# 日本腦炎、恙蟲病之診斷與治療

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# 節肢動物傳播的病毒性疾病

| 病毒分類 | 病毒名稱 | 傳染媒介 | 脊椎動物宿主 | 感染後症狀 | 流行區域 |
|---|---|---|---|---|---|
| TOGAVIRIDAE Alphavirus | Chikungunya | 蚊子 | 人類、靈長類 | 發熱、關節痛、出疹 | 非洲、東南亞、菲律賓 |
| FLAVIVIRIDAE Flavivirus | Dengue 1, 2, 3 and 4 | 斑蚊 | 人類、靈長類 | 發熱、出血、出疹 | 遍及熱帶地區 |
| | **Japanese encephalitis** | 家蚊 | 鳥、豬 | 腦炎、發熱 | 亞洲、太平洋島嶼、澳洲北部 |
| | West Nile | 家蚊 | 鳥 | 發熱、腦炎、出疹 | 非洲、北美、印度地區、中東、前蘇聯、歐洲 |
| | Yellow fever | 斑蚊 | 人類、靈長類 | 出血熱 | 非洲、中美洲 |
| BUNYAVIRUS Phlebovirus | Rift Valley fever | 斑蚊、瘧蚊、沼蚊、家蚊 | ? | 發熱、出血、腦炎、視網膜炎 | 非洲、阿拉伯 |

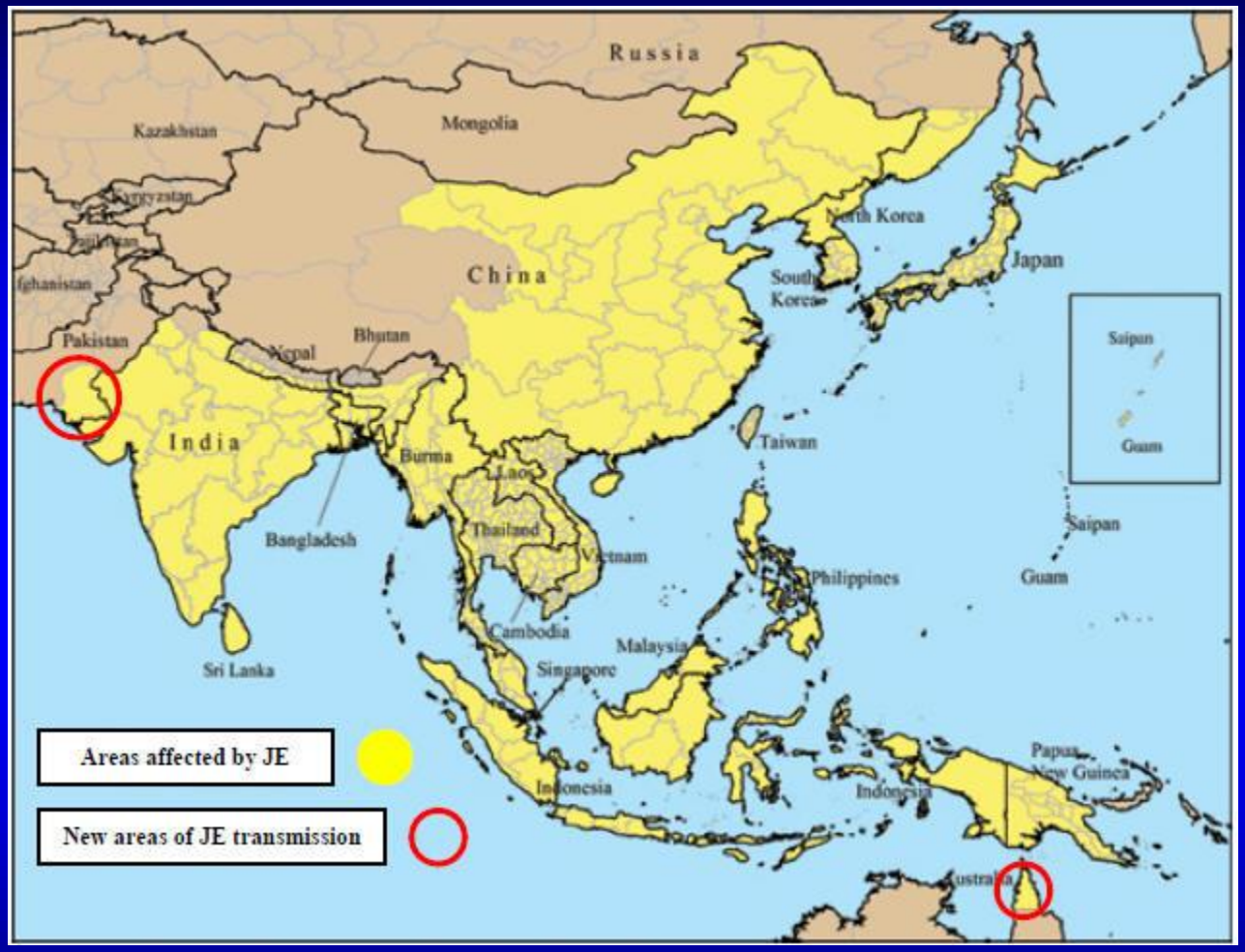



**Figure 1 : Global distribution pattern of Japanese encephalitis. The areas shaded in yellow are Japanese encephalitis risk-prone regions. The areas encircled in red, such as Karachi (Pakistan) and Torres Strait islands (Australia) and parts of the northern Australian mainland are newer areas affected by Japanese encephalitis.**

Kaushik Bharati http://www.antimicrobe.org/mid

# 日本腦炎

- 1924年在日本爆發大流行
- 1938年日本學者得知經由蚊蟲為媒介而傳染
- 1956年發展出不活性的疫苗。
- 臺灣地區每年都有日本腦炎病例發生，流行地區遍部全省。

| Year | Incident |
|---|---|
| 1871 | First recorded clinical case of JE, reported from Japan |
| 1924 | Large outbreak of JE in Japan with >6,000 cases and a fatality rate of 60%; Isolation of JEV from human brain |
| 1933 | First cases of JE reported from the Korean peninsula |
| 1935 | Isolation of Nakayama strain of JEV |
| 1938 | Isolation of JEV from *Culex tritaeniorhynchus* mosquitoes |
| 1940 | First cases of JE reported from the Chinese Mainland |
| 1950 | First cases of JE reported from the Philippines |
| 1950s | Elucidation of transmission cycle of JEV, with pigs and ardeid birds identified as amplifying hosts and *Culex tritaeniorhynchus* as primary vector species |
| 1955 | First cases of JE reported from Vellore, India |
| 1965 | Major epidemic in northern Vietnam |
| 1969 and 1970 | Major epidemic in Chiang Mai Valley, Thailand |
| 1973 | First epidemic in India, in the state of West Bengal |
| 1978 | Major epidemic in Terai region of Nepal |
| 1983 | JE reaches Pakistan, the furthest geographical extension to the West |
| 1985-86 and 1987 | Major epidemics in Sri Lanka |
| 1995 | JE reaches Papua New Guinea and Torres Strait islands (Australia), the furthest geographical extension to the South |
| 2005 | Major epidemic in Gorakhpur, Uttar Pradesh state of India. 5,737 cases, with 1,344 deaths;<br>India imports live-attenuated SA 14-14-2 vaccine from China |

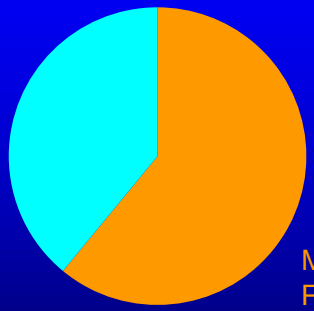
**Table 1 : Japanese Encephalitis : An Historical Timeline**

# 日本脳炎

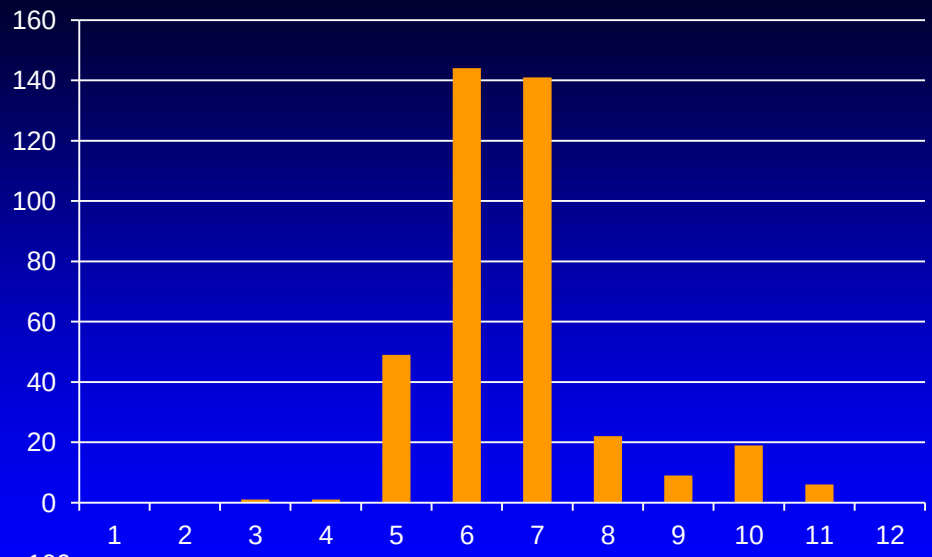
- All world
- Approximately 35,000-50,000 people suffer from JE every year, with a mortality rate of 10,000-15,000 people per year. China still accounts for 50% of the reported JE cases worldwide.
-

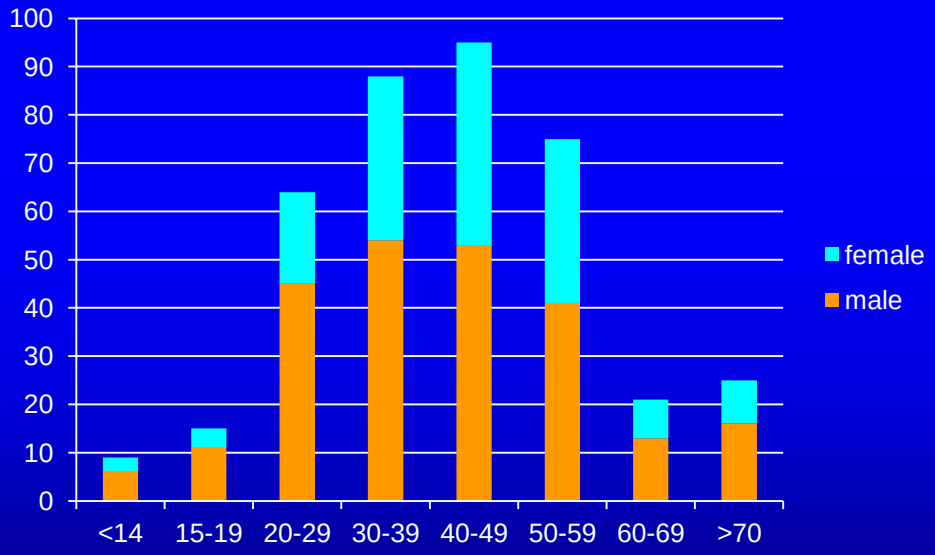
Zheng Y Rev Med Virol. 2012 Mar 8

| | |
|---|---|
| 台北區 合計 | 55 |
| 北區 合計 | 34 |
| 中區 合計 | 91 |
| 南區 合計 | 89 |
| 高屏區 合計 | 80 |
| 東區 合計 | 43 |




Male :239 cases
Female:153 cases




**Japanese encephalitis cases**
**from 1998 to Feb.2013 in Taiwan**

http://www.cdc.gov.tw

# 2012年5月

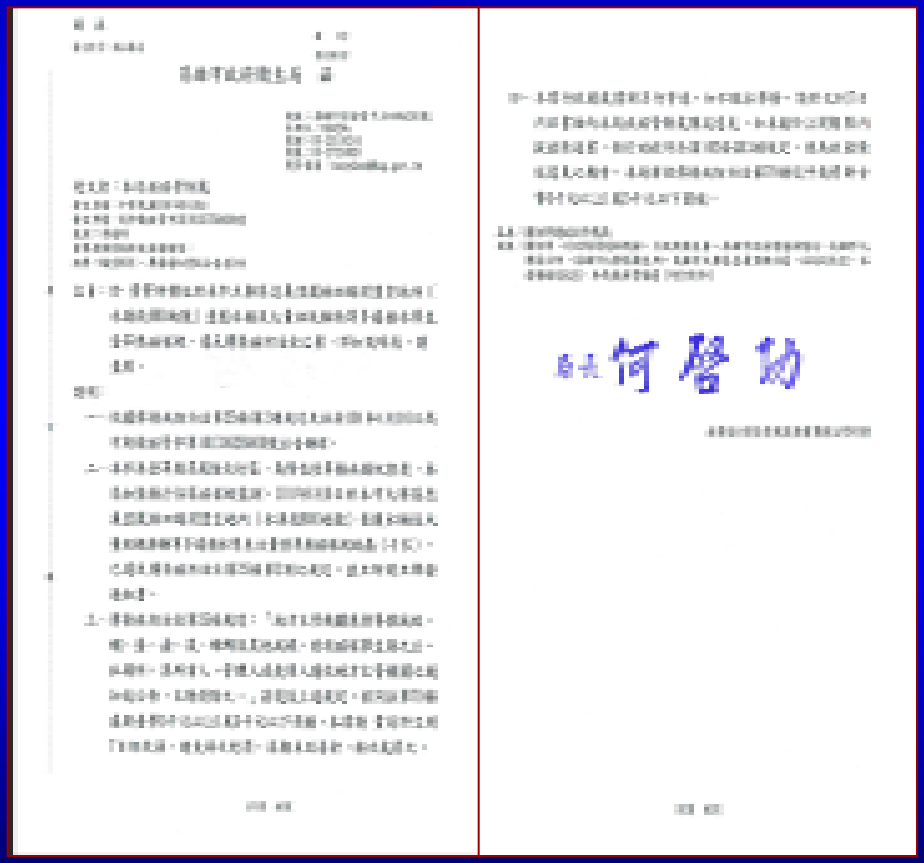
- **高雄市出現首例本土型日本腦炎病例，籲請市民提高警覺**
- 高雄市出現今年(2011)首例本土型日本腦炎確定病例，個案為64歲男性美國人，居住於高雄市大寮區。患者於5月16日開始出現頭痛、發燒、全身無力等症狀，5月19日出現行動及反應遲緩，5月20日因意識混亂由友人護送至市立聯合醫院急診求治，並由醫院通報為日本腦炎疑似個案採檢送驗，6月5日經行政院衛生署疾病管制局綜合研判結果為陽性。該患者於5月26日因出現呼吸急促等危急症狀，已由醫師給予插管呼吸器輔助呼吸，目前意識狀況呈現昏迷，昏迷指數約7分，持續於加護病房加強照護中。

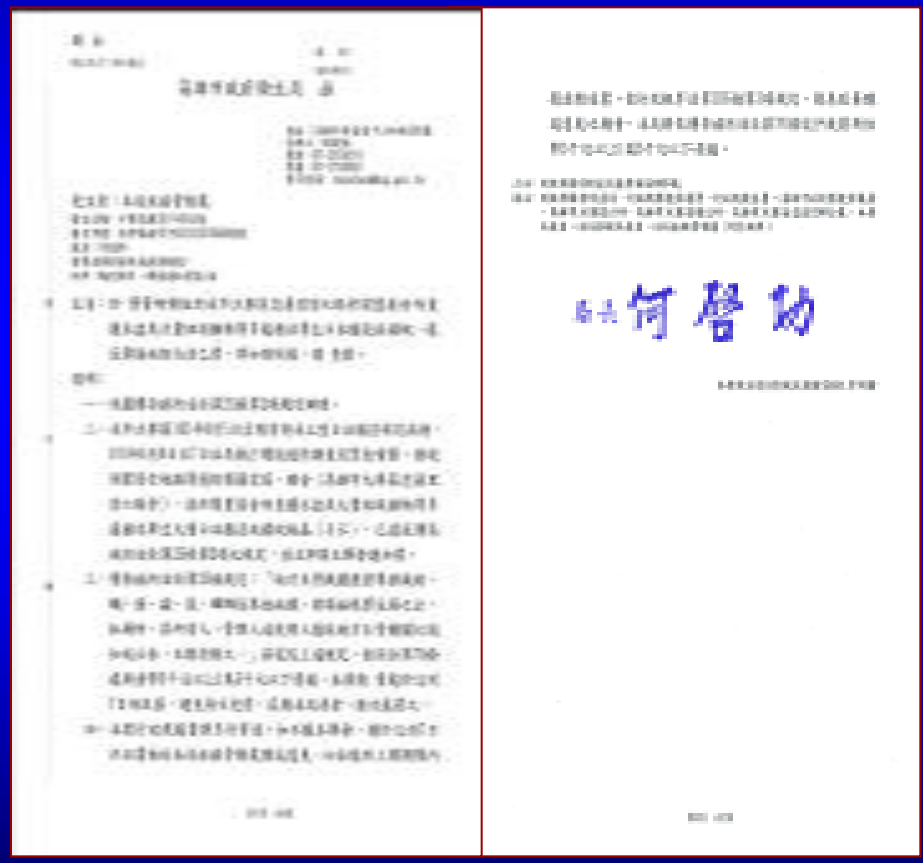
# 疫情調查

- 經環境調查該名個案居住地點周邊有大量雜草叢生的空地，防疫人員在空地內側隱密處查獲民眾飼養豬支，豬圈舍前方即為水池，現場亦捕獲數隻斑蚊與家蚊，整體衛生環境條件不良，是十分有利傳播日本腦炎的病媒蚊-三斑家蚊孳生的環境

# 大寮戰區防治作為

## 本府衛生局已依傳染病防治法對國防部總政治作戰局及國有財產局權管之影劇七新村病媒蚊孳生源開出舉發通知書





# 臨床症狀

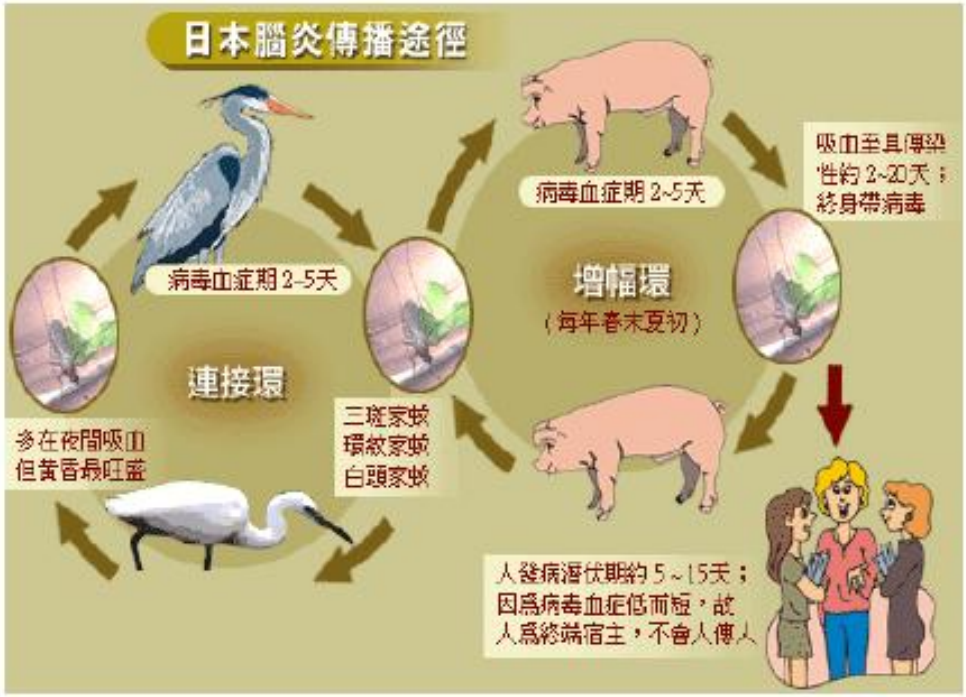
- **患者通常在經過5~15天的潛伏期後出現臨床症狀，其典型的病程演進可分為四個時期：**
  - 前驅期 (2~3天)
    - 前驅症狀發作快，主要出現頭痛、噁心、嘔吐、食慾不振、精神不安、發燒或輕微呼吸道感染症狀。
  - 急性期 (3~4天)
    - 高燒、部份兒童呈現抽筋症狀，頸部僵硬、四肢僵硬、深部及淺部反射異常、震顫、言語困難、神智不清、對人時、地不能辨別、甚至昏迷或死亡。
  - 亞急性期 (7~10天)
    - 中樞神經的侵犯較緩，部分病例仍有生命危險
  - 恢復期 (4~7週)
    - 大部分存活病例的神經功能缺損仍存在，其中包括四肢僵硬、無力、腦神經及錐體外徑路的異常。

# 病媒蚊
## 在台灣傳播日本腦炎之病媒蚊

- 三斑家蚊、環紋家蚊
  孳生於
  - 水稻田
  - 灌溉溝渠
  - 地上小水池
  - 牛足印
  - 水泥槽
  - 池塘
  - 溪流
  - 濕地
  - 人工容器
- 白頭家蚊
  孳生於
  - 濕地
  - 溪流
  - 臨時性積水窪地

# 傳染方式

- 許多動物(主要為豬、鳥)因被帶有日本腦炎病毒的病媒蚊叮吮而受到感染，但本身不發病。
- 未帶病毒的病媒蚊則在叮吮正處於病毒血症的動物時受到感染
- 而病毒在蚊蟲體內大量增殖2-20天後，即可經過唾液傳給健康民眾，而這隻病媒蚊則終生具有傳播病毒的能力。



# 潛伏期與可傳染期

- 潛伏期
  - 5 ~ 15天
- 可傳染期
  - 人不會經由人直接傳染給人
  - 蚊子一旦被感染則終生具感染力
  - 豬及鳥類的病毒血症期通常為2~5天
- 感染性及抵抗力
  - 通常小孩及老人感染後較容易發生臨床症狀，其他年齡層則較多不顯性感染。

# 病例定義

- 臨床病例
  - 出現下列急性神經症狀：發燒、意識障礙、嘔吐、頸部僵硬、抽筋、肌張力異常、頭痛、腦膜刺激症狀及精神症狀（譫妄、意識不清等）。

# 檢體採檢送驗事項

| 項目 | 檢體種類 | 採檢目的 | 採檢時機 | 採檢規定 | 運送條件 | 注意事項 |
|---|---|---|---|---|---|---|
| 日本腦炎 | 血清 | 抗體檢測（ELISA）；病原體檢測（Real-time RT-PCR） | 急性期（立即採檢）；恢復期（發病14-40天之間） | 以無菌試管收集3 mL血清。 | 低溫 | 1.若無法取得急性期之血液，請採間隔7天之恢復期血清，分2次送驗。<br>2.檢體勿加入任何添加物。<br>3.血清檢體見附錄一2.7.3及2.7.4備註說明，血清採檢步驟請參考附錄一第3.3節。<br>4.腦脊髓液採檢步驟請參考附錄一第3.6節，由醫師採檢。 |
| | 腦脊髓液 | | 住院期間 | 以無菌容器收集腦脊髓液2-3 mL。 | 低溫 | |

# 實驗室診斷

- 符合下列檢驗結果之任一項者，定義為檢驗結果陽性：
  - 臨床檢體（組織、腦脊髓液或其他體液）分離並鑑定出日本腦炎病毒。
  - 臨床檢體分子生物學核酸檢測陽性。腦脊髓液中日本腦炎病毒特異性之IgM抗體陽性。
  - 急性期（或初次採檢）血清中，日本腦炎病毒特異性IgM或IgG抗體為陽性者。
  - 在最近未接受預防注射及排除其他黃病毒交叉反應的情形下，成對血清（恢復期及急性期）中，日本腦炎病毒特異性IgM或IgG抗體（二者任一）有陽轉或≧4倍上升。

# 疾病分類

- 極可能病例
  - 符合臨床條件及檢驗結果陽性定義之第三項。
- 確定病例
  - 符合檢驗結果陽性定義之第一、二、四項之任一項。

# 法定傳染病規範

- 疾病分類
  - 屬第三類傳染病
- 通報定義
  - 具有下列任一個條件
    - 符合臨床條件
    - 醫師高度懷疑與確定病例具有流行病學上相關
- 通報期限
  - 於1週內進行通報

# 實驗室檢查

- 白血球上升 嗜中性白血球增加 輕微貧血.
- 腦脊髓液蛋白質約 50%個案會上升
- 腦脊髓液早期會以嗜中性白血球為主
- 腦脊髓液晚期為淋巴球為主

# KMHKH

- Case presentation:
- 23 male
- consciousness change and
- irritable mood
- CSF Glu:60
  TP: 32
  Lactate:1.1
  Appear:clear
  cell count:0
  PMN/MN:0
  VDRL(-)
  Cryptococcus (-)
  HSV IgM(-)
  blood Glu:85
  Lactate:1.8
  IgG:1240

# Chief Complaint and Present Illness

- 43 yrs old, ♂, Car repair workers
- Admission Date：2009/10/11
- Chief Complaint:

  Sudden onset of left lower limb weakness for one day

  Present Illness:

  suffered from fever, muscle soreness since 2 days ago, sudden onset of progressive left proximal lower limb weakness noted 1 day before admission.
- headache, dizziness, general malaise, vomiting, intermittent left thigh numbness and neck pain.
- visited LMD but in vain, then visited our ER (10/11)

# Physical Exam

- **Consciousness** :Alert, E4V5M6
  BP：113/ 68 mmHg, PR：109 bpm. RR：18cpm, BT：37.9℃

**Lower limbs**： left lower limb weakness, free activity

Muscle Power

| | R't | L't |
|---|---|---|
| **upper limbs** proximal | 5 | **4** |
| distal | 5 | **4+** |
| **lower limbs** proximal | 5 | **2** |
| distal | 5 | **3-4** |

| DTR：(0- + + + + +) | R't | L't |
|---|---|---|
| Biceps reflex | + + | + + |
| Triceps | + + | + + |
| Brachiaradia is | + + | + + |
| Knee jerk | + + | - |
| Ankle jerk | + + | + + |

# Differential diagnosis

- **Cranial nerve: intact**
- **MP**
  - R L
  - 5 5
  - 5 2
  - 5 4-
- **DTR**
    - R L
    - 2 2
    - 2 2
- **EPS**
- Rigidity (-)
- Bradykinesia (-)
- Bilateral upper limbs postural Tremor (+)

- **D/D:**
- L2~L3 level (no sensory level)
- Suspect drug related (EPS?)
- L-spine radiculopathy
- Myopathy
- Femoral nerve lesion

- **Plan**
- GOT/GPT
- CK, lactate
- T3,T4, TSH
- influenza

# Admitted on 10/11

- 10/11
- Fever up to 39 (19:30)
- Give stin and  Blood culture
- Intermittent bilateral upper limbs tremor and spasm (20:30), left predominant, tonic –flexor posture, suspect seizure, 30 seconds~1 min
- Suspect novamin induced EPS

# Clinical Course

**10/12**

- Generalized skin rash (00:40) and fever, suspect stin allergy
- Drowsy consciousness, generalized skin rash + fever, suspect stin allergy
- WBC = 12.53 10^3/ul ; Segament Neutro = 88.6 %; CRP = 69.4 mg/l
- Highly suspect meningoencephalitis
- Focal seizure →

  Consult Infection, check HIV, TB, JBE

# Clinical Course

**10/13**

**Course**

- Drowsy consciousness, E3V3M5
- Lumbar puncture for suspected CNS infection (open pressure 218mmHg)
  →Transfer to KMU- NICU

**Lab**

- Cell count = 177X11/9 mm^3 [0~5]
- PMN/MN = 86/14 % [2/98~5/95]
- TP = 0.19 g/dl [6.60~8.52]
- Glu = 59 [120~200], Smear: CSF, negative.
- Pathology: Increased leukocytes and lots of neutrophils suggest meningitis

**Medication**

- Ceftriaxone 2g IV Q12H + Vancomycin 1g IVD Q8H + Acyclovir 750mg IVD Q8H
- Doxycycline 100mg PO QD

# 10/17-10/24 at KMUH

- 10/17 respiratory failure →Intubation →Right lower lobe pneumonia
- EEG, no seizure wave was found.
- lumbar puncture again due to consciousness not improved→

  CNS infection was partial relieved. WBC was lymphocyte dominent→ stop using Vancomycin→ Consciousness was improved
- 10/24: consciousness and pneumonia improved gradually →Extubation

# 10/30

- Pneumonia  relieved gradually.
- Pre-renal acute renal failure was impressed, so we increased fulid amount of hydration. Following renal function improved gradually.
- transferred to general ward on 10/28.
- JBE confirmed by positive IgG and IgM. (98.10.13)

# 治療及預後

- 治療方式
  - 無針對日本腦炎病毒之抗病毒藥物
  - 依病情給予支持療法
  - 嚴重時要加護病房照護
- 併發症
  - 神經性後遺症
    - 不正常肌張力
    - 語言障礙
    - 運動肌無力等
  - 精神性後遺症
    - 脾氣暴躁
    - 性格不正常
    - 智力不足
      - 常發生在年輕的小孩

# 日本腦炎防治策略

- 早期診斷 早期治療
- 病媒蚊防治
  - A)降低幼蟲
  - B)病媒蚊控制
- 預防 施打疫苗
- 國內自民國57年起，新生兒全面施打日本腦炎疫苗，之前出生的人多半都沒有接種過疫苗。

# 疫苗接種條件及限制

- 接種對象
  - 年滿15個月的幼兒，應接受2劑注射，其間相隔2週，隔年再接種一劑，小學一年級時再追加接種一劑。
  - 工作或生活中有感染之虞且有意願接種的成人可前往全國26家署立醫院或分院自費接種。
- 接種時程
  - 每年3至5月
- 禁忌
  - 發高燒
  - 患有嚴重疾病者

# 疫苗接種條件及限制

- 保護力
  - 疫苗的有效性約85%
- 副作用
  - 局部
    - 紅腫、腫脹、疼痛
  - 全身
    - 發燒、惡寒、頭痛、倦怠感
  - 通常2~3天內消失

# 避免病媒蚊叮咬

- 盡量避免於病媒蚊活動的高峰期(黃昏)，在豬舍、其他動物畜舍或病媒蚊孳生地點附近活動。
- 請穿著長袖長褲、身體裸露處塗抹防蚊藥劑，避免蚊蟲叮咬，以降低感染風險。
- 居家環境管理：疏通水溝、清除雜草、處理積水及家中需設置紗門、紗窗，以消滅病媒蚊及其幼蟲。

# 立克次體屬疾病之流病特色

| 抗原分類 | 疾病名稱 | 致病原 | 傳染媒介 | 動物宿主 | 感染症狀 | 流行區域 |
|---|---|---|---|---|---|---|
| Typhus fevers | Epidemic typhus 〈流行性斑疹傷寒〉 | *Rickettsia prowazekii* | 體蝨 | 人類、 老鼠 | 頭痛、發燒、畏寒、出疹 | 非洲、亞洲、中南美洲的高山寒冷地區 |
| | Endemic typhus 〈地方性斑疹傷寒〉 | *R. typhi* | 跳蚤 | 老鼠、貓 | 頭痛、發燒、畏寒、出疹，症狀較溫和 | 全世界 |
| Spotted fevers | Rocky Mountain spotted fever 〈落磯山斑疹熱〉 | *R. rickettsii* | 蜱〈Tick〉 | 嚙齒類 | 頭痛、發燒、腹痛、出疹 | 墨西哥、美國中南美洲 |
| | Mediter- ranean spotted fever 〈地中海斑點熱〉 | *R. conorii* | 蜱〈Tick〉 | 嚙齒類 | 發燒、焦痂、 局部腺病、末端出疹 | 非洲、印度、歐洲、中東、地中海、美國 |
| | Oriental spotted fever | *R. japonica* | 蜱〈Tick〉 | 嚙齒類 | 發燒、焦痂、 局部腺病、 有時會出疹 | 日本 |
| Orientia | Scrub typhus 〈恙蟲病〉 | Orientia tsutsuga-mushi | 蟎〈Mite〉 | 嚙齒類 | 發燒、頭痛、盜汗、 焦痂、出疹、 | 印度南部、中亞、東亞、 東南亞、澳洲、 |
| Coxiella | Q fever 〈Q 熱〉 | *Coxiella burnetii* | 吸入被病原體污染微粒 蜱〈Tick〉 | 山羊、綿羊、牛、家畜 | 發燒、頭痛、畏寒、盜汗、肺炎、肝炎、心內膜炎 | 全世界 |

# Rickettsial Infection

1. Gram (-) , obligate intracellular bacteria
2. Vectorborne ( tick , mite , fleas…)
3. Spotted fever and typhus groups

   ─ vasculitis

   ─ rickettsiae proliferate in the endothelial lining cells of small arteries , capillaries , and veins

# Topic1.Scrub typhus-history

- AD 313, 晉朝”葛洪” “人行經草處,沙地被依微小沙虱叮咬,即發生紅疹,三日後發熱,叮咬局部潰瘍節痂”
- 1810: Hakuju  Hashimoto, Japanese, first described this disease
- 1927:緒方規雄(Ogata norio), patient serum injected into the rabbit's testis-repeat this procedure 5 times-gall bladder swelling -isolated Rickettsia orientia
- 1931 Formal name: Rickettsia tsutsugamushi
- 範圍:西至巴基斯坦、阿富汗;

  東至日本本州北端;南到整個東南亞至;

  澳洲東北部及西南太平洋群島

# Scrub typhus-pathogen

- 1.恙蟲病 (Tsutsugamushi disease，
  tsutsu是惡疾之意，而mushi是指恙蟲)
  又名叢林型斑疹傷寒〈Scrub typhus〉
- pathogen: *Orientia tsutsugamushi*
  ( *Rickettsia tsutsugamushi)*
  vector: *Leptotrombidium deliense*
- 2.Transmitted by a bite of chigger
  (a larval stage mite), through the chigger's saliva,
- Endemic in Asia, Australia, New Guinea, Pacific Islands

# Host

- *Orientia tsutsugamushi* in mites *will be* vertical transmission in every stages including ovary、larva、deutonymph、adult→ permanent infection
- Animal host: rodents、mammals (sheep、pig、dog、cat)、avian (bird、chicken). Rodents are the major host.

Jerome Goddard Infect Med 17(4):236-239, 2000.

# Transmission method

- **Incubation period**

  - 1~2 weeks，usually 9~12 days , not human to human

- **Immunity protection**

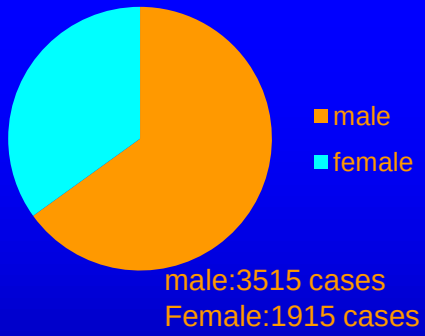
  - One man got secondary infection of scrub typhus, he may have long term immunity for protection if the strain of scrub typhus is same as previous, but only short term immunity for protection if the strain of scrub typhus is different from previous.

  - Second or third infection of scrub typhus in endemic area may occur, but the symptoms and signs will be mild.

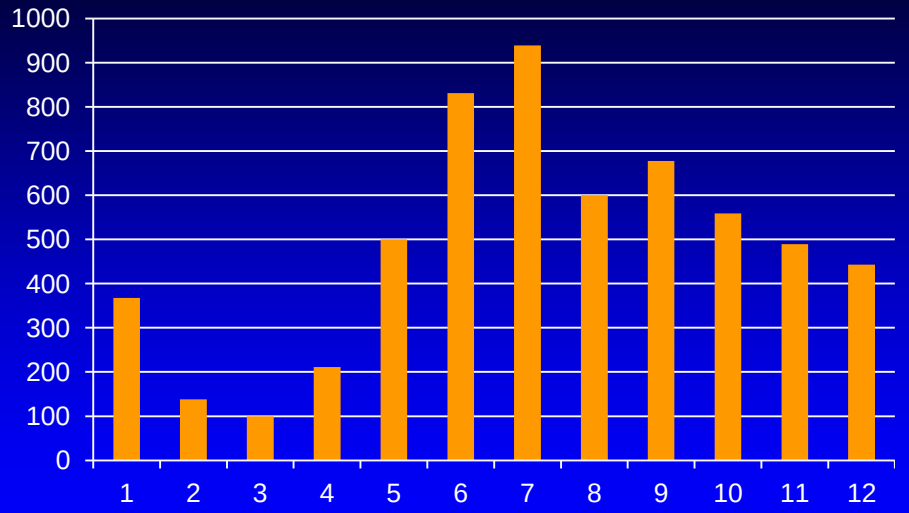
http://www.cdc.gov.tw

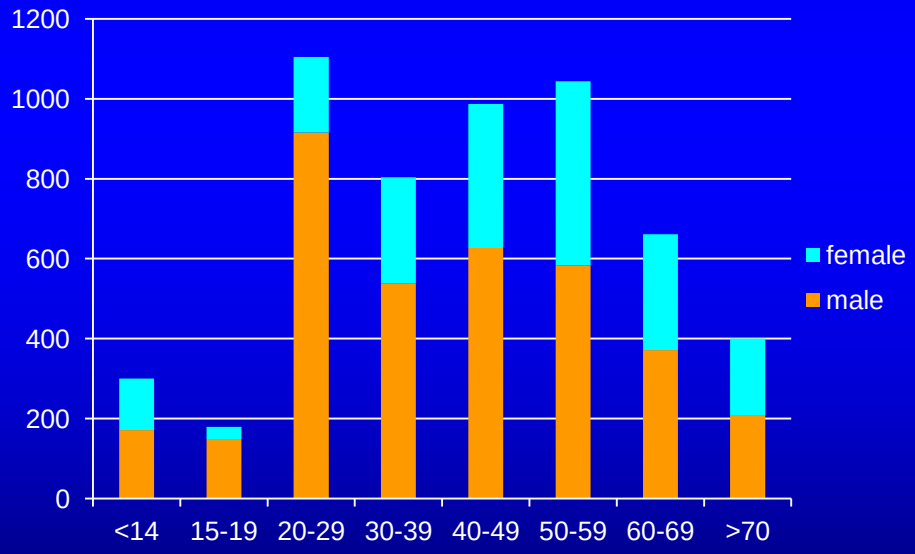
Scrub typhus 1996~2013.2

| | |
|---|---|
| 台北區 合計 | 1636 No.1 |
| 北區合計 | 230 |
| 中區合計 | 640 |
| 南區合計 | 216 |
| 高屏區合計 | 1277 No.3 |
| 東區合計 | 1481 No.2 |
| 合計 | 5480 |




male:3515 cases
Female:1915 cases




**Scrub typhus cases from 1996 to Feb.2013 in Taiwan**

http://www.cdc.gov.tw

# Epidemioloy

- **Seasons: all year in Taiwan, the peak period May~December**
- **Location: scrub typhus favor high temperature and high humidity, outsides grass**
- **occur in Taiwan, high prevalence in Kingman, Matsu, Penghu, Lanyu, Hualien, Taitung, Kaohsiung**
- genotype: Karp, Gilliam, Kato, Kawasaki, Boryong, Taguchi, Kanda/Kawasaki,

# Clinical Manifestation (1)

- Fever, chills ,headache, muscle pain, lymphadenopathy,
- Rash:
  - 5 days after insect bite, 9-10 days later subsided,
  - from trunk to extremities
  - macule→papule

  Eschar (about 50-80% in scrub typhus patients, painless)
- Splenomegaly may be seen
- Complication:
  - Pneumonia, ARDS, myocarditis, renal failure, septic shock
  - After two weeks incubation, central nervous system occur meningoencephalitis, acute transverse myelitis

http://www.cdc.gov.tw

# SCRUB TYPHUS IN JAPAN: EPIDEMIOLOGY AND CLINICAL FEATURES OF CASES REPORTED IN 1998

- A total of 462 cases
- Seventy-six percent of the patients were more than 51 years old, and 36% and 16% of the patients were engaged in farm work and forestry, respectively.
- Fever, rash, and eschar were detected in 98%, 93%, and 97% of
- the patients, respectively.
- Elevated levels of C-reactive protein, aspartate transaminase, and alanine transaminase were detected in 96%, 87%, and 77% of the patients, respectively.
- Disseminated intravascular coagulation developed in 34
- cases and had a unique regional distribution.

*Am. J. Trop. Med. Hyg.*, 67(2), 2002, pp. 162–165

# Acute respiratory distress syndrome in scrub typhus.

- 72 patients with scrub typhus from 1998.1 to 2006.8 in KCGMH in Taiwan.
- Eight of 72 scrub typhus patients with ARDS included in the study; the other patients without ARDS were used as controls. The mortality rate for the scrub typhus patients with ARDS was 25%.
- Initial presentations of dyspnea and cough, white blood cell count, hematocrit, total bilirubin, and delayed used of appropriate antibiotics use were significant predictors of ARDS.
- Multivariate analysis showed that albumin, prothrombin time, and delayed use of appropriate antibiotics were independent predictors of ARDS.

Am J Trop Med Hyg. 2007 Jun;76(6):1148-52.

# Scrub typhus complication

- Be aware of the potential for complications, scrub typhus are older (≥ 60 years), presents without eschar, or WBC counts > 10, 000/mm3, and serum albumin level ≤ 3.0 g/dL. Close observation and intensive care for scrub typhus patients with the potential for complications → reduction in its mortality rate. Kim *et al. BMC Infectious Diseases* 2010,1**0**:108

- Bilateral simultaneous facial palsy following scrub typhus meningitis: a case report and literature review.

  Lin,WL Kaohsiung J Med Sci. 2011Dec;27(12):573-6.

# Diagnosis

- 1. PCR amplification of *O. tsutsugamushi* DNA from blood of febrile patients or eschar lesion

  2. IFA (indirect fluorescent antibody): acute stage IgM Ab ≧1：80 and IgG Ab ≧1：320

  3. IFA (acute stage & recovery stage）IgM or IgG Ab seroconversion or ≧4x elevation

- Weil-Felix slide agglutination test: lower sensitivity and specificity

  half patients have antibody reaction to

  Proteus spp. OX-K,

  Weil-Felix slide agglutination test is not specific.

  sensitive or specificity is not high.

  Proteus spp.have similar antigen with rickettsial antigen. When human got rickettsial infection, human body will induce anti-rickettsial antibody which will be cross reaction with Proteus spp.

  Proteus OX-K (+) ---may be associated with scrub typhus infection

  Proteus OX19 (+) -- may be associated with murine typhus infection

  Proteus OX-K(-), OX19(-), OX2(-)—Q fever

# Treatment and prophylaxis

- 1. inadequate treatment (insufficient treatment course) induce high relapse tendency, all patient need two weeks treatment course doxycycline: 100 mg bid p.o for 7-14 days,
  tetracycline, minocycline
- 2.ciprofloxacin, levofloxacin, chloramphenicol, rifampicin
  3. oral azithromycin was administered in a 500mg dose on the first day, followed by 250 mg daily on days 2 to 5.
  ( in children and pregnant women)

Prophylaxis: doxycycline 200 mg/ every week, keep 3-4 weeks, wearing long-sleeve clothes and trousers, bootleg, use insect repellent,

Prognosis: treatment-mortality less than 5%

第四類法定傳染病, 一週內通報

# Scrub typhus prevention

**Personal prevention**

- wearing long-sleeve clothes and trousers bootleg while in adventure travel
- use insect repellent, Diethyltoluamide (DEET), for prevention mite bite
- After leaving an endemic area, take a bath and wear the clean dress

**Environment improve**

grass cutting nearby a residence house for decreasing the possibility of mite contact

**Deratization- decresae the numbers of mites**

http://www.cdc.gov.tw

# Patient profile & Chief complaint

- Age:58 y/o , female
- Occupation: housewife
- Residence: 高雄縣大寮鄉
- Admission date: 94.11.14 via ER
- C.C: sudden onset fever up to 39.2 degrees on and off for 2-3 days.

# Present illness

- This 58 female, a case with hypertension with diet and activity control, without other major systemic diseases.
- About 7 days ago, she came back from 澎湖娘家 and then felt general malaise, headache since last W2(11/8).

# Present illness

- Due persistent symptoms, she went LMD for help and medications was prescibed on last W6(11/12) for tonsillitis.
- However, after LMD visit, fever on and off was noted for 2-3 days and chillness, dizziness, sore throat persisted.

# Present illness

- she came to our ER for help.
- Other associated symptoms/signs:

- Fever(+), chillness(+), general malaise(+), headache(+), myalgia(-), arthralgia(-), retro-orbital pain(-), night sweating(-), rash(-).
- Neck stiffness(-), conscious change(-), facial muscle weakness(-), photophobia(-), seizure(-), limb weakness(-).
- Sorethroat(+), cough(-), rhinorrhea(-),dyspnea(-)
- Abdominal pain(-), diarrhea(-), nausea/vomiting(-)
- Painful urination(+), low back soreness(+), frequency(-), urgency(-)

# Physical examination

- Consciousness: alert, oriented.
- Vital signs: BT: 37.8 BP: 130/80 PR: 84
  RR: 20
- HEENT:

  Sclera: mildly pink but not icteric

  Oral cavity: swelling of injected bil. Tonsils, discharge(-)

# Physical examination

- Neck:

-Lymphadenopathy (+) over left side of neck, 2 lymph nodes, size 1x1 cm, tenderness(-), movable.

-Jugular vein engorgement(-)

-Kernig's sign(-), Brudzinski's sign(-)

Chest:

-Heart sound: regular heart beat, no murmur, no S3,S4, normal S1,S2

-Breath sound: bil. clear. No crackles. No wheezing.

# Physical examination

- Abdomen:

-Soft, flat, tenderness(-), Murphy's sign(-)

-Liver/spleen: impalpable

-RUQ knocking pain(+)

-R't flank knocking(+)

-Normoactive bowel sound

# Physical examination

- Extremities:

  -Lower legs pitting edema(-)

- Skin:

  -Erythematous maculopapules(+) over lower abdomen, itching(-), pain(-).

  -Black-central scared wound (+) with erythematous base, over r't inguinal area, itching(-), pain(-), discharge(-). →Eschar

# Clinical impresison

- Fever:

→Acute tonsillitis
(sore throat, swelling tonsils)
→susp. APN, r't
( kocking pain)
→susp. Viral infections
Reckettsia infection (scrub typhus)
Dengue fever
( hx., eschar, regional lymphadenopathy, rash)
→susp. Liver disease
( RUQ knocking pain)

# Plans

- General survey: CBC/DC, CRP, electrolytes, liver function, renal function,, coagulation profile, GOT/GPT, bilirubin, AC sugar.
- HBsAg, anti-HCV.
- Urine routine.
- Abdominal echo
- Chest X-ray, 12-lead EKG
- Well-Felix test, LDH
- IFA, PCR?
- Antibiotics: Cefazolin 1g IV q8h.
  Doxycyclin 100mg bid

# Laboratory surveys

| CBC | 11/14 ER | 11/16 | 11/18 |
|---|---|---|---|
| WBC x1000/ul | **4.03** | **4.67** | 6.99 |
| RBC x10^6/ul | 4.09 | 3.88 | 3.92 |
| HGB g/dl | 11.7 | 11.2 | 10.6 |
| HCT % | 34.5 | 32.6 | 32.9 |
| MCV fl | 84.8 | 84 | 83.9 |
| PLT x1000/ul | 94 | 105 | 182 |
| SEGEMENT /BAND% | | | 28/2 |
| LYMPH % | 17.94 | | 44 |
| EOSIN % | 0.24 | | 1 |
| MONO % | | | 5 |
| BASO % | 0.74 | | |
| RDW-CV % | | | |
| RDW-SD fl | | | |
| CRP ug/ml | 64 | | |

# Laboratory surveys

| Urine | 11/14 ER | Urine | 11/14 |
|---|---|---|---|
| GLU | - | RBC /HPF | 2-5 |
| BIL | - | **WBC /HPF** | **0-2** |
| KET | - | Epith /HPF | 0-2 |
| SG | =<1.005 | Crystal | - |
| OB | + | Cast | - |
| PH | 7.0 | | |
| PRO | - | | |
| URO | 0.1 | | |
| NIT | - | | |
| **WBC** | **-** | | |
| Color | Yellow/Clear | | |

normal

# Laboratory surveys

| **Blood chemistry** | 11/14 ER | 11/15 | 11/16 |
|---|---|---|---|
| T-BIL mg/dl | | 0.47 | |
| D-BIL mg/dl | | 0.13 | |
| GOT IU/L | 56 | | |
| GPT IU/L | 46 | | |
| PRO mg/dl | | 6.02 | |
| ALB mg/dl | | 3.28 | |
| GGT U/L | | 23 | |
| ALK-P IU/L | | 145 | |
| LDH | | | 1207 |
| Cholestreol | | 147 | |
| TG | | 185 | |
| PT p second | | 11.9 | |
| PT c second | | 10.8 | |
| PT(INR) | | 1.07 | |
| PTT P | | 35.7 | |
| PTT C | | 28.2 | |

# Laboratory surveys

| | 11/14 ER | 11/18 |
|---|---|---|
| BUN mg/dl | 5.8 | |
| CREA mg/dl | 0.76 | |
| NA m mol/L | 129 | 133 |
| K m mol/L | 4.1 | 3.8 |
| Sugar(AC) mg/dl | 108 | |

# Abdominal echo

Finding: Liver cyst at S2, single, <5 cm.

Splenomegaly(-), hepatic parenchyma change(-),

normal kidney size, parenchyma, hydronephrosis(-).

# Tentative Diagnosis

- Atypical infection, suspect  scrub typhus

  (thrombocytopenia, normal or low WBC, impaired liver function, eschar, relative bradycardia, rash, lymphadenopathy, travel history)

  Differentials: Dengue fever, typhoid fever, leptospirosis, other viral infections
- Acute tonsillitis

→Cefazolin and Doxycyclin use

→Watch out CNS, pulmonary, renal complications

→Dx. Confirmation

# Progression

- Fever(+) but decreased gradually under treatment with Cefazolin and Doxycyclin
- No complications occurred during admission.
- Fever subsides on 11/19 (day 6) and due to stable condition, MBD arranged with OPD F/U and oral antibiotics prescribed.
- Her husband?

# D/D Dengue fever and Rickettsial diseases

**Fever with headache without obvious focus**

**Relative bradycardia**

**No**

Endemic area:south-east asia
headache、muscle pain、joint pain、retrobulbar pain、back pain、rash
Laboratory：

❶WBC＜5000/ul or normal
❷PLT＜100,000/ul
❸GOT、GPT elevation and GOT ＞ GPT
❹aPTT prologation、PT normal

initial 3 days Segment elevation
the 4th ~6th day after infected
monocytosis

One or two items compatible but not very likely

May inform CDC

Endemic + 2 kind clinical symptoms + laboratory

Inform CDC

**Yes**

Eschar

**Yes**

mountains Climbing, Taitung or Hualien travel history

suspect scrub typhus

**No**

❶ WBC＜5000/ul or normal
❷PLT lower
❸GOT、GPT elevated and GOT < GPT
❹aPTT prolongation、PT normal
Animal contact
Anticardiolipin Ab elevation

suspect Q fever

❶ WBC＜5000/ul or normal
❷PLT lower
❸GOT、GPT elevated and/or GOT > GPT
❹aPTT prolongation、PT abnormal
OX 19 (+)

suspect Murine typhus


Thank you!