaccine is only about 70%. In post monsoon period, patient from JE endemic district presenting fever with altered sensorium, history of JE vaccination can rule out JE as case of AES.

In Nepal research has shown that typhoid fever is more commonly transmitted by drinking contaminated water than human-to-human transmission. Drinking “dhughedhara” (stone spouts) water seems to predispose even more to suffering from enteric fever than drinking tap water. Because of the lack of municipal tap water many people may be drinking stone-spout water. Asking the source of the water supply in the household therefore may be an important point in history- taking in a febrile patient.

After a proper and comprehensive history, a good physical examination is important. This includes removing “patukas” or cummerbund as causative problem (an abscess, for example) may be hidden behind the contours of the patuka and the patient may think this is unimportant. So, it is very useful to disrobe the patient for proper examination so that we include all clues to make the correct diagnosis. Many health care workers will not open bandages applied on the

patients or disrobe the patient adequately and hence may miss an important diagnosis. They may miss observing jaundice because of examination in poor light and thus viral hepatitis, leptospirosis, malaria, dengue, scrub typhus as a cause of fever may not be considered. Suffused conjunctiva without discharge usually observed in dengue, leptospirosis and rickettsial fever. So, proper lighting of the surroundings and a good light source during examination is essential. Also, abdominal rash (maculopapular) in dengue, rickettsial fever and typhoid fever, eschar lesion in scrub typhus and purpura, petechiae in haemorrhagic fever including dengue.

Undifferentiated Febrile Illnesses

Undifferentiated febrile illness (UFI) are an important group of "fevers" seen by health care workers in Nepal. So a clear- cut approach is vital. But certain background points about these diseases in the context of Nepal is important.

Typhoid, typhus, leptospirosis are 3 common treatable UFIs to keep in mind in Nepal so that treatment can be promptly established without leading to unnecessary complications. It is crucial to rule out malaria first if the patient comes from a malaria zone, especially if falciparum malaria is suspected as this kind of malaria can turn life- threatening very quickly as in the above example. Dengue, typhus, chikungunya also has to be considered especially in the Terai region in a patient with fever and rash (often like sunburn) with pain on eye movement. Established viral hepatitis along with leptospirosis, malaria, dengue and typhus as mentioned above will present with jaundice and always needs to be considered.

Enteric fever (typhoid and paratyphoid fever) are the commonest bacterial organisms (*Salmonealla typhi* and *paratyphi*) that are cultured in the blood from Nepali patients (probably from all South Asian patients). This gives an idea of the pervasive nature of this organism. However, in most areas in South Asia including Nepal blood culture may not be available and empirical treatment started in most cases. Most cases of enteric fever present as UFIs with no focus of infection.

Although Rickettsial illnesses (typhus fever) had been recognized to be an important cause of fever in Nepal since 2004, this fact had not been well -grasped until post- earthquake 2015. Post-earthquake there were outbreaks of scrub typhus in various parts of Nepal, some of which were fatal. This event brought a great awareness in the health care professionals so that typhus now is more readily considered as a cause of fever in Nepal. One interesting hypothesis as to why there have been outbreaks of typhus post-earthquake suggests that with the destruction of houses, the rats also moved to the human shelters and lived in closer proximity to humans, thus facilitating the transmission of typhus.

In the past when a large study was carried out to ascertain the cause of fever in Nepali patients, although in the final diagnosis typhus fever ranked second as the commonest cause of UFIs,

none of the enrolled patients (about 700) had typhus fever initially in their differential diagnosis listed by the treating physician. One distinguishing feature in the Nepali patients with scrub typhus who have been studied at Patan Hospital showed that most of these patients did not have an eschar, a characteristic of typhus fever. In Nepal as a recent study showed, murine typhus which is transmitted by rat fleas is more common in the cities (for e.g. Patan area) compared to scrub typhus which seems to be more common in rural areas where there are more shrubs, where mites which are vectors for scrub typhus, may reside.

Since rats are in plentiful supply in Nepal, it is not surprising that besides scrub and murine typhus which have been documented to cause febrile illness in Nepal, leptospirosis, which may also be transmitted by rat-carriage, is also a well- known cause of UFIs.

As mentioned earlier all of the three UFIs mentioned (typhoid, typhus, and leptospirosis) may also present with complications like pneumonia, encephalitis or multi organ failure including renal failure; but in the initial stages before complications set in very often, they will present as UFIs. Hence, there is importance of prompt recognition and treatment.

True vs False Diagnosis of UFIs

Microbiological diagnosis of the UFIs is fraught with problems because for example, for typhoid fever diagnosis a blood culture facility is necessary and most patients may not have access to such a facility. The dubious Widal test is done even in remote areas of Nepal which should be discouraged as the test results are not scientifically helpful. Many commercial rapid diagnostic kits for UFIs (for example for typhoid and typhus and leptospirosis fevers) are available whose value in making a diagnosis may be no better than the Widal test. Hence, for any purported diagnostic testing the specificity and sensitivity of the test (i.e. the accuracy of the test) must be independently verified before blindly accepting the test result and prescribing incorrect therapy. On the contrary there are reliable rapid diagnostic tests, for example in the diagnosis of falciparum malaria and dengue fever. It is now well known that in the diagnosis of falciparum malaria using rapid diagnostic tests like the Optimal test is much more reliable (more sensitive results) than using the traditional thick and thin smear blood films.

For the diagnosis of typhus or leptospirosis, rising serum titres are necessary and not immediately helpful for the patient as three weeks in between titres are necessary to study the rise. Furthermore these studies are not available in Nepal and these tests (like PCR diagnosis) have to be sent abroad at great expense for the patient with little use in the treatment of the index patient.

Empirical Treatment

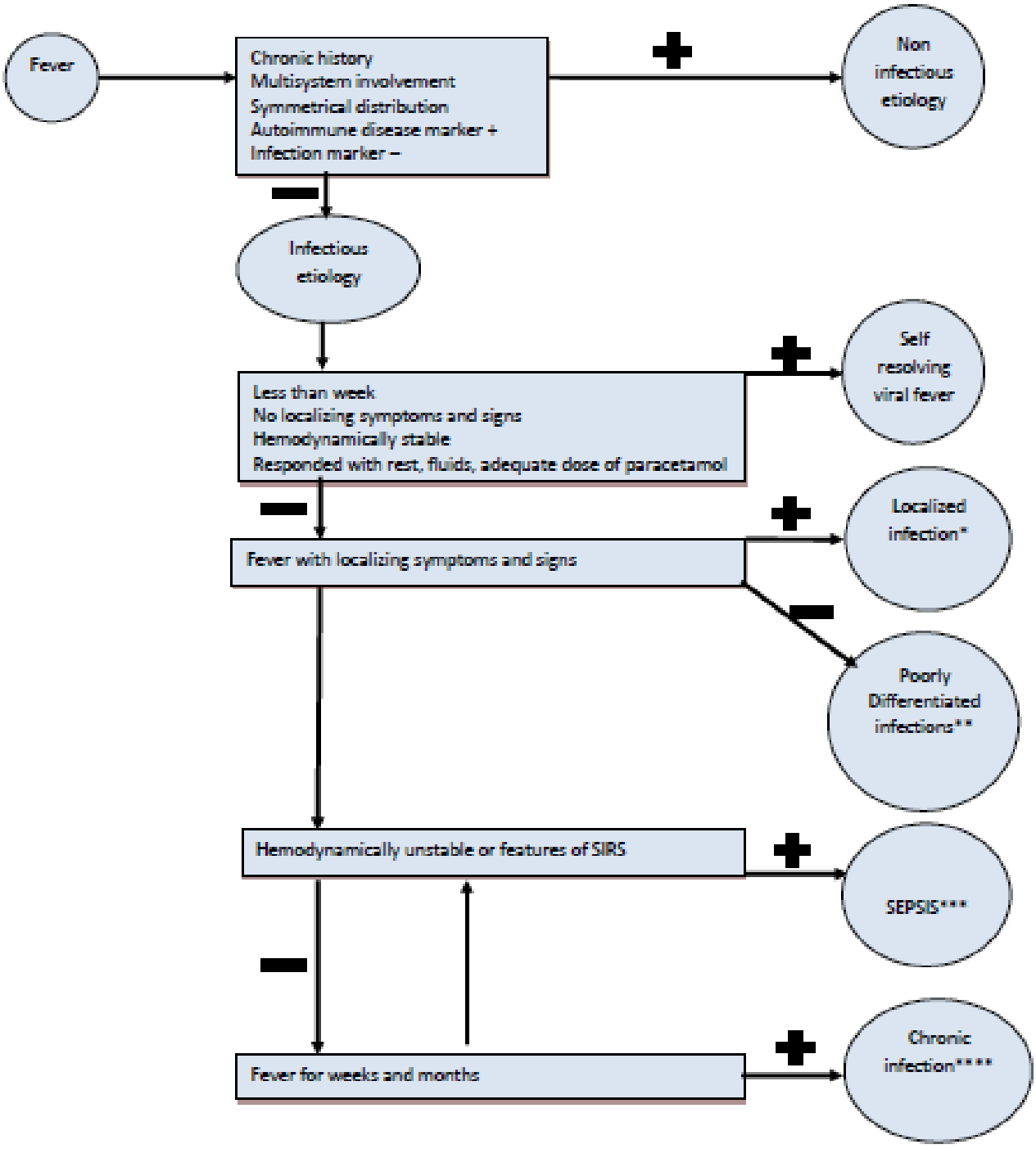
Hence when a patient presents with high fever for three or four days with no focus of infection, empirical treatment is often started in the belief that the patient may have typhoid fever. Often ciprofloxacin or ofloxacin is started. It has now been shown that fluroquinolones (even the fourth generation ones like gatifloxacin, see further reading below) should not be used in the empirical treatment of typhoid fever in Nepal, including in all probability, the whole of South Asia due to resistance caused by mutant typhoid organisms, specifically a clade designated as H58.

It is best to start empirical treatment on an outpatient basis with azithromycin for typhoid fever. And because it will not be known at the start of therapy whether the patient has typhoid, typhus or leptospirosis (or other causes), it is best to also include doxycycline which is the drug of choice for both typhus and leptospirosis. Studies done at Patan Hospital have shown that 20 to 25 % of patients who present as “typhoid fever” actually have typhus fever for which the treatment as noted is different. If the patient is very ill, then a combination of ceftriaxone and doxycycline should be used in the empirical treatment of UFIs in Nepal.

Finally, antimicrobial resistance is a burgeoning problem worldwide especially in low income countries like ours. It is crucial that when a patient presents with fever, we do not just “throw” expensive unnecessary antibiotics at the patient but stop to consider what may be the common organisms in our epidemiological setting and treat accordingly. Many patients in Nepal receive “last resort” antibiotics like imipenam and colistin for uncomplicated UFIs and this will do more harm than good and create mutant strains like the H58 mutant typhoid strain referred to above which will make treatment very difficult.

In conclusion, in the approach to fever in a Nepali patient, a comprehensive history including travel history is crucial followed by a complete physical exam. In the diagnosis of fever, reliability of commercial rapid tests have to be carefully assessed before accepting the diagnosis. Finally, in the empirical treatment of fever, due consideration has to be given as to the likely cause of fever in our epidemiological setting. The diagnosis in our setting is based mostly on history and physical examination due to the unavailability of diagnostic tests in most cases. Antibiotics may have to be prescribed accordingly. Although access to antibiotics in many parts of Nepal is very difficult, excess use of antibiotics for fever in many towns and cities is also common. Hence a balance between “excess and access” has to be struck and antibiotics have to be used judiciously in the treatment of “fever” to avoid antimicrobial resistance.

Algorithm for Fever



Clinical Decision Making

The content learned in medical school may need to be contextualized. We read sciences that looks like black and white but when we practice there are lot of gray zones.

Threshold for offering investigations and prescribing treatment in day to day clinical practices varies from individual to individual. It depends upon clinical competency, nature of diseases, availability of investigations and drugs and other social factors. All clinical scenarios may not be what we have read in medical schools. For example; the definitive diagnosis of enteric fever is four fold rises in serology or proven body fluid culture in a clinical suspected case. However, when we see these two test they have pros and cons. If a clinician chooses paired sera (paired WIDAL) to prove the diagnosis of enteric fever s/he need to take two blood sample most probable on first week and third week of fever. It did not help in decision making to that particular patient because by the third week the patient might have been cured or worsened or collapsed. The strong part of serology is, it is positive in majority of clinical cases but it is time based. It does not help clinician to know about the antibiotic sensitivity, treatment response and previous or recent subclinical infections. If another clinician chooses blood culture it tells about antibiotic sensitivity, treatment response and result is in clinician hand by 48 to 72 hours. However, the test is not available in all clinical setting and blood culture positivity rate is low in majority of febrile cases (5% to 20%). Hence, those majorities of patient (80% to 95%) who had negative blood culture cannot be ruled out as enteric fever. Decision making in negative test with low sensitivity and positive test with low specificity makes betting as black or white in a gray zone area. Choosing both tests increases the cost and may not complement each other.

Decision making in clinical setup especially to choose between error of commission (false positive) and error of omission (false negative) is very tough job. The clinical threshold is balancing between these two errors. In other words clinical threshold means the magnitude of ruling in as a wrong disease/ diagnosis is equivalent to ruling out right disease/ diagnosis in a patient. It means error of tagging/ treating with antitubercular drugs to a patient with symptoms, signs and investigations finding likely to be tuberculosis but was something else (brucellosis, sarcoidosis, invasive fungal infections, malignant serositis) is equally error as not tagging/ treating a patient with unusual presentation of tuberculosis. The consequences of both this situation has to be analyzed and the threshold has to be determined.

The classical teaching method in medical schools says diagnosis is made on basis of tripod of clinical history, physical examination and investigations. History taking and clinical examination increase the pre-test probability. The clinical method helps to look if the characteristics of patient resembles to prevalent population or not. Prevalence of the disease determines the post-test probability however clinical threshold has to be determined by clinician beforehand. Prevalence does not determine the clinical thresh hold. If post-test probability crosses the threshold then it is justified to take action. Asking kala azar antibody test in non-febrile case may lead to more error as compared to chronic febrile one. Asking same test in chronic febrile case may lead to more error than chronic fever with splenomegaly. This is so because chronic fever with splenomegaly has the highest pre-test probability followed by chronic fever than a febrile one. Hence clinician should decide threshold for asking an intervention

before s/he sees the patient and if those characteristics are present should execute the intervention. Asking test in patient without poor characterization of patient may lead to unnecessary intervention and further decision making may not be progressed i.e. increase cost of the treatment.

Suppose a clinician makes a minimal threshold of 70% to start treatment of Kala azar. S/he agrees error of leaving 30 Kala azar patients (false negative) equals error of treating 3 non Kala azar patients (false positive) as Kala azar. Higher clinical threshold lowers the intensity to treat a patient i.e. seeking strong evidence to support the diagnosis. Lower the threshold higher the intensity to treat. Hence if clinical threshold to treat Kala azar is kept lower he will be treating many patient (true positive and false positive) but many of them will be false positive. Otherwise he will be missing the diagnosis of many disease patients.

If we have following data available from the past record of 1000 kala azar (VL) patients among 11000 total patient over an year.

Table 1: characterization of VL in a hospital visit population

	Number of VL Patients	Sensitivity	Total non VL patient	Specificity
Fever	950/1000 (TP)	95%	5000/10000 (FP)	50%
Splenomegaly	500/1000 (TP)	50%	3000/10000 (FP)	70%
Positive rK 39	950/1000 (TP)	95%	10/100 (FP)	90%
1100 patient went under rK 39 of them 100 were non VL cases of them 10 were positive (false positive) and 90 were negative (true negative)				

Now the pre-test probability of this patient is prevalence of VL among all hospital cases i.e. 1000/11000*100% = 9.09% =9.1%.

Mathematically Post-test probability

$$= \frac{\text{True positive}*100\%}{\text{Total positive}}$$

$$= \frac{\text{population}*\text{prevalence}*\text{sensitivity}*100\%}{[\text{Population}*\text{prevalence}*\text{sensitivity}+\text{population}*(1-\text{prevalence})*(1-\text{specificity})]}$$

$$= \frac{\text{prevalence}*\text{sensitivity}*100\%}{[\text{Prevalence}*\text{sensitivity}+(1-\text{prevalence})*(1-\text{specificity})]}$$

If a male patient present with fever than his probability of VL will be

$$= 950*100\% / (950+5000)$$

$$= 15.96\%$$

$$= 16\%$$

If he has fever and splenomegaly then his pre-test probability (prevalence) of VL will be 16% and post-test probability will be:

(16/100*50/100)*100% / [(16/100*50/100) + {(1-16/100)*(1-70/100)}]

=24.09%

If he has fever splenomegaly and rK 39 positive then his pre-test probability (prevalence) of VL will be 24%. His post-test probability will be:

(24/100*95/100)*100% / [(24/100*95/100) + (1-24/100)*(1-90/100)

= 75%.

If the clinician threshold is 70% then he need to have chronic fever, splenomegaly and positive rK 39 test to start the treatment. Let us see if a patient comes with chronic fever and positive rK 39 test will he crosses the threshold or not.

Now the post-test probability with fever is 16% that is prevalence for fever and positive rK 39. Now, the post-test probability with fever and positive rK 39 will be

= (16/100*95/100)*100 / [(16/100*95/100)*100 + (1-16/100)*(1-90/100)

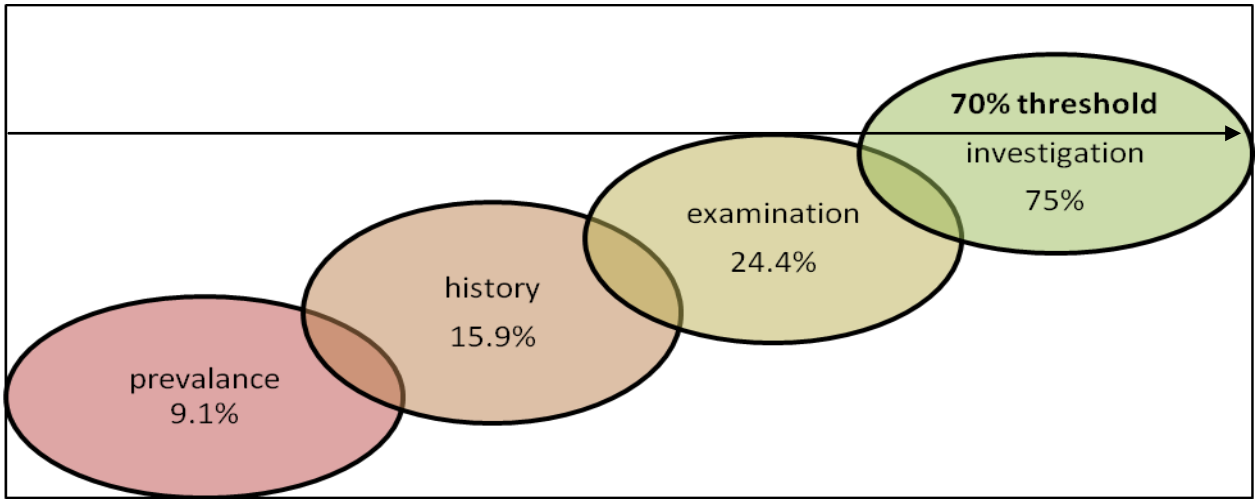
=64.4%

It showed that absence of splenomegaly is likely to decrease the post-test probability and if we set up threshold below this post-test probability many patient with kala azar will not be diagnosed as kala azar (more false negative) or many patient without kala azar will be diagnosed as kala azar (more false positive). Just asking rK 39 in patient with chronic history may not help for decision making to start the treatment because post-test probability is lower than the benchmark (threshold) that was kept 70%. This means we need another test to increase our threshold i.e bone marrow or PCR. It did not change the treatment plan but gives new perspective provided the false positive has been excluded.

The final post-test probability exceeds our threshold which we determined beforehand. Hence with this threshold patient most go further for treatment. If we make threshold more we need another tools with higher specificity to overshoot it so this may be bone marrow or PCR which might not be feasible or more expensive. If we keep our threshold low we may be treating all fever with splenomegaly as VL which might be other than VL like leukemia, lymphoma, and tropical splenomegaly. Clinical threshold is making choice to prefer false negative (error of omission) verses false positive (error of commission).

The following figure summarizes the need of good history taking clinical methods and when to ask for investigations.

Figure 1: Graphical representation of probability and threshold



In our medical schools we are taught about the investigations especially in ideal set up which might not be same when we practice in community. There has been development of lots of rapid diagnostic test (RDT) kit for the diagnosis of common infectious disease. This made laboratory available at the community level. Knowing about these RDTs sensitivity, specificity and their complements (false negative and false positive) help us to establish more strong evidences to rule in/out the clinical diagnosis. If an RDT is antigen detection test the clinician should know the appropriate time of sample collection when the sample has adequate amount of antigen. NS1 antigen detection test may be negative before day 2 and after day 10 of fever hence requesting this test may be false negative on these time frames. If an RDT is antibody detection test it takes time to be positive and may last lifelong. The rK39 test done in a patient with chronic fever and if test is positive it could be naive leishmaniasis case or past treated case of leishmaniasis with some other cause of fever. Hence knowing type of RDT and its' false positive and negative gives better interpretation of the test.

The post-test probability of these RDTs depends upon prevalence of the disease in a community, sensitivity and specificity. For example if a test is 90% sensitive and 80% specific then we cannot calculate post-test probability unless we have pre-test probability which is usually prevalence. So if a disease is 5% prevalent in population A and 10% prevalent in population B the post-test probability will be 19% and 33%. This is so because if there are 1000 population in A then disease will be 50 and test will detect 45 as true positive and 5 as false negative. Also there will be 950 people disease free and test will rule in disease free (true negative) as 760 and 190 as false positive. The total number of cases detected by test if used to screen all the population will be 235 (45 and 190). Hence, post-test probability will be 45 out of 235 i.e. 19%. So with this test likely of treating 4 non diseased populations for 1 patient exist (190/45). Likely for population B with sample size of 1000 there will be 100 diseases with 90 as true positive and 10 as false negative whereas there will be 900 disease free with 720 as true negative and 180 false positive. The total number of cases detected by test if used to screen all the population B will be 270 (90 and 180). Hence, post-test probability will be 90 out of 270 i.e. 33%. So with this test likely of treating 2 non diseased populations for 1 patient exist (180/90). Hence prevalence changes the post-test probability.

Table 2: prevalence effect on post-test probability

Population A	1000	**PREVALENCE**	**5%**	**Population B**	1000	**PREVALENCE**	**10%**
	TEST +	TEST -	TOTAL		TEST +	TEST -	TOTAL
DISEASE	45 (TP)	5 (FN)	50	DISEASE	90 (TP)	10 (FN)	100
NON DISEASE	190 (FP)	760 (TN)	950	NON DISEASE	180 (FP)	720 (TN)	900
Post-test pro.			**19%**				**33%**

If we offer another test with sensitivity of 80% and specificity of 90% then post-test probability will be 30% and 47% for population A and B.

Table 3: prevalence effect on post-test probability with higher specificity

Population A	1000	**PREVALENCE**	**5%**	**Population B**	1000	**PREVALENCE**	**10%**
	TEST +	TEST -	TOTAL		TEST +	TEST -	TOTAL
DISEASE	40 (TP)	10 (FN)	50	DISEASE	80 (TP)	20 (FN)	100
NON DISEASE	95 (FP)	855 (TN)	950	NON DISEASE	90 (FP)	810 (TN)	900
Post-test pro.			**30%**				**47%**

Hence, increase in specificity increases the post-test probability. So with this test B likely of treating 2 non diseased people for 1 patient exist with population A (95/40) and treating 1 non diseased people for 1 patient exist with population B (90/80).

Threshold is when error of making false negative equals error of making false positive. So if the a third test has sensitivity of 82% and specificity of 98% then for population B error of making false positive is equal to false negative. The post-test probability will be 82%.

Table 4: Comparison between false positive to false negative

Population A	1000	**PREVLANCE**	**5%**	**Population B**	1000	**PREVLANCE**	**10%**
	TEST +	TEST -	TOTAL		TEST +	TEST -	TOTAL
DISEASE	41 (TP)	9 (FN)	50	DISEASE	82 (TP)	**18 (FN)**	100
NON DISEASE	19 (FP)	931 (TN)	950	NON DISEASE	**18 (FP)**	882 (TN)	900
Post-test pro.			**67%**				**82%**

If another test has sensitivity of 82% and specificity of 99% then the number of error of commission and omission will be same for population A.

Table 5: Comparison between false positive to false negative

Population A	1000	**PREVLANCE**	**5%**	**Population B**	1000	**PREVLANCE**	**10%**
	TEST +	TEST -	TOTAL		TEST +	TEST -	TOTAL
DISEASE	41 (TP)	**9 (FN)**	50	DISEASE	82 (TP)	**18 (FN)**	100
NON DISEASE	**9 (FP)**	941 (TN)	950	NON DISEASE	**9 (FP)**	882 (TN)	900
Post-test pro.			**82%**				**90%**

If another test has sensitivity of 60% and specificity of 45% then the number of error of commission and omission will be same for population B.

Table 6: Comparison between false positive to false negative

Population A	1000	**PREVLANCE**	**5%**	**Population B**	1000	**PREVLANCE**	**10%**
	TEST +	TEST -	TOTAL		TEST +	TEST -	TOTAL
DISEASE	30 (TP)	**20 (FN)**	50	DISEASE	60 (TP)	**40 (FN)**	100
NON DISEASE	**428 (FP)**	522 (TN)	950	NON DISEASE	**40 (FP)**	860 (TN)	900
Post-test pro.			**82%**				**60%**

If we observe last three tables the post-test probability is equal to sensitivity of the test when the number of false positive equals false negative. If we consider error of not treating a disease patient (as test showed it as false negative) equals error of treating a patient with different diagnosis (as test was false positive) then it is the threshold. As per table 4 and as per table 5 the threshold for population B and population A is made 82% respectively however the specificity for the population B is 98% and 99%. If we observe table 6 for population B we made threshold of 60% and specificity 45%. Hence if we choose high sensitivity test (low error of omission) than we need to choose high specificity test (low error of commission) to have equal number of errors and reverse. So while screening a disease it is better to use high sensitive test and while conforming diagnosis it is better to use high specificity test. This applied for even clinical methods too. While suspecting a disease in a patient in OPD/Inpatient it is better to ask common clinical manifestation which means it is very sensitive clinical methods. Suspecting malaria in an acute febrile patient from tropical is very sensitive (low error of omission) but less specific (high error of commission) clinical methods. However it is not very specific but presence of splenomegaly makes the clinical methods less sensitive (higher error of omission as compared to previous situation) but more specific (lower error of commission as compared to previous situation). The ideal methods or test is one with maximum sensitivity and specificity but it does not occur in real scenario. In real scenario if we increase sensitivity the specificity drops and vice versa. This means if we try to decrease error of omission the error of commission increases and vice versa. Clinical threshold depends upon matching between these two errors.

If disease is life threatening or becomes severe within few days or highly infectious or patient is unlikely to follow up it is better to choose low error of omission and accept high error of commission. All febrile cases were treated as Ebola in Africa during the outbreak though some of them mightn't not have Ebola. The threshold for treatment was low as they used low specificity criteria. Similarly if the disease has prolong duration of course or less infectious or patient is likely to have follow up it is better to choose high specificity test provided it is affordable. That means the clinical threshold to treat this patient is high. Clinical threshold for treating malaria (acute fever) might be kept low as compared to Kala azar (chronic fever). Likely clinical threshold to treating suspected pulmonary tuberculosis should be kept low as compared to non-pulmonary non severe form of tubercular effusion. Clinical threshold to treat suspected tubercular meningitis should be kept low as compared to non-severe form of suspected pulmonary tuberculosis. Clinical threshold to treating suspected pulmonary tuberculosis in a lactating

woman should be kept low as compared to non-lactating woman. A minimal respiratory symptom of sarcoidosis patient tagged as tuberculosis and treated with antitubercular drugs is less error than invasive fungal infection of lungs being treated as tuberculosis. The likely of patient having worsened with invasive fungal infection is more as compared to sarcoidosis. Similarly not diagnosing/treating a tuberculosis patient (cervical tubercular lymphadenitis) seems less error than a laryngeal tuberculosis patient. Being not able to diagnosis/treat highly contagious (High pathogenic avian influenza) and difficult to treat (MDR TB) have more adverse outcome. Hence acceptability of clinical decision of commission error and omission error depends upon availability of the test/ treatment, outcome of the patient and its consequences. Hence patient factor, logistic supply of investigation and drugs, disease nature and drugs factor determines the clinical threshold. Clinician should determine benchmark to accept these errors.

A lower threshold for these errors should be kept if the disease is life threatening, highly contagious, very difficult to treat and patient is of vulnerable group (extreme of ages, pregnancy, and underlying non communicable disease). Hence over treatment (error of commission) is justified than under treatment (error of omission) if these characteristics are observed in a patient provided the both treatment is effective. However if one treatment plan is likely to have more side effects then it will have more adverse consequences. For example a trail of non tubercular bacterial pneumonia is safer than tubercular from treatment point of view. Miltefosine has lesser side effects than Amphoteracin B however Miltefosine is not preferred due to more relapses seen in Visceral Leishmaniasis. A very high threshold should be kept if the disease is of benign or self limiting in nature, slow progressing and with low contagious. Hence under treatment (error of omission) is justified than over treatment (error of commission) in these scenarios. Suspecting bacterial sore throat in majority of common cold patient and over treating with antibiotics may be practiced in our clinical set up however we know more than 90% of common cold is viral. This error of commission practices makes immense use of antibiotics when they are really not required and seems ill justified. There are lots of recommendations for prescribing antibiotics. Here are some of them.

1. Threshold to initiate antibiotics treatment in fever with sore throat is more than 1 Centor score

- **Centor Criteria** (presence of each clinical feature scores 1 point)

    a. History of fever
    b. Tender anterior cervical lymphadenopathy
    c. Absence of cough
    d. Tonsillar exudates

2. Threshold to initiate immediate antibiotics in bronchitis if any of the following

- **>80 years of age with one of the following (The age factor may be slight low in south Asian set up):**

    a. Hospitalization in the past year
    b. Diabetic
    c. On oral corticosteroids

- **CHF OR >65 years of age with 2 of the following**.

    a. Hospitalization in the past year
    b. Diabetic
    c. On oral corticosteroids

3. All acute clinical cases of pneumonia will benefit by antibiotics and CURB-65 score is benefit tool. Threshold for inpatient management of Pneumonia
   Assess **CRB-65 score**: Each scores 1:
    a. Confusion
    b. Respiratory rate ≥30 breaths/min
    c. BP systolic ≤ 90mmHg or diastolic ≤ 60mmHg
    d. Age ≥65 yrs

   (Score 3-4 admit urgently Score 1-2 arrange same day secondary care assessment or admission Score 0 likely to be able to treat at home)

4. Threshold to initiate Antibiotic indication in COPD
    a. Treat exacerbations with antibiotics promptly if there is purulent sputum and increased shortness of breath and/or increased sputum volume
    b. Exacerbation with consolidation on a CXR or clinical signs of pneumonia

5. Threshold to initiate Antibiotics in urinary tract infections
    a. Men/ Women with severe/≥ 3 symptoms (frequency, urgency, dysuria, polyuria, suprapubic tenderness, haematuria)
    b. Women with mild/ ≤ 2 symptoms and positive dipstick
    c. Male, Pregnancy, Diabetic with mild/ ≤ 2 symptoms and positive dipstick

If patient is not sick and not responding to antibiotics discontinue all non-essential medications. If fever resolves after 72 hours it is drug fever if not revise your diagnosis and upgrade your investigations.

If patient is sick and not responding to antibiotics for 48 -72 hours then upgrade antibiotics and investigations watch for 48 hours. If responded treatment is appropriate if not revise your diagnosis.

2 How to approach to the patients with Jaundice

Jaundice is the clinical manifestation of elevated serum bilirubin. The normal serum concentration of bilirubin is less than 1 mg/dL (17 µmol/L). Typically, jaundice is not detectable clinically until serum bilirubin reaches 2.5 mg/dL. It is first seen in the sclera which have a particular affinity for bilirubin due to their high elastin content. It is also seen in oral mucous membranes such as the hard palate or under the tongue. Increased serum bilirubin levels occur when an imbalance exists between bilirubin production and clearance.

How patient present?

In Nepal people seldom say about yellowish discoloration of eyes, they usually say that they are suffering from jaundice disease. They may present with dark urine. When deep jaundice is present they present with complaints of yellowish discoloration of whole body. People often use crazy terms like black jaundice, white jaundice or even unseen jaundice. Another peculiar feature is that they refer jaundice as disease and other symptoms like nausea, vomiting, loss of appetite, pain abdomen as symptoms of jaundice.

History taking in jaundiced patients

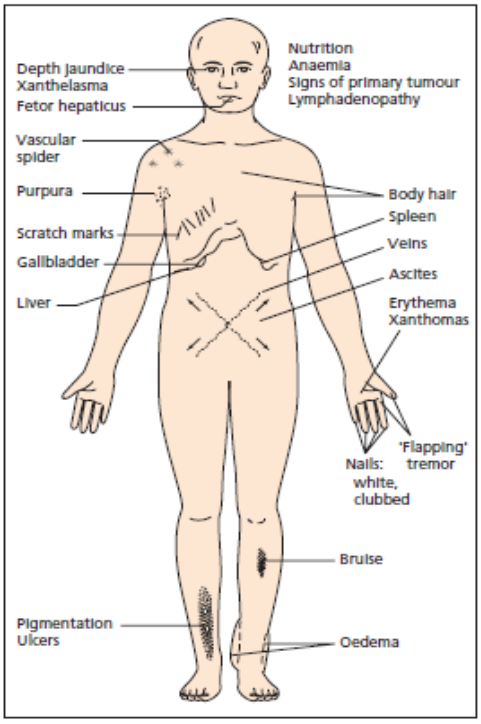
Following points should be considered while taking history. Detailed history taking can lead to diagnosis in many patients.

- Duration of jaundice – recent, chronic, recurrent
- Anorexia, nausea vomiting
- Previous attacks of jaundice
- Pain abdomen
- Chills, fever, systemic symptoms
- Itching
- Exposure to drugs (prescribed and illegal)
- Biliary surgery or any other surgery in past
- Weight loss
- Color of urine and stool
- Contact with other jaundiced patients
- History of IV drug abuse
- Blood transfusions
- Occupation

Examination of a jaundice patient

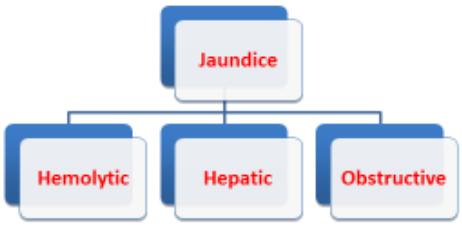
- Degree of jaundice
- Scratch marks
- Stigmata of chronic liver disease: Palmar erythema, spider nevi, clubbing, white nails, Dupuytren's contracture, gynecomastia, caput medusa
- Assessment of the nutritional status
- Jugular venous pulsation
- Pigmentation, ecchymosis
- Per abdominal examination
    - Liver: Size, surface, edge, tenderness
    - Palpation of gall bladder
    - Splenomegaly
    - Abdominal mass and lymph nodes

Physical signs to be seen in patients with jaundice



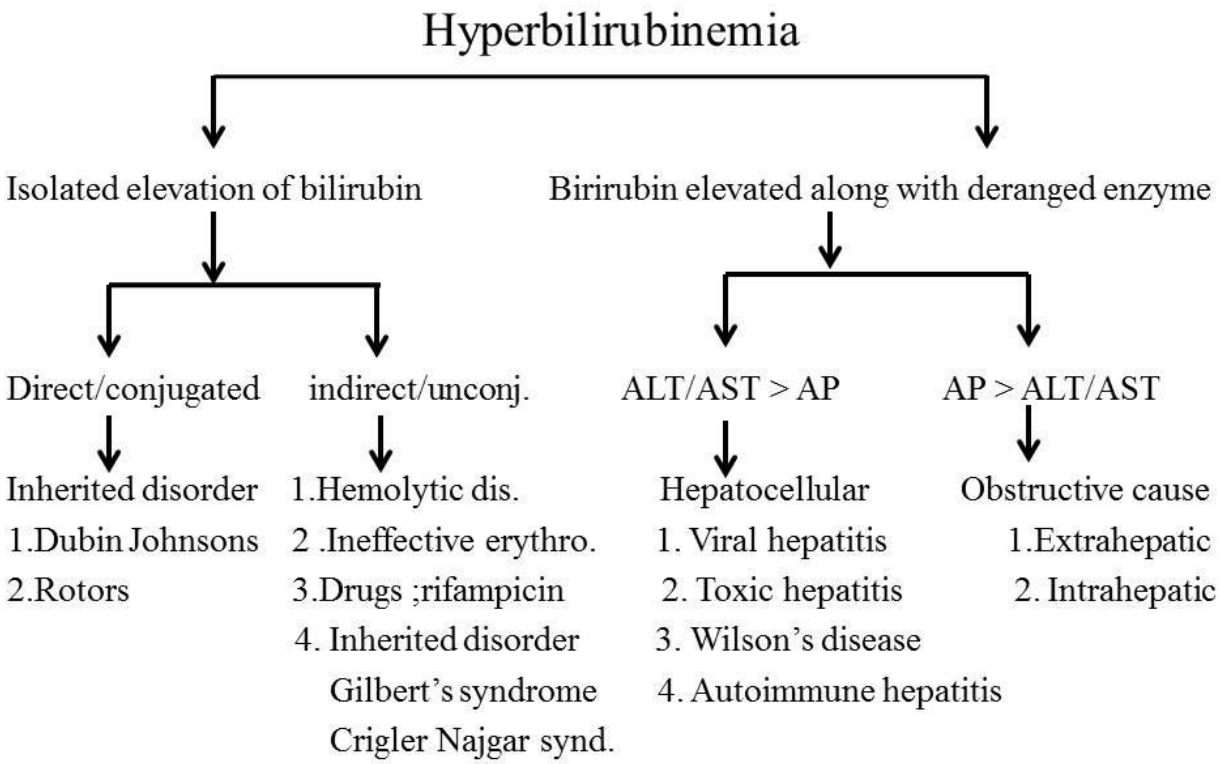
Jaundice

- **Normal Serum Bilirubin (SB) is 0.3 to 1.0 mg%**



Approach to a patient with suspected infective jaundice (most likely infective jaundice)

Algorithm for Suspected Infective Jaundice



Relevant points in history

• How long been jaundiced?

• Ever been jaundiced before?

• Any associated fevers or abdominal pain or weight loss?

• Pale stool and dark urine?

• Any recent foreign travel (hepatitis, malaria)?

• Any risk factors for hepatitis (tattoos, IVDU, high risk professions, blood transfusions, multiple sexual partners)?

• PMH of blood disorders (e.g. SCD, thalassemia)?

• DH any new medications that can cause jaundice?

• SH excess alcohol intake

• FH of jaundice (inherited disorders of bilirubin metabolism)

An Approach to Jaundice

• Is it isolated elevation of serum bilirubin?

• If so, is the ↑ unconjugated or conjugated fraction?

• Is it accompanied by other liver test abnormalities?

• Is the disorder hepatocellular or cholestatic?

• If cholestatic, is it intra- or extrahepatic?

Examination findings

• Icterus

• Signs of chronic liver disease

• Palpable gallbladder

• Scratch marks over body

USG Abdomen

• Liver size, Shape, Echotexture, SOL.

• Intrahepatic biliary radical

• CBD

• Gallbladder

• Pancreas

MRCP

• CBD stone

• Benign biliary stricture

• Malignant biliary stricture

• Chronic pancreatits

CECT abdomen

• Liver SOL

• Carcinoma GB

• Pancreatic Carcinoma

• Lymphnodal mass causing external compression

Biochemical test for intrahepatic cause

• HBsAg

• IgM Anti HAV

• IgM Anti HEV

• Autoimmune Markers

• Serum Ceruloplasmin

Management

• Depends on type of jaundice.

• Intrahepatic cause- Except for few causes no specific treatment available

• In acute viral hepatitis use of antivirals is a debatable.

• In wilsons disease use of chelating agents.

• In autoimmune liver disease use of steroids and other immunosuppressors

- Obstructive cause
- ERCP for CBD stone, benign biliary stricture.
- ERCP stenting for malignant CBD stricture, carcinoma head of pancreas and external compression.
- Surgical bypass for malignant stricture and carcinoma head of pancreas.
- Percutaneous or ERCP based stenting for carcinoma Gall bladder.

Diet

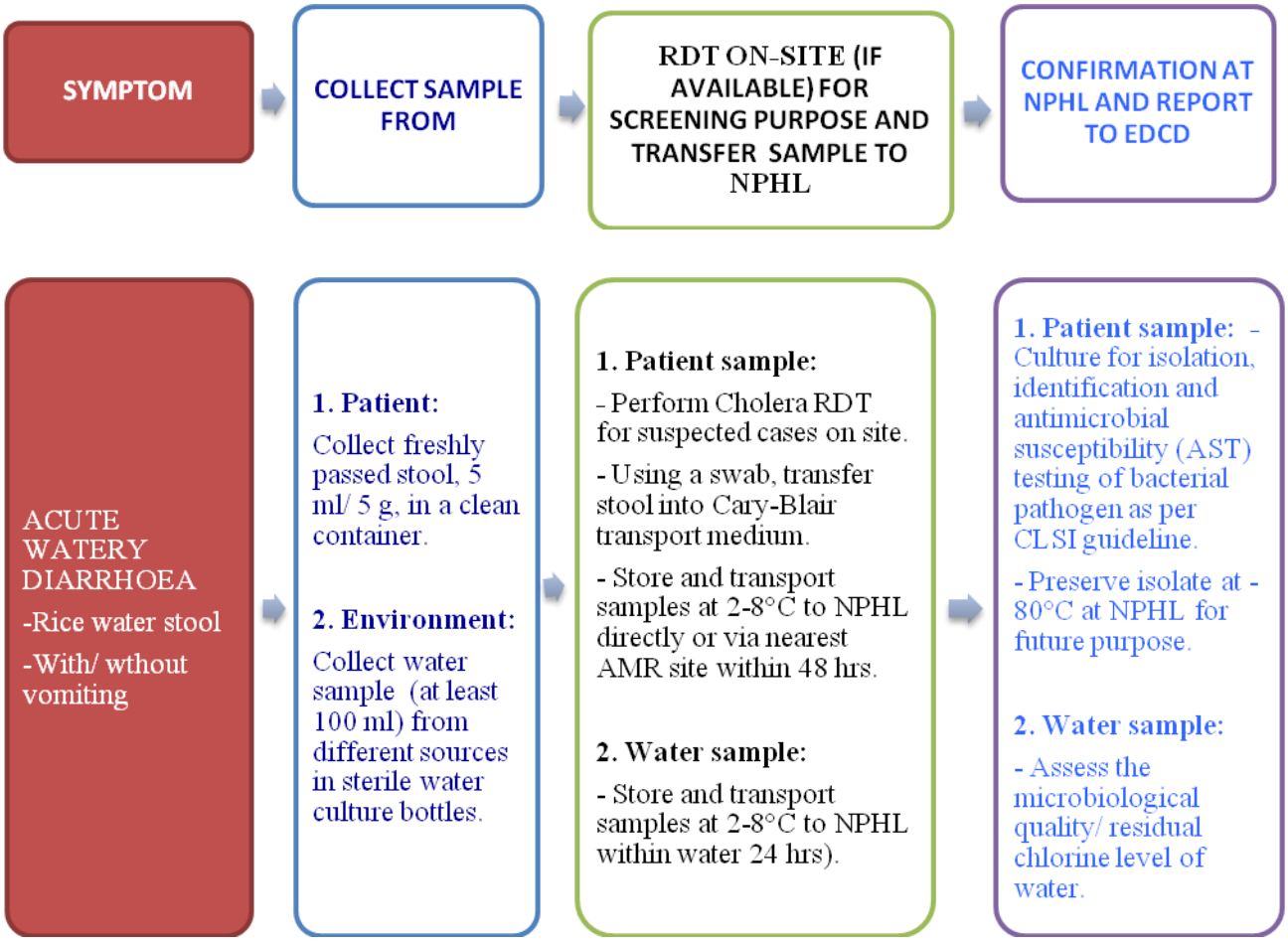
- A normal wholesome diet is recommended in any jaundice.

ACUTE WATERY DIARRHOEA (rice watery stool with/ without vomiting)

Definition

Patients with painless rice watery diarrhea (with or without vomiting) more than three times in a day is usually suspected cholera case.

Investigation chart

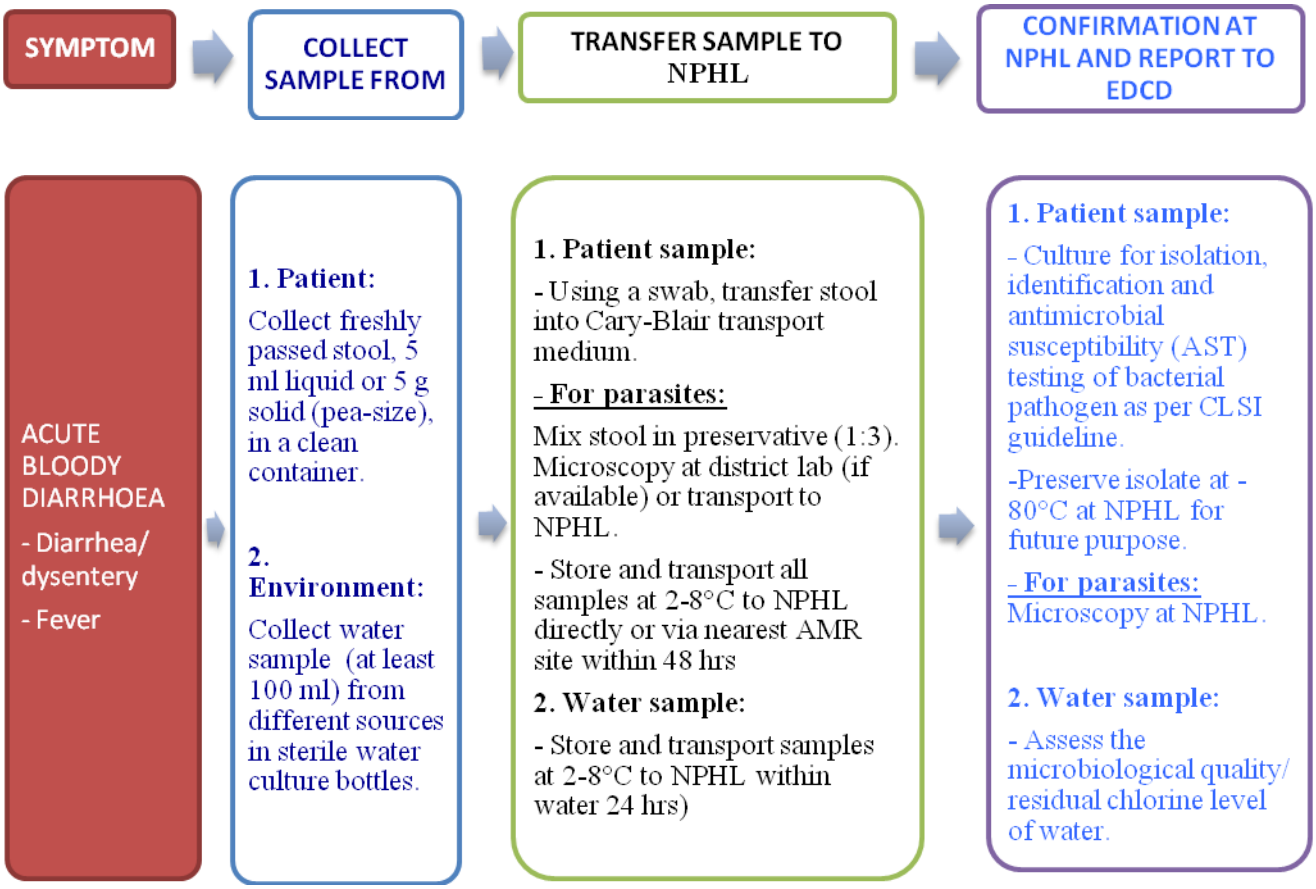


ACUTE BLOODY DIARRHOEA (with fever)

Definition

Dysentery is bloody diarrhea, i.e. any diarrhoeal episode in which the loose or watery stools contain visible red blood. Dysentery is most often caused by *Shigella* species (bacillary dysentery) or *Entamoebahistolytica* (amoebic dysentery).

Investigation chart

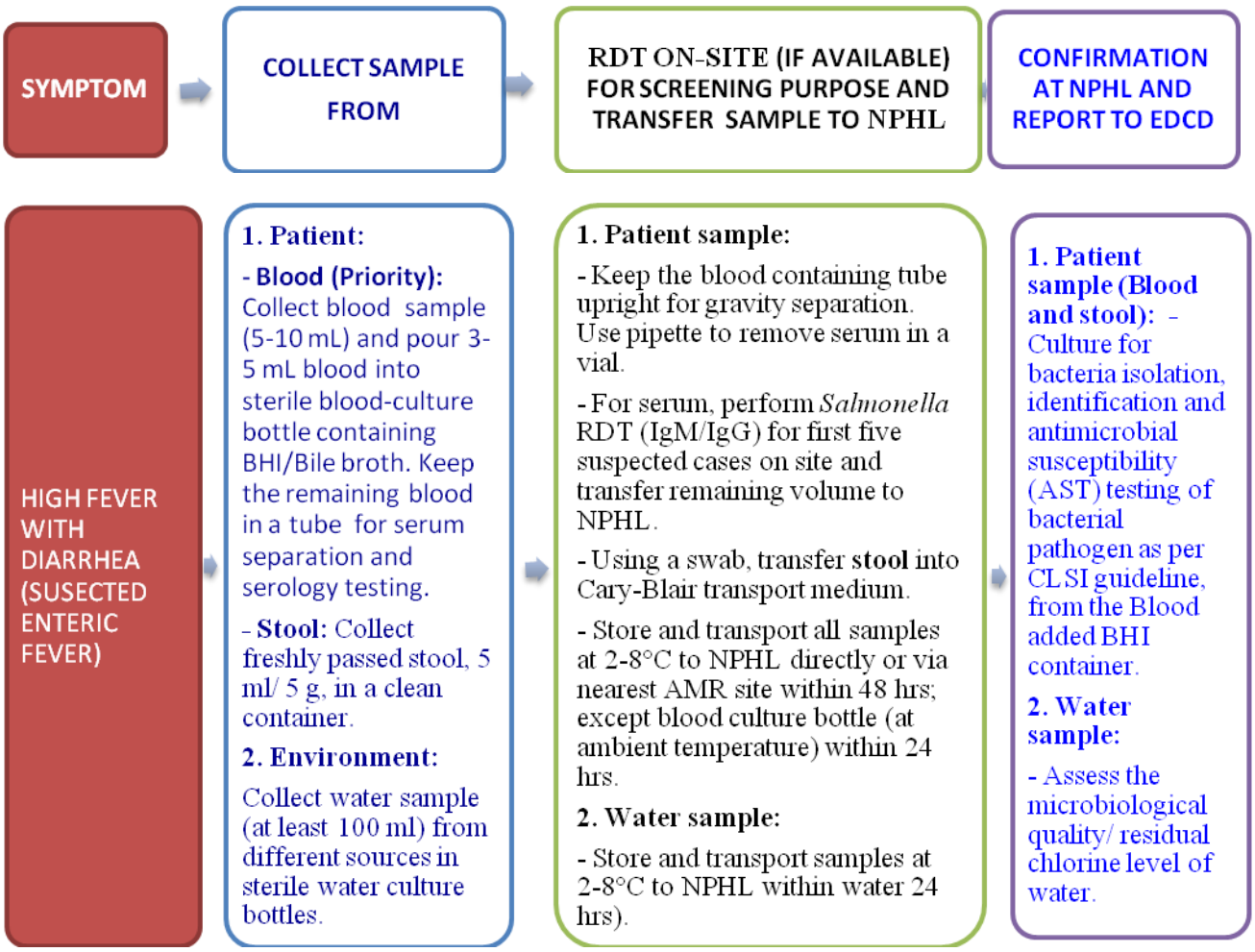


HIGH GRADE FEVER WITH DIARRHEA (SUSPECTED ENTERIC FEVER)

Definition

Typhoid fever is a life-threatening illness caused by the bacterium *Salmonella Typhi/ Paratyphi*, transmitted through eating food or drink contaminated with *Salmonella* spp.

Investigation chart

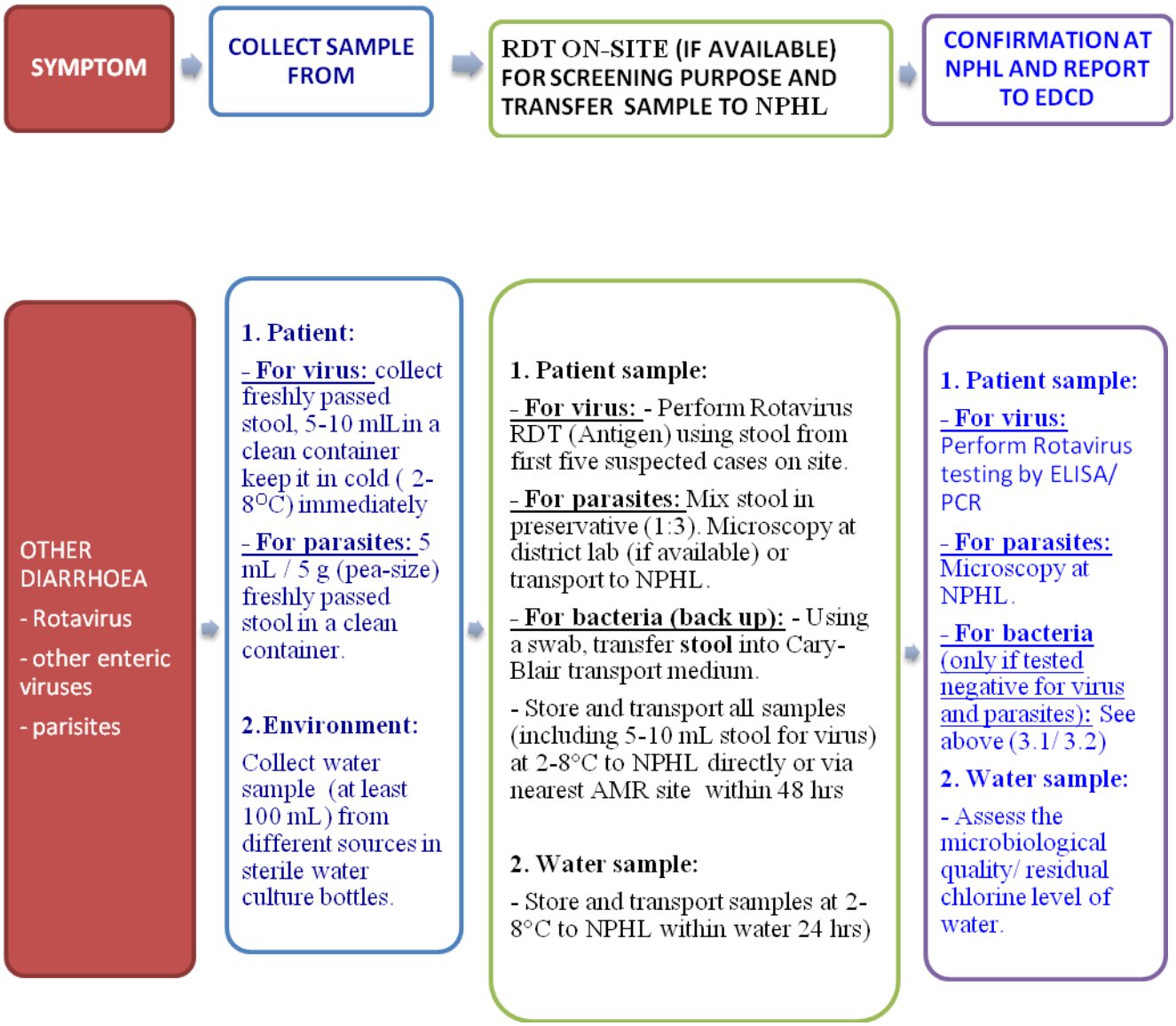


OTHER DIARRHOEA

Definition

Patient with typical diarrhea for few days without blood/ mucus and no sign of cholera and enteric fever

Investigation chart

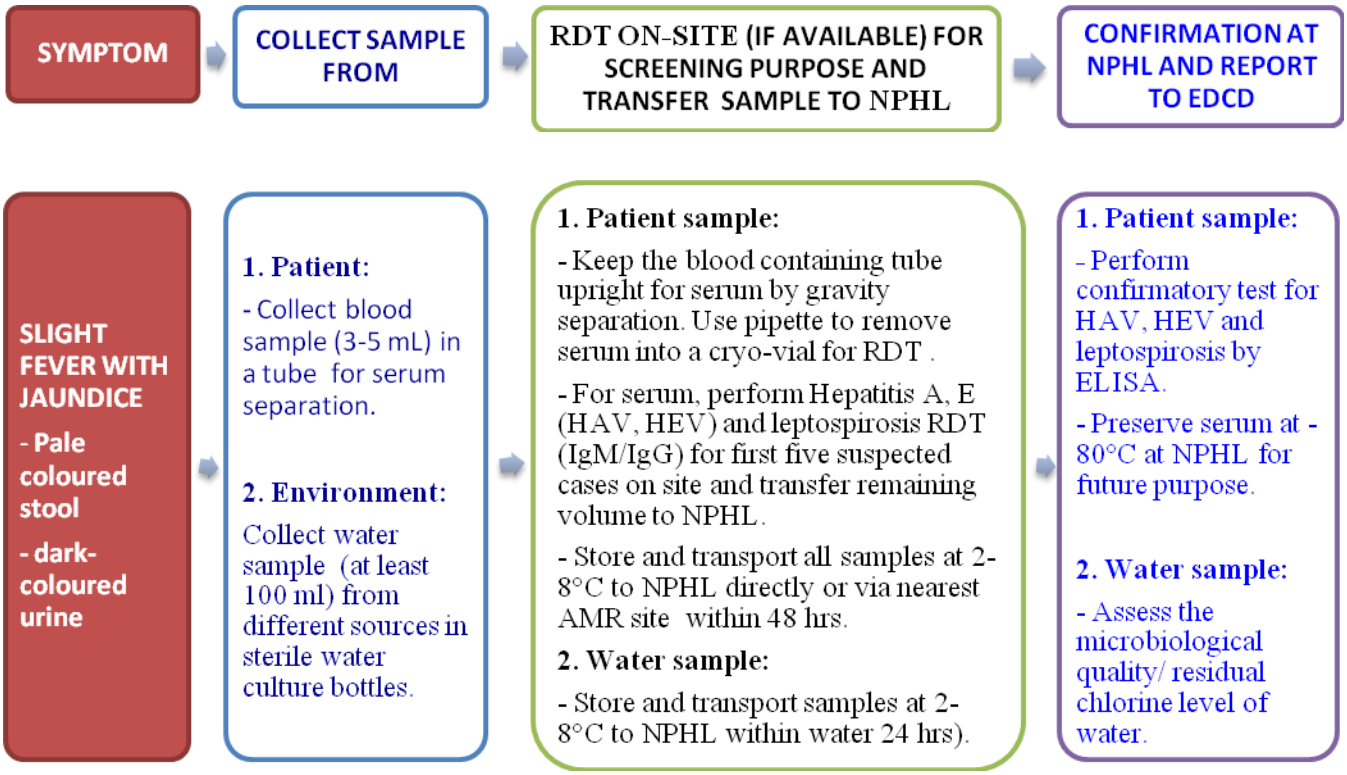


SLIGHT FEVER WITH JAUNDICE

Definition

Patient with sign of Jaundice**(**Nausea**,** slight fever**,** Pale colored stool**,** dark-colored urine, etc.)

Investigation chart

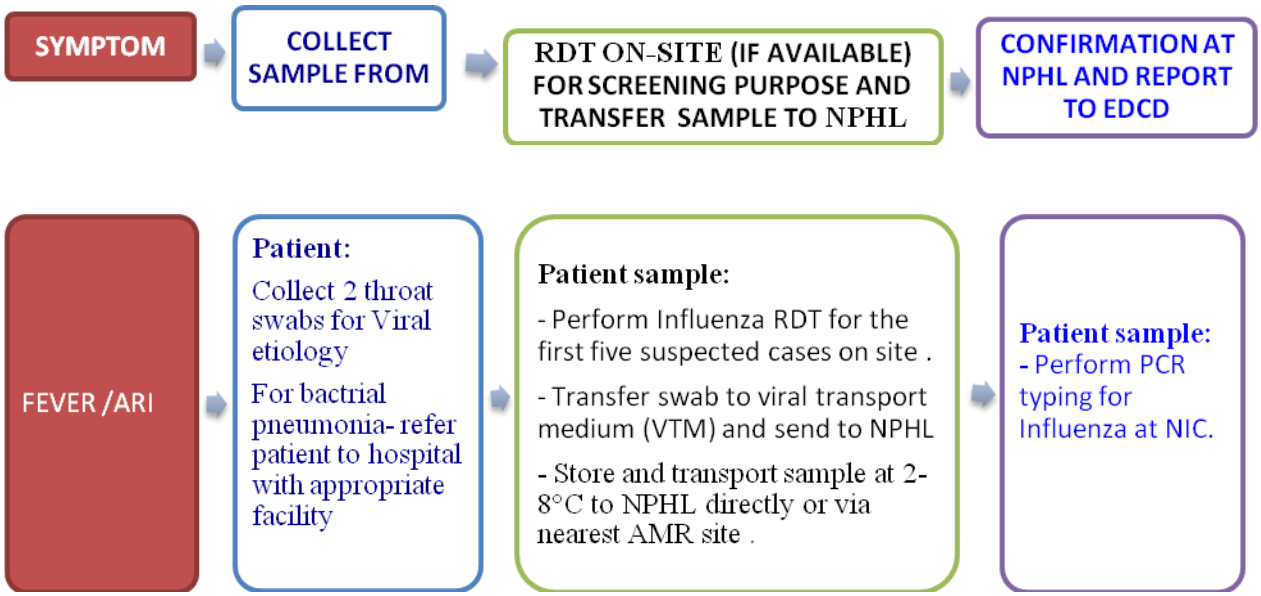


ACUTE RESPIRATORY INFECTION (ARI/ILI/SARI)

Definition

A patient with flu like symptoms and with/without fever > 38^0C, cough, shortness of breath or difficulty in breathing plus history of exposure in the 7 days prior to the onset of symptoms.

Investigation chart

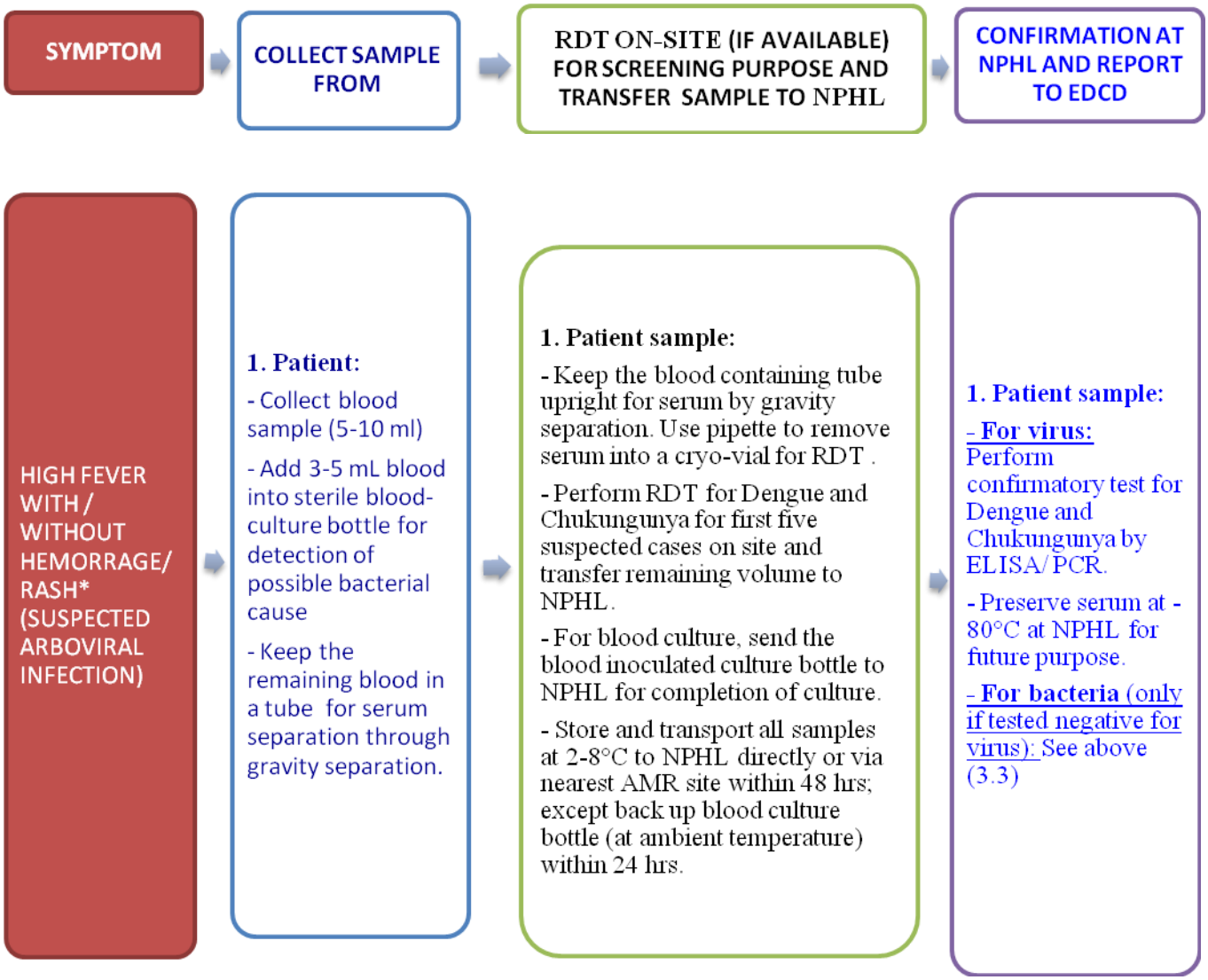


HIGH FEVER WITH OR WITHOUT HEMORRAGE/ RASH (SUSPECTED ARBOVIRAL INFECTION)

Definition

Patients with fever plus headache, myalgia, retro-orbital pain, arthralgia, rashes nausea/ vomiting, etc. with epidemiological link are suspected of Dengue/Chikungunya or other hemorrhagic fevers.

Investigation chart

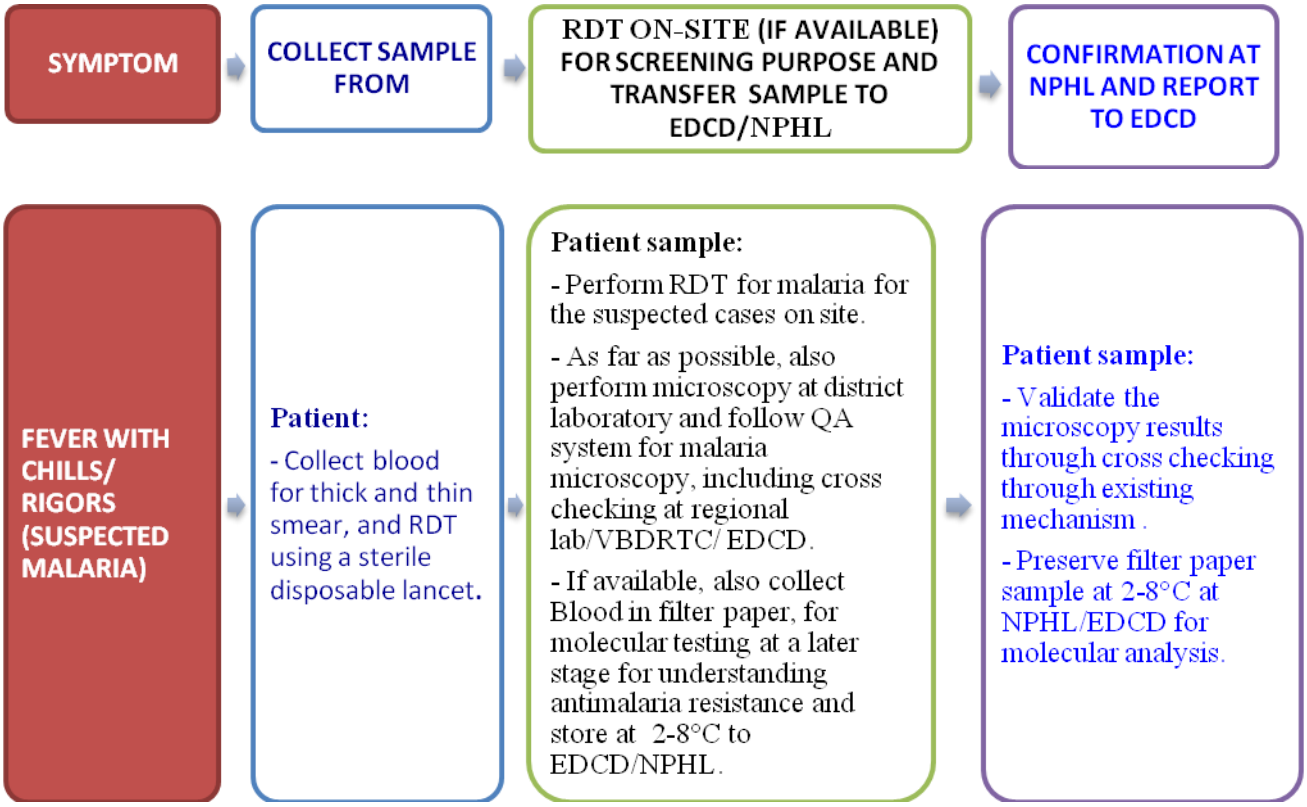


FEVER WITH CHILLS (SUSPECTED MALARIA)

Definition

Patients with intermittent fever plus chills, rigors, headache, etc. with epidemiological link.

Investigation chart



Chapter III: Respiratory Illness

Severe Acute Respiratory syndrome (SARS)

Disease name	**Severe Acute Respiratory syndrome (SARS)**
ICD-10 code	ICD-10 UO4.9
Epidemiology	**Background/causative agent:** SARS is rapidly progressive acute respiratory illness, caused by SARS-coronavirus (SARS-CoV); an enveloped RNA virus that can infect mammals and birds. SARS was first recognized in mid-November 2002 in the Guangdong province of China. By late February 2003, it had spread internationally and epidemic ended in July 2003. The disease infectivity (Ro) is between 2-4. **Incubation period** 2-10 days prior to onset of first symptom typically fever. Peak viral load is at day 12-14 of infection **Reservoir** Animals possibly palm civets (similar to cats) or bats **Transmission** SARS spread by direct contact and large respiratory droplets of stool, and body fluids, and in some situation by fomites. Nosocomial transmission has been a striking feature in most outbreaks. Transmission does not occur before clinical signs and symptoms and maximum period of communicability is less than 21 days. **There is no documented human-to-human transmission since 2004.**
Clinical features	**A two staged illness** **1. Prodromal phase-** a. prodrome of fever (>38^{0}C). with or without rigors b. non-specific systemic systems- headache, myalgia and malaise **2. Respiratory phase-** a. Starts 3-7 days after the prodromal phase with dry cough and breathlessness and may progress to respiratory failure requiring ventilatory support in ICU b. Large volume watery diarrhea with or without blood or mucus in 70% patients *Presence of cough, myalgia, diarrhea, and rhinorrhea or sore throat has 100% sensitivity and 76% specificity for identifying patient with SARS* *Physical examination reveals minimal signs.*
Investigations	1. WBC- normal or reduced, thrombocytopenia 2. Raised creatine phosphokinase, SGPT and LDH. Raised LDH is associated with poor outcome 3. CXR- may be normal or show diffuse bilateral interstitial

	infiltrates in lower and peripheral zones. Cavitation, hilar lymphadenopathy and pleural effusion are uncommon. 4. CT chest- interstitial infiltrates, ground glass opacities and interlobular septal thickening 5. Respiratory samples and stool samples should be collected for real time polymerase chain reaction (RT-PCR). RT-PCR has sensitivity 80% in respiratory samples. RT-PCR assay can detect virus in stool for more than 4 weeks after onset of illness.
Differential diagnosis	Bacterial pneumonia, TB, viral pneumonia, atypical pneumonia, cardiac and other systemic illnesses
Diagnosis/ Case definition	**Suspected SARS-CoV:** • Fever >38^0C **PLUS** • One or more symptom of lower respiratory tract illness- cough, breathlessness **PLUS** • Radiological infiltrate consistent with pneumonia or ARDS, or autopsy finding consistent with pneumonia or ARDS without identifiable cause **PLUS** • No alternate diagnosis to explain the illness **Probable SARS-CoV:** • Clinical criteria PLUS epidemiological linkage (for e.g. contact with a confirmed SARS-CoV infected patient, traveling from or living in SARS-CoV prevalent area) **Confirmed SARS-CoV:** • Above features PLUS lab confirmation of SARS-CoV infection
Investigation	**Laboratory:** • Positive laboratory findings for SARS-CoV based on one or more of -PCR positive for SARS-CoV for two separate samples -Seroconversion by ELISAor IFA • -Virus isolation
Management of patient	1. No specific treatment other than general supportive care. Ribavarin is NOT recommended. 2. Steroid (e.g. prednisolone 1mg/kg) has been found to reduce fever and need of oxygen, and has been used if • PaO_2< 70 mmHg or SpO_2< 90% on room air. No controlled trialhas shownreduction in mortality 3. Broad spectrum antibiotics to cover organisms causing community acquired pneumonia or as per antibiogramifavailable
Case fatality rate	9.5% but fatality rate was 43% for those aged ≥ 60 years
Management of contacts and immediate	1. Trace the contact systematically. A contact is defined as a person who cared for or lived with confirmed case of SARS or a person under investigation or who had direct contact with their respiratory secretions,

management	body fluids and/or excretions. 2. Informthe signs,symptoms and modes of transmission of SARS to each contact 3. Place the contact for surveillance for 10 days and explain that fever is the first symptom to occur in most cases
Prevention and control measures	1. Identify all suspected and probable cases 2. Health care workers involved in patient management should wear a face mask with eye protection, and gloves and should wash hands before and after contact with any patient. 3. Disinfect with hypochloride solution (non-metallic objects) or 70% alcohol (metals) 4. Patient care- minimization of aerosol generating procedures- nebulization, steam inhalation, bronchoscopy and ventilation (CPAP, BiPAP)
Special considerations	SARS-CoV infection is a reportable case to EDCD, DPHO, and other concerned authorities as soon as it is confirmed.
Message to the general public	Methods to prevent the spread of infection, like washing hands, avaiding direct contacts and timely reporting and getting tested

Nipah virus (NiV) disease

Disease name	**Nipah virus (NiV) disease**
ICD-10 code	**ICD-10 B 33.8**
Epidemiology	**Background/causative agent:**Nipah viral disease is one of zoonotic infections caused by Nipah virus, a member of the family Paramyxoviridae, genus Henipavirus. It was first identified and isolated in Malaysia in 1999 during outbreak of encephalitis and severe respiratory illness among pig farmers and people with close contact with pig. Virus was named after SungalNipah, a village in Malaysia Peninsula. Another outbreak occurred in Bangladesh in 2001 and repeated outbreaks have been reported there since then. Outbreak in Siliguri, India occurred in 2001 with reports of human-to-human transmission in hospital settings. **Incubation period:** 5-14 days **Reservoir** Fruit bats members of genus *Pteropus*are the major reservoirs. Pig is an intermediate host but infected cows, goats and dogs have been reported **Transmission** **3 known pathways** 1. Drinking of contaminated fresh date palm sap- majority of cases in Bangladesh 2. Via direct contact with infected bats, pigs, or from other NiV infected people's secretions. **3.** Direct contact with NiV-contaminated fruit bat secretions**Risk groups** All age groups are susceptible. People who come in close contact with infected swine are at increased risk
Clinical features	Manifestations of NiV infection range from asymptomatic infection to acute respiratory illness to fatal encephalitis. 1. Patient may present with **influenza-like symptoms**- fever, headache, myalgia, vomiting and sore throat. 2. Neurological symptoms- Drowsiness, dizziness, seizures, followed by altered mental status and neurological deficit **(encephalitis**). These may progress into coma and death within 24-48 hours. Majority of patients who survive will have full recovery but 20% of cases will have neurological deficit. 3. Some patients present with pneumonia leading to ARDS

Diagnosis	Diagnosis can be established in a patient with clinical history suggestive of NiV by direct virus isolation or polymerase chain reaction(RT-PCR) in blood, CSF, throat and nasal swabs and urine at the early stage of infection. At a later stage, antibody (IgM and IgG) can be detected by ELISA. In fatal cases, tissues (eg. brain, spleen) can be used for virus isolation, RT-PCR and immunohistochemistry.
Differential diagnosis	Other causes of encephalitis and severe respiratory illness need to be considered. 1. Viral encephalitides e.g. Herpes simplex encephalitis, Japanese encephalitis (JBE), 2. Bacterial meningitis 3. Cerebral malaria 4. Influenza and influenza like illness
Case fatality rate	40-75%; variation in different outbreaks
Case definition	**Suspected case** A person fulfilling both of the following criteria. 1. Features of acute encephalitis: a. Acute onset of fever AND b. Evidence of acute brain dysfunction manifested as i. Altered mental status OR ii. New onset of seizures OR iii. Any other neurological deficit 2. Epidemiological linkage a. Drinking raw date palm sap OR b. Occurring during Nipah season OR c. Patient from Nipah endemic area **Probable case** A person with features of acute encephalitis a. during a Nipah outbreak in the area OR b. with history of contact with confirmed Nipah patient Respiratory features may present in patients with suspected or probable cases with or without encephalitis. The respiratory features are a. Onset of illness < 7 days duration AND b. Acute onset of fever AND c. Severe shortness of breath, cough AND d. Chest radiograph showing diffuse infiltrates **Confirmed case** A suspected or probable case of Nipah virus infection with microbiological confirmation either by a. IgM antibody against Nipah virus by ELISA in serum or CSF b. Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid
Management of	There is no definite therapy for Nipah viral disease. Management is supportive.

patient	Because of the risk of person-to-person transmission, standard infection control practices and proper barrier nursing techniques should be followed. Ribavirin has been found effective only in vitro and usefulness in clinical practice remains uncertain. **ICU management is indicated if** a. signs of impending respiratory failure: respiratory rate > 30/min in adult and > 70/min in children b. Oxygen saturation <90% and central cyanosis despite oxygen supplementation of 5 litres/min through mask c. Uncontrolled seizures d. GCS <8 e. Hemodynamic instability i.e., bradycardia, hypotension and capillary refilling time > 3 seconds f. Multi-organ failure
Prevention and control measures	1. Prevention of person-to-person transmission a. Through hand washing with soap water after contact with patient b. Maintenance of distance of >1meter c. Keeping personal items separately d. Washing used items of the patient separately 2. Boiled date palm sap is safe 3. Prevention of transmission to health care workers a. Admission of suspected cases to the isolation ward b. Use of mask and gloves during clinical examination, sample collection and care giving c. Following standard precautions of infection prevention 4. Contacts and source of infection should be searched to identify missed cases. 5. Outbreaks of Nipah viral disease in animals have preceded human cases, animal health surveillance system should be established
Vaccine	Post-exposure prophylaxis by using human monoclonal antibody targeting the G glycoprotein of NiV has been found effective in experimental animals
Special considerations	1. Case should be reported to the health authority at once 2. Following epidemic measures should be carried out a. Animal handlers should practice precautionary measures- protective clothing, gowns, boots, gloves and face shield b. Culling of infected swine with burial or incineration of carcasses should be done under supervision with biosecurity protection c. Movements of animals from infected farms to other areas should be restricted d. Infected person should be isolated to prevent person-to-person transmission
Message to the general public	

Middle East respiratory syndrome corona virus (MERS-CoV)

Disease name	**Middle East respiratory syndrome coronavirus (MERS-CoV)**
ICD-10 code	
Epidemiology	**Background/causative agent:** MERS-CoV, an enveloped RNA virus was first identified in June 2012 in a 60-year old man in Saudi Arabia who died due to acute pneumonia and renal failure. By June 2014, 699 cases of laboratory confirmed cases including at least 209 deaths had been reported to WHO. **Incubation period:** Approximately 5 days (range 2-14 days) **Reservoir** Reservoirs remain unknown. Closely related beta-coronavirus has been found in numerous batsin Middle east including insectivorus bats. **Camels** Tr**ansmission** 1. Non-human to human: route of transmission from animals to human is not fully understood **2.** Human-to-human: while providing unprotected care to infected persons. There have been clusters of cases in health care facilities when infection prevention and control practices are inadequate. No evidence of sustained human to human transmission was found in republic of Korea. **Risk groups** The main risk factor is contact with with a person infected with MERS-CoV. Commonly reported co-morbidities associated with severe disease or death are diabetes, immunosuppression and heart disease. Health care workers involved in procedures which generate aerosol- Nebulization or intubation and ventilation are at greastest risk.
Clinical features	Clinical picture ranges from asymptomatic or mild respiratory symptoms to severe acute respiratory disease and death. 1. A typical presentation is fever, cough and dyspnea. 2. Pneumonia is a common finding and severe illness can cause respiratory failure requiring intensive care support including mechanical ventilation. 3. Many have acute kidney injury and diarrhea, 4. DIC and pericarditis also seen.

	5. More severe disease was found in older people, immunocompromised persons and those with diabetes, chronic lung disease and cancer. 6. There are reported cases of co-infection with other respiratory viruses- influenza A(H1N1), parainfluenza virus, influenza B, and rhinovirus.
Diagnosis	Travel history to the Middle East and Korea should be obtained to any patient presenting with a febrile acute respiratory illness. Serum and respiratory samples from upper and lower tract should be collected for RT-PCR. **Confirmed case**: a positive PCR test result on at least two specific genomic targets for MERS- CoV or a single positive PCR target with sequence confirmation from a different genomic site
Differential diagnosis	Other causes of encephalitis and severe respiratory illness need to be considered. 1. Viral encephalitides e.g. Herpes simplex encephalitis, Japanese encephalitis (JBE), 2. Bacterial meningitis 3. Cerebral malaria 4. Influenza and influenza like illness
Case fatality rate	Approximately 36% of reported cases have died.
Case definition	
Management of patient	No vaccine or specific antiviral therapy is currently available. Treatment is supportive and based on the patient's clinical condition. It is advised to start antibiotic treatment for community acquired pneumonia at the time of admission
Management of immediate contacts and environment	1. Identify all close contacts of confirmed case. 2. Keep the contacts under active surveillance for 10-14 days with self-monitoring of respiratory symptoms 3. Paired serum samples (as soon after exposure as possible and after 4-6weeks later) should be taken from identified contact to identify MERS-CoV infection and asymptomatic cases. 4. Discard the suspect or probable case if alternative diagnosis can fully explain the illness.
Prevention and control measures	5. Identify all probable and possible cases 6. Apply standard infection control measures 7. Place the patient in a single room when possible and limit movement. When movement outside the room is required, ensure that patient

	wears appropriate personal protective equipment.
Special considerations	
Message to the general public	

LEGIONELLOSIS

Disease name	**LEGIONELLOSIS**
ICD-10 code	ICD-10 A48.1
Epidemiology	**Background/causative agent:** Legionella is obligatory aerobic, fastidious, gram-negative bacilli that stain poorly with Gram stain. L. pneumophilia causes both epidemic and sporadic infections. Out of 18 serogroups, serogroup 1 is most commonly associated with the disease. It accounts for 2-6% of community acquired pneumonia in immunocompetent hosts.. Legionella is acquired through inhalation of contaminated aerosols or aspiration. Outbreaks linked to contaminated portable water systems, ultrasonic mist devices, air conditioning condensates etc Indigenous cases have been reported within kathmadu valley in 3 patients without travel history during 2014. . **Incubation period:** 2-10 days, most often 5-6 days **Reservoir** Legionellosis is a waterborne disease and common reservoirs are potable water system (showers), air-conditioners, cooling system and decorative fountains. Warm water (25-42*C) stagnation, scale and sedimentation favor growth of bacteria. Tr**ansmission** Airborne transmission although other modes including aspiration of water are possible. Human-to-human transmission has been reported. **Risk groups** Outbreaks of legionellosis are most common in travelers and hospitalized patients. **Risk factors (personal)** • Exposure to contaminated water, • Increasing age (>50 years) • Cigarette smoking, • Alcohol use • Diabetes, cancer, • Chronic lung disease • Immunosuppression including organ transplant and corticosteroid use • End-stage renal disease, and **Risk factors (environmental)**

	• Proximity to sources of transmission, • poor design or poor maintenance of cooling water systems, • inadequate staff training
Clinical features	**a.** General- Lethargy, headache, fever (temperature may reach to 40.5·C in 1/3rd patients and may be sustained), recurring rigors, anorexia, and myalgia are early symptoms **b.** Respiratory- after several days cough becomes more pronounced with occasionally watery or purulent sputum develops. Dyspnea and pleuritic chest pain will develop in about half and one-third cases respectively **c.** Extrapulmonary- GI- watery diarrhea, nausea, vomiting, abdominal pain Neurological- headache, confusion, obtundation, seizures, hallucinations **d.** Physical findings- relative bradycardia, pleural rubs, generalized abdominal tenderness, hepatosplenomegaly, nuchal rigidity and focal neurological deficit **Laboratory findings** 1. CBC- leucopenia and thrombocytopenia especially in severely ill cases 2. Hyponatremia and hypophosphatemia are present in > 50 % cases 3. Mild elevations in serum creatinine, CPK and liver enzymes are common 4. Urine- Hematuria and proteinuria are common. Occasionally frank rhabdomyolysis. 5. CXR- radiological findings typically lag behind the early illness. Small pleural effusion develop in half of cases. Multilobar opacities are commonly seen in CT chest but frank cavitation is rare. 6. Immunological- a. Urinary antigen- the most commonly used method for diagnosis (sensitivity 60-80% and specificity > 95% for L. pneumoplilia serotype 1) b. Direct fluorescent antibody assay for sputum- sensitivity 33-68% and specificity > 95%. c. PCR-based assays for sputum have sensitivity > 80% and specificity > 90% **Situations suggesting legionellosis disease** a. Gram stains of respiratory samples showing many polymorphonuclear leucocytes with few or no organisms b. Hyponatremia c. Pneumonia with prominent extrapulmonary manifestations- diarrhea, confusion, neurological symptoms d. Failure to respond to beta-lactams, aminoglycosides or both antibiotics **ICU referral-** Earlier the better • Respiratory failure (PaO2 < 8kPa) despite high flow oxygen

	• Tiring patient with rising CO2 • Worsening metabolic acidosis despite antibiotics and fluid management • Hypotension despite adequate fluid resuscitation
Diagnosis	Clinical features and laboratory tests (see above in clinical features and laboratory tests)
Differential diagnosis	
Case fatality rate	The mortality in community-acquired Legionella is about 15%. Factors associated with poor outcome are- immunodeficiency state, delayed initiation of appropriate antibiotic therapy, comorbidities and need for dialysis or ventilatory support
Case definition	**Confirmed cases:** Clinical or radiological evidence of pneumonia and a microbiological diagnosis by culture of the organism from respiratory specimens, or a fourfold rise in serum antibodyb levels against L. pneumophilaserogroup 1, or detection of L. pneumophilaantige in urine or positive direct immunofluoresence assay (DFA) test. **Presumptive cases**: Clinical or radiological evidence of pneumonia and a microbiological diagnosis of a single high antibody level against L. pneumophilaserogroup 1 or a seroconversione demonstrated against Legionella species and serogroups other than L. pneumophila1.
Management of patient	1. Preferred antibiotic is fluoroquinolone PO or IV 2. Alternative- Clarithromycin PO/IV (azithromycin is an option) 3. Rifampicin is added in severely ill or immunocompromised patient but not used alone. Duration of therapy is 14-21 days
Poor prognostic factors in pneumonia	Those with 2 or more adverse prognostic factors should be managed for severe CAP • Age ≥ 65 years • Comorbidities- diabetes, cardiac disease, COPD, stroke • RR ≥ 30/min • Confusion- abbreviated mental test score (AMMT) ≤ 8 • Blood pressure- SBP ≤ 90 mmHg & or DBP ≤ 60 mmHg • Hypoxemia with PaO2 < 8 kPa and need for assisted ventilation • Urea ≥7 mmol/L • Albumin < 35 g/L • WBC >20 or < 4x109 • Radiology bilateral or multilobar involvement • Microbiology- positive blood culture
Management of	1. Additional case finding measures and environment assessment should be

immediate contacts and environment	taken ≥ 2 cases of legionellosis occurring in travelers from same destination during a 1-year period ora single case of laboratory-confirmed health care associated legionnaires disease
Prevention and control measures	1. Proper maintenance and disinfection of drinking-water supplies whirlpool spas and cooling towers 2. Maintening hot water system temperatures at 50*C or above
Special considerations	Cause for the outbreaks need to be established 1. Identify common exposure 2. Review maintenance logs for water system 3. Water and biofilm swabs collection for culture. At least 250 ml of water to be collected from each site.
Message to the general public	

Influenza

Disease name	**Influenza**
ICD code	ICD-10 J10,J11 (seasonal influenza)other influenza ICD-10 J09
Epidemiology	**Background and causative agents:** Influenza virus belongs to the family Orthomyxoviridae. Three distinct types: Influenza A, B and C Influenza A is divided into different subtypes based on envelop glycoproteins- hemagglutinin (HA) and Neuraminidase (NA). At least 18 highly divergent and antigenically distinct HAs (H1-H18) and 11 distinct NAs (N1-N11) have been described in influenza A. Both influenza A and B can cause seasonal and sporadic outbreaks. Influenza C virus causes minor local outbreaks and infection is milder. Clinically important subtypes: H1N1 (Swine Flu) H5N1, (Avian Influenza) H7N9 (novel avian influenza) **Incubation period**: 1-4 days Adult contagious for 7 days and children for 21 days from onset of illness **Reservoirs:** aquatic birds are primary reservoir of influenza virus. Recent studies indicate that bats are potentially and likely ancient reservoirs of diverse pool of influenza viruses. **Transmission:** All routes of transmission- droplet, droplet nuclei and contact have a potential role and relative significance depends upon the circumstances acting at a given time.
Clinical features	Clinical picture is variable- depends upon influenza subtype in part 1. Asymptomatic infection 2. Flu- acute onset of fever, cough, headache, coryzal symptoms, sore throat, myalgia 3. Complications a. Bronchitis, bronchiolitis b. Primary influenza viral pneumonia - Onset typically within 48 hours of onset of fever - Dry cough or productive, hemoptysis may occur - Bilateral crackles or wheezes on chest examination - May progress rapidly to respiratory failure and death (more common in avian influenza H5N1 and H7N9 and pandemic H1N1) often associated with lymphopenia, thrombocytopenia, abnormal liver functions and multi-organ failure c. Secondary viral pneumonia- - onset typically 4-5 days after initial fever, during early convalescence - pathogens: S. pneumonia, S. aureus, H. influenza, mixed

	d. GI symptoms- watery diarrhea, more frequently described during influenza A H1N1 and H5N1 than seasonal infection e. Neurological- encephalitis, transverse myelitis, acute necrotizing encephalitis, GBS f. Cardiovascular- ECG abnormalities, myocarditis, pericarditis g. Otitis media, conjunctivitis h. Myositis, myoglobinuria and ARF
Diagnosis	**Need to put tests available in our part- ???? RDT for influenza A and B, PCR-genotyping**
Differential diagnosis	Other respiratory pathogens- adenovirus, RSV, rhinovirus, parainfluenza, C, pneumonia, legionella, Mycoplasma and S. pneumonia Very high fever favors influenza
Case definition	
Management of patient	**Severity assessment** 1. Patients with uncomplicated influenza do not require hospital admission 2. For influenza related pneumonia, a CURB-65 score of ≥3 indicates severe pneumonia with high risk of death 3. Patients with CURB-65 score 0-1 may be considered for home treatment 4. Bilateral CXR infiltrates consistent with primary viral pneumonia should be treated as severe pneumonia irrespective of CURB-65 score (see approach to pneumonia) **Treatment** **A. Supportive care** • Oxygen • IV fluids • Nutritional support • Admission to ICU if one or more of o Primary viral pneumonia o CURB-65 score ≥ 4 o PaO2 < 8 kPa despite high flow O2 o Progressive hypercapnia o pH <7.26 o Septic shock o Mechanical ventilation, NIV may be used for patients with COPD and type 2 respiratory failure B. **Antiviral treatment:** Antiviral drugs can shorten the illness duration by 1 day, hospitalization and may reduce the risk of complications from influenza (e.g., otitis media in young children, pneumonia, and respiratory failure).

	Two types **1.** M2 inhibitors- amantidine, rimantidine **2.** Neuraminidase inhibitors- oseltamivir, zanamivir • Early treatment of hospitalized patients can reduce death. • In hospitalized children, early antiviral treatment has been shown to shorten the duration of hospitalization. • Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of influenza illness onset. • Antiviral treatment is recommended **as early as possible** for any patient with confirmed or suspected influenza who: - is hospitalized; - has severe, complicated, or progressive illness; or - is at higher risk for influenza complications. • Antivirals are also indicated in patients with suspected H5N1 or H7N9, regardless of duration of symptoms **Persons at higher risk for influenza complications recommended for antiviral treatment include:** • children aged younger than 2 years • adults aged 65 years and older • persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), and metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)

	• persons with immunosuppression, including that caused by medications or by HIV infection • women who are pregnant or postpartum (within 2 weeks after delivery) • persons aged younger than 19 years who are receiving long-term aspirin therapy • persons who are morbidly obese (i.e., BMI ≥ 40) • residents of nursing homes and other chronic care facilities. **Drugs** 1. Oseltamivir 75 mg bd for 5 days (75 mg od if creatinine clearance < 30 ml/min). antiemetics may be required for nausea 2. Inhaled zanamivir 10 mg bd via inhaler if resistant to oseltamivir. 3. Antiviral prophylaxis may be considered for health care workers caring for patients with suspected avian influenza as well as patients household contacts. **C. Treatment of influenza-related pneumonia** according to severity.
Outcome	Uncomplicated influenza typically resolves within 7 days but cough and malaise may persist for several weeks. Reported mortality from primary viral pneumonia is about 40%. Risks of viral pneumonia are increased in older patients with cardio-respiratory diseases or diabetes. Pandemics may shift the age distribution- in 2009 pandemic, children and young adults had high morbidity and mortality.
Management of contacts and immediate management	Specific role of antiviral management. (see above)
Prevention and control measures	**Vaccination** A. **Inactivated influenza vaccine**- modified annually based on recent viral strains now includes antigen from 2009 pandemic H1N1. Provides partial protection against influenza illness, hospitalization and death. It is not protective against H5N1 avian influenza but may make simultaneous co-infection with human and avian influenza less likely- reduce likelihood of viral genetic reassortment **Indications** • Annual influenza vaccination for everyone above 6 months of age

	• Age >65 years • Chronic morbidity • Nursing home residents or health care workers B. **Oseltamivir** 75 mg OD to high risk individuals throughout the period of exposure
Special considerations	
Message to the general public	

Crimean Congo Hemorrhagic Fever

Disease name	**Crimean Congo Hemorrhagic Fever**
ICD code	ICD-10 A98.0
Epidemiology	**Background/causative agent:** Crimean-Congo Heemorrhagic Fever (CCHF) is a viral hemorrhagic fever caused by bunyavirus of genus Nairovirus. The disease was first described in Crimea in 1994 and identified in Congo in 1956. Though case of CCHF was first reported in Pakistan in 1976, number of cases increased since 2000 and there are about 50-60 cases annually. Sporadic cases have been reported from Punjab and Jammu Kashmir of India. **Incubation period:** 1-3 days, with maximum of 9 days following tick bites and 5-6 days following contact with infected blood or tissue **Reservoir:** Hares, birds and Hyalomma ticks are believed to be reservoir and domestic animals (sheep, goats and cattle) are amplifying hosts. **Transmission:** a. transmitted to humans by the bite of the Hyalomma tick or b. by direct contact with blood of an infected animal or human **Risk groups** Health care workers, abattoir workers and livestock owners are at increased risk
Clinical features	Can be divided into 2 phases 1. **Prehemorrhagic phase:** sudden onset of fever, myalgia, dizziness and headache. Gastrointestinal symptoms such as diarrhea,vomiting and nausea occur occasionally along with congested sclera and conjunctivitis. 2. **Hemorrhagic phase:** develops later characterized by petechial rash spreading from chest aand abdomen to the whole body. There may be bleeding from gums, nose, lungs, uterus urinary tract and GI tract 3. Constantly elevated temperature for 5-12 days and can be biphsic. **Laboratory abnormalities** 1. Blood cells- leucopenia and thrombocytopenia 2. LFT- elevated ALT and AST 3. Coagulation profile- prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT)
Diagnosis	During acute phase of illness, virus can be detected by RT-PCR, virus isolation

	or antigen or antibody (IgM, IgG) detection by ELISA
Case fatality	2%-30% with most fatalities occurring in 5-14 days after onset of symptoms
Case definition	**Suspected case** Patients with sudden onset of illness with high grade fever >38.5°C for >72 hours and <10 days especially in endemic area and among those in contact with sheep and other livestock. **Probable case** Suspected case with history of illness ≤ 10days AND Thrombocytopenia < 50,00/mm3 AND Any 2 of the following a. Petechial or purpuric rash, epstaxis, hemetemesis, melena, hemoptysis, gum bleeding or other manifestation b. No known predisposing factors for hemorrhagic manifestations **Confirmed case** Probable case with a. Presence of IgG or IgM antibodies in serum by ELISA b. Detection of viral nucleic acid in specimen by PCR c. Isolation of virus
Management of patient	**General** 1. Patient should be admitted in isolated single room with negative pressure if possible 2. Patient should be cared with barrier-nursing techniques 3. Intensive monitoring and replacement of fluid and blood products **Definite treatment** Intravenous ribavirin given early in the course of illness may be of benefit. Dose of ribavirin: 2 gm loading dose followed by 4 gm/day in 4 divided dose for 4 days and 2gm/d in 4 divided dose for 6 days
Management of contacts and immediate management	1. Known direct contact with the blood or secretions of probable or confirmed case such as needle stick injury or contact with mucus membranes have baseline blood investigation done and start ribavirin therapy 2. Household or other contact should monitor temperature and if temperature goes ≥ 38.5° C, he/she should be considered for probable case and should be admitted and ribavirin needs to started.
Prevention and control measures	1. Public should be educated about the mode of transmission of disease 2. Visiting to tick-infested areas should be avoided if feasible. To minimize exposure, covering the body with light clothing and use of tick repellant such as diethyltolumide should be practiced 3. People working with livestocks or other animals in the endemic area should protect themselves with use of repellents on skin (eg. DEET), clothing (eg. permethrine) and wearing gloves or other protective clothing to prevent contact of skin with infected blood or tissue 4. All health care workers should wear disposable gloves and masks and gowns (should be autoclaved before sending to laundry or incineration)

Chikungunya fever

Disease name	Chikungunya fever
ICD code	ICD-10 A92.0
Epidemiology	Background/causative agent: Chikungunya fever is a viral illness caused by arbovirus (Chikungunya virus). It is a RNA virus that belongs to Alphavirus genus of Togaviridae. The virus was first isolated in Tanzania in 1952-53 from human and mosquito during an epidemic of fever that was similar to Dengue fever clinically. The Chikungunya virus was isolated in India in 2006 outbreak. Aedes mosquito that breeds in domestic settings such as flower vases, water-storage containers, air coolers, tyres, plastic bottles, metal cans etc. is the vector responsible for transmission of disease. A.aegypti is the common vector responsible for transmission in urban areas whereas A. albopictus is common in rural areas. The adult female mosquito rests in cool shady domestic and peridomestic areas and bites during day time. **Incubation period:** 2-4 days from the mosquito bite. Viremia persists for upto 5 days from the clinical onset **Reservoir:** primates **Transmisssion:** 1. By bites of mosquitoes. Humans are infectious to mosquitoes for the first few days after onset of illness. 2. Exposure to infected blood has infected health care workers and neonates during delivery
Clinical features	1. Fever (92%) is the commonest symptoms with abrupt onset in some cases and associated with chills and rigors. It may be low grade or can reach up to 39-400C and can last for 3-4 days. 2. Arthralgia/arthritis (87%): Ankle, wrist and small joints of hand are mostly affected but can involve knee and spine. Migratory arthritis with effusion can be found in 70% cases. Joint pain is usually worse in the morning and relieved by mild exercise. 3. Headache (62%). 4. Transient maculopapular rash is seen in up to 50 % patients that typically resolve in 7-10 days and may show mild desquamation 5. Photophobia, retro-orbital pain, vomiting, diarrhea are less common 6. Infrequent are meningeal syndrome and encephalopathy
Diagnosis	1. Hematological findings are non-specific with leucopenia with lymphocyte predominance. Thrombocytopenia is rare. 2. Most commonly diagnosed by serological testing that shows IgM antibodies in acute serum sample after 1 week of onset of illness and rising in virus-specific titers between acute and convalescent samples 3. RT-PCR in serum 4. Virus isolation from blood
Differential diagnosis	1. Leptospirosis 2. Dengue fever

	3. Malaria 4. Rheumatic fever
Case definition (ECDC)	**Clinical criteria:** Acute onset of fever >38.5°C and severe arthralgia/arthritis not explained by other medical conditions **Epidemiological criteria:** Residing or having visited epidemic areas, having reported transmission within 15 days prior to the onset of symptoms **Laboratory criteria:** At least one of the following tests in the acute phase: a. Virus isolation b. Presence of viral RNA by RT-PCR c. Presence of virus specific IgM antibodies in single serum sample collected in acute or convalescent stage. d. Four-fold increase in IgG values in samples collected at least 3 weeks apart On this basis, cases are to be categorized as **Possible case:** a patient meeting clinical criteria **Probable case:** a patient meeting both the clinical and epidemiological criteria **Confirmed case:** a patient meeting the laboratory criteria, irrespective of the clinical presentation
Management of patient	There is no antiviral drug for Chikungunya fever and management is entirely symptomatic. 1. Paracetmol is the drug of choice for fever and joint pain. If pain relief is inadequate other analgesia can be used- Hydroxychloroquine 200 mg or chloroquinesulphate 300 mg once daily. Steroids and aspirin are avoided. 2. Patient is encouraged to drink plenty of fluids 3. Rest with refrain from exercise 4. **Referral to tertiary care centre** if a. Fever persisting for >7 days b. hemodynamic instability (syncopal attacks, hypotension(systolic blood pressure <90 mmHg) c. oliguria (urine output less than 500 ml in 24 hours), d. altered sensorium or e. bleeding manifestations
Management of contacts and immediate management	A search should be carried out for unreported or undiagnosed cases where the patient lived during the 2 weeks prior to onset of fever.
Prevention and control measures	General measures applicable to vector and other prevention should be used. 1. Risk communication to the household members 2. Minimize the vector population 3. Minimize the vector-patient contact (Aedes mosquitoes bite mostly in the morning and late afternoon) 4. Reporting to the nearest public health authority
Special	Eliminate or treat all potential places of mosquito breeding with larvicides

considerations	
Message to the general public	

Chapter IV: Zoonotic Diseases

Taeniasis andCysticercosis

Category	Description
Disease name	Taeniasis and Cysticercosis (**ICD 10 code B68 & B69**)
Epidemiology	**Introduction**: Taeniasis is caused by ingestion of larval form of the tapeworm from undercooked meat. The larvae develop into adult and approximately 2 to 3 months after the adult tapeworm is established in the upper jejunum it hatches eggs that is excreted on feces. Cysticercosis is caused by ingestion of eggs that had been defecated from definitive host. The eggs developed into larvae and those larvae get inoculated into brain, spinal

	cord, skeletal muscle, cardiac muscle, eye and other tissues. **Causative agent**: Adult stages (Taeniasis) and larval stages (Cysticercosis) of tapeworm (*T. saginata found in cattle* and *T. solium found in pork).* **Host factors**: Definitive host (human) and intermediate hosts (pigs, cattle, humans). Household contact with an individual infected with *T solium*increase the risk of cysticercosis. **Environmental factors**: Undercooked pork and beef meat is associated with Taeniasis. Consumption of Food and Water contaminated by feces of definitive host is associated with Cysticercosis. **Mode of transmission**: Animal can transmit larval stage to human while consuming undercooked meat. Animal can get infected with tapeworm eggs when exposed to human feces while feeding. Autoinfection in human is likely to occur with cysticercosis.
Clinical features	**Taeniasis**: Patient may present with mild epigastric discomfort, nausea, flatulence, diarrhea and hunger pains. On microscopic examination of stool presence of proglottids confirms the diagnosis. **Cysticercosis**: Clinical manifestation depends upon site and number of cyst present in different tissue/organ. The cysts are viable at the beginning but later one dies and calcified unless ingested by definitive host. a. **Neurocysticercosis**: It is one of the most serious forms of the disease. Patient commonly present with seizures. Other manifestations of neurocysticerci are hydrocephalus, stroke and myelopathy. b. **Ocular cysticercosis**: Ocular cysticercosis may affect almost all eye tissues. Usually unilateral eye involvement is seen. Decreased vision, pain, diplopia and recurrent redness of the involved eye followed by blindness over 3-5 years if untreated are common symptoms. c. **Muscular/subcutaneous cysticercosis**: Patient is usually asymptomatic however may present as nodular painful swelling.
Diagnosis	a. **Neurocysticercosis**: Clinical presentation of Neurocysticercosis with following investigation finding 1. CT scans or MRIs: showing Cystic lesions and scolex. 2. CSF: enzyme-linked immunosorbent assay (ELISA) for detection of anticysticercal antibodies or cysticercal antigens. 3. Serum:anticysticercal antibodies demonstrated by immunoblot assay b. **Ocular cysticercosis**: 1. Funduscopic examination: Direct visualization of subretinal parasites. 2. Serum:anticysticercal antibodies demonstrated by immunoblot assay **c. Muscular/subcutaneous cysticercosis:** 1. Biopsy proven
Case definition	**Suspected case**: Clinical presentation **Probable and confirmed case**: Please refer Del Brutto criteria
Management of patient	**Taeniasis:** Praziquantel (5-10 mg/kg, single-administration) or niclosamide (adult and children over 6 years: 2 g, single-administration after a light breakfast, followed after 2 hours by a laxative; children aged 2-6 years: 1 g; children under 2 years: 500 mg) **Cysticercosis**:No treatment required for muscular or subcutaneous disease**.**

	A. Neurocysticercosis 1. Praziquantel(50 mg/kg/day for 15 days) or **albendazole** (15 mg/kg/day in 2 divided doses for 15 to 21 days) 2. Steroid and antiepileptic drugs 3. Surgery **B. Ocular cysticercosis** 1. Praziquantel(50 mg/kg/day for 15 days) or **albendazole** (15 mg/kg/day in 2 divided doses for 28 days) 2. Steroid 3. Surgery
Prevention and control measures	Well cooked meat consumption prevents **Taeniasis**. Food and water safety prevents **Cysticercosis**.
Special considerations	Praziquantel is pregnancy category B whereas Albendazole is pregnancy category C.
Message to the general public	

Toxoplasmosis

Category	**Description**
Disease name	Toxoplasmosis
Epidemiology	**Introduction:**Toxoplasmosis is caused by infection with an obligate protozoan intracellular parasite. *The parasite* infects a large proportion of the world's population (perhaps one third) but rarely causes clinically manifestations in immune-competent human. **Causative agent**: *Toxoplasma gondii*

	Host factors: Definitive host is cat and intermediate host is human and other mammals. **Environmental factors:** A cat becomes infected by eating *T gondii* cyst containing raw meat of mammals, wild birds, or mice. In the cat's gastrointestinal tract there is development of oocyst from the cyst. The cat can excrete millions of oocyst that may remain infectious for more than one year in warm humid environments. **Mode of transmission:** 1. *T gondii* oocysts, tachyzoites(rapidly dividing cyst), and bradyzoites (slowly dividing cyst) ingestion occurs during handling of contaminated soil or cat litter. 2. Transmission of tachyzoites to the fetus can occur via the placenta following primary infection in mother. 3. Transmission can also occur via ingestion of tissue cysts (bradyzoites) in undercooked or uncooked meat. **Risk groups:** Individuals at risk for toxoplasmosis include fetuses, newborns, and immunologically impaired patients (hematologic malignancies, bone marrow and solid organ transplants, or acquired immunodeficiency syndrome).
Clinical features	**Immuno competent**: Eighty to ninety percentage of infected are asymptomatic. However patients may have cervical lymphadenopathy with discrete, usually nontender nodes smaller than 3cm in diameter. Other clinical presentations are fever, malaise, night sweats, myalgias, sore throat and pain abdomen (due to retroperitoneal and mesenteric lymphadenopathy). **Immuno compromised**: 1. **CNS toxoplasmosis**: Patients present with seizure, cranial nerve deficits, altered mental status, focal neurologic deficits, and headache. 2. **Toxoplasmic pneumonitis**: Patient present with nonproductive cough, dyspnea, chest discomfort, and fever. 3. **Ocular toxoplasmosis** (toxoplasmicretinochoroiditis) is relatively uncommon in patients with AIDS. It commonly manifests as ocular pain and loss of visual acuity. Funduscopic examination usually demonstrates necrotizing lesions, which may be multifocal or bilateral. **Congenital toxoplasmosis**:The classic clinical triad of retinochoroiditis, cerebral calcifications, and convulsions defines congenital toxoplasmosis.Infected newborns have anemia, thrombocytopenia, and jaundiceat birth. Microcephaly, hydrocephalus, organomegalyhas been reported. Affected survivors may have mental retardation, seizures, visual defects, spasticity, hearing loss or other severe neurologic sequelae**.**
Diagnosis	Diagnosis depends upon clinical suspicion with laboratory finding as mentioned below 1. Blood smear, body fluids (Amniotic fluid/Sputum) or tissue biopsy onmicroscopy demonstrating*T gondii*confirms the diagnosis. 2. Molecular diagnosis PCR if available also confirms the diagnosis. 3. CT and MRI head may add diagnosis in immune compromised cases. 4. Detection of IgG, IgM by immunological study is surrogate marker of Toxoplasmosis. (IgM is used in case of acute infection especially in primary maternal infection and congenital toxoplasmosis)
Case definition	**Suspected**: Clinical manifestation as mentioned above **Probable**: Clinical manifestation as mentioned above with indirect evidences by immunoglobulin detection (IgG/IgM) or imaging methods(CT and MRI). **Confirmed:** Clinical manifestation as mentioned above with demonstration of *T gondii*organisms in blood, body fluids, tissue or molecular diagnosis.
Management of	**Immuno-competent**

patient	1. Pyrimethamine (100mg loading dose orally followed by 25-50 mg/day) plus sulfadiazine (2-4 g/day divided 4 times daily) **OR** **2.** Pyrimethamine (100-mg loading dose orally followed by 25-50 mg/day) plus clindamycin (300 mg orally 4 times daily). **AND** Folinic acid (leucovorin) (10-25 mg/day) should be given to all patients to prevent hematologic toxicity of pyrimethamine. **OR** 3. Trimethoprim (10 mg/kg/day) and sulfamethoxazole (50 mg/kg/day) for 4 weeks **Pregnancy :** 1. Spiramycin 1 g orally every 8 hours 2. If the amniotic fluid test result for *T gondii* is positive: 3 weeks of pyrimethamine (50 mg/day orally) and sulfadiazine (3 g/day orally in 2-3 divided doses) alternating with a 3-week course of spiramycin 1 g 3 times daily for maternal treatment **OR** 3. Pyrimethamine (25 mg/day orally) and sulfadiazine (4 g/day orally) divided 2 or 4 times daily until delivery (this agent may be associated with marrow suppression and pancytopenia) **AND** Leucovorin 10-25 mg/day orally to prevent bone marrow suppression **Immuno-compromised** Pyrimethamine 200 mg orally initially, followed by 50-75 mg/day orally plus folinic acid 10 mg/day orally plus sulfadiazine 4-8 g/day orally for as long as 6 weeks, followed by suppressive therapy (Suppressive therapy for patients with AIDS (CD4 count < 100 cells/µL) is pyrimethamine 50mg/day orally plus sulfadiazine 1-1.5 g/day orally plus folinic acid 10 mg/day orally till CD>500/ml for three readings)
Prevention and control measures	Do not eat undercooked meat. Wash hands after handling raw meat. Keep children's play areas free from cat and dog feces. Wash your hands thoroughly after touching soil that may be contaminated with animal feces.
Message to the general public	Protecting children's and pregnant from exposure to cat litter. Pregnant women and those with HIV should be screened for toxoplasmosis.

Plague

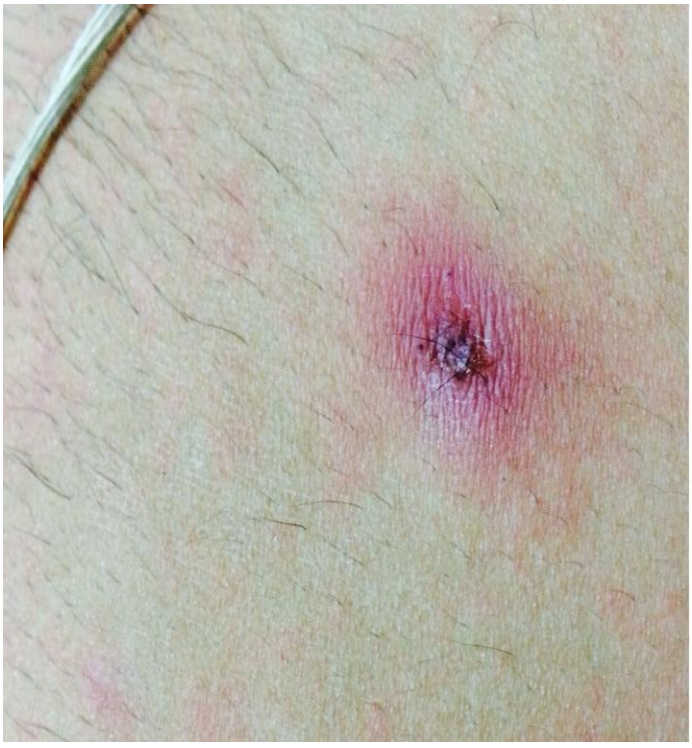
Category	Description
Disease name	Plague ICD – 10: A 20
Epidemiology	**Introduction:** A zoonotic disease infecting human caused by gram-negative bacteria which is transmitted by rodents and their fleas. **Causative agent**: *Yersinia pestis*

	Host factors: Human and other vertebrates **Environmental factors**: Outbreak of Plague usually occurs when sylvian rodents with infected flea transmit the bacteria to domestic animals. The domestic animals transmit the disease to human. **Reservoir**: Wild rodents (especially ground squirrels) are the natural vertebrate reservoir of plague. Lagomorphs (rabbits and hares), wild carnivores and domestic cats may also be a source of infection to people. **Mode of transmission, Incubation period, Period of communicability**: Clinical manifestation occurs within a week from bite of infected flea or droplet infection. Fleas may remain infective for months under suitable conditions of temperature and humidity. Pneumonic plague can be transmitted directly from human to human however bubonic plague is unlikely to have human to human transmission.
Clinical features	There are 3 forms of plague infection depending on the route of infection: 1. **Bubonic**: The most common form of plague and is caused by the bite of an infected flea. Non specific symptoms are fever, chills, headache, muscle pain and weakness.The lymph node draining the bite site becomes inflamed, tense and painful, and is called a "bubo". *Y. pestis* multiplies in the lymph node and can lead to suppurative discharge. Contact to suppurative lesion is infectious. If untreated can develop into septicaemia. 2. **Septicaemic**: It occurs when infection spreads directly through the bloodstream without forming a “bubo". Patient present with features of sepsis, DIC and MODS if untreated. 3. **Pneumonic**: It is the most virulent, highly fatal and least common form of plague. Patient get infection form aerosolized infective droplets. Patient present with fever, cough, shortness of breath and bloody sputum production.
Diagnosis	Under clinical suspicion laboratory investigations help to confirm the diagnosis. 1. Sample of fluid from a bubo, or blood or sputum or lumph node aspirationon Gram, Wright, Giemsa, or Wayson's stained smears visualizing bipolar-staining, ovoid, Gram-negative organisms with a "safety pin" appearance. 2. Blood cultures: 3. Rapid dipstick tests (if available) have been validated for field use to quickly screen for *Y. pestis* antigen in patients.

Case definition	**Suspected:**Clinical manifestation as mentioned above **Probable & confirmed**: Clinical manifestation as mentioned above with positive laboratory test.
Management of patient	Clinical management of patient should be done under clinical suspicion. Also it should be reported as EWARS. Antibiotics susceptible for plague are:
Management of contacts and immediate environment	This section will not apply to all diseases, only for diseases where contacts are to be identified and traced (tuberculosis, meningitis, measles, etc…)
Prevention and control measures	This would be according to the current public health prevention and control of the disease according to international guidelines: - See previous EWARS guidelines - See IHR recommendations
Special considerations	For e.g., reporting, epidemic measures, focal points

Scrub Typhus

Disease name	**Scrub Typhus**
Epidemiology	**Background/causative agent:** Scrub typhus is an acute, febrile, infectious illness that is caused by *Orientia* (formerly *Rickettsia*) *tsutsugamushi*. It is also known as *tsutsugamushi disease*. It is an obligate intracellular gram-negative bacterium from the Rickettsiaceae family. Scrub Typhus has now been confirmed from different parts of Nepal. However, the distribution of the disease is still under study by EDCD. **Incubation period:** About 5 to 20 days (mean, 10-12 days) after the initial bite **Risk groups:** Agricultural workers, people living in houses with shrubs/ bush nearby, and travelers in areas with potential exposure to mice and mites, for e.g. camping, rafting, or trekking. **Transmission/reservoir:** Humans acquire the disease from the bite of an infected trombiculid mite (chigger). The mites are both the vector and reservoir of the disease. The mite is very small (0.2 – 0.4mm) and can only be

	seen through a microscope or magnifying glass. The larva is the only stage that can transmit the disease to humans and other vertebrates. **There is no human to human transmission.** <u>period of communicability</u>
Clinical features	• Fever is high grade (>104^{0}F) and usually lasts 14 days. • The site of insect bite is usually painless and a black eschar (scab) is seen in 40% of cases *(see image alongside)*  • Maculopapular rash is seen over trunk, which is transient, and is seen around day 7 of fever. • Severe headache • Profuse sweating • Conjunctival injection • Lymphadenopathy **Complications:** - Cough and X-ray evidence of pneumonitis are common and may progress to ARDS. - Diarrhea and features of acute gastroenteritis is also possible. - Neurological findings may suggest meningo-encephalitis. - Spontaneous abortion may occur during pregnancy if infected.
Diagnosis	Clinical findings with laboratory confirmation gives the diagnosis of Scrub Typhus. **Supportive laboratory investigation:** • Total Leucocytes Count during early stages may be normal but

	may be elevated to more than 11,000/cu mm later in the course of disease. • Thrombocytopenia (low platelet count), usually <1,00,000/cu mm is seen in majority of patients. • Elevated liver transaminases (AST, ALT) is also seen in many patients. **Specimen for diagnosis:** • Heparinized blood: Conserve at -80°C and then ship in dry ice for culture. • EDTA blood: Conserve at +4°C and then ship at room temperature for PCR. • Serum: Conserve at +4°C, then ship at room temperature. Collect two serum specimens 10 days apart. • Skin or lymph node biopsy can also give the diagnosis. **Note:** The sample collected at the site should be sent to National Public Health Laboratory (NPHL), Teku, Kathmandu through courier / WHO surveillance mechanism following IATA guidelines (triple packing and biosafety). The information on the sample shipment should be intimated to NPHL (Focal point), EDCD (Focal point), and WHO Communicable Diseases Surveillance Unit. **Contact details of all three are available at the end of this document.**
Case definition	**Suspected/clinical case:** Acute undifferentiated febrile illness of 5 days or more with or without eschar should be suspected as a case of Rickettsial infection. (If eschar is present, fever of less than 5 days duration should be considered as scrub typhus.) **Probable case:** A suspected clinical case with an IgM titer > 1:32 and/or a four-fold increase of titers between two sera confirm a recent infection. **Confirmed case:** The one in which: • Rickettsial DNA is detected in eschar samples or whole blood by PCR **OR,** • Rising antibody titers on acute and convalescent sera detected by Indirect Immune Fluorescence Assay (IFA) or Indirect Immunoperoxidase Assay (IPA)
Management of patient	**Clinical management of patient:** **Pediatric treatment:** Azithromycin for less than 8 years 500mg orally single dose **For more than 8 years:** Doxycycline 2.2mg/kg orally twice daily for 3 days after resolution of fever (usually 5-10 day course) **- Adult treatment:** Azithromycin 500mg orally single dose; **OR**

	Doxycycline 100mg orally twice daily for 5 to 10 days. **- Pregnant women:** Azithromycin 500mg orally single dose Combination with Rifampicin can be given in areas where Tetracycline has been noted. Chloramphenicol is another alternative. Supportive treatment for management of complications.
Management of contacts and immediate environment	
Prevention and control measures	Early case detection by healthcare workers is needed. *Other strategies are to make public aware and give preventive information like:* • Wear protective clothing. • Insect repellents containing dibutyl phthalate, benzyl benzoate, or diethyl toluamide can be applied to the skin and clothing to prevent chigger bites. • Do not sit or lie on bare ground or grass; use a suitable ground sheet or other ground cover. • Clear vegetation spray insecticides on the soil to break up the cycle of transmission. **Prophylaxis:** Single oral dose of chloramphenicol or tetracycline given every five days for a total of 35 days, with 5-day non-treatment intervals (for endemic regions). **No vaccine is available for scrub typhus.**
Special considerations	**Timely reporting of any suspected or confirmed case should be done to EDCD *(see contact details at the end of this document).*** For e.g., reporting, epidemic measures, focal points
Message to the general public	

Chapter V: Food and Water borne Diseases

Hepatitis A

Disease name	**Hepatitis A**
Epidemiology	**Background/causative agent:** Hepatitis A is caused by infection with the hepatitis A virus (HAV). It is the most common form of acute viral hepatitis in the world. Major geographical differences in endemicity of hepatitis A are closely related to hygienic and sanitary conditions and other indicators of the level of socioeconomic development. In developing countries, 90% of children have been infected and developed protective immunity by the age of 10 and clinical illness is uncommon in elderly. It is caused by a RNA virus in the hepatovirus genus of the picornavirus family. **Incubation period:** 15 – 50 days. **Risk groups:** Children on endemic areas Travelers from non-endemic area Family members of infected persons Childrenin the areas of poor sanitation and open sewerage Age group 5 to 14 years rarely adults **Transmission:** -Feco-oral route -Blood transfusion **Reservoir:** Human ; rarely chimpanzees and other primates <u>period of communicability</u> one to two weeks before the onset of illness and a week after appearance of jaundice
Clinical features	➢ Asymptomatic in children less than 6 years (only 10% develops jaundice) ➢ Fever, malaise, Loss of appetite, nausea, vomiting, diarrhoea, pain

	abdomen, dark colored urine and jaundice ➢ In up to 5% cases there may not be jaundice throughout the course of illness. ➢ Itching is present in few cases and may be confused with obstructive jaundice ➢ Adults are more prone to severe disease **Complications:** ➢ Acute liver failure (Fulminant hepatic failure) ➢ Pancreatitis ➢ Acute kidney injury ➢ Vasculitis and arthritis ➢ Polyradiculopathy& ➢ Meningoencephalitis
Diagnosis	**Supportive laboratory investigation:** Liver function test: ➢ conjugated hyperbilirubinemia ➢ raised liver enzymes (ALT and AST)2.5 times the upper values (*Very high values such as more than 1000 IU/mL do not point toward very serious disease*) ➢ Prolonged prothombin time ➢ USG abdomen ➢ Anti HAV IgM **Specimen for diagnosis:** ➢ Serum **Differential diagnosis:** ➢ Viral hepatitis(A, B etc.) ➢ Leptospirosis ➢ Epstein Barr virus ➢ Cytomegalo virus ➢ Dengue fever ➢ Measles, varicella, Q fever ➢ Drug induced hepatitis
Case definition	**Clinical description** An acute illness typically including acute jaundice, dark urine, anorexia, malaise, extreme fatigue and right upper quadrant tenderness. Biological signs include increased urine urobilonogen and >2.5 times the upper limit of serum alanine aminotransferase **Note:** Most infections occur during early childhood. A variable proportion of adult infections are asymptomatic

	Laboratory criteria for diagnosis positive for IgM anti-HAV
Management of patient	**Clinical management of patient:** ➢ There is no specific treatment for HAV ➢ Supportive treatment: • Adequate nutritional supports,(*250 grams of sugar in one litter of water per day for about two weeks*) • Fluid replacement for diarrhoea and vommiting • Antipyretic- paracetamol • Anti-emetic –metoclopramide or domperidone or ondansetron • Anti-spasmodic-hyoscine butyl bromide or drotaverin • Anti-pruritic-ursodeoxycholic acid or cholestyramine **When to admit patients:** ➢ unable to take food normally ➢ secondary bacterial infections ➢ chronic liver disease, specially liver cirrhosis ➢ pregnancy, particularly in third trimester ➢ encephalopathy and or coagulopathy Where to refer: Nearby tertiary center if complication develops
Management of contacts and immediate environment	
Prevention and control measures	Food safety, sanitation modification and vaccination are main strategies in prevention of HAV The spread of hepatitis A can be reduced by: • adequate supplies of safe drinking water; • proper disposal of sewage within communities; and • personal hygiene practices such as regular hand-washing with safe water Once the disease is detected in community: • Search for the source (Water source) • Open sewerage and broken water pipes should be reported and prompt repair should be demanded. • Taking boiled water and cooked food should be advised **Hepatitis A vaccines** • There are two HAV vaccines • HAVRIX (GSK) • VAQTA (Merck) • TWINRIX (GSK) is in combination with the hepatitis B vaccine

Special considerations	Timely reporting of focal outbreaks or epidemics should be done to DPHO/ EDCD
Message to the general public	Acute HAV hepatitis is most common jaundice causing illness in children. It is a self-limiting disease. Since it can be present in many conditions, proper diagnosis is important. Diet restrictions complicate the disease and may even cause death. There are no special types of foods for jaundice. Since this is a liver disease, taking alcohol can take lives.

Hepatitis E

Disease name	**Hepatitis E**
Epidemiology	**Background/causative agent:** Hepatitis E is a form of viral hepatitis caused by Hepatitis E virus (HEV). It is responsible for large outbreaks involving up to several thousand persons in developing countries. Although it is a self-limiting disease but one of the important cause of morbidity and mortality in developing countries. Hepatitis E virus isthe causative agent of Hepatitis E which is a non-enveloped, positive-sense, single-stranded RNA virus. **Incubation period:** 15 to 60 days **Risk groups:** ➢ Clinical attack rates are highest in young adults aged 15–49 years ➢ Pregnant women are more likely to experience severe illness including fulminant hepatitis and death ➢ Young adults in endemic areas are at risk. Travellers from non-endemic areas travelling to endemic areas are also at risk. **Transmission:** ➢ Feco-oral route **Reservoir :** ➢ Domestic Pig, ➢ Rarely wild boar meat, bandicoot rat, black rat and Asian house shrew (food borne infection can occur from pork, boar, and deer meat). <u>period of communicability</u> ➢ the period of communicability is not known, however HEV has been detected in stool 14 days after the onset of jaundice (4 weeks after ingestion of contaminated food and water) ➢ the virus persist in contaminated food and water for 2 weeks
Clinical features	Short prodromal phase, and a period of symptoms or jaundice lasting days to several weeks Fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, jaundice, dark urine, clay-colored stool, joint pain Young patients may present with fever as the first symptoms in some cases.

	With passage of time jaundice deepens and peak reaches in 7-10 days' time Other symptoms gradually become milder with deepening of jaundice. About 25% of the patients present with pruritus **Complications:** ➢ Acute liver failure ➢ Fulminant hepatitis occurs more frequently during pregnancy ➢ Pregnant women are at greater risk of obstetrical complications and mortality (20%) from hepatitis E in their third trimester ➢ Chronic hepatitis in immune compromised and transplant patients Other less common complications are ➢ pancreatitis ➢ acute kidney injury. ➢ The rare complications are ➢ transient arthralgia and skin rashes, ➢ vasculitis and arthritis, ➢ polyradiculopathy and meningoencephalitis, ➢ gullainbarree syndrome, bilateral brachial plexus neuritis, ataxia, peripheral demyelinating polyradiculoneuropathy, peripheral neuropathy
Diagnosis	**Supportive laboratory investigation:** Liver function test: ➢ conjugated hyperbilirubinemia ➢ raised liver enzymes (ALT and AST) 2.5 times the upper values ➢ Prolonged prothombin time ➢ USG abdomen ➢ Anti HEV IgM ➢ Detection of HEV RNA in stool and serum-reverse transcription-PCR assay. ➢ IgM anti-HEV strongly suggests acute infection ➢ IgG anti-HEV indicates the convalescent phase or past infection **Specimen for diagnosis:** ➢ Stool and serum **Differential diagnosis:** ➢ Viral hepatitis (A, B etc.) ➢ Leptospirosis ➢ Epstein Barr virus ➢ Cytomegalo virus ➢ Dengue fever ➢ Measles, varicella, Q fever

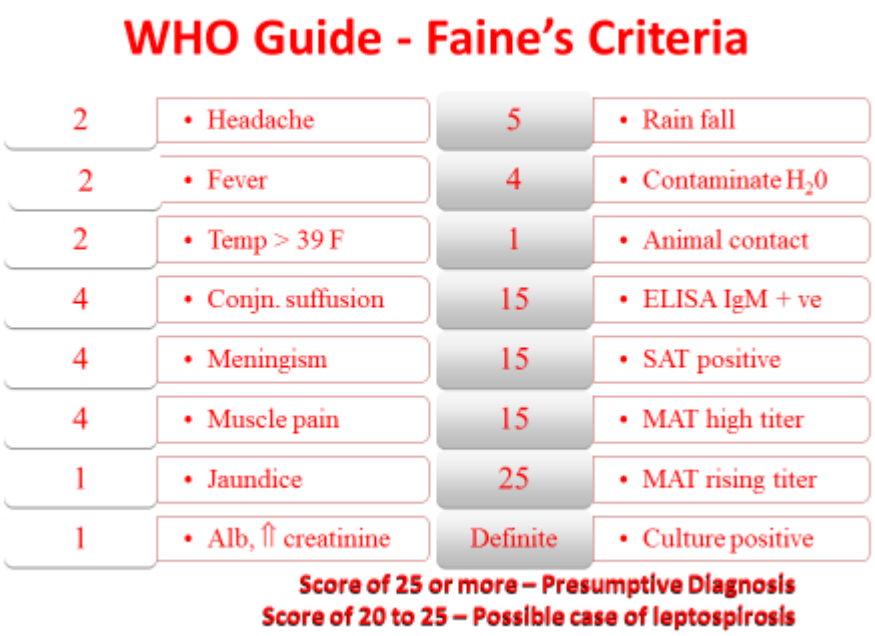
	➢ Drugs induced hepatitis
Case definition	**Suspected/clinical case:** **Probable case:** **Confirmed case:**
Management of patient	**Clinical management of patient:** Self-limiting disease. There is no specific treatment for HEV Supportive treatment: ➢ Adequate nutritional support,(250 grams of sugar in one litter of water per day for about two weeks) ➢ Fluid replacement for diarrhoea and vommiting ➢ Antipyretic- paracetamol ➢ Anti-emetic –metoclopramide or domperidone or ondansetron ➢ Anti-spasmodic- hyoscine butyl bromide or drotaverin ➢ Anti-pruritic-ursodeoxycholic acid (15-20mg/kg body weight) or cholestyramine 4gram (upto TDS, examine PT regularly, as it can increase PT) (with fruit juice) ➢ Vitamin B-complex for one month (to replete the liver store) When to admit patients: ➢ unable to take food normally ➢ secondary bacterial infections ➢ chronic liver disease, specially liver cirrhosis ➢ pregnancy, particularly in third trimester ➢ encephalopathy and or coagulopathy ➢ neurological complication Where to refer: Nearby tertiary center if complication develops
Management of contacts and immediate environment	
Prevention and control measures	Food safety, sanitation modification and vaccination are main strategies in prevention of HAV The spread of hepatitis A can be reduced by: ➢ adequate supplies of safe drinking water; ➢ proper disposal of sewage within communities; and ➢ personal hygiene practices such as regular hand-washing with safe water Once the disease is detected in community: ➢ Search for the source (Water source) ➢ Open sewerage and broken water pipes should be reported and prompt repair should be demanded. ➢ Taking boiled water and cooked food should be advised

Special considerations	Timely reporting of focal outbreaks or epidemics should be done to DPHO/EDCD
Message to the general public	Acute HEV hepatitis is most common jaundice causing illness. Since it is a self-limiting disease it should not be treated with herbal medicines. Diet restrictions complicate the disease and may even cause death. There are no special types of foods for jaundice. Since this is a liver disease, taking alcohol can take lives.

Leptospirosis

Disease name	**Leptospirosis**
Epidemiology	**Background/causative agent:** Leptospirosis is a widespread and potentially fatal zoonosis that is endemic in many tropical regions and causes large epidemics after heavy rainfall and flooding. Its abundance is due to their ability to infect a range of animal species, including humans, as well as the ability to survive outside the host, if environmental conditions are favorable. Infection results from direct or indirect exposure to infected reservoir host animals that carry the pathogen in their renal tubules and shed pathogenic leptospires in their urine. Leptospires are spirochaetes in the order Spirochaetales, family of Leptospiraceae and include two genera, Leptospira and Leptonema. Leptospiraare obligate aerobes with an optimum growth temperature ranging from 28°C to 30°C. The genus Leptospirawas divided into two species based on serological classification: Leptospirainterrogans, which comprises all the pathogenic strains and Leptospirabiflexa, the environmental saprophytic strains. **Incubation period:** 2 to 26 days **Risk groups:** Farmers Sewerage workers Veterinarians Gardeners Fish farming Livestock farmers Water sportsman Mine workers Soldiers **Transmission:** Contact of the skin (especially if abraded or after prolonged immersion) or mucus membrane with : • Moist soil or vegetation contaminated with urine of infected animals • Contaminated water • Urine, fluids or tissue of infected animal

	Reservoir: ➢ Pathogenic leptospires are naturally carried in the renal tubules and genital tract of wild and domestic animal ➢ Rats, swine, cattle, dogs and raccoons ➢ The shed leptospires can remain viable for weeks or months under moist soil or water at 28-32 degree Celsius Other less common reservoir ➢ small mammals ➢ large herbivores ➢ bats and pinnipeds ➢ poikilothermic animals such as frogs and toads
Clinical features	➢ Leptospirosis ranges in severity from a mild, self-limited febrile illness to a fulminant life-threatening illness ➢ Multiple organ systems may be involved, reflecting the systemic nature of the infection ➢ sudden onset of fever, chills, and headache ➢ The headache is often severe and has been described as a bitemporal, frontal throbbing headache accompanied by retro-orbital pain and photophobia. ➢ Muscle pain (calves and lower back) ➢ conjunctival suffusion (dilatation of conjunctival vessels without purulent exudates) ➢ subconjunctival hemorrhages and icterus ➢ Rash is uncommon ➢ nonproductive cough ➢ Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal pain ➢ dehydration ➢ high-outputnonoliguric renal failure. ➢ Severe leptospirosis - multiple organs including the liver, kidneys, lungs, and brain. ➢ The combination of jaundice and renal failure, known as Weil's disease ➢ There is a strong association between infection with the Icterohaemorrhagiaeserogroup and jaundice. ➢ Acute hemolytic anemia can be seen in leptospirosis patients with glucose-6-phosphate dehydrogenase deficiency ➢ bleeding are common and occur in the majority of patients with severe leptospirosis ➢ Most bleeding manifestations are mild, including petechiae, ecchymoses, and epistaxis ➢ However, some patients have severe gastrointestinal (melena or hematemesis) or pulmonary hemorrhage. ➢ The kidney is a major target organ ➢ It is manifested by elevations in serum blood urea nitrogen and creatinine levels ➢ findings on urinalysis of pyuria, hematuria, and elevated urine protein levels

	➢ When poor oral intake due to nausea and high-output renal failure combine to cause dehydration, patients are at risk of oliguria and renal failure. ➢ Progression to severe leptospirosis and circulatory collapse may be accompanied by acute respiratory distress syndrome (ARDS). ➢ Headache is frequently severe and when accompanied by meningismusmay prompt performance of lumbar puncture ➢ A typical finding on CSF examination is usually consistent with aseptic meningitis ➢ Rarely neurologic complications may also occur including hemiplegia, transverse myelitis, and Guillain–Barré syndrome. **Complications:** ARDS, Renal failure, pulmonary hemorrhage and neurological complications 
Diagnosis	**Supportive laboratory investigation:** ➢ Blood routine, Renal function test, Liver function test (Bilirubin is markedly increased, upto 40 mg/dL; SGPT/SGOT mildly increased) ➢ Urine routine (hematuria, pyuria, proteinuria is possible) and deranged RFT ➢ CSF ➢ Microscopic agglutination test (MAT; detects antibody >1:400) **Specimen for diagnosis:** ➢ Blood ➢ Urine ➢ CSF

	Differential diagnosis: ➢ Influenza; Typhoid fever, ➢ Lobar pneumonia; ➢ Viral hepatitis; ➢ Viral meningitis; ➢ Epidemic hemorrhagic fever
Case definition	**Suspected/clinical case:** **Probable case:** **Confirmed case:**
Management of patient	**Clinical management of patient:** ➢ Most leptospirosis cases are mild and resolve spontaneously ➢ Early initiation of antimicrobial therapy may prevent some patients from progressing to more severe disease ➢ A range of antibiotics are used to treat hosts with leptospirosis, with IV C-Penicillin (2M units 6 hourly for 5-7 days) being commonly used in severe adult human cases ➢ Other antibiotics that can be used are ampicillin (1 g IV 6 hourly), ceftriaxone (1 g IV once a day), or cefotaxime (1 g IV 6 hourly) ➢ Ceftriaxone has been shown to be noninferior to penicillin for serious leptospirosis ➢ The less severe cases are usually treated orally with antibiotics such as doxycycline, azithromycin, ampicillin or amoxycillin.
Management of contacts and immediate environment	
Prevention and control measures	➢ avoiding high risk exposures to infected water sources ➢ chemoprophylaxis and vaccination of animals ➢ Prophylactic doxycycline in highly endemic areas and in areas after natural disaster where flooding or contaminated bodies of water are present. ➢ Exposure to freshwater or moist soil which has been contaminated with spirochetes from infected mammalian urine is a major risk factor for contracting leptospirosis ➢ Humans can help prevent infection by avoiding exposure to stagnant water, properly draining farm water runoff, and keeping food away from animal waste contamination. ➢ Occupational activities that put workers at risk through exposure to contaminated water or infected animals should be identified. Personal protective equipment such as gloves, boots, goggles, and overalls for workers in high-risk occupations are important to prevent exposure of mucous membranes and skin, but can be difficult to implement in hot

	and humid environments.
Special considerations	
Message to the general public	This is an occupational disease and farmers are more at risk. The disease may be sometimes confused with flu like illness and complications can appear if not treated on time. If there is fever, jaundice, red spots in the body and red eyes, physician's consultation should be done at earliest.

Cholera

Disease name	**Cholera**
Epidemiology	**Background/causative agent:** Cholera is a disease caused by gram negative comma shaped bacteria *Vibrio Cholerae*. It is a facultative anaerobic bacterium which has a flagellum at one pole. *Vibrio cholerae*serogroup 01 includes two biotypes-classical and EI Tor-each of which includes organisms of inaba, Ogawa and rarely Hikojimaserotypes.The pathogenesis of *V. cholerae* is related to the cholera toxin which can induce secretary diarrhoea leading to watery diarrhoea. **Incubation period:** 2 hours to five days,usually 2-3 days. **Risk groups:** ➢ lowest socioeconomic groups ➢ people without access to safe drinking water and adequate sanitation ➢ gastric achlorhydria ➢ Person with blood group O are more vulnerable to severe cholera if infected. **Transmission/reservoir:** -Through ingestion of food or water contaminated directly or indirectly with feces or vomitus of infected persons. -environmental reservoirs exist, apparently in association with copepods or other zooplankton in brackish water or estuaries.
Clinical features	Sudden onset, profuse, painless watery stools. Nausea, severe vomiting occurs early in the course of illness **Complications:** ➢ Rapid dehydration ➢ Acidosis ➢ circulatory collapse ➢ hypoglycemia in children and renal failure can lead rapidly to death ➢ In severely dehydrated cases (cholera gravis), death may occur within a few hours and case fatality rate may reach 50%.
Diagnosis	**Supportive laboratory investigation:**

	➢ Stool microscopy can show highly motile bacteria with characteristic motility (shooting star, darting movement) ➢ Stool microscopy and culture ➢ Rapid diagnostic kit can detect cholera in stool. ➢ PCR for serotyping and bio typing **Specimen for diagnosis:** Stool **Differential diagnosis:**
Case definition	**Suspected Cholera:** A case of cholera should be suspected when: ➢ In an area where the disease is not known to be present, a patient aged 5 years or more develops severe dehydration or dies from acute watery diarrhoea; ➢ In an area where there is a cholera epidemic, a patient aged 5 years or more develops acute watery diarrhoea, with or without vomiting. **A case of cholera:** ➢ A case of cholera is confirmed when *Vibrio cholerae* O1 or O139 is isolated from any patient with diarrhoea.
Management of patient	**Clinical management of patient:** ➢ Rapid rehydration by Intravenous route using crystalloids (Normal saline) ➢ Oral rehydration solution ➢ Doxycycline (100mg) capsule-3 capsule stat ➢ Azithromycin (500mg) - 2 tablets stat (for pregnant women and children less than 8 years old) ➢ Tetracycline*(500 mg) 4 times a day, and children 12.5 mg/kg 4 times daily, for 3 days ➢ TMP-SMX (320 mg trimethoprim and 1600 mg sulfamethoxazole twice daily for adults and 8 mg/kg trimethoprim and 40 mg/kg sulfamethozazole daily in 2 divided doses for children, for 3 days); ➢ Furazolidone (100 mg 4 times dailyfor adults and 1.25 mg/kg 4 times daily for children, for 3 days); ➢ Erythromycin (250 mg 4 times daily for adults and 10 mg/kg 3 times daily for children, for 3 days) ➢ Ciprofloxacin, 250 mg once daily for three days (**avoid in children younger than 8 years)* **(Annex for plan A/B/C)**
Management of contacts and immediate environment	➢ Surveillance of person who shared food and drink with a cholera patient for 5 days from last exposure ➢ Investigate possibilities of infection from polluted drinking water and food. Meal companion for the 5 days should be interviewed.
Prevention and control measures	➢ There should be inter-sectorial collaboration and multidisciplinary approach in reducing cholera outbreaks in endemic areas and control outbreaks.

	➢ Health education on safe water drinking, sanitation, food preparation, food preservation and food safety should be given in endemic areas. ➢ Communities should be reminded of basic hygienic behaviors, including the necessity of systematic hand-washing with soap after defecation and before handling food or eating, as well as safe preparation and conservation of food. ➢ Public campaign through media, such as radio, television or newspapers should be involved in disseminating health education messages. ➢ Community and religious leaders should also be associated to social mobilization campaigns Water treatment (annex) Immunization : There are 2 WHO pre-qualified oral cholera vaccines (OCVs) (Dukoral® and Shanchol®) are available.
Special considerations	All outbreaks (clinical cases) should be reported immediately to the respective DHO/DPHO, Regional Health Services Directorate and the EDCD/DHS for immediate investigation and, if possible, laboratory confirmation.
Message to the general public	Cholera is severe diarrhoea which can claim life if untreated so do not waste time in local (traditional healers) treatment. Take patients as soon as possible to nearby health care facility and provide ORS to patient on the way to hospital if possible. Hand washing and water preparation can prevent disease.

Acute Gastroenteritis

Disease name	**Acute Gastroenteritis**
Epidemiology	**Background/causative agent:** diarrheal disease of rapid onset, with or without accompanying symptoms, signs, such as nausea, vomiting, fever, or abdominal pain **(1)Bacterial** a)Inflammatory diarrhea Aeromonas, Campylobacter jejuni, Clostridium dificile, E. coli:enteroinvasive, O157:H7 Plesiomonas, shigelloides, Salmonella, Shigella, Vibrio parahaemolyticus, Yersinia enterocolitica b) Non-inflammatory E. coli: enteropathogenic, enterotoxigenic, Vibrio cholerae **(2) Viral** Rotavirus, Enteric adenovirus, Astroviruus, Calcivirus, Norwalk, CMV, HSV **(3) Parasites** Giardia lamblida, Entamoebahistolytica, Strongyloidesstercoralis, Balantidium coli, Cryptosporidium parvum, Cyclosporacayetanensis, Isospora belli **Incubation period:** Few hours to few days

	Risk groups: Infant and children under five years old, Older population, Immunocompromised patients, malnourished children **Transmission/reservoir:** Feco-oral route period of communicability
Clinical features	**Complications:** ➢ dehydration ➢ acidosis ➢ circulatory collapse ➢ hypoglycemia in children and renal failure can lead rapidly to death
Diagnosis	**Supportive laboratory investigation:** Routine stool examination, Culture and sensitivity **Specimen for diagnosis:** Stool **Differential diagnosis:**
Case definition	➢ Acutegastroenteritis:sudden onset of diarrhoea and/or vomiting, usually three or more bouts of diarrhoea or vomiting and diarrhoea. ➢ Food poisoning: Diarrheal disease following ingestion of food or watercontaminated by bacteria, toxins or protozoa. ➢ Acute watery diarrhoea: lasts several hours or days, and includes cholera; ➢ Acute bloody diarrhoea: also called dysentery
Management of patient	**Clinical assessment of the rehydration (annex)** **Clinical management of patient:** Oral rehydration therapy: ORS should be given to all the patients Intravenous rehydration: Normal saline/Ringers lactate according to the level of dehydration **(Annex for plan A/B/C)** Adjunctive therapy: • Antimicrobial drugs Infant with acute watery diarrhoea best managed without antibiotics Antibiotics are required for systemic spread, cholera and dysentery Ciprofloxacin, Ofloxacin, Cotrimoxazole, Tetracycline Metronidazole for giardiasis and amoebic dysentry • Antimotility drugs: SHOULD BE AVOIDED Nutritional supplement: Vitamin A, Zinc, give nutrient-rich foods – including breast milk

Management of contacts and immediate environment	
Prevention and control measures	➢ access to safe drinking-water; ➢ use of improved sanitation; ➢ hand washing with soap; ➢ exclusive breastfeeding for the first six months of life; ➢ good personal and food hygiene; ➢ health education about how infections spread; ➢ rotavirus vaccination; ➢ Water treatment (see annex)
Special considerations	
Message to the general public	

Chapter VI: Vector Borne Diseases

Malaria

Category	Description
Disease name	Malaria ICD-10 B50-54
	Introduction*:* Malaria is a preventable and treatable acute public health problem in the globe. It is caused by infection of red blood cell by Plasmodium protozoa after being injected by female anopheles mosquito. **Causative agents**: Plasmodium *vivax, falciprum, malariae, ovale and knowleski*. **Host factor:** Children and pregnant are more prone for malaria. Travel to endemic area within a month or residing at endemic area increases likelihood of disease. Mortality is seen more in children probably due to fewer incidences of subclinical infections that gives partial immunity as compared to adults. **Environmental factor:** Monsoons and hot climate increases the breeding of mosquito hence the incidence rate increases with it. The mosquito prefers to bite during dusk and dawn. Despite of presence of mosquito the likelihood of being infected by malaria decreases when the environmental temperature remains lower than 16^{o}C as the parasite couldnot complete life cycle in the vector. **Mode of transmission, Incubation period, Period of communicability:** The infected vector injects sporozoites into human. By two weeks the parasite completes its preerythrocytic pathway and prepares to infect RBC. The parasites infect RBC and multiplies over there so that they can infect other RBC; the clinical presentation. Some of the parasite released from RBC develops as gametocytes which will be taken by mosquito during blood meal. Around a few weeks later the gametocyte develops into adults in the mosquito guts hence ready to infect new host.
Clinical features	A first symptom is fever +/- chills and rigor usually for less than two weeks. On addition patient may present with non specific symptoms like headache, abdominal discomfort, fatigue (due to anemia), lassitude (due to hypoglycemia), muscle and joint aches. Poor feeding, vomiting, altered sensorium and fits are common presentation in children below five. Jaundice, respiratory failure, hypoglycemia and renal shut down are common presentation in pregnant women. If untreated the disease is fatal within few hours to days due to MODS.

	Chronic complications of treated malarial cases are Hyperactive malarial spleenomegaly, Quartan malarial nephropathy, Burkitts lymphoma and increase risk for EBV infections.
Diagnosis	The diagnostic tests are demonstration of malarial antigen by Optimal (Plasmodium LDH +/- histidine rich protein) and Quantitative buffy coat. Demonstration of parasite in blood smear or PCR is gold standard test. Presence of shock or any of the following laboratory findings anemia, thrombocytopenia, hypoglycemia, jaundice, transaminitis, acidosis, deranged coagulation profiles, elevated urea and creatinine and hypoxia in an acute febrile patient from malaria endemic area or with travel history within a month should be highly suspected of malaria until proven otherwise.
Case definition	**Suspected case**: An acute febrile case from malaria endemic area or with travel history within a month. **Definite cases**: Clinical suspicion with positive antigen detection test (RDT) or smear or PCR. Repeat RDT after 6-12 hr incase first test was negative yet there is strong clinical suspicion. **Sever malaria**: Those malaria patient who are unable to take per orally **Complicated malaria:** Malaria with organ involvement due to sequestration of parasite on the organ or high parasite load.
Management of patient	1. **Patient who can take oral medication**: Artemether 5-24mg/kg plus Lumefantrine 29-144mg/kg over three days in six divided doses. OR Artisunate 4mg/kg plus Amodiaquine 10mg/kg OD for three days. OR Artisunate 4mg/kg plus Mefloquine 8.3mg/kg OD for 3 days OR Diahydroartemisinin 4mg/kg plus 18mg/kg and 24mg/kg Piperaquine for >25yrs and above < 25kg respectively. 2. **Patient who can't tolerate oral medication**: Injection artesunate 2.4 -3.0 mg/kg IV OD for 5 days plus Injection clindamycin 10mg/kg BD for 7 days. OR Injection Artemether 3.2mg/kg loading dose with 1.6m/kg OD for 5 days. (switch to oral once patient tolerates) 3. **Pregnancy:** Diahydroartemisinin 4mg/kg OD for 5 days plus 10mg/kg clindamycin BD for 7 days. Quinine can be given in option to artemisin derivatives however other drugs are not recommended during pregnancy especially at first trimester. **Radical cure:** 0.25-0.50mg/kg Primaquine OD for 15 days in case of P. *vivax* infection. The G6PD level should be at least 30% of the normal else patient will develop hemolysis due to Primaquine.
Prevention and control measures	Prevention of mosquito bites between dusk and dawn is the first line of defense against malaria. Measures to prevent mosquito bites include sleeping under long-lasting insecticidal nets, and using protective clothing and insect repellents. Vaccine (RTS, S) is recently approved. Chemoprophylaxis for traveler to malaria endemic area is recommended.

	Mefloquine and Doxycycline are preferred choice given prior to, during, and upon return from the travel.
Special considerations	Artesunate plus Amodiaquine therapy on HIV/AIDS co infected patient is associated with neutropenia in ZDV/AZT and hepatotoxity in EFV combination. Use of quinine in Rifampicin receiving patient are likely to have relapse or recrudescence.
Message to the general public	

Kala-azar

Category	Description
Disease name	Leishmaniasis ICD-10 B50-54
	Introduction: Leishmaniasis is caused by protozoa Leishmania and spread by the bite of sand flies. It present in three forms: Cutaneous, Mucocutaneous, and Visceral leishmaniasis. **Causative agents**: Leishmania *donovani/chagasi* **Host factor:** People from low socioeconomic background are prone for the disease. For every one clinical cases there has been more than one subclinical cases hence active case finding at field is better way for disease control. **Environmental factor:** Houses with mud walls and near to livestock's shelter are risk factor. Disease occurs in rural set up in tropics and subtropical region however outbreaks in hills (Okhaldhunga, Bhojpur, Doti) of Nepal have been documented. Evidences from Nepal support livestock as reservoir in South Asian region. **Mode of transmission, Incubation period, Period of communicability:** The infected sandfly injects promastigotes into human. These promastigotes change into amastigotes by end of two weeks inside the macrophages and multiply at tissues leading to clinical manifestations. L. *donovani* multiplies at viscera hence named visceral leishmaniasis whereas L. *chagasi* prefers into skin and subcutaneous tissues hence named cutaneous and mucocutaneous leishmaniasis respectively. People resided or visited to middle east or sub Saharan Africa are prone for cuteneous and mucocutaneous disease. Usually clinical symptoms present after 2-6 months however incubation periods can last for years depending upon patient immunity.
Clinical features	**Visceral leishmaniasis (more common in Nepal)** Patient usually present with fever for more than two weeks with constitutional symptoms like loss of weight, appetite, bleeding from natural

	orifices. On examination low BMI, pallor, edema Lymphaenopathy, **Significant Spleenomegaly** and Hepatomegly are common findings. It is lethal if untreated. Post/Para Kala azar Dermal Leishmaniasis (PKDL) is one of the complications seen in treated cases. **Dermal leishmaniasis:** Nodular lesion especially over face that grows as painless ulcer. On examination volcano like chronic ulcers with painless base is highly suggestive. The disease is not lethal if untreated. **Mucocuteneous leishmaniasis:** It presents as Localized or Disseminated lesion depending upon patient immune status. Chronic mucocutaneous ulcers especially over face (nose, lips, cheeks, soft palate) and limbs is common manifestation which may heals with ugly scars if untreated. Some presents with nasal stiffness, nasal bleeding and later as nasal perforation.
Diagnosis	Antibody detection test rK 39 remains positive in naïve patients, subclinical cases and previously treated patients. Bone marrow and spleenic aspiration or skin lesion biopsy showing amstigotes is gold standard. PCR helps if tissue aspiration and biopsy do not support. Pancytopenia especially leucopenia is highly suggestive in clinical cases. Hypoalbumenia, jaundice, transaminitis and anemia are other non specific laboratory findings.
Case definition	**Suspected case**: 1. **Visceral leishmaniasis**: A chronic febrile case with spleenomegaly +/- hepatomegaly, lymphadenopathy. 2. **Cutaneous/Mucocutaneous leishmaniasis:** Chronic skin or mucocutaneous lesion as described above. **Definite cases**: Suspected cases with positive rK-39 in naïve cases. Suspected cases with tissue/biopsy or PCR proven in previously treated/subclinical cases. **PKDL** Skin lesion in previously treated case of VL which shows amatigotes or positive on PCR.
Management of patient	**Management of Leishmaniais:** **1. Mono therapy**: Inj. Liposomal Amphoteracin B 10mg/kg single dose. **OR** Injection Liposomal Amphoteracin B 5mg/kg/day OD for 3 days. **OR** Tablet Miltefosine 50mg BID for 28 days. **OR** Injection Amphoteracin B 1mg/kg OD for 14 doses. Liposomal Amphoteracin B is preferred regimen due to better compliance, lesser side effects, more safety profile and relapses **2. Combined regimen: (**preferred in case of relapse, reinfection and treatment failure**)** Injection parmomycin 15mg/kg/day for 10 days plus tab Miltefosine 50 mg BID for 10 days **OR**

	Liposomal Amphoteracin B 5mg/kg day 1 followed by Injection parmomycin 15mg/kg/day for 10 days plus injection **Management of PKDL:** Inj. Liposomal Amphoteracin B 5mg/kg/day for 2 days per week 3 weeks. **OR** Tablet Miltefosine 50mg BID for 12 weeks. **OR** Injection Amphoteracin B 1mg/kg OD for 60-80 doses.
Prevention and control measures	Prevention of sandfly bites includes sleeping under long-lasting insecticidal nets, using protective clothing, insect repellents and destroying sandfly habitat (cracks and crevices in wall).
Special considerations	Miltefosine is contraindicated in pregnancy, lactation, child below 2yrs, severe anemia and renal and hepatic failure. Parmomycin has to be given IM and is contraindicated in pregnancy, lactation, severe anemia, child below 12yrs and renal and hepatic failure. Liposomal Amphoteracin B/ Amphoteracin B is category B in pregnancy and lactation, is relatively safe in mild hepatic impairment. Liposomal Amphoteracin B can be given upto creatinine 2.4mg/dl. (Always prepare with distill water and dissolve in 5% dextrose. Always use filter while injecting Liposomal Amphoteracin B from vial to D5) Start HAART despite of CD4 count in case of HIV co infection as they are highly likely to have relapse and reinfection. rK-39 may be negative in HIV/AIDS patients.
Message to the general public	

Dengue

Category	**Description**
Disease name	Dengue ICD-10 A 90
	Introduction*:* Dengue is a mosquito-borne tropical disease caused by the dengue virus (DENV). The virus has four serotypes DENV-1 to DENV-4. Infection with one serotype usually gives lifelong immunity to that serotype, but only short-term immunity to the others. **Causative agents**: Dengue virus is an RNA virus of the family *Flaviviridae*. **Host factor:** Humans are the primary host of the virus but it also circulates in nonhuman primates. Severe disease is more common in extreme of ages, female sex, high body mass index, high viral load, reinfection with another serotype and presence of chronic diseases such as diabetes, sickle cell and asthma. **Environmental factor**: An Aedes mosquito is the vector. Aedes *aegypti* is

	particularly involved in transmission, as it prefers to lay its eggs in artificial water containers, to live in close proximity to humans, and to feed on people rather than other vertebrates. An infection can be acquired via a single bite. Aedes prefer to bite more than one site before it completes its meal. The mosquito prefers to bite during dusk and dawn. Monsoons and hot climate increases the breeding of mosquito hence the incidence rate increases with it. **Mode of transmission, Incubation period, Period of communicability:** A female mosquito that takes a blood meal from a person infected with dengue fever, during the initial 2–10 day febrile period, becomes itself infected with the virus in the cells lining its gut. About 8–10 days later, the virus spreads to other tissues including the mosquito's salivary glands and is subsequently released into its saliva. Cases of vertical transmission and contaminated blood product consumption related transmission have been reported. Incubation period is less than two weeks.
Clinical features	Dengue presents in two forms; Dengue fever and Severe Dengue. **Dengue fever** presents as high grade fever, headache especially retro orbital pain, and rashes (triad of dengue). It may be associated with muscle, abdomen, bone and joint pain. Children usually presents with vomiting, diarrhoea and dehydration whereas adults usually presents with bleeding manifestation. Febrile phase may last for seven days however patient may remain afebrile for a few days after initial few days fever. **Severe dengue** manifest as bleeding and/or fluid loss in third space leading to hypovolumic shock. Any of the warning signs (Mucosal bleeding, Worsening abdominal pain, Ongoing vomiting, Liver enlargement, High hematocrit with low platelets, Lethargy or restlessness, Serosal effusions and Shock) during first week of fever needs scrutiny for Severe Dengue. Complications of Dengue are Myocarditis, Transverse myelitis, Guillain Barre Syndrome, Acute liver failure, Encephalitis and DIC but rare.
Diagnosis	Laboratory finding suggestive of dengue are Leucopenia, Atypical lymphocytsis, Thrombocytopenia, Hemoconcentration, raised ESR, LDH, urea and liver enzymes (ALT>AST). Honeycomb sign in USG is specific findings. Antigen detection test NS1 remains positive from day of fever to first week. Antibodies (IgG/IgM) are positive at the end of first week to first few months. Molecular technique PCR can be done during the period of positivity of NS1 antigen test.
Case definition	**Suspected case**: An acute febrile case with any of above clinical presentation from tropics or with travel history within a last two weeks. **Definite cases**: Clinical suspicion with positive antigen detection test (NS1) or PCR or four fold rise in IgM/IgG titer. **Severe dengue:** Definite dengue case with any one of the warning signs (Mucosal bleeding, Worsening abdominal pain, Ongoing vomiting, Liver enlargement, High hematocrit with low platelets, Lethargy or restlessness,

	Serosal effusions, Shock)
Management of patient	**Dengue fever**: There is no specific medication for treatment of a dengue infection. Avoid NSAIDS, steroids and antibiotics. Encourage patient to drink plenty of fluids. Paracetamol and cold sponging is recommended for fever. **Severe dengue**: Patient needs admission. Fluid management is crucial to save life. The rate of fluid administration is titrated to a urinary output of 0.5–1 mL/kg/h, stable vital signs and normalization of hematocrit. Platelets transfusion is **indicated** if there is ongoing spontaneous bleeding or very severe thrombocytopenia.
Prevention and control measures	Prevention of mosquito bites between dusk and dawn is the first line of defense against malaria. Measures to prevent mosquito bites include sleeping under long-lasting insecticidal nets, and using protective clothing and insect repellents. Dengvaxia is one of the most popular vaccines of dengue being approved and reviewed by around 20 countries in Asia and Latin America.
Special considerations	Dengue fever is not life threatening however severe dengue if not supported with treatment is highly fatal.
Message to the general public	

Filariasis

Refer to filaria treatment and control guideline of EDCD

Chapter VII: Laboratory Perspective for Infectious Disease Control

Method of sample collection, packaging/shipment and waste management

4.1 Collect patient information in the form (see Annex- 4. Case investigation form)

4.2 Label specimen collection container – unique identification number (location and number), date and time of collection, type of sample

4.3 Specimen collection:

4.3.1. Stool Sample

- Collect freshly passed stool, 5 ml liquid or 5 g (pea-size), in a container.
- Using a swab transfer the stool specimen to pre-refrigerated/ cold sterile bacterial transport media (Cary-Blair transport medium).
- Try to ensure that the swab is pushed to the bottom of the tube. Break off and discard the excess top portion of the swab sticks.
- **Infant stool sample –**
    a. Moisten two swabs in sterile saline, insert swab tip just past the anal sphincter and rotate gently and withdraw.
    b. Try to ensure that visible fecal material is present on each swab.
    c. After obtaining the two fecal swabs, insert both into the same tube of sterile transport medium and push them to the bottom of the tube.
    d. Break off and discard the excess top portion of the swab sticks.
- **Stool sample for viral (possible rotavirus) diagnosis-**

a. Large a quantity as can be obtained (preferably, at least 10 mL), in a leak-proof, clean, dry container, and refrigerate at 2-8 C immediately.

4.3.2 Respiratory track sample

- Hold the tongue down with the tongue depressor.
- Use a strong light source to locate areas of inflammation and exudate in the posterior pharynx and the tonsillar region of the throat behind the uvula.
- Rub the area back and forth with a Dacron or calcium alginate swab.
- Withdraw the swab without touching cheeks, teeth or gums and insert into a screw cap tube containing transport medium.

4.3.3 Blood/ Serum Sample

- Place a tourniquet above the venipuncture site.
- Disinfect the tops of blood culture bottles.
- Palpate and locate the vein.
- Disinfect the veinpuncture site meticulously with 10% povidone iodine or 70% isopropyl alcohol by swabbing the skin concentrically from the center of the venipuncture site outwards.
- Let the disinfectant evaporate.
- **Perform venipuncture:**
    a. If withdrawing with conventional disposable syringes, withdraw 5-10 ml of whole blood from adults, 2-5ml from children and 0.5-2ml for infants.
    b. Using aseptic technique, transfer the specimen to relevant cap transport tubes and culture bottles.
    c. Secure caps tightly. If withdrawing with vacuum systems, withdraw the desired amount of blood directly into each transport tube and culture bottle. Remove the tourniquet.
    d. Apply pressure to site until bleeding stops, and apply band-aid.
    e. Do not recap used sharps/ needles. Discard directly into the sharps disposalcontainer.

- **Serum separation –**
    - Stand tube up right to allow for gravitational flow.

- Remove serum (approximately 2mL for 5mL blood sample) with pipette to 3-5 mL container (cryo-vial) for serum sample.

Sample collection for thick/thin blood smear preparation for malaria microscopy

- Holding patient's left hand, select the ring finger (second or third finger). (The big toe can also be used with infants).
- Clean the finger with a piece of cotton soaked with 70% alcohol to remove grease and dirt from the ball of the finger
- Puncture the ball of the finger with a new sterile disposable lancet, using a quick rolling action (not too close to the nail bed).
- Apply gentle pressure (but do not squeeze) to the finger to express the first drop of blood and wipe it away with a dry piece of cotton wool.
- Working quickly and handling clean slides only by the edges, touch the slide on the ball of blood to obtain a single small drop (approximately 2 µl) of blood on the 1/3 corner of the slide for the **thin film** and at a distance of 1 cm apart put 3 small drops (approximately 6 µl) of blood for **thick film**.
- Get another clean slide to be used as a spreader. Place the spreader in front of the single drop of blood, at an angle of 45° pull-back the spreader and hold it until the blood is evenly spread along the edge of the slide, making like a tongue.
- For making thick film, with one corner of the spreader slide, spread the blood connecting 3 drops of blood together and in a circular motion (with 3 to 6 movements) to make a circle with a diameter of 1.2 cm finishing off at the center.
- Let the blood film be air-dried. Using lead pencil or diamond pencil, label the upper 1/3, thin portion of the thin smear with the patient's ID and date of collection.

4.3.4 Water Sample

- Collect at least 100 mL of water sample from different water sources into the sterile water culture bottle (supplied by NPHL) and seal properly.
    - **Water course or reservoir**– collect from a depth of at least 20 cm.
    - **Dug well**– do not allow the bottle to touch the sides of the well.

4.4 Packaging and rapid transport to reference laboratory (NPHL)

Stool specimens –

- Should be transported at 2-8°C.
- **Suspected parasite infection-** should be mixed with 10% formalin or PVA, 1 part stool to 3 parts preservative.
- Transport all the specimens in such a way that they can be tested within 48 hrs.

Respiratory specimen –

- All respiratory specimens except sputum are transported in appropriate bacterial/ viral media.
- For transport periods up to 24 hours, transport specimens for viruses at 2-8°C in VTM.

Blood/serum specimen–

- **Blood/serum—** should be transported at 2-8°C within 48 hrs.
- ***Blood culture bottles–*** Should be transported at ambient temperature (25-36^{0}C) within 24 hrs.
- ***Blood samples on filter paper–***Should be transported at 2-8°C hrs within 1 week or at ambient temperature within 48 hrs.
- ***Blood smear*** – Should be transported at ambient temperature in a slide box with desiccant.
- ***Water specimen*** – Should be transported at 2-8°C and test refrigerated sample within 24 hrs.

4.5 Waste disposal

- ***Sharps***– do not recap needles, discard all sharps directly into the sharps disposal container.
- ***Infectious waste*** – place into sealed bag for disposal in waste container/red bag.
- ***General waste*** – dispose in leak proof plastic bag/black.

Annexes

WHO's rehydration plan C/B/A:

Pregnancy Category for Drugs (A-X):

Contact details:

EDCD: Dr. Babu Ram Marasini, Director, EDCD (9851066412); Email: marasini2@yahoo.com
Dr. GunaNidhi Sharma, Deputy Health Administrator, EDCD (9851064774); Email: drgunish@gmail.com
Tel: **01-4255796**; Fax: 01-4262268; Email: **ewarsedcd@gmail.com**

WHO: Communicable Diseases Surveillance and Response Unit, WHO
Dr. KK Yogi
Tel: **9801010037**; 9801010006 (alt); 9801010021 (alt); 9841796122 (alt)
Email: **yogik@who.int**; singhn@who.int (alt); ghimirep@who.int (alt); vivekdhungana@gmail.com (alt)

NPHL: Dr. GeetaShakya, Director, NPHL (9851115089)
Tel: **01-4252421**; Fax: 01-4252375; Email: **nphl@wlinnk.com.np**

References