GP Handbook v8.2

Infectious Diseases

ANTIBIOTICS **3**

Causes of Antibiotic Resistance 3

ANTI-TB CHEMOTHERAPY **4**

General 4
Uncomplicated Pulmonary Tuberculosis 4
Drug-Resistant Tuberculosis 5
Extrapulmonary Tuberculosis 5
Pulmonary TB associated with Other Conditions 6
Children 6
Silico-tuberculosis 6
Geriatric Tuberculosis 6
Liver Dysfunction 7
Renal Impairment 7
Fixed-dose Combination Tablets 7
Dosages of Anti-TB Drugs 8

AVIAN FLU **9**

Symptoms 9
Transmission 9
Prevention 9
Laboratory Diagnosis 10
Clinic Management 10
Amantadine 10

BOTULISM **12**

Clinical Features 12
Treatment 12
Prevention & Control 12

CHOLERA **13**

General Information 13
Diagnosis & Treatment 13
Cholera Vaccination 13
Vibrio parahaemolyticus 14

DENGUE FEVER **15**

Mode of Transmission 15
Clinical Features 15
Laboratory Diagnosis 15

TREATMENT 16
PREVENTION 16
INFLUENZA 17
MODE OF TRANSMISSION 17
CLINICAL FEATURES 17
LABORATORY DIAGNOSIS 18
OPTIONS FOR CONTROLLING INFLUENZA 18
JAPANESE ENCEPHALITIS 20
MODE OF TRANSMISSION 20
CLINICAL FEATURES 20
LABORATORY DIAGNOSIS 20
TREATMENT 20
PREVENTION 20
MALARIA PROPHYLAXIS 22
ANTI-MOSQUITO MEASURES 22
ANTI-MALARIAL DRUGS 22
AFTER RETURNING HOME 23
NOROVIRUS INFECTION 24
CLINICAL FEATURES 24
MANAGEMENT 24
PREVENTION 24
NOTIFIABLE INFECTIOUS DISEASES 25
HOW TO NOTIFY 25

ANTIBIOTICS

In most Western countries, people can buy antibiotics only by prescription. In Hong Kong antibiotics can be obtained in most pharmacies no more difficult than buying toothpaste. Antibiotics are commonly referred to as "anti-inflammatory drugs" not only by patients, but also by some doctors. This misnomer confuses the lay public, which in turn aggravates the problem of antibiotic abuse as patients use or request antibiotics as quick fixes in any inflammatory conditions, regardless of the cause of the diseases.

Perhaps the most widespread and unwarranted use of antibiotics is in the treatment of URTI. These infections are mostly viral, and do not respond to antibiotic treatment. Doctors may come under pressure from patients (or their parents in paediatric cases) to prescribe antibiotics. If a child is ill with an ear infection and is screaming with pain, the mother may not be in the mood for an academic discussion on the problems of emerging bacterial resistance. If she thinks there is even a small chance that antibiotics will hasten the end of this illness, she will ask for newer and better antibiotics.

Causes of Antibiotic Resistance

- Prescribing antibiotics for infections that are viral and/or self-limiting
- Abuse of potent, broad-spectrum antibiotics when more narrow spectrum antibiotics would work equally well
- Neglecting the importance of bacterial culture and sensitivity testing in specific infections (eg urinary tract infection)
- Acceding to unreasonable request from patients to give antibiotics when none are needed
- Failure to stress the importance of completing a course of antibiotics

ANTI-TB CHEMOTHERAPY

General

- Tuberculosis (TB) remains a very important infectious disease in Hong Kong. In 2000, there were about 7,500 notifications of TB and about 300 deaths, which corresponded to crude notification and death rates of 111.7 per 100,000 and 4.4 per 100,000, respectively.
- A 6-month standard regimen with 4 drugs in the initial phase is recommended for uncomplicated new cases of pulmonary TB, while a 9-month regimen starting with 5 drugs is recommended for retreatment cases.
- Patients with disease that is resistant to isoniazid or rifampicin may require modified regimens and expert help.
- Multidrug-resistant tuberculosis should be managed in specialised centres, using multiple drugs as guided by in vitro susceptibility tests.
- Recommended regimens to treat extrapulmonary tuberculosis are based on limited current evidence, although shorter regimens may be acceptable when better evidence emerges.
- A longer duration of treatment is required for diabetic, immunocompromised, or silicosis patients.
- During pregnancy, streptomycin should be avoided; the safety profiles of second-line drugs have not yet been ascertained.
- Hepatotoxic drugs should be used with caution in patients with liver dysfunction
- Dosage reductions are required if streptomycin and ethambutol are used in patients with renal impairment.
- Apart from antituberculosis drugs, short courses of corticosteroids can be useful in managing TB pericarditis, advanced stages of TB meningitis, certain cases of TB lymphadenitis, TB pleural effusion, TB pyrexia, genitourinary TB, and suppression of severe hypersensitivity reactions to antituberculosis drugs.

Uncomplicated Pulmonary Tuberculosis

New cases

Recommendation : 2 HRZ + (E or S) / 4 HR

- Four drugs isoniazid, rifampicin, pyrazinamide, and either ethambutol or streptomycin are recommended for the 2-month initial phase of treatment, as the rate of initial resistance to isoniazid is more than 4% in Hong Kong.
- Two drugs - isoniazid and rifampicin are recommended for the 4-month continuation phase, which makes a total treatment duration of 6 months.
- The drugs may be given daily or intermittently (3x/week) in both the initial and the continuation phase.
- For patients with extensive disease, the 2-month initial phase may be extended to 3 or 4 months, depending on clinical, bacteriological, and radiological responses, while the total duration of treatment may remain at 6 months.
- If there is suspicion of drug-resistant TB (eg contacts of patients with drug-resistant TB), the initial phase of treatment may be similarly extended, pending the drug sensitivity results.

Retreatment (those who have received treatment within the previous 5 years)

Recommendation: 3(4) HRZES / 6(5) HR ± E

- Five drugs - isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin - are recommended for the initial 3 to 4 months, depending on the timing of the availability of the sensitivity results, smear results, extent of the disease, and probability of drug-resistance.
- Isoniazid and rifampicin (also with ethambutol if the disease is extensive or the sensitivity test pattern is unknown) are recommended for the continuation phase; the total treatment duration is 9 months.
- If the sensitivity test results that are available subsequently are unfavourable, the above regimen may need to be modified.

Drug-Resistant Tuberculosis

Comparatively less data is available for categorical recommendation of regimens for drug-resistant TB. It is important to avoid the "addition phenomenon" — namely, adding a single drug to a failing regimen. Otherwise, acquired resistance to the newly added drug may develop. Instead, add at least 2, 3, or more drugs to which the organisms are known to be susceptible, or which have not already been taken by the patient. In general, patients with multi-drug resistant pulmonary TB should be referred to a chest physician for specialist care.

Extrapulmonary Tuberculosis

As there have been few large-scale studies on the treatment of extrapulmonary TB, consensus is often lacking, especially in relation to the duration of treatment. Generally speaking, the initial phase should be advisably given on a daily basis. Adjunctive corticosteroid therapy can be useful.

Tuberculous meningitis (including CNS tuberculoma)

Recommendation: 3 HRZE ± S / 9 HR ± E

Depending on CT findings and treatment response, some authorities may further prolong the total duration of treatment for central nervous system tuberculoma. Extended treatment may also be considered for those presenting at an advanced stage (eg stage III) of TB meningitis.

Miliary tuberculosis

Recommendation 3 HRZ + (E or S) / 9 HR ± E

Tuberculosis of bones and joints

Recommendation 2 HRZ + (E or S) / 10 HR

The total duration of treatment may be reduced to 6 or 9 months in the case of TB of the spine or in other settings with mild disease.

Tuberculous lymphadenitis

- For peripheral disease which commonly involves the cervical region and where there are only solitary / few affected lymph nodes together with normal chest X-ray, the treatment for new cases of pulmonary TB is recommended.
- Other situations are treated as above, but with the continuation phase extended such that the total duration of treatment is 9 months.

- The clinical response of TB lymph nodes during treatment may be quite unpredictable, sometimes with paradoxical increases in size probably due to immunological reactions. Residual nodes may still be palpable after completing the full course of treatment

Tuberculous pericarditis, tuberculous peritonitis, and genitourinary tuberculosis
The recommendation is the same as for treating new cases of pulmonary TB, but the continuation phase is extended such that the total duration of treatment becomes 9 months. For some cases that involve limited gut and genitourinary disease, 6 months of treatment may be adequate.

Pulmonary TB associated with Other Conditions

Diabetes mellitus
The recommendation is the same as in treating new cases of pulmonary TB, but the continuation phase is extended such that the total duration of treatment becomes 9 months.

Immunocompromised patients
The recommendation is the same as in treating new cases of pulmonary TB, but the continuation phase is extended such that the total duration of treatment becomes 9 months. For patients infected with the HIV, the total duration of treatment should be 9 months. For all practical purposes these patients should be referred for specialist care.

Pregnancy
Basically, rifampicin, isoniazid, ethambutol, and pyrazinamide can still be used, although the manufacturers of rifampicin advise caution during pregnancy. Pyridoxine is sometimes recommended for pregnant women receiving isoniazid. Streptomycin should be avoided because of ototoxicity to the foetus. The safety profiles of the second-line drugs and ofloxacin have not been ascertained and thus these drugs should also be avoided. Taking antituberculous drugs itself is not an absolute contraindication to breast feeding. The infectivity of the mother, however, must be considered.

Children

The treatment regimens are essentially similar to those for adults, except that ethambutol should be avoided in children until they are at least 6 years old and capable of reporting symptomatic visual changes accurately. The drug dosages need to be calculated according to the body weight and may have to be adjusted, especially during the period of adolescent growth spurt.

Silico-tuberculosis

A longer duration of treatment is required for patients with silico-tuberculosis. These patients should be referred to a chest physician for specialist care.

Geriatric Tuberculosis

- The treatment of tuberculosis in the elderly does not markedly differ from that in the younger population.
- As the risk of hepatotoxicity is higher especially in those with malnourishment, some individual tailoring of dosage, say by using isoniazid 200mg instead of 300 mg once daily and pyrazinamide 1 gm instead of 1.5 gm once daily may be necessary.
- Pyridoxine supplement should also be considered for those with poor nutritional

intake or at increased risk of neuropathy.

- When the drug susceptibility pattern of the cultured bacilli is known to be favourable, use of rifampicin and isoniazid together may prove sufficient for diseases with limited bacillary load. A total duration of 9 months is required for co-administration of these 2 drugs.
- Use of ethambutol can be problematic in many old patients with poor baseline visual function and / or difficulty in assessing visual acuity.

Liver Dysfunction

Impaired LFT is relatively common during antituberculosis chemotherapy and do not signify true hepatotoxicity. Drug-induced hepatitis which occurs more commonly in patients with compromised liver reserve such as in chronic hepatitis B and C infection and alcoholic liver disease necessitates cessation of therapy.

When the tuberculous disease is mild or has improved markedly, one can wait until the liver chemistry has normalized before retrial of the conventional antituberculosis drugs, by gradual re-institution. Whenever possible, isoniazid and rifampicin should be included in the regimen, so that treatment duration will not be unduly prolonged.

In the face of extensive disease when delay in therapy might be detrimental to the patient's health, ofloxacin can be used together with streptomycin and ethambutol as an interim regimen for treatment. Incorporation of ofloxacin as a component of a definitive regimen should only be considered when the patient cannot tolerate the co-administration of rifampicin and isoniazid. Current experience shows that 400 - 600 mg once daily can be tolerated by most patients in this setting. The optimum duration of ofloxacin plus either rifampicin or isoniazid together with ethambutol as a definitive therapeutic regimen appears to be at least 1 year.

Renal Impairment

The development of antituberculosis drug-related renal impairment necessitates the withdrawal of the drug(s). Examples include streptomycin and rifampicin. In general, isoniazid, rifampicin and pyrazinamide can be used in normal dosages in mild to moderate renal impairment. In severe renal impairment, the dosage of isoniazid should be reduced and pyridoxine supplementation is needed to prevent the development of peripheral neuropathy. Streptomycin and aminoglycosides should be avoided or must have dosages adjusted in the presence of renal impairment. Ethambutol, ofloxacin and ciprofloxacin are also predominantly removed by the kidney. Dosage reduction is also mandatory. Therapeutic monitoring of serum drug concentrations may help to optimize therapy and minimize toxicity. Patients on dialysis should be referred for specialist care.

Fixed-dose Combination Tablets

Only rifater (R + H + Z) and rifinah (R + H) are available in Hong Kong.

Advantages

- reduced risk of acquired drug resistance
- simplified prescription
- improved compliance

Disadvantages

- higher cost
- lack of flexibility in dosing

Dosages of Anti-TB Drugs

Isoniazid (H)
Daily dosage: ~ 5mg/kg (~300mg)
Intermittent dosage: 10-15mg/kg 3 times per week

Rifampicin (R)
Daily dosage: ~ 10mg/kg (ie < 50kg: 450mg; > 50kg: 600mg)
Intermittent dosage: 10-12mg/kg 3 times per week (ie 600mg 3 times a week)

Streptomycin (S)
Daily dosage: 12-15mg/kg (ie < 50kg: 500-750mg; > 50kg: 750mg)
Intermittent dosage: 12-15mg/kg 3 times per week (ie < 50kg: 500-750mg; > 50kg: 750-1000mg)

Pyrazinamide (Z)
Daily dosage: 25-30mg/kg (ie < 50kg: 1.0-1.5gm; > 50kg: 1.5-2.0gm)
Intermittent dosage: 30-40mg/kg 3 times per week (ie < 50kg: 2.0gm; > 50kg: 2.5gm)

Ethambutol (E)
Daily dosage: ~ 15mg/kg
Intermittent dosage: ~30mg/kg 3 times per week

Rifater (rifampicin 120mg + isoniazid 50mg + pyrazinamide 300mg)
Daily dosage: 1 tablet/10kg (eg 50-60kg: 5 tablets, >60kg: 6 tablets)

Rifinah (Rifinah-150: R 150mg + H 100mg; Rifinah-300: R 300mg + H 150mg)
Daily dosage: < 50kg: 3 tablets of Rifinah-150; > 50kg: 2 tablets of Rifinah-300

AVIAN FLU

Influenza or 'flu' can be caused by different types of influenza viruses. It spreads mainly by respiratory droplets generated by coughing and sneezing or contact with contaminated surfaces. It is important to differentiate the 3 different types of flu:-

Seasonal influenza
This occurs in human populations. In Hong Kong, influenza peaks in January to March and July to August every year. The commonest circulating strains are influenza A (H1N1 and H3N2) and influenza B.

Avian influenza
Avian influenza normally infects birds, including poultry. It was known previously to infect birds only, but 18 human cases caused by the H5N1 strain were documented in Hong Kong in 1997 and another 2 were documented in 2003. The possible strains include influenza A (H5, H7 and H9) viruses. Human cases of avian influenza have been reported, mostly resulting from close contact with sick birds. Efficient spread between human beings is not known.

Influenza pandemic
This occurs when a new viral strain emerges and spreads rapidly among the human race which does not possess immunity to the disease. The new viral strain may originate from a human influenza virus or an avian influenza virus. As large numbers of people will fall ill or die from it, great human, social and economic loss will result.

Symptoms

The initial symptoms of avian influenza are similar to those of other influenza viruses, including fever, headache, muscle pain, runny nose, cough and sore throat. However, it is more likely to result in high fever, chest infection, respiratory failure, multi-organ failure, and death.

It is Worthing noticing that it is impossible to differentiate between avian influenza and SARS by symptoms alone. Confirmation of diagnosis will depend on laboratory tests on clinical samples from the patient.

Transmission

Avian influenza is transmitted from infected live birds to humans. Human-to-human transmission is inefficient. People in close contact with poultry are more susceptible to contracting avian flu. The elderly, children and people with chronic illness have a higher risk of developing complications such as bronchitis and pneumonia. There is no evidence that avian influenza can be transmitted through eating poultry or eggs.

Prevention

- Avoid touching live poultry or their droppings
- Wash hands thoroughly with liquid soap and water immediately after contact with live poultry, birds or their droppings
- Develop good body resistance and have a healthy lifestyle
- Observe good personal and environmental hygiene

- Keep hands clean and wash hands properly and frequently
- Cover nose and mouth while sneezing or coughing, and dispose sputum or secretions wrapped in tissue paper into rubbish bins with lids
- Maintain good indoor ventilation

Vaccination

At present there is no vaccine for preventing avian influenza in humans. Influenza vaccine cannot prevent avian influenza. However, the vaccine can help reduce the chance of complications and hospitalization from human influenza. Influenza vaccine can also reduce the chance of genetic re-assortment and subsequent emergence of influenza strain with pandemic potential.

Antiviral Drugs

As prophylactic treatment, oseltamivir (Tamiflu) lasts only as long as it is being taken and ceases once it is stopped. Self-medication is not encouraged because of potential side effects and possibility of emergence of antiviral resistance.

Laboratory Diagnosis

Laboratory testing for human H5N1 influenza is similar to testing for other human influenza viruses, in terms of the clinical samples to be collected, and the testing procedures to be performed.

Diagnostic tests include slide immunofluorescence, viral culture, serology and molecular detection of viral nucleic acid (currently the preferred method). Nasopharyngeal aspirate samples provide a good diagnostic yield for respiratory viruses in general. Modern diagnostic virology laboratories can produce accurate, reliable results within one working day, provided that a good quality sample which is correctly labelled, stored, transported, arrives in good time for all the diagnostic testing to be performed.

Clinic Management

If there is a high index of suspicion of avian influenza A (H5/H7/H9) case:

- ensure that the patient has put on a face mask
- call for ambulance and transfer the patient to the nearest A&E department
- alert the A&E department and the Centre for Health Protection (CHP)
- keep a record and contact numbers of patients / accompanying persons / health care workers who share the waiting area with the affected patient
- disinfect the potentially contaminated area before seeing the next patient

If a probable / confirmed patient with avian influenza (H5/H7/H9) has attended the clinic, regardless of the identity of the affected individual, our CSC (Clinic Support Centre) here in TY will work with CHP and other relevant public health authorities to monitor and contain the avian flu virus infection.

Amantadine

It has been shown that the H5N1 virus is sensitive to amantadine, an effective agent for the treatment and prophylaxis of influenza A (but not B). However, the influenza viruses can rapidly develop resistance to this drug. Hence, doctors are advised to use the drug appropriately for treatment or prophylaxis of influenza A.

Close contacts, i.e. home contacts and medical staff providing direct care to patients with H5N1

infection, should be put on medical surveillance. If they develop symptoms compatible with influenza (fever of 38°C or higher, together with cough or sore throat), they should have a throat swab or nasopharyngeal aspirate taken for viral cultures.

Dosages

Amantadine 100mg bd for 5 days can be used (while pending viral culture results) to treat cases of suspected H5N1 infection. If started within 48 hours of the start of illness, amantadine can reduce the severity and shorten the duration of illness. Doses should be reduced for children and elderly, and those with underlying renal diseases. For children aged 1 to 9, the dosage is 5mg/kg/day in 2 divided doses up to 150 mg. For children aged greater than 9, adult dosage can be used but if the body weight of the child is less than 40kg, use the regime of 5mg/kg/day in 2 divided doses up to 150 mg.

Adverse reactions

Amantadine can cause neurological and gastrointestinal side effects. In one study of healthy adults, approximately 13% of those treated with amantadine developed side effects. Neurological side effects include nervousness, anxiety, difficulty in concentrating and dizziness. More serious neurological side effects like marked behavioural changes, delirium, hallucinations, agitation and seizures have been observed. Gastrointestinal side effects include nausea, vomiting abdominal pain and constipation. These side effects will stop after the drug has been withdrawn. Cautions must be exercised for people with renal insufficiency and in the elderly age group. The drugs are contraindicated for persons with seizure disorders.

BOTULISM

Clostridium butyricum is an anaerobic spore-forming organism widely distributed in the soil. The pathogenic effect of *C butyricum* depends on its ability to produce botulinum neurotoxin. The toxin is heat sensitive, and can be destroyed by heating at 80°C for 10 minutes or at boiling temperature for a few minutes. The spores are more resistant to heat and therefore may be found in canned food treated with temperatures 100°C or less.

Clinical Features

Foodborne botulism
This results from ingestion of preformed toxin present in contaminated food, and is characterized by acute bilateral cranial nerve impairment and descending weakness or paralysis, usually occurring within 12-36 hours after ingestion of the toxin. The patient typically remains alert and afebrile, and sensory deficits are absent. Vomiting and constipation or diarrhoea may occur initially.

Infant botulism
This is a result of spore ingestion and subsequent outgrowth and in-vivo toxin production in the intestines by the bacteria. It affects infants under 1 year of age almost exclusively. The incubation period is undetermined. The disease typically begins with constipation, followed by lethargy, listlessness, poor feeding, ptosis, difficulty swallowing, and hypotonia. Death may occur in severe cases.

Laboratory diagnosis
Botulism is confirmed by detecting botulinum toxin in serum, stool, gastric aspirate or incriminated food, or by culture of the organism from gastric aspirate or stool in a clinical case.

Treatment

Good supportive care in a hospital is the mainstay of therapy for all forms of botulism. The respiratory failure and paralysis may require intensive supportive care including ventilatory support. If diagnosed early (within 48 hours of onset), foodborne botulism can be treated with a polyvalent antitoxin that blocks the action of circulating toxin in the blood. Although this can prevent patients from worsening, recovery still takes many weeks. Antitoxin is not routinely given for treatment of infant botulism, because circulating toxin is in most cases absent.

Antibiotics are not necessary in foodborne or infant botulism. Some antibiotics such as aminoglycosides and tetracyclines may worsen the muscle paralysis.

Prevention & Control

Adequate heat treatment is the most important means of control. Prevention of introduction of bacteria and/or spores during food processing is critical especially in the preparation of high-risk canned food. Appropriate storage temperature and addition of other preservatives, such as salt or acid, could be useful.

CHOLERA

General Information

- Cholera is an acute infectious disease caused by *Vibrio cholerae*, a Gram-negative, facultatively anaerobic rod in the family Vibrionaceae. Two serogroups, 01 and 0139 ("Bengal"), can cause disease. Serogroup 01 contains two serologically indistinguishable biotypes, classical and El Tor. Mild or asymptomatic infections are seen more often with the El Tor biotype.
- Cholera is transmitted through faecal-oral route, with an incubation period ranging from a few hours to 5 days. Infected patients suffer from mild to severe "rice-water" diarrhoea without pain or colic. The patient can die from severe dehydration. Cholera can occur in large-scale epidemics where proper sanitary measures have broken down.
- The risk of cholera to travellers in general is so low (cholera : hepatitis A = 1 : 700) that the vaccine is not likely to benefit them. Travellers who follow the usual tourist itinerary and who use standard accommodations in countries affected by cholera are at virtually no risk of infection.
- The traveller's best protection against cholera, as well as against many other enteric diseases, is to avoid food and water that might be contaminated.

Diagnosis & Treatment

For rapid diagnosis, a wet mount of liquid stool is examined microscopically. The characteristic motility of vibrios is stopped by specific antisomatic antibody.

Treatment of cholera consists mainly of fluid and mineral replacement. Oral or intravenous fluid may be given. Appropriate antibiotic (tetracycline or doxycycline) can shorten the duration of diarrhoea and diminish the severity of illness.

Vibrio cholerae is susceptible to many disinfectants, including 0.05% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, 8% formaldehyde, 10% hydrogen peroxide and iodine-based disinfectants.

Cholera Vaccination

No country requires proof of cholera vaccination as a condition for entry. The traditional cholera vaccine by injection only provides incomplete protection of short duration and can convey a false sense of security. Its use for prevention is therefore not recommended. Two recently developed vaccines for cholera are licensed and available in other countries. Both of them appear to provide a somewhat better immunity than the previously available vaccine. However, neither is available in Hong Kong.

Nowadays, cholera vaccines are indicated only:

- when a country affected or threatened by cholera requires evidence of cholera vaccination for entry, or
- in special high-risk groups (eg healthcare workers, military personnels) that work and live in highly endemic areas under less than sanitary conditions.

Immunization Schedule

- Complete primary immunization consists of two doses of 0.2ml vaccine given intradermally at least 1 week apart, although one dose of vaccine will usually satisfy the requirements of

countries requesting evidence of cholera vaccination for entry.
- Booster doses may be given every 6 months if necessary for travel or for residence in highly endemic, unsanitary areas.

Physicians administering cholera vaccine to travellers should emphasize that an International Certificate of Vaccination is valid only for 6 months, beginning 6 days after vaccination.

Precautions
- Vaccination may result in 1-2 days of pain, erythema, and induration at the injection site, which may be accompanied by fever, malaise, and headache.
- Vaccine is not recommended for infants less than 6 months of age.
- No specific information exists on the safety of cholera vaccine during pregnancy.

Vibrio parahaemolyticus

Vibrio parahaemolyticus is in the same family Vibrionaceae. It lives in saltwater and is present in higher concentrations during summer. Most people get infected by eating raw and uncooked shellfish, particularly oysters. When ingested, *Vibrio parahaemolyticus* causes watery diarrhoea often with abdominal cramping, nausea, vomiting fever and chills. Usually these symptoms occur within 24 hours of ingestion. Illness is usually self-limited and lasts about 3 days. Severe disease is rare and occurs more commonly in persons with weakened immune systems.

DENGUE FEVER

Dengue fever (DF) is an acute febrile viral disease caused by dengue viruses which are flaviviruses (4 serotypes). It is on the increase across the Asia Pacific region. Reported cases and deaths due to dengue started to show a rising trend in the year 2000 beginning in May and June. The hardest hit countries so far have been Cambodia, Vietnam, Singapore, Malaysia, the Philippines, and in the Pacific, French Polynesia and Samoa.

In Hong Kong, DF has been a statutory notifiable disease since March 1994. About 3-15 cases of DF were notified each year. Most of them acquired the infection from outside Hong Kong, most commonly from Southeast Asian countries.

Mode of Transmission

Dengue viruses are transmitted to humans through the bites of infective female Aedes mosquitoes, principally Aedes aegypti. This is a day biting species, with increased biting activity for 2 hours after sunrise and several hours before sunset. Mosquitoes generally acquire the virus through feeding on the blood of an infected person. Once infective, a mosquito is capable of transmitting the virus to susceptible individuals for the rest of its life. Hence, once introduction into a community, it is virtually impossible to eradicate the disease without total elimination of the vector. The disease is not directly transmitted from person to person or through droplet spread. Patients are infective for mosquitoes from shortly before to the end of the febrile period, usually a period of 3-5 days.

Clinical Features

DF is an acute febrile infection with an incubation period of 3 to 14 days. It is characterized by sudden onset, fever for 3-5 days, intense headache, myalgia, arthralgia, retroorbital pain, anorexia, gastrointestinal disturbances and rash. A generalized maculopapular rash usually appears about the time of defervescence. Minor bleeding phenomena, such as petechiae, epistaxis or gum bleeding may occur at any time during the febrile phase. Recovery may be associated with prolonged fatigue and depression. Lymphadenopathy and leukopenia with relative lymphocytosis are usual; thrombocytopenia (less than 100×10^9/L) and elevated transaminases occur less frequently.

Dengue haemorrhagic fever (DHF) is characterized by increased vascular permeability, hypovolaemia and abnormal blood clotting mechanisms. It is recognized principally in children, but occurs also in adults. The risk factor described best is the circulation of heterologous dengue antibody, acquired passively in infants or actively from an earlier infection.

Dengue shock syndrome (DSS) includes the more severe DHF patients plus signs of shock, and is a life-threatening condition.

Laboratory Diagnosis

Diagnosis of DF/DHF can be made using serological tests. A fourfold or greater rise in IgG or IgM antibody titres using haemagglutination-inhibition test in paired serum samples confirms the infection. IgM antibody, indicating current or recent infection, is usually detectable by day 6-7 after onset of illness. A number of commercial kits are available in the market.

During the acute febrile state of illness, virus can be isolated from blood or virus specific nuclei acid

sequences may be detected by PCR.

Treatment

There is no specific treatment for DF. No isolation of patient is required. Patients should be encouraged to drink plenty of fluid. Aspirin is contraindicated both because of its anticoagulant effects and the increased risk of developing Reye's syndrome.

Prevention

No vaccine is current available for DF. At present, the only method of controlling or preventing DF and DHF is to combat the vector mosquitoes. Vector control is implemented using environmental management and chemical methods through community-based programmes.

INFLUENZA

Influenza A and B are the 2 types of influenza viruses that cause epidemic human disease. Influenza A viruses are categorized into subtypes on the basis of 2 surface antigens: hemagglutinin and neuraminidase. Currently circulating influenza B viruses are separated into 2 distinct genetic lineages but are not categorized into subtypes.

Immunity to the surface antigens reduces the likelihood of infection. Antibody against one influenza virus type or subtype confers limited or no protection against another type or subtype of influenza virus. Frequent emergence of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics as well as the reason for annually reassessing the need to change one or more of the recommended strains for influenza vaccines. More dramatic antigenic shifts can result in the emergence of a novel influenza A virus with the potential to cause a pandemic.

In Hong Kong, influenza occurs throughout the year. It usually peaks in February and March but may have a secondary peak during summer time.

Mode of Transmission

Influenza viruses are spread from primarily through respiratory droplet transmission. This requires close contact between the source and the recipient, because droplets do not remain suspended in the air and generally travel only a short distance (< 1 m) through the air. Contact with droplet contaminated surfaces is another possible route. Airborne transmission is possible, although supporting data are limited.

Clinical Features

	Common Cold	**Influenza**
Onset	Gradual	Sudden
Fever & chills	Rare	Common (>80%)
Cough	More productive	Usually dry
Sore throat	Common	Rare
Nasal symptoms	Common	Rare
Headaches & myalgia	Rare	Common
Tiredness	Rare	Common
Pathogens	Rhinoviruses Parainfluenza Influenza B Influenza C Corona virus RSV	Influenza A Influenza B

Influenza viruses cause disease among persons in all age groups. Rates of infection are highest among children, but the risks for complications, hospitalizations, and deaths from influenza are higher among persons aged > 65 years, young children, and persons with chronic medical conditions such as asthma, kidney diseases, diabetes, heart diseases, lung diseases and any other conditions associated with impaired immunity (eg HIV infections).

The incubation period is 1-4 days. Adults can be infectious from the day before symptoms begin through approximately 5 days after illness onset. Young children also might shed virus several days before illness onset, and children can be infectious for >10 days after onset of symptoms. Furthermore, young children are less likely to report typical influenza symptoms (eg fever and cough).

Uncomplicated influenza is characterized by the abrupt onset of constitutional and respiratory symptoms. Uncomplicated influenza typically resolves after 3-7 days, although cough and malaise can persist for > 2 weeks. However, influenza can cause primary viral pneumonia; exacerbate underlying medical conditions (eg pulmonary or cardiac disease); lead to secondary bacterial pneumonia, sinusitis, or otitis; or contribute to co-infections with other viral or bacterial pathogens.

Laboratory Diagnosis

Diagnostic tests include slide immunofluorescence, viral culture, serology and molecular detection of viral nucleic acid (currently the preferred method). Nasopharyngeal aspirate samples collected in a hospital setting with proper infection containment facilities provide a good diagnostic yield for influenza viruses.

Options for Controlling Influenza

Vaccination

The CHP has been providing recommendations on the use of influenza vaccine for the local medical community. In TY however, we have been following the guidelines provided by the Advisory Committee on Immunization Practices (ACIP) of the Center for Disease Control (CDC), ie routine annual vaccination is recommended for:-

- young children and the elderly
- institutionalized persons
- patients with chronic diseases (eg asthma, diabetes…)
- health-care workers
- pregnant women who will be in the 2nd or 3rd trimester during the flu season
- **all persons who want to reduce the risk of becoming ill with influenza or of transmitting influenza to others**

Agrippal from Novartis is what we use in TYMP for the 2007/2008 influenza season. It is a trivalent inactivated vaccine that contains purified viral proteins from the following influenza virus strains:

- A/Solomon Islands/3/2006 (H1N1)-like
- A/Wisconsin/67/2005 (H3N2)-like
- B/Malaysia/2506/2004-like

For adults and children from 36 months, a single dose (0.5 ml) of the vaccine will be injected intramuscularly or subcutaneously. For children aged 6 months to 35 months, half a dose (0.25 ml) is to be administered (discard half the contained volume up to the mark indicated on the syringe barrel before injection). Children who have not been previously infected with influenza, or who are receiving the vaccine for the first time, should receive a second dose after an interval of at least 4 weeks.

Like all current inactivated influenza vaccines, Agrippal contains trace levels of egg protein and should not be administered to individuals with egg protein allergies.

Tamuflu (oseltamivir)

This is the first orally active neuraminidase inhibitor commercially developed. It is indicated for **treatment** of uncomplicated influenza caused by viruses types A and B in patients > 1 year old with flu symptoms for < 48 hours. It is also indicated for **prevention** of influenza in patients > 1 year. Tamiflu is not a substitute for annual flu vaccination. Studies have shown that those who had flu symptoms and were treated with Tamiflu had reduced recovery times of up to 30%.

Adult dosages (reduce dosages by 50% for patients with creatinine clearance 10-30 ml/min):

- Treatment: 75 mg bd x 5/7
- Prevention (post-exposure): 75 mg qd x 10/7
- Prevention (seasonal): 75 mg qd during a community outbreak (safety and efficacy demonstrated for up to 6/52, and duration of protection lasts for as long as dosing is continued)

Dosages for patients aged 1 and older (or adults unable to swallow a capsule):

Body weight (kg)	Treatment	Prophylaxis (post-exposure)
< 15	30 mg bd	30 mg qd
> 15 – 23	45 mg bd	45 mg qd
> 23 - 40	60 mg bd	60 mg qd
> 40	75 mg bd	75 mg qd

Tamiflu is normally not recommended for use during pregnancy or nursing, as the effects on the unborn child or nursing infant are unknown. Efficacy of Tamiflu has not been established in immunocompromised patients.

Nonpharmacologic interventions for your patients

- Build up good body immunity by having a proper diet, regular exercise and adequate rest, reducing stress and avoiding smoking
- Maintain good personal and environmental hygiene
- Wash hands after sneezing, coughing or cleaning the nose
- Maintain good ventilation and avoid visiting crowded places with poor ventilation
- Wear face masks and consult doctors promptly for influenza-like symptoms

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) is an acute viral infection of the central nervous system caused by JE virus which is a flavivirus (a group B arbovirus). According to the World Health Organization, JE occurs in a large number of countries/areas of Asia, including Cambodia, China, Indonesia, Japan, Lao People's Democratic Republic, Malaysia, Myanmar, the Philippines, Republic of Korea, Thailand, Vietnam, south-eastern Russian Federation and the Indian subcontinent. In recent decades, JE has gradually spread to previously non-affected Asian regions, and a small outbreak was recently reported from islands in the Torres Strait off the Australian mainland. In Hong Kong, no more than 2 cases of human JE were reported each year. Both local and imported cases have occurred.

In Hong Kong, DF has been a statutory notifiable disease since March 1994. About 3-15 cases of DF were notified each year. Most of them acquired the infection from outside Hong Kong, most commonly from Southeast Asian countries.

Mode of Transmission

The virus is transmitted by the bite of infected Culex mosquitoes. *Culex tritaeniorhychus* is the principal vector of the disease. The mosquito becomes infected by feeding on pigs and wild birds infected with the JE virus. The infected mosquitoes then transmit the virus to humans and animals during the feeding process. The transmission reaches its dead end in human. The disease is not directly transmitted from person-to-person.

Clinical Features

The incubation period of JE is usually 4 to 14 days. Mild infections may occur without apparent symptoms other than fever with headache. More severe infection is marked by rapid onset, headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions (especially in infants) and paralysis. Case fatality rates range from 10% to 35%. Neurological and psychiatric sequelae are common among survivors.

Laboratory Diagnosis

Diagnosis of JE infections can be made by serological tests, such as haemagglutination-inhibition test, by demonstrating a fourfold rise in antibody titres in paired sera. This test is available at the Government Virus Unit of the Department of Health (DH).

Treatment

There is no specific treatment for JB. No isolation of patient is required. Treatment is mainly supportive.

Prevention

As JE is a mosquito-borne disease, measures should be taken to eliminate mosquito breeding sites and

prevent mosquito bites. Vaccination is indicated mainly for persons spending 30 days or more in an epidemic region, or an endemic area during the transmission season. Currently one inactivated JE vaccine (distributed by a Japanese company called Biken) is licensed in Hong Kong. The vaccine is derived from mouse brain, and is given subcutaneously.

For initial immunization of adults and children 3 years and older, usually 2 doses (1 ml each) are administered at an interval of 1-2 weeks. Immunity may take one month to develop. Another dose (1 ml) can be given in 1 year, and every 3 years thereafter as boosters. For children between 1-2 years old, the dosages are reduced by half. Common reported side effects include local reactions at the injection site, and mild systemic symptoms such as headache, myalgia, gastrointestinal symptoms and fever.

The vaccine is not generally recommended for pregnant women (unless the risk of infection outweighs the risk of the immunization), and persons with a history of multiple allergies or hypersensitivity to components of the vaccine. There are no data about the safety and efficacy of the vaccine in infants less than 1 year of age. Limited data suggest that immunogenicity is not compromised by the simultaneous administration of diphtheria, pertussis, and tetanus vaccine.

Because the vaccine may cause severe delayed allergic reaction (anaphylaxis), which can occur within minutes, or up to as many as nine days after receiving an immunization, use of the vaccine requires careful evaluation of risks and benefits.

The JE vaccine comes in a freeze-dried powder form and must be reconstituted with its diluent before use. The vaccine should be refrigerated between 2° and 8 °C and not frozen at any time. It is stable (ie retains its original potency) at 4 °C for at least 1 year and retains more than 90% of its potency after 28 weeks at 22 °C. At 37 °C, the vaccine retains 95% of its original potency after 4 weeks. Once reconstituted, the vaccine is stable for at least 2 weeks at 22 °C, but at 37 °C, potency declines to 85% after 2 weeks.

MALARIA PROPHYLAXIS

Malaria occurs in over 100 countries and more than 40% of the people in the world are at risk. Large areas of Central and South America, Hispaniola (Haiti and the Dominican Republic), Africa, the Middle East, the Indian subcontinent, Southeast Asia, and Oceania are considered malaria-risk areas. The World Health Organisation estimates that yearly 300-500 million cases of malaria occur and more than 2 million people die of malaria.

Symptoms of malaria include fever and flu-like syndrome, including chills, headache, muscle aches, and tiredness. Nausea, vomiting, and diarrhoea may also occur. Malaria may cause anaemia and jaundice because of the loss of red blood cells. Infection with one type of malaria, *P falciparum*, if not promptly treated, may cause renal failure, seizures, mental confusion, coma, and death.

For most patients, symptoms begin 10 days to 4 weeks after infection, although one may feel ill as early as 8 days or up to 1 year later. Two kinds of malaria, *P vivax* and *P ovale*, can relapse; some parasites can rest in the liver for several months up to 4 years after a person is bitten by an infected mosquito.

Anti-Mosquito Measures

- Pay special attention to mosquito protection between dusk and dawn. This is when the type of mosquito whose bite transmits malaria is active.
- Wear long-sleeved shirts, long pants, and hats.
- Use insect repellents that contain DEET (diethylmethyltoluamide).
- Do not put repellent on wounds or broken skin.
- Do not breathe in, swallow, or get into the eyes (DEET is toxic if swallowed). If using a spray product, apply DEET to your face by spraying your hands and rubbing the product carefully over the face, avoiding eyes and mouth.
- Purchase a bed net impregnated with the insecticide permethrin or deltamethrin if you are going to sleep in areas without air-conditioning. Or, spray the bed net with one of these insecticides if you are unable to find a pretreated bed net.

Anti-Malarial Drugs

Mefloquine (Mephaquin in HK, Lariam in US)

- The adult dosage is 250mg (one tablet) once a week.
- Take the first dose of mefloquine 1 week before arrival in the malaria-risk area.
- Take mefloquine once a week (same day each week), while in the malaria-risk area.
- Take mefloquine once a week for 4 weeks after leaving the malaria-risk area.
- Mefloquine should be taken on a full stomach, eg after dinner.
- The most commonly reported minor side effects include headache, nausea, dizziness, difficulty sleeping, anxiety, vivid dreams, and visual disturbances. Mefloquine has rarely been reported to cause serious side effects, such as seizures, depression, and psychosis. Mefloquine should be used with caution in persons with psychiatric disturbances. Minor side effects usually do not require stopping the drug. Travellers who have serious side effects should see medical attention.

- Contraindications: allergy to mefloquine, epilepsy or other seizure disorders, active depression or a history of psychosis, cardiac arrhthymias.

Doxycycline (Vibramycin or Doxymycin in HK)

- The adult dosage is 100mg once a day.
- Take the first dose of doxycycline 1 or 2 days before arrival in the malaria-risk area.
- Take doxycycline once a day (same time each day), while in the malaria-risk area.
- Take doxycycline once a day for 4 weeks after leaving the malaria-risk area.
- Taking doxycycline may cause travellers to sunburn faster (photosensitivity).
- Take doxycycline on a full stomach to lessen nausea; do not lie down for 1 hour after taking the drug to prevent reflux of the drug.
- Women who use doxycycline may develop a vaginal yeast infection.
- Contraindications: allergy to tetracyclines or doxycycline, children under the age of 8 (teeth may become permanently stained), pregnancy.

Atovaquone-proguanil (Malarone in HK)

- Malarone is a new antimalarial drug indicated for prevention AND treatment of acute, uncomplicated malaria.
- Malerone is effective against drug sensitive and drug resistant P falciparum.
- It is an alternative for travellers who cannot or choose not to take doxycycline or mefloquine.

- FOR PROPHYLAXIS, the adult dosage is 1 tablet (250mg atovaquone/100mg proguanil) once a day.
- Take the first dose of Malarone 1 to 2 days before travel to the malaria-risk area.
- Take Malarone once a day while in the malaria-risk area.
- Take Malarone once a day for 7 days after leaving the malaria-risk area.
- Take the dose at the same time each day with food or milk.

- FOR TREATMENT, the adult dosage is 4 tablets as a single dose for 3 days.

- Side effects are rare: abdominal pain, nausea, vomiting, and headache can occur.
- Contraindications: severe renal impairment, pregnancy, breast-feeding, infants weighing less than 11kg.
- In residents (semi-immune subjects) of endemic areas, the safety and effectiveness of Malarone has been established in studies of up to 12 weeks.

After Returning Home

Continue taking the anti-malarial drug for 4 weeks (doxycycline or mefloquine) or 7 days (atovaquone/proguanil) after leaving the risk area. Any patients becoming ill with a fever or flu-like illness either while travelling in a malarious area or after returning home (for up to 1 year) therefrom should seek immediate medical attention.

NOROVIRUS INFECTION

This infection is caused by a group of viruses known as noroviruses, also known as "Norwalk-like viruses" or small round structured viruses (SRSVs). These viruses are a common cause of sporadic cases of acute gastroenteritis as well as outbreaks of food poisoning and acute gastroenteritis, especially in elderly homes and schools. The disease affects people of all age groups and tends to be more common during winter. In July 2006, there were 30 confirmed norovirus outbreaks in elderly homes and 12 in public hospitals affecting 206 and 93 persons respectively.

Clinical Features

Norovirus infection is transmitted:

- by food or water contaminated with the virus;
- by contact with vomitus or faeces from infected persons;
- by contact with contaminated objects; or
- by aerosol spread.

The disease is usually self-limiting with symptoms of nausea, vomiting, diarrhoea, abdominal pain, low-grade fever and malaise. The incubation period is usually 24 to 48 hours, and the subsequent symptoms usually last the same (ie 24 to 48 hours).

Management

- Supportive care (eg fluid replacement)
- Symptomatic treatment
- Antibiotics are of no value in treatment.

Prevention

- Maintain high standard of personal, food and environmental hygiene.
- Wash hands thoroughly before handling food and eating and after going to toilets and handling vomitus or faecal matter.
- Wear gloves while disposing of vomitus and faeces, and wash hands afterwards.
- Clean and disinfect soiled linens, clothes and surfaces promptly and thoroughly with household bleach (5.25%) diluted in a ratio 1 in 49 units of water.
- Food handlers and caretakers developing vomiting or diarrhoea should refrain from work and seek medical advice.
- No vaccine is available for Norwalk-like viruses infection.

Disinfection of environment after vomiting incidents

- Keep children away from the area during the cleaning process.
- Wear gloves and a mask while removing the vomitus.
- Use disposable towels to wipe away all the vomitus from outside inward, before applying diluted bleach (1:49) to the surface and the neighbouring area (eg within 2m of the vomitus).
- Leave bleach on the soiled surface for about 30 minutes to allow time for the bleach to inactivate viruses before rinsing the surface with water. Leave the surface to dry.
- Floor mops should not be used for cleaning the vomitus.

NOTIFIABLE INFECTIOUS DISEASES

Although it is widely believed that infectious diseases are grossly under-notified (especially in the private sector) here in Hong Kong, a registered doctor has a statutory duty to notify the Department of Health of the occurrence of the following 31 infectious diseases under the Quarantine and Prevention of Disease Ordinance (Cap. 141).

Acute Poliomyelitis
Amoebic Dysentery
Bacillary Dysentery
Chickenpox
Cholera
Dengue Fever
Diphtheria
Food Poisoning
Influenza A (H5), Influenza A (H7), Influenza A (H9)
Japanese Encephalitis
Legionnaires' Disease
Leprosy
Malaria
Measles
Meningococcal Infections
Mumps
Paratyphoid Fever
Plague
Rabies
Relapsing Fever
Rubella
Scarlet Fever
SARS
Streptococcus suis Infection
Tetanus
Tuberculosis
Typhoid Fever
Typhus
Viral
Whooping Cough
Yellow Fever

In 2006 (as at 10 August), the 5 most frequently notified infectious diseases were chickenpox, tuberculosis, food poisoning, viral hepatitis and scarlet fever.

How to Notify

Name of Form	Fax	Enquiry
Tuberculosis Notification	2574 2439	2572 3487
Notification of Infectious Diseases other than Tuberculosis	2893 9425	2961 8570

Forms can be downloaded, and e-mail notification is available, at:
http://www.dh.gov.hk/english/useful/useful_forms/useful_notify.html