Common Infectious Diseases & Diagnostics in HIV & Traveling Medicine

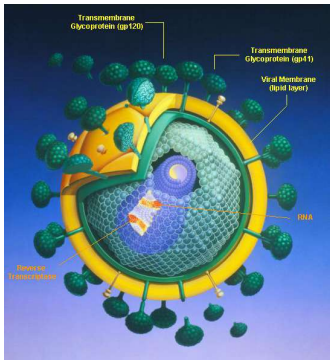
Professor Ivan Hung
MD FRCP (Lon, Edin)

HIV
愛滋病病毒

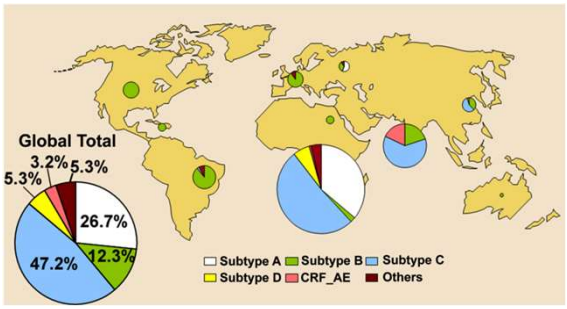
The HIV Virus

- Retrovirus (RNA virus), genus Lentivirus, family Retroviridae
- failing immune system - life-threatening opportunistic infection
- leads to AIDS
- Bodily fluid: blood, semen, vaginal fluid or breast milk
- Free virus particles or virus in infected immune cells

Human Immunodeficiency Virus



Map Showing HIV Subtypes



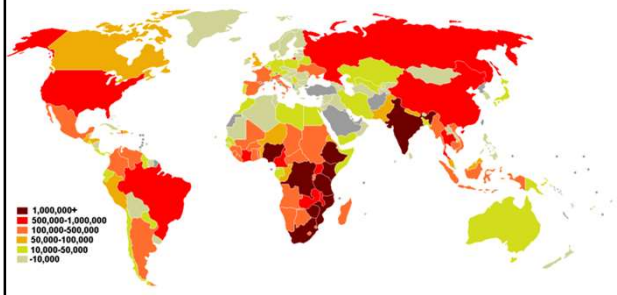
Origin & Discovery

- From SIV to HIV
- Early 20th century
- Two species: HIV-1 and 2
- HIV 1: southern Cameroon; jump from wild chimpanzees (*Pan troglodytes troglodytes*)
- HIV-2: Gabon: Sooty Mangabey (*Cercocebus atys*)
- HIV-1 more virulent: cause of global HIV pandemics

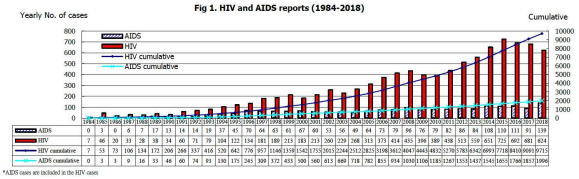
Historical Perspective: Human

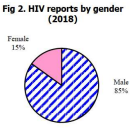
- **June, 1981** by CDC: unusual clusters of PCP caused by *Pneumocystis jirovecii* in five homosexual men in LA
- **1983**: Retrovirus identified
- **1985:** Serological test
- **1987**: antiretroviral drugs
- **1996:** HAART
- **1996 -:** 60-80% decreased in mortality, AIDS and hospitalization

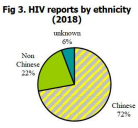
People Living with HIV

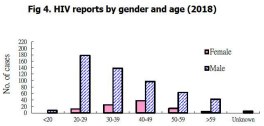


59 millions worldwide; 20 millions died





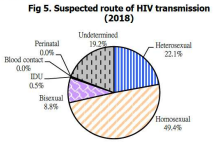




Sexual contact remained the major route of transmission for HIV

Sexual contact contributed to around 80% of all reported HIV cases in 2018 (homosexual 49.4%, heterosexual 22.1%, bisexual 8.8%). (Fig 5). There were 3 cases of infection via injecting drug use (IDU) in 2018. 19.2% of cases in 2018 did not have risk factor ascertained due to inadequate information.

Note: The percentage may not add up to 100% due to rounding.



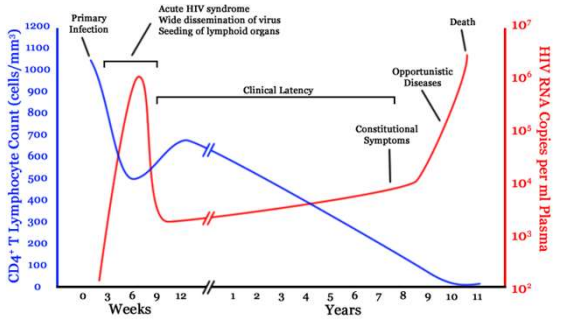
Viral Transmission

- sexual intercourse (hetero/ homosexual route)
- Blood-borne: IVDU/ exposure to contaminated blood (0.3%)
- perinatal transmission
- breast milk

Risk Factors

- High HIV viral load
- Lack of circumcision
- Sexual risk: unprotected sex, ♂ to ♀ 0.08% per act,
- ♀ to ♂ 0.04% per act;
- receptive anal 1.7% per act
- Presence of ulcerative STDs; eg genital herpes, syphilis (10 to 300 times)
- HIV superinfection (infected with second strain after first strain); coinfection (two strains simultaneously)

Clinical Course of Infection



Acute HIV Infection

- Thrush
- Vaginal candidasis
- Oral hairy leukoplakia (EBV)
- Herpes zoster x 2 or > 1 dermatone
- Peripheral neuropathy
- Bacillary angiomatosis (Bartonella)
- Cervical dysplasia
- Cervical carcinoma in situ
- Fever or diarrhea > 1 month
- ITP
- PID
- Listeriosis

AIDS Defining Conditions

- All patients with CD4 count < 200/ mm3
- Pneumocystis pneumonia — 42.6 %
- Esophageal candidiasis - 15.0 %
- Wasting — 10.7 %
- Kaposi's sarcoma — 10.7 %
- Disseminated *M. avium* infection — 4.8 %
- Tuberculosis — 4.5 %
- Cytomegalovirus disease — 3.7 %
- HIV-associated dementia — 3.6 %
- Recurrent bacterial pneumonia — 3.0 %
- Toxoplasmosis — 2.6 %
- Immunoblastic lymphoma - 1.9 %
- Chronic cryptosporidiosis - 1.5 %
- Burkitt lymphoma - 1.5 %
- Disseminated histoplasmosis - 1.0 %
- Invasive cervical cancer - 0.9 %
- Chronic Herpes simplex — 0.5 %
- *Penicillium manarffei* infection in Asia

HIV antibodies testing
愛滋病病毒抗體測試

- 2-step testing
  二步法測試
- Screening by enzyme-linked immunosorbent assay (ELISA)
  利用[酶聯免疫吸附測試]作篩查
- Confirmation by Western blot (WB)
  以[免疫蛋白印迹法]作確診
- Free confirmation for screening positive results by Public Health Laboratory Centre of Centre for Health Protection, DH
  衞生署衞生防護中心轄下的公共衞生檢測中心提供免費確診服務予初篩陽性的個案

3

Window period
空窗期

- The time period between contracting HIV and testing positive for HIV antibody, is usually taken to be 3 months.

從感染了愛滋病病毒至愛滋病病毒抗體測試呈陽性反應的期間，一般視爲三個月。

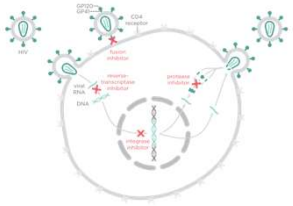
3

Treatment

- Currently no vaccine or cure
- Post exposure prophylaxis: 4 weeks: Truvada (emtricitabine + tenofovir)
- HAART: (start CD4 <350; HK)
- 2x NRTI + PI or NNRTI
- Average life expectancy: >30 years from time of infection
- Side effects: lipodystrophy, dyslipidemia, insulin resistance, CVS risks

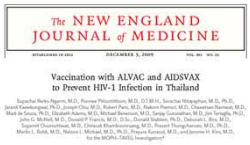
Classes

- Fusion inhibitor: maraviroc (CCR5) enfuvirtide (gp41)
- NRTI: zidovudine, lamivudine, tenofovir, stavudine
- NNRTI: efavirenz
- Integrase inhibitor: raltegrase, dolutegravir
- PI: ritonavir, lopinavir
- Early commencement increase survival
- CD4 around 500

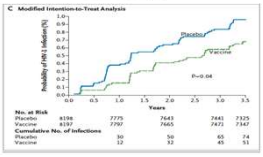


HIV Vaccine: Challenges & Prospects

- AIDSVAX (recombinant gp120) and ALVAC (recombinant canarypox vector)
- 16,402 healthy subjects
- 2009: efficacy 26.1% to 31.4%



- Extraordinary mutability
- Genetic diversity
- Rapid integration with host DNA leading to latency (narrow window)
- Early destruction to CD4 T cells
- T-cell vaccine: induce broad neutralizing Ab and cytotoxic T lymphocytes



Rerks-Ngarm S et al. N Engl J Med 2009;361:2209-20
Johnston MI et al. N Engl J Med 2008;359:888-90

Case 1

- 23M, Vietnamese prisoner
- IVDA
- Admitted 21/8/2006
- Fever, 3 weeks
- Cutaneous lesions: arms 2 weeks, face 3 days
- 4 kg weight loss
- Poor appetite
- Denied chill, myalgia, cough or diarrhea

Physical Examination

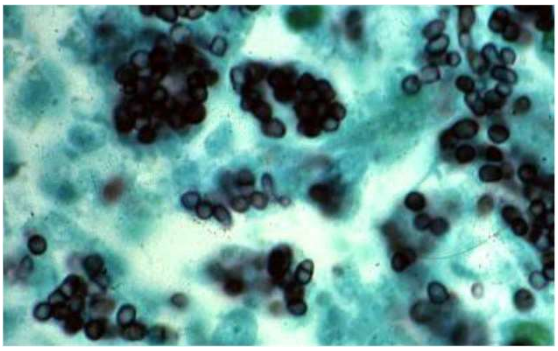
- Unwell and fatigue
- T 38.2, pulse 84/min
- Bilateral cervical LN
- Numerous skin-colour cutaneous papules, with umbilication
- Face and both arms
- Lesions on the buccal mucosa and soft and hard palates
- Normal lungs and heart
- Enlarged liver 2 cm below R costal margin

Blood Results

- WCC 2.2 (N 2.0, L 0.2)
- Plt 185
- ALP 85, ALT 50, Bil 23
- **1. Abnormality?**
- **2. Differential diagnosis?**

Differentials

- Abnormality: severe lymphopenia
- Differentials:
- *Penicillium marneffei* infection
- *Cryptococcus neoformans* infection
- Molluscum contagiosum
- Bacillary angiomatosis



Diagnostic Results

- BMA: hypocellular marrow with numerous yeasts
- Blood and skin scrapping: *Penicillium marneffei*
- CD4 count 78 cells/ml

Diagnosis

- *Penicillium marneffei* infection
- 馬爾尼菲青黴菌
- HIV +ve
- AIDS

Treatment

- Amphotericin B (0.6mg/kg daily): 2 weeks
- Oral itraconazole 200mg bid for 10 weeks
- Fever and skin lesions resolved
- Referred ITC
- HAART
- Prophylaxis: Trimethprim sulfamethoxazole + azithromycin
- Secondary prophylaxis: itraconazole 200mg daily

Case 2

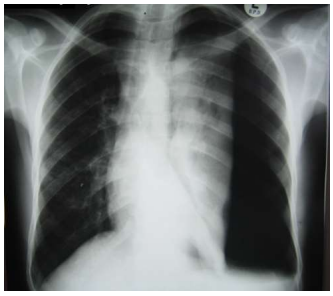
- Man in his twenties with HIV
- Cough, fever and SOB
- Unwell for 2 months
- Cough with white sputum, poor appetite and wt loss
- Clinic visit 3 weeks ago: CXR normal, sputum culture -ve
- Short course of antibiotics: no improvement
- No pleuritic chest pain, haemoptysis or leg swelling

Past Medical Hx

- HIV +ve; unknown CD4 count
- No history of asthma
- Smoked 10 cigarettes per day

Physical Examination

- Cachectic
- Mild respiratory distress
- Body temp: 37.5C
- Pulse: 126 beats/ min
- Oral thrush with no LNs
- Trachea deviated to R
- Clear chest and absent breath sounds and hyperresonance to percussion L side
- WC 6.4 L 0.2 CD4 78
- ABG: pH 7.47 pCO2 4kPa pO2 18kPa (2LO2)

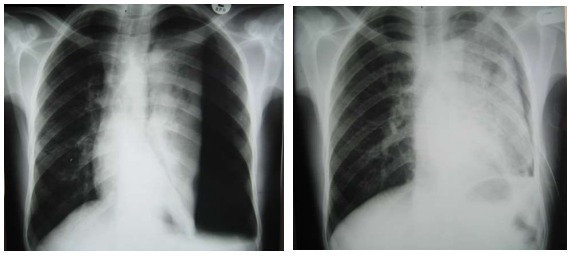


1. Abnormalities?
2. Differentials?

Differentials

- Pneumocystis jiroveci pneumonia
- Pulmonary tuberculosis
- Pulmonary cryptococcosis
- Pulmonary Kaposi's sarcoma
- Chronic obstructive pulmonary disease

Diagnostic Result & Procedure



Urgent sputum smear: AFB +ve

Follow-up

- Diagnosis: pulmonary tuberculosis 肺結核
- Started on HRMZ
- Chest drain clamped and removed 1 week
- CXR: fully expanded
- Discharge and follow-up in HIV clinic
- HAART started

Discussion

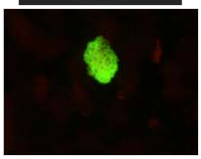
- HIV/ AIDS increased risk of spontaneous pneumothorax
- DDx: *Pneumocystis jiroveci,* pulmonary TB
- Rupture of cavitary lesion into pleural space
- Less common: pulmonary cryptococcosis, pulmonary Kaposi's sarcoma
- Small pneumothoraces (<1cm rim): conservatively with O2 supplement
- Large: tube thoracostomy
- Complication: bronchopleural fistula require pleurodesis

Case 3

- 52M
- Known HIV
- Defaulted FU
- SOB 1 week
- CD4 250
- HIV RNA 130,000
- SaO2 93% (5L O2)
- Afebrile
- Fine crackles
- DDx?

DDx

- MTB
- *Legionella pneumophila*
- *Strep pneumoniae*
- *Mycoplasma*
- *Pneumocystis jirovecii*



Dx & Treatment

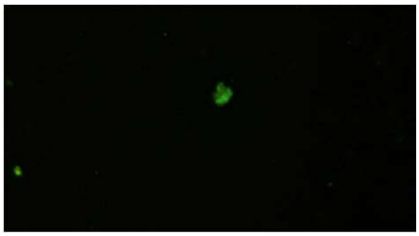
- Pneumocystis pneumonia 肺囊蟲性肺炎
- *Pneumocystis jirovecii*
- IF staining positive
- Septrin + prednisolone 40mg BD

Case 4

- HIV +ve woman
- Fever, malaise
- Tinnitus, decreased hearing
- Painful pustular lesions left ear
- CD4 478
- On HAART

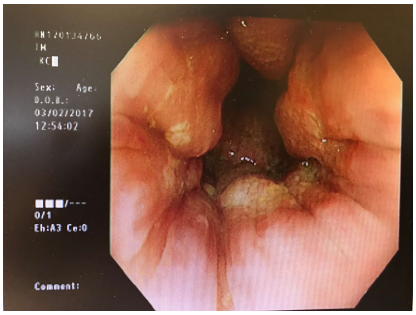
DDx

- Streptococcal cellulitis of the external ear
- *Pseudomonas* otitis media (malignant otitis externa)
- Herpes simplex virus
- Varicella zoster virus
- Contact dermatitis

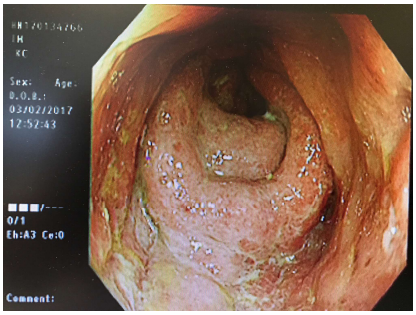


VZV Ab +ve, Ramsey Hunt Syndrome
水痘帶狀皰疹, 拉姆齊亨特綜合徵

Case 5: PR Bleed



Returned from Thailand



Case 5

DDx

1. ulcerative proctitis
2. LGV proctocolitis
3. GI lymphoma
4. HPV associated SCC of the anal canal

Case 5

- Anti-HIV 1 +ve (EIA/ Western blot)
- Anal swab culture: *Chlamydia*
- Anal & urethral swab NAT: *Chlamydia trachomatis* DNA +ve
- 沙眼衣原體
- Anal swab culture: *Neisseria gonorrhoeae* 淋病
- Syphilis VDRL 1:16 梅毒
- Histology: granulation tissue, lymphocytic infiltration, no crypt abscess, proctitis
- Doxycycline 100mg bid 3 weeks
- Ceftriaxone 250mg IMI x 1
- Benzathine penicillin IMI weekly x 3
- Referred ITC
- CD4 362
- HIV 320,000 copies/mL
- Plan to commence Truvada and Dolutegravir
- Repeat colonoscopy in 1 month

Infectious Diseases Associated with Returned Traveler

History

- 34 M admitted to Medical Ward
- Chinese; non-smoker, non drinker
- Good past health
- Fever, malaise for 3 days

History

- What would you ask?

History

- OTCC

History

- Occupation: businessman
- Travel: N Thailand/ Burma border 2 weeks ago
- Contact: no contact with febrile patient or animal
- Cluster: 2 friends and well

What Else?

- Dates of travel and duration of stay
- Type of accomodation
- Activities
- Insect bite
- Needle/ blood exposure
- Sex Hx
- Soil/ water contact
- chemoprophylaxis

History

- Stayed in **** Hotel for 1 week
- Played war game once at rural area in late evening with soil and water contact
- Insect/ mosquito bites +
- Denied sexual contact
- Denied needle or blood exposure

Differentials?

Differentials:

- Malaria
- Dengue fever
- Tyhoid fever
- Rickettsioses
- Leptospirosis
- Melioidosis

Physical Examination

- Mild jaundice
- Splenomegaly

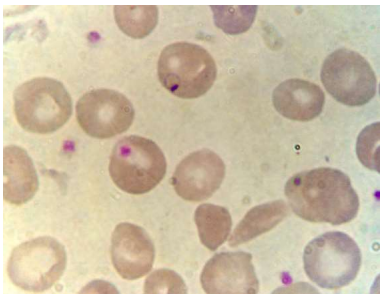
Investigation

- CBC
- LRFT
- Blood/urine/stool culture
- Blood smear for malaria
- Throat swab/ culture
- CXR

Results

- WCC 5000
- Platelet 100,000
- Hb 10.5
- Aspartate transaminase (AST) 220
- Bilirubin 60
- Ustix: RBC +++

Thin Blood Smear



Diagnosis

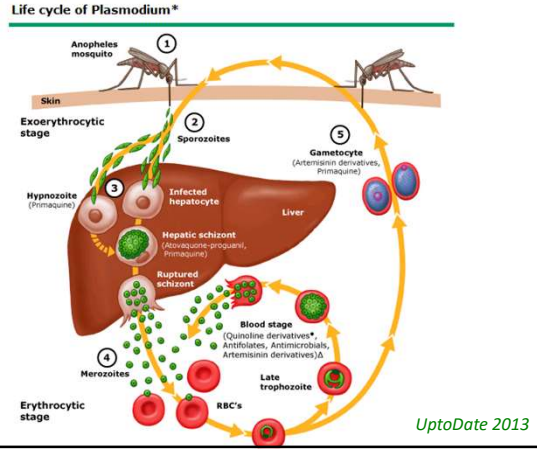
- Plasmodium falciparum
- 瘧疾，惡性瘧原蟲

Treatment

- Artensunate/ mefloquine combined treatment
- No parasite seen on day of discharge

Malaria

- 5 species of Plamodia: P falciparum, P vivax, P ovale, P malariae, P knowlesi (previously simian)
- Most: PF and PV
- Mortality PF
- Co-infection: 5 %
- Transmitted by female Anopheline mosquito
- Problems: resistance of parasites to chemotherapy, resistance of Anopheles to insecticide, climate change and international travel
- 500 million cases and 2.7 million deaths



Symptoms & Signs

- Asymptomatic for 1 week after bitten
- Incubation 2 weeks to 1 year
- Fever, chills, headache, abdominal pain, diarrhea and cough
- Febrile paroxysms co-ordinated with rupture of red cells: 24 hours for PF, PV and PO, 3 days for PM
- Hepatosplenomegaly, thrombocytopenia and jaundice

P falciparum

- World wide in tropical and subtropical areas
- Severe malaria: multiply rapidly in blood and lead to severe anemia
- Small blood vessel occlusion and cytokine storm: tissue damage and organ failure

Severe PF Malaria

- parasitemia > 5 %
- altered consciousness or seizure
- oliguria
- jaundice
- severe normocytic anemia
- hypoglycemia
- organ failure

Complications

Complication	Incidence (%)
Hemolysis	46.2
Jaundice	21
Cerebral	20
Thrombocytopenia	18.2
Pancytopenia	6
Diarrhea	6
Systemic inflammatory response	6
Acute respiratory distress[a]	4.5
Acute renal failure[a]	3
Death	1

Treatment: P falciparum

- Artemisinin-based (Qinghaosu)discovered by Tu Youyou; 2015 Nobel Prize laureate (prof of 3 noes)
- Artesunate 2.4mg/kg iv twice daily on first day, then 2.4mg/kg iv daily till oral therapy (total 9.6mg/kg in 3 days) + Doxycycline 100mg bid for 1 week
- Quinine-based:
- Quinine gluconate 10mg/kg loading dose in NS, then 0.02mg/kg per min or
- Quinine dihydrochloride 20mg salt/kg loading dose in D5; followed by 10mg/kg every 8 hours

Treatment: P falciparum

- Emergence of quinine resistant PF in SEA and central Asia (efflux pump)
- Open-label study: mortality decreased by 1/3 with Artemisinin based therapy
- Cardiotoxicity and hypoglycemia with quinine therapy
- Recommend Artemisinin based therapy

Supportive Measures

- ICU
- semi-prone position
- monitor RR, BP, GCS every 4 hrs
- monitor T and reduce T with anti-pyretics and tepid sponging
- Transfusion: Hb< 7 g/dL
- Monitor fluid output
- Haemodialysis for patients with oliguria not responding to fluid challenge
- Monitor O2 saturation: ARDS: mechanical vent
- Blood glucose
- Vit K: DIC
- Diazepam for seizure
- Blood film q6 hours

Treatment: PV, PM & PO

- Chloroquine 600mg base PO stat and 300mg base 6 hrs later, 300mg daily for 2 days + Primaquine 15mg base po daily for 14 days in **PV + PO** to eradicate hyponozoites in the liver
- Mefloquine for chloroquine resist PV

Prevention

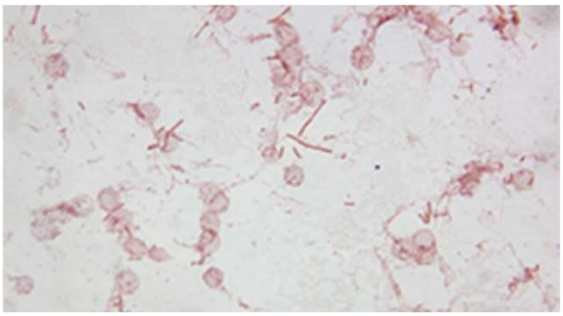
- Mosquito netting, long sleeve clothing
- Insect repellent
- Prophylaxis regime: (active against all species)
- 1st choice: Atovaquone-proguanil (malarone) (1 day before and 1 week after); can be used in pregnancy
- 2nd choice: Doxycycline (1 day before and 4 weeks after); teratogenic

Case 2

- 20F
- Recurrent fever
- Returned from Bangladesh
- Non-bloody diarrhea
- Mosquito bites
- Did not drink exclusively from bottled water

DDx

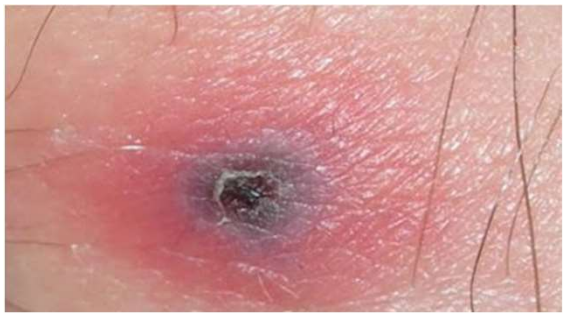
- Chikungunya fever
- Dengue fever
- Typhoid fever caused by *Salmonella typhi*
- Paratyphoid fever caused by *Salmonella paratyphi*
- Leptospirosis
- Malaria



G-ve rods; Salmonella typhi 傷寒沙門氏菌

Case 3

- 35M
- Policeman
- Mui Wo, Lantau Island
- Fever, headache, cough
- Splenomegaly, lymphdenopathy
- Shock and DIC
- ICU care

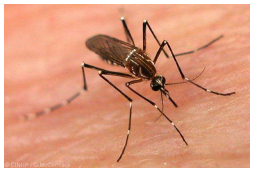


Dx

- Scrub typhus 斑疹傷寒
- Chigger bites
- Weil Felix test +ve
- Specific Ab for O. tsutsugamushi +ve
- Doxycycline 100mg bd for 1 week

Dengue 登革熱

- 50 millions; 12,000 deaths
- tropical and subtropical
- Outbreaks: Singapore, Rio de Janeiro, Pueto Rico, Hawaii
- Aedes aegypti
- Flavivirus
- 4 different serotypes
- Life-long immunity after primary infection of the same serotypes (not the others)

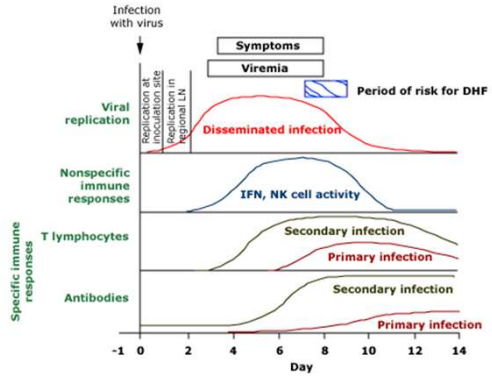


Dengue Fever: primary infection

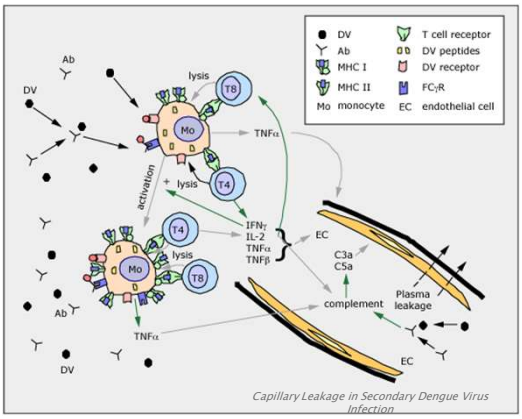
- Incubation period: 4-7 days
- Asymptomatic for children under 15 years
- **Classic** dengue fever: Influenza like illness: fever (5-7 days), headache, retro-orbital pain and myalgia
- 50% lymphdenopathy, diffuse erythema, non-specific maculopapular rash (more common in primary dengue)
- Nausea and vomiting
- Cough/ sore-throat
- Hemorrhage: skin > nose > GIB
- O/E: pharyngeal erythema, lymphadenopathy, hepatomegaly, conjunctival injection
- Leucopenia, thrombocytopenia, raised AST

Dengue Hemorrhagic Fever: secondary infection

- 4 cardinal features
- Increased vascular permeability: hemoconcentration (20% rise in hematocrit), pleural effusion or ascites
- Marked thrombocytopenia
- Fever 2-7 days
- Hemorrhagic tendency: positive tourniquet test or spontaneous bleeding
- + shock – becomes DSS



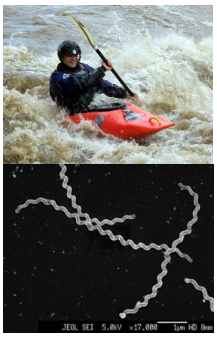
UptoDate 2013



UptoDate 2013

Leptospirosis 鉤端螺旋體病

- Leptospira spp (spirochaete)
- Fresh water exposure (rafting or kayaking)
- Cross country running
- Myalgia, headache and rash
- Deranged liver and renal fx
- Biphasic, aseptic meningitis, uveitis, liver and renal failure, ARDS, myocarditis and rhabdomyolysis
- Clinical + convalescence titre x 4
- Penicillin or tetracycline



The Ten Commandments

- Thou shalt not drink the water
- Thou shalt not eat the food
- Thou shalt not have sex with strangers
- Thou shalt not travel in unsafe vehicles with unsafe drivers
- Thou shalt not swim in lakes
- Thou shalt not forget your malarial prophylaxis
- Thou shalt not forget to use your sun protection cream
- Thou shalt not walk barefoot
- Thou shalt not forget to use your insect repellents
- Thou shalt empty your shoes each morning for snakes

Thank You!