梅毒 (Syphilis)
大綱 (Outline)

• Introduction (簡介)
• Diagnosis (診斷)
• Treatment (治療)
• Prevention (防治)
Introduction

• Syphilis (梅毒)
  – Pathogen: *Treponema pallidum* (梅毒螺旋體)
  – Mode of transmission:
    • Transfusion of blood
    • Intercorse or sexual behavior
    • Trans-placental
    • Percutaneous following contact with infectious lesions
  – Incubation period: 10-90 days
Epidemiology of Syphilis

- **Epidemiology**
  - Worldwide
  - 20-35 year
  - city > country
  - Risk factor:
    - Multiple sexual partners
    - Prostitute
    - MSM (men sex with men)

**Taiwan**
- Gender: male
- Age: 30-49 year, 70 year cured
- Area: Taipei
Clinical Manifestations

• Primary (初期梅毒)
  – 2-4 weeks
  – Highly contagious

Symptom
  – Painless sore
  – Chancre
Clinical Manifestations

• Secondary (二期梅毒)
  – 4-6 weeks
  – Highly contagious

**Symptom**
– Rash
– Fever
– Lymphadenopathy
– Malaise
– Syphilitic alopecia
Clinical Manifestations

• **Tertiary (三期梅毒)**
  - 3-7 years
  - contagious

**Symptom**
- Organ damage
- Gumma
- CNS invasion
- Cardiovascular invasion
Clinical Manifestations

• **Cardiovascular** (心臟性梅毒)
  – Derived from Tertiary syphilis without treatment
  – Male > Female; Black > Caucasian

**Symptom**
– coronary artery stenosis
– chest pain
– heart attack
– heart failure
Clinical Manifestations

• Nervous system (神經性梅毒)
  – Derived from Tertiary syphilis without treatment
  – Male > Female; Caucasian > Black

Symptom
  – Headache
  – Memory loss
  – Epilepsy
  – Dementia paralytica
Clinical Manifestations

• **Congenital syphilis** (先天性梅毒)
  – non-hereditary
  – Syphilis can’t transmit across placenta in 4 month of pregnancy

**Symptom**

– Vesicular lesions instead of chancre (secondary syphilis)
– Hutchinson’s Teeth
– Mulberry molar (第一臼齒桑葚狀)
Clinical Manifestations

• **Latent (隱性梅毒)**
  – Early latent :
    – Asymptomatic $\leq$ 1 year
    – contagious
  
  – Late latent :
    – Asymptomatic $> 1$ year
    – weakly contagious
Diagnosis

The Common Methods

• Serology
  – Mainstay for syphilis testing
  – Two classes of serologic tests
    • Non-treponemal
    • Treponemal

The Uncommon Methods

• Rabbit Infectivity Test (RIT)：Limited to research settings
• Dark Field Microscopy：Useful only during primary infection
• Immunostaining：Direct fluorescent antibody or silver stain
• Polymerase Chain Reaction (PCR)：Not commercial available
Diagnosis

Non-treponemal tests:
- Rapid Plasma Reagin (RPR)
- Venereal Disease Research Laboratory (VDRL)

Principle:
- *T. pallidum* infection leads to the production of reagin
  - **Reagin** – Antibodies to substances released from cells damaged by *T. pallidum*
  - Reagin reacts with cardiolipin
    - **Cardiolipin** – a phospholipid component of certain eukaryotic and prokaryotic membranes
Diagnosis

RPR and VDRL are agglutination assays

Reagin → Reactive

Charcoal → Weak Reactive

Cardiolipin → Weak Reactive (Minimally)

Nonreactive
Diagnosis

Non-treponemal tests:

- **Advantages**
  1. Rapid turnaround time – Minutes
  2. Inexpensive
  3. No specialized instrumentation required
  4. Usually revert to negative following therapy
  5. Can be used to monitor response to therapy

- **Limitations**
  1. Results are subjective
  - Intra- and Inter-laboratory variability
  2. Non-specific:
  - False positive can result from other infectious or non-infectious conditions (EBV, Lupus, Autoimmune disease, etc.)
  3. Limited sensitivity in early/primary syphilis and in late/latent syphilis
Diagnosis

• **Treponemal Assays:**
  – Fluorescent treponemal antibody (FTA-ABS)
  – Treponema pallidum particle agglutination (TP-PA)
  – Enzyme Immunoassay (EIA)
  – Multiplex Flow Immunoassay (MFI)
  – Microhemagglutination assay (MHA)

• **Principle:**
  – Infection leads to production of specific antibodies directed against *T. pallidum*
  – Treponemal tests detect IgG or total IgM/IgG antibodies directed against *T. pallidum*
Bound beads are passed through the laser detector

Labeled anti-IgM and anti-IgG reporter antibody added

Patient Serum Added

Syphilis IgG beads

Laser 1 identifies the bead (IgM vs. IgG)

Laser 2 determines if the target antibody is present (presence or absence of fluor)

Yellow wells = positive
Diagnosis

Treponemal Assays:

• Advantages
  1. High Specificity
  2. Possibly higher sensitivity during early and late syphilis stages compared to non-treponemal tests
  3. Newer Methods
     – Objective result interpretation
     – Automation option
     – High throughput
     – High reproducibility/precision

• Limitations
  1. Remain positive despite treatment
     • Cannot be used to monitor response to therapy
  2. Conventional Methods
     • Subjective interpretation requiring technician expertise to read
  3. Expensive instrumentation and higher cost/test
Syphilis Screening Algorithms: Traditional versus Reverse Screening

Non-treponemal test (e.g., RPR)

Reactive

Treponemal test (e.g., FTA)

Reactive

Syphilis

Non-reactive

Non-reactive

Negative for syphilis

Negative for syphilis
病例定義（Case definition）
（一）梅毒通報範圍
1、活性梅毒通報定義：同時符合通報條件1+2 或僅符合通報條件3 者。
2、非活性梅毒通報定義：僅符合通報條件2 者。
（二）通報條件
1、臨床症狀出現硬下疳或全身性梅毒紅疹等臨床症狀。
2、未曾接受梅毒治療或病史不清楚者，RPR (+) 或VDRL (+)，且TPHA=1:320 以上(包括320)。
3、曾經接受梅毒治療者，VDRL 價數上升四倍。
（三）需1週內通報。
（1）一期、二期或早期隱性梅毒—適用長效盤尼西林，1次注射完成治療；對不能每天接受注射，以及合作程度不好的病人最適宜。方法：診斷後即時接受Benzathine penicillin, 2.4 m.u. IM ST

（2）對盤尼西林過敏之病患—可用下列任一種方法：
- Doxycycline, 100 mg bid p.o. ×14 days
- Tetracycline, 500 mg q6h p.o. ×14 days

（3）晚期梅毒
- Benzathine penicillin, 2.4 m.u. IM qw ×3 weeks

（4）神經性梅毒—下列任一種方法：
- Crystalline penicillin G, 2～4 m.u.IV q4h ×10～14 days
- Crystalline penicillin G, 2～4 m.u.IM + probenecid
- 500mg p.o. q4h ×10～14 days