



瘧疾的預防性投藥

衛福部 疾病管制署
中區傳染病防治醫療網
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教學大綱

- 一. 瘧疾的流行病學
- 二. 疫區旅遊忽視預防性投藥之案例分享
- 三. 瘧疾的致病機轉
- 四. 瘧疾的治療
- 五. 瘧疾的預防性投藥

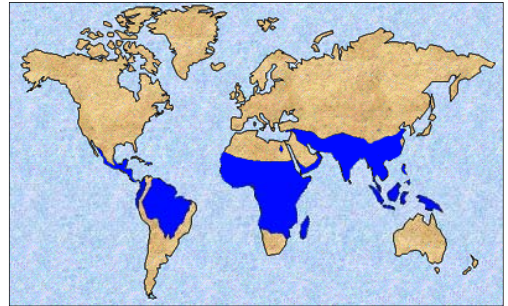


一、瘧疾的流行病學



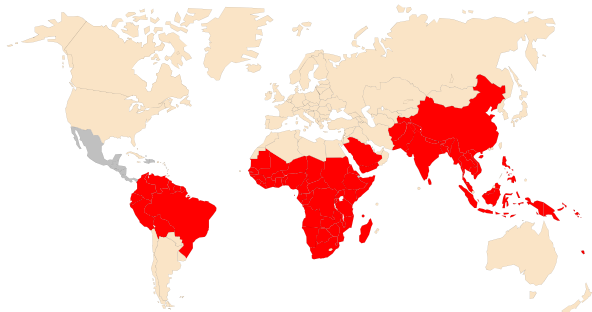
Where does malaria occur?

Areas at risk:



P. falciparum resistance to chloroquine

Source: WHO global database on drug resistance 1996-2004

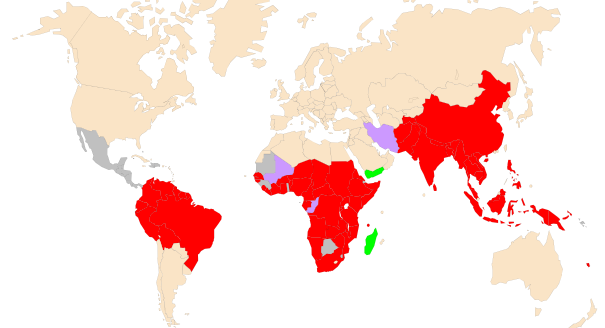


■ Countries with at least one study indicating chloroquine total failure rate > 10%
■ Chloroquine total failure rate < 10%
■ No failure reported
■ No recent data available



P. falciparum resistance to sulfadoxine/pyrimethamine

Source: WHO global database on drug resistance 1996-2004



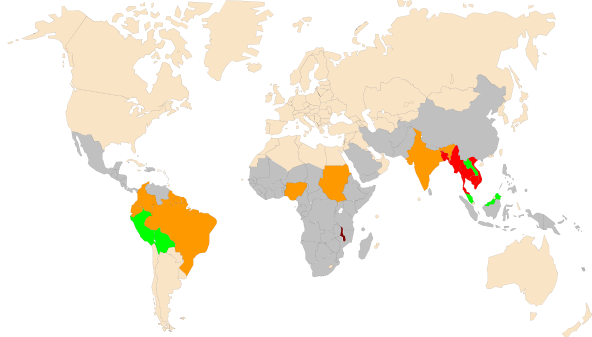
■ Countries with at least one study indicating pyrimethamine-sulfadoxine total failure rate > 10%
■ P. pyrimethamine-sulfadoxine total failure rate < 10%
■ No failure reported
■ No recent data available



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P. falciparum resistance to mefloquine

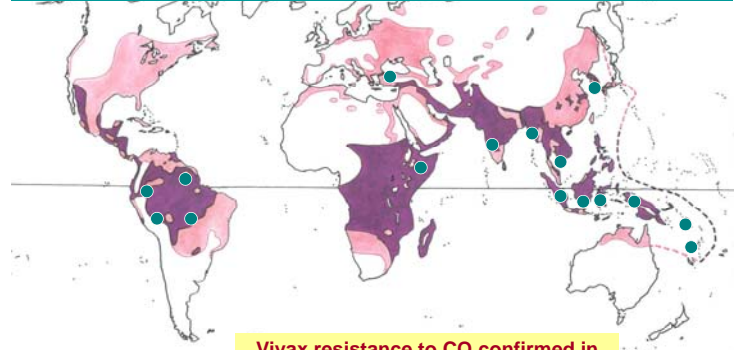
Source: WHO global database on drug resistance 1996-2004



- Countries with at least one study indicating mefloquine total failure rate \geq 20%
- Countries with at least one study indicating mefloquine total failure rate \geq 10%
- Mefloquine total failure rate < 10%
- No failure reported
- No recent data available

Taiwan CDC
<http://www.cdc.gov.tw>

P. vivax malaria distribution and Reported Treatment or Prophylaxis Failures or True Resistance, 2004



Vivax resistance to CQ confirmed in Guyana, Indonesia and Peru

Source: WHO RBM Department, 2004



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二、疫區旅遊忽視預防性投藥之案例分享

Taiwan CDC
<http://www.cdc.gov.tw>



衛生福利部疾病管制署

Malaria in Canadian Travellers

- In the 1990s ...
 - 9 Canadian travellers died from malaria (+/- unreported / undiagnosed cases)
- We continue to see (on average)...
 - 538 cases of malaria each year
 - one death from malaria each year
- In 2006 in Saskatchewan...
 - 2 patients admitted to ICU for severe / complicated malaria

Taiwan CDC
<http://www.cdc.gov.tw>



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Fact or Myth?

- Death can occur in as little as 24-48 hours from onset of the first symptoms.

Fact!

- Progression from mild to severe disease can be very rapid and unpredictable.

Taiwan CDC
<http://www.cdc.gov.tw>



衛生福利部疾病管制署

19 year old woman

- Travel to Ghana
- Doxycycline for malaria prophylaxis
 - Discontinued because of vivid dreams
- First symptoms: April 18 (after return home)
 - 1st visit: April 18... 'viral', no testing
 - 2nd visit: April 19...insisted on testing
 - Smear examined April 20 am... 'rare parasites'
 - Repeat blood smears drawn April 20 am...20% parasitemia!
 - IV quinine not available (at designated regional site)....could not be located
 - Transferred....first dose of quinine at 2400 hours

Taiwan CDC
<http://www.cdc.gov.tw>



Delay....

- **62 hour treatment delay**
 - Failure to consider dx - 24 hours
 - Failure to obtain test results - 24 hours
 - Failure to access drug - 14 hours



37 year old woman

- Travel to Tanzania for 10 day safari
- Chose not to use anti-malarials
 - Concerned about side effects
- First symptoms: July 4 (Tuesday)
 - 1st visit: July 4 pm....'viral', no testing
 - 2nd visit: July 6.... smears sent to referral lab by bus
 - 3rd visit: July 7.... Worse, dyspneic, no results available from blood smear
 - July 7, 2000 hours...Severely ill, transfer arranged, first dose of IV quinine at 0200



Delay...

- **88 hour delay in treatment!**
 - Failure to consider dx – 48 hours
 - Failure to obtain test results – 40 hours



Malaria

- Possible malaria should be considered a **medical emergency** even if symptoms are mild.
- Prompt diagnosis is medically (and medico-legally) essential.
- Blood smear results should be available in 4-6 hours – if not, transfer of the patient to a site that can provide results promptly is necessary.



Fact or Myth?

- People who grew up with malaria do not require chemoprophylaxis because they are immune.

Myth!



Immunity to Malaria

- Develops **slowly** and only after multiple episodes of clinical disease.
- Is **incomplete** and never fully protective against disease, severe disease or death.
- Is **transient** – and lost within 3-6 months of leaving an area of continuous exposure.



VFRs: high risk group

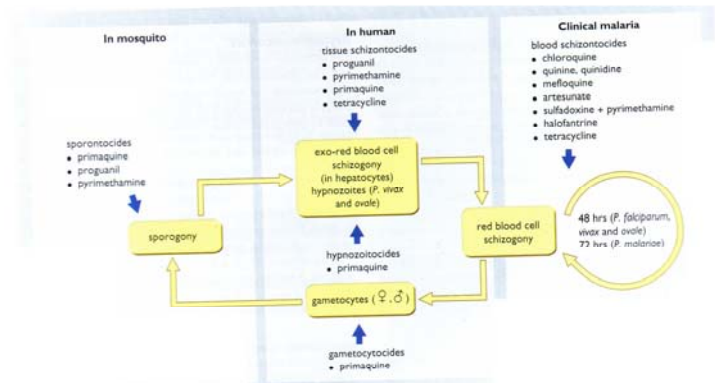
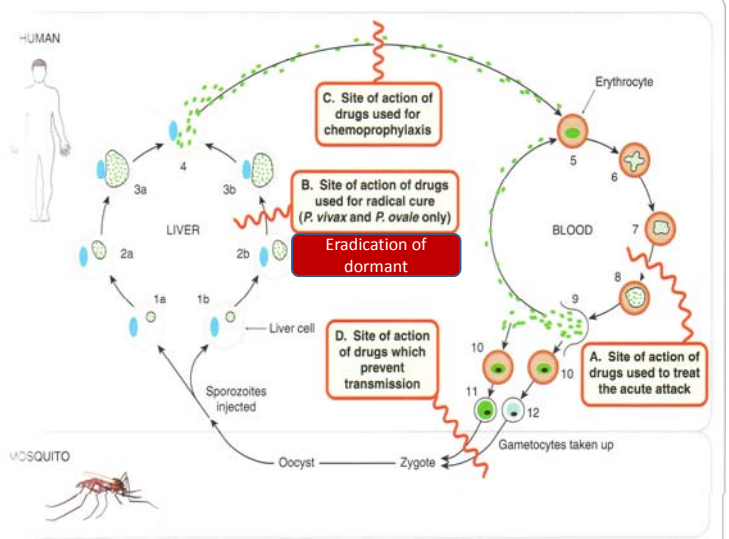
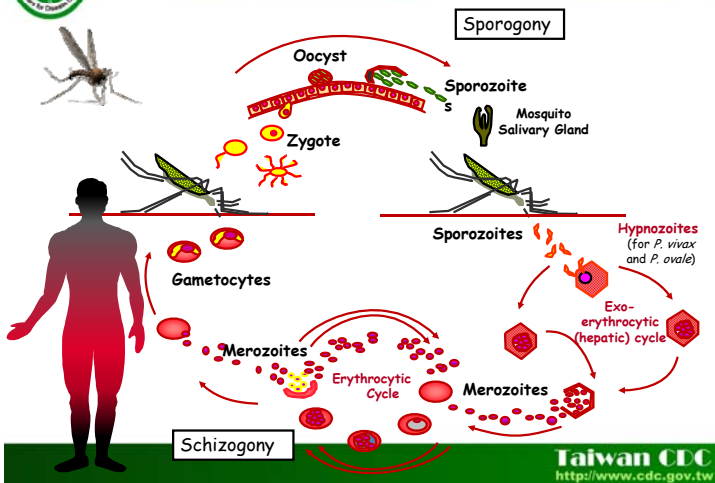
- VFRs = “visiting friends and relatives”
 - Travel home to endemic areas
 - Often don't seek pre-travel advice
 - Do not perceive themselves at risk
 - Consider malaria a minor disease
 - Consider themselves immune
- Periodic health exam can provide a good opportunity to ask about possible future travel.



三、瘧疾的致病機轉



Malaria Life Cycle



四、瘧疾的治療



Different clinical needs have to be considered

- P. Falciparum vs. P. Vivax
- 1st line drugs
- 2nd line drugs
- Severe malaria
- Pregnancy
 - Treatment
 - Prevention

➔ ACT's were first introduced in S.E Asia and rapidly expanded to many other countries



Malaria Resistance

- About 90% of malaria deaths occur in sub Saharan Africa.
- The key factor contributing to ↑ malarial morbidity & mortality is ↑ resistance of *P.falciparum* to chloroquine, sulfadoxin-pyrimethamin [SP] & amodiaquine.
- Artemisinin compounds produce a very rapid therapeutic response ,active against multi-drug resistant *P.falciparum*, well tolerated by the patient, ↓ gametocyte carriage, no resistance is detected.
- Artemisinins cure falciparum malaria in 7d, if combined with another drug in 3d.



抗瘧藥物合併治療的理論基礎

- Advantages of combining two or more antimalarial drugs:
 - First **cure rates are usually increased.**
 - Second, in the rare event that a mutant parasite which is resistant to one of the drugs arises de-novo during the course of the infection, it will be killed by the other drug. This mutual protection **prevents the emergence of resistance.**
- Both partner drugs in a combination must be **independently effective.**
- Risks: Increased costs and increased side effects



artemisinin combination therapy (ACT)

Combinations which have been evaluated:

artemisinin +	mefloquine piperazine	artesunate +	chloroquine amodiaquine sulfadoxine-pyrimethaminine mefloquine proguanil-dapsone chlorproguanil-dapsone atovaquone-proguanil clindamycin tetracycline doxycycline
artemether +	mefloquine lumefantrine		
dihydroartemisinin +	mefloquine naphthoquine		

There are now more trials involving artemisinin and its derivatives than other antimalarial drugs, so although there are still gaps in our knowledge, there is a reasonable evidence base on safety and efficacy from which to base recommendations.



Comparison of different combinations

criteria	AS+CO	AS+AQ	AS+S/P	AS+MQ	AM+LF 6doses
efficacy	>82% d14	>90% d14	90% d14	>95% d42	>95% d42
duration of Rx	3	3	3	3	3 (2 x/d)
safety	good	good	good	moderate	good
co-formulation	no	developing	blister	developing	yes
cost (adult Rx) in \$	1	1.5	1.2	2.5-4	2.4
resistance	high	moderate	variable	low	no

Choice of cost effective drugs depends on the resistance of *P. Falciparum* inside the country



Response to increasing resistance

Combination therapies recommended by WHO

WHO Technical Consultation on "Antimalarial Combination Therapy" – April 2001

- Artemether/lumefantrine
- Artesunate + amodiaquine
- Artesunate + SP
- Artesunate + mefloquine



WHO recommendations

- WHO recommends that all countries experiencing resistance to conventional monotherapies should use combination therapy, preferably containing artemisinins [ACTs -artemisinin-based combination therapies].
- WHO recommends the following therapeutic options:-
 - Artemether/lumefantrine
 - Artesunate+amodiaquine
 - Artesunate+SP
 - Artesunate+ mefloquine [area with low to moderate transmission.
 - Amodiaquine+SP



Remember about ACT's

- Short shelf life (24 months)
- Increased costs
- Longer lead time for deliveries
- Challenging implementation
- Strong commitment from all the partners
- Upscaled production from the manufacturers
- Shared knowledge and experience
- Global building capacity



五、瘧疾的預防性投藥



抗瘧藥物的臨床應用(一)

1. **Prophylactic**:-to prevent clinical attack
 - A. **Suppressive prophylaxis**:-use of blood schizontocides to prevent acute attack
 - B. **Causal prophylaxis**:-use of tissue schizontocides to prevent the parasite from establishing in the liver
2. **Curative**:-suppressive treatment of the acute attack usually with blood schizontocides.



抗瘧藥物的臨床應用(二)

3. **Prevention of transmission**:- eradication of infection in mosquitos using gametocytocides or sporontocides.
4. **Prevention of relapse**:-Primaquine



瘧疾預防性投藥

- 瘧疾預防性投藥在疫區是不建議的，因為必須長期服用，要考慮價格與副作用。只建議在疫區旅遊的旅客或短期居留者。
- 旅客必須在抵達前1-2週就開始服藥，並持續服藥至離開後4週。



- ✦ Include [mefloquine](#) ,[doxycycline](#), and the combination of [atovaquone](#) and [proguanil](#) (only needs be started 2 days prior and continued for 7 days afterwards).

Travelers to areas endemic for chloroquine-susceptible disease	Chloroquine
Travelers to areas endemic for chloroquine-resistant disease	Mefloquine



謝謝聆聽