Update on management of Malaria

Dr Owen Tsang

2 May 2017

IDIC forum

2015 Nobel Prize winner Tu You You 屠呦呦

Since the year 2000

Average malaria infection prevalence declined **46%** in children aged 2–10, from 26% to 14% in 2013.

The number of malaria infections at any one time dropped **26%**, from 173 million to 128 million in 2013.

Malaria mortality rates have decreased by **47%** worldwide and by **54%** in the WHO Africa Region.

WHO 2014 Malaria report

World situation

Table 8.3 Estimated number of a) malaria cases and b) malaria deaths by WHO region, 2000, 2005, and from 2010 to 2013

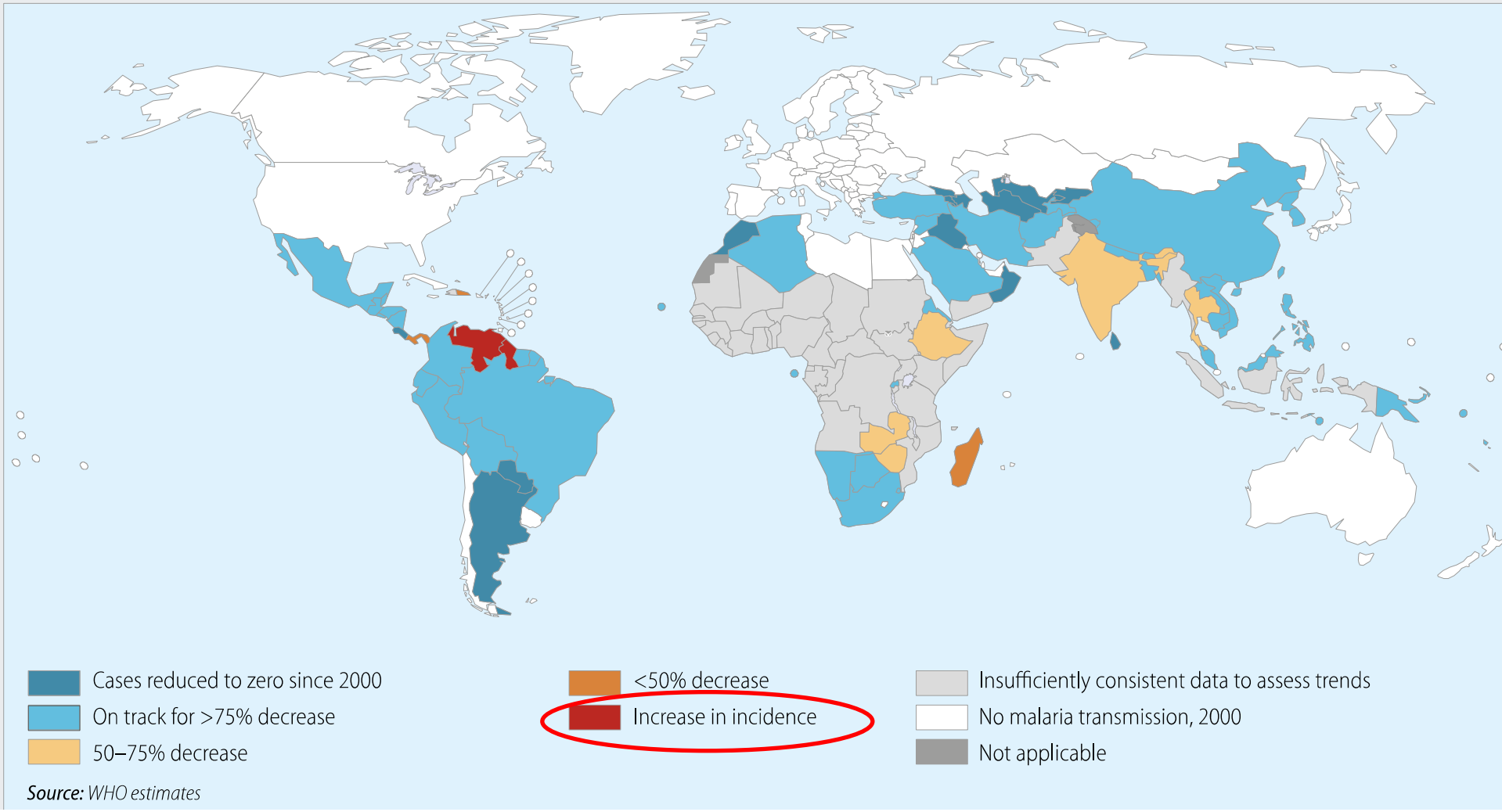
(a) Number of cases (000's)	2000	2005	2010	2011	2012	2013
Africa	174 000	192 000	167 000	163 000	163 000	163 000
Americas	2 500	1 700	1 100	800	800	700
Eastern Mediterranean	14 000	10 000	9 000	11 000	10 000	9 000
Europe						
South-East Asia	33 000	34 000	28 000	28 000	27 000	24 000
Western Pacific	4 000	2 000	2 000	1 000	1 000	1 000
World	**227 000**	**240 000**	**207 000**	**203 000**	**202 000**	**198 000**
Lower bound	150 000	155 000	133 000	129 000	127 000	124 000
Upper bound	304 000	328 000	287 000	282 000	281 000	283 000

(b) Number of deaths	2000	2005	2010	2011	2012	2013
Africa	801 000	761 000	576 000	543 000	530 000	528 000
Americas	2 300	1 800	1 300	1 000	900	800
Eastern Mediterranean	17 000	13 000	12 000	13 000	12 000	11 000
Europe	3					
South-East Asia	53 000	50 000	46 000	44 000	43 000	41 000
Western Pacific	9 500	4 700	3 900	3 300	3 500	3 300
World	**882 000**	**830 000**	**639 000**	**605 000**	**590 000**	**584 000**
Lower bound	599 000	547 000	405 000	384 000	376 000	367 000
Upper bound	1 104 000	1 029 000	795 000	755 000	742 000	755 000

Source: *WHO estimates*

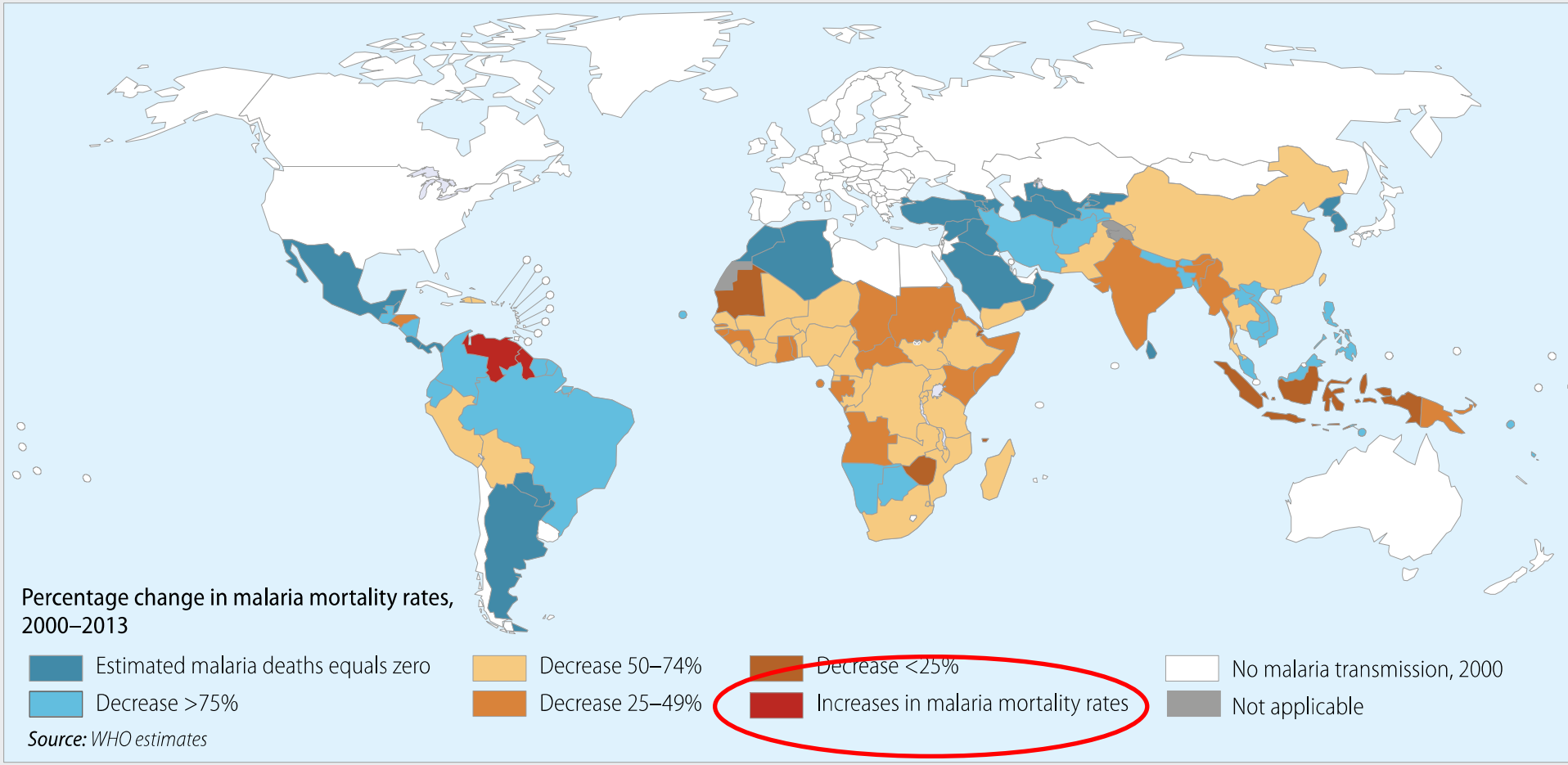
WHO proposed Artemisinin Combination Therapy in 2006

Figure 8.2 Projected changes in malaria incidence rates, by country, 2000–2015



WHO 2014 Malaria report

Figure 8.9 Percentage change in malaria mortality rates, 2000–2013



WHO 2014 Malaria report

Hong Kong situation

South China Morning Post
scmp.com

1996

Malaria man died following 36-hour delay in treatment

PATRICIA YOUNG and MICHELLE CHIN

PUBLISHED : Saturday, 05 October, 1996, 12:00am
UPDATED : Saturday, 05 October, 1996, 12:00am

A teacher died of malaria after his treatment was delayed for 11/2 days because a hospital could not process his blood test quickly and then failed to forward the results, an inquest heard yesterday.

Simon Davies was airlifted to hospital after a private doctor suspected he had contracted the disease.

A 34 year-old Briton died from falciparum malaria after coming back from Burma

要聞港聞 2002年09月25日 國泰空姐瘧疾遲送院枉死

蚊叮奪命疑案專家作供 國泰空姐瘧疾遲送院枉死

2002

9

讚 0 分享 0 Tweet 0 0

A 讚 熱帶病專家鍾世文醫生昨出庭作供。 梁家亮攝

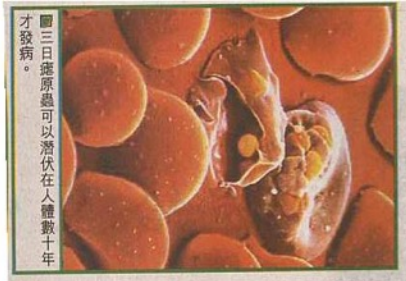
【本報訊】三十二歲國泰日籍空姐出勤往南非疑遭瘧蚊叮，返港後不適及發燒，到診所求醫惟未見好轉，最後入院證實染上瘧疾死亡。熱帶病專家昨在死因庭作供指，若該名空姐能及早送院治理，獲救機會極高；由於瘧疾與感冒的病徵相若，醫生對持續發燒病者應詢問其旅遊經歷及進行驗血，專家意見認為機組人員甚至市民對瘧疾的知識明顯不足。

第二名替死者診斷的劉醫生表示，知道該空姐之前曾求醫但未見好轉，且連續發燒四天，他經診斷後認為病人患感冒，當時沒有詢問她的旅遊經歷及建議進行驗血，只開出感冒藥及建議兩日後覆診。

瘧疾似感冒易誤診

熱帶病專家鍾世文醫生供稱，該空姐知念明子於去年十二月十一日深夜被送往嘉勒撒醫院，由他負責診斷。病人當時神志不清，病況嚴重，其後證實患上一種名為（ Cerebral Malaria）的瘧疾，由於病人出現心律不正，曾替她進行換血

瘧疾絕迹20年 首度爆發



圖三日瘧原蟲可以潛伏在人體數十年才發病。

威爾斯親王醫院去年接獲一宗罕見的瘧疾個案，患者七十七歲老婦發病後，三次入院，花了五個月時間才確診。醫生指出，病人發病初期，沒有發燒和發冷等典型瘧疾病徵，直至處方類固醇給她治療其他疾病，令她免疫力下降，瘧原蟲乘機大量繁殖，才驗血發現。醫生指瘧疾絕迹本港廿年，估計病人多年前受感染，瘧原蟲在體內潛伏長達最少廿年才發病。

患者一九四九年由內地移居本港後，一直住在大埔的村屋，期間從沒有返回內地。她本身患糖尿病，二〇〇四年十一月因膠膽數周入院，當時沒有發燒症狀，超聲波檢查發現她的肝脾發大，脾臟長度更達廿七厘米，是正常的三倍。她的血細胞數量減少，主動脈旁的淋巴結輕微腫脹，但她拒絕驗骨髓，故當時無法確定淋巴結腫脹原因。

去年二月，她首次感到間歇性發燒和發冷，每四日發燒一次，但血液、尿液和痰樣本種不到細菌，三月抽取的兩個血液樣本均對瘧疾呈陰性反應。醫生在她同意下終抽驗骨髓，驗出骨髓細胞異常及有少量淋巴瘤細胞，給她處方類固醇舒緩病情後讓她出院。

瘧原蟲潛伏廿載

但病人一個月後再次因間歇性發燒入院，這次留醫期間再驗血，即驗出「三日瘧原蟲」。醫生隨即對症下藥，處方抗瘧疾藥物，三日後已將病人體內瘧原蟲清除，血細胞數量回升，發大的脾臟經三個月跟進治療後開始消退。

衛生署表示，去年接獲威院呈報此個案，相信屬復發個案，病人早在多年前已受感染，去年再復發，未能確定在本地或外地感染。署方指出，文獻曾報道過四十年後甚至更長時間才復發個案。

曾治療患者的中文大學內科及藥物治療學系副教授李禮舜指出，瘧疾在港絕迹最少廿年，未能確定她在本港或五十多年前在內地感染瘧原蟲，但相信她早在廿年前已受感染，瘧原蟲潛伏體內，當她服類固醇令抵抗力下降，瘧原蟲迅速繁殖，驗血才能驗出。他估計，瘧原蟲在她體內潛伏時，可能不斷攻擊淋巴細胞，引致淋巴瘤。■記者蘇家欣

2006

欣擊，原體她

衞生署近年接獲的瘧疾個案

年份	個案
2006年（截至1月）	3
2005年	32
2004年	37
2003年	28
2002年	54
2001年	47

註：本港近年的瘧疾個案全部由外地傳入，主要來自南亞、非洲及東南亞。

遊東非遇蚊叮

港婦瘧疾命危

今年七宗傳入個案 西貢兩公里揪媒蚊

本港錄得瘧疾個案 *截至8月16日

年份	宗數
2013	20
2014	23
2015*	7

今年7宗瘧疾傳入地點

印度	2	巴基斯坦	1
印尼	1	馬達加斯加	1
科特迪瓦	1	未能分類	1

資料來源：衞生防護中心

提高警覺

本港有市民到東非旅遊時被蚊叮感染瘧疾，目前情況危殆。該名居於西貢的女患者曾兩度到將軍澳醫院急症室求醫，第二次求診才獲入院治療。衞生防護中心昨表示，至今無發現同村居民出現感染，食物環境衞生署將在患者居所外方圓兩公里調查瘧疾媒蚊。有傳染病專家指出，本地瘧疾個案自九八年起絕迹，迄今發現的病例屬外地感染。殺傷力大的瘧原蟲可在人體內高速繁殖，經血液入侵器官，若及早知道患者旅遊史，可盡早以快速測試確診及作適切治療。

女患者四十四歲，過往健康良好，居於西貢南山村浪尾。她於七月廿一至三十一日與丈夫到訪東非馬達加斯加，返港後在八月九日開始出現發燒及屙嘔病徵，分別於十三日及十四日到將軍澳醫院急症室求醫，十四日入院，目前情況危殆，於深切治療部留醫。患者丈夫趙先生證實事件，他昨探訪太太，形容她病情已趨穩定。食環署表示，過去一年平均每星期到西貢南山村浪尾滅蚊一次。為審慎起見，將派員到患者處所調查，並向村民宣傳防蚊。

瘧原蟲經血液侵器官致衰竭

將軍澳醫院表示，女病人十三日求診時透露曾前往非洲國家，當天沒有發燒，醫生臨床診斷為腸胃炎並處方藥物。但翌日再求診時，病人發高燒及神志混亂，急症室醫生診斷為懷疑傳染病，並抽血化驗，其後病人情況轉差，十五日轉送深切治療部。

連同此個案，衞生防護中心今年至今共錄七宗瘧疾，當中六宗屬外地傳入，一宗未能分類。中文大學感染及傳染病學教授李禮舜指出，近年在港發現個案均由外地傳入，以印度、巴基斯坦及非洲國家傳入佔多。他解釋，瘧疾由按蚊將瘧原蟲傳人，瘧原蟲可分五種，殺傷力各有不同，以惡性瘧原蟲殺傷力最大。惡性瘧原蟲進入人體後，可在血液高速繁殖，再經血液入侵器官，導致多重器官衰竭，甚至死亡。

到高危地區前應先求醫配藥

李禮舜透露，上周他亦接獲一名南亞商人士自巴基斯坦回港後確診瘧疾，幸及時得知旅遊史，盡快進行緊急血液測試，確診後立即處方抗瘧疾藥物及支援性治療，病人現況穩定。他提醒，市民若準備到瘧疾高危國家，可於出發前求醫獲取預防藥物，出發前直至離開該地區後一至四周仍要服用。若返港後出現發燒、肌肉痛等徵狀，應盡快求醫，並清楚報告旅遊史。

瘧原蟲

■女患者位於浪尾的居所。（朱先儒攝）

2015

- 44 years old lady with good PH
- To Madagascar 31/7 – 31/7
- 9/8: Fever, diarrhoea & vomiting
- 13/8: To AED, Dx: GE
- 14/8: To AED with confusion
- 15/8 To ICU in critical condition
- Subsequently discharged

April 2017

初診未透露上月遊非洲加納

港女染瘧疾失知覺命危

一名40歲女子曾於上月到訪非洲加納，返港約兩周後因咳嗽、發燒及肌肉疼痛等到瑪麗醫院急症室求診，當時她未有向分流護士透露曾外遊，而醫生臨床診治為上呼吸道感染。三天後，她因上腹部疼痛、嘔吐、血尿等症狀再求醫，此時才向急症室醫生表明外遊紀錄，但病情已急轉直下，同日安排入院不久已失去知覺，出現腦水腫，需要急救及插喉協助呼吸，經血液化驗證實病人感染瘧疾，現情況危殆。瘧疾傳播途徑是被受感染的瘧蚊叮咬，不會在人傳人，但可透過血液傳播，而瘧疾亦可在懷孕或生產時經母體傳給胎兒或初生嬰兒。　本報港聞部報道

瘧疾是一種可致命的嚴重疾病，現時藥物可有效治療，但及早確診和治療對徹底治癒瘧疾尤為重要。根據瑪麗醫院昨天公布的資料，該名肇事女病人相信錯過治療的黃金時機。該病人仍在成人深切治療部留醫，情況危殆。院方會繼續跟進病人情況提供適切治療。

肝功能受損 出現腦水腫

瑪麗醫院發言人昨天公布一宗外地傳入病人感染罕見及嚴重瘧疾個案，患者一名40歲女子，她於上周三中午因咳嗽、發燒、喉嚨痛及肌肉疼痛到瑪麗醫院急症室求診。分流護士曾詢問病人最近十日的外遊紀錄，病人表示並無外遊，醫生診斷病人患上上呼吸道感染，病人獲處方治療上呼吸道感染的藥物後離開急症室。

該名病人於本月1日早上，因為上腹部疼痛、嘔吐、血尿等症狀再到該院急症室。急症室醫生於上午8時半左右為她診治，並安排抽血檢驗，初步血液報告顯示其肝功能受損，於是安排病人轉往內科病房作進一步治療，其間急症室醫生再次查詢病人的病歷，病人表示曾於3月8日至16日到訪非洲加納。

病人中午左右轉抵內科病房，但下午情況轉差，於下午2時十分失去知覺，需要急救及插喉協助呼吸。及後腦部掃描證實病人出現腦水腫，而血液報告亦證實病人感染瘧疾，病人隨即被轉往成人深切治療部，微生物學醫生亦到場會診，並於下午4時半左右展開瘧疾的藥物治療。

瘧疾屬於須呈報的傳染病，瘧疾常見於非洲、東南亞及南美洲等氣候溫暖的熱帶及亞熱帶地區，市民如須前往有關地區，應注意防蚊，並在出發前最少六個星期諮詢醫生意見，以便採取預防措施及於需要時獲取預防瘧疾的藥物。

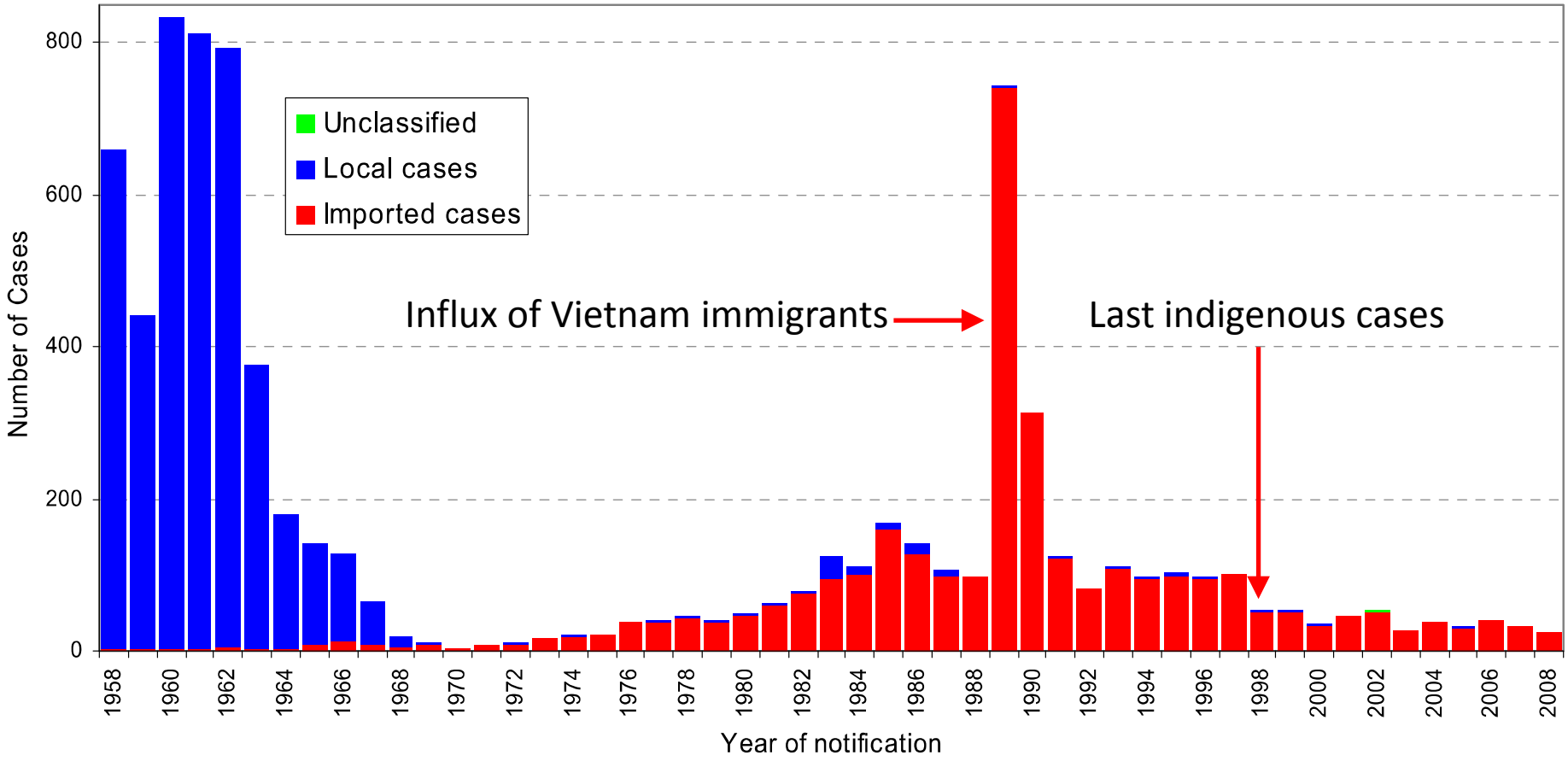
潛伏期可達數月或更長

一般而言，瘧疾的潛伏期會因應不同的致病瘧原蟲種類而有所不同，通常在被受感染的瘧蚊叮咬七至三十日天後出現病徵，但潛伏期可達數月或更長。患者通常有間歇性發燒、發冷、冒汗、頭痛、疲倦、噁心、嘔吐及肌肉疼痛等徵狀，併發症包括貧血、肝臟及腎臟衰竭、嚴重個案可引致腦部水腫、誘發痙攣、神志不清及昏迷。如在外遊期間或回港後出現瘧疾徵狀，應立即求診並主動透露近期的外遊紀錄，以便盡快安排治療。

一宗嚴重瘧疾個案時序 資料來源：瑪麗醫院

3月8日至16日	一名40歲女子到訪非洲加納
3月29日中午	她因咳嗽、發燒、喉嚨痛及肌肉疼痛到瑪麗醫院急症室求診，當時病人無向分流護士提及曾外遊。醫生診斷病人患上呼吸道感染，獲處方治療藥物後離開
4月1日	
上午8時30分	該女子因上腹部疼痛、嘔吐、血尿等症狀再到瑪麗急症室求診，急症室醫生安排她抽血檢驗，初步血液報告顯示其肝功能受損，於是安排病人轉往內科病房作進一步治療。期間，急症室醫生再查詢病歷，病人表示曾外遊
中午12時半	轉抵內科病房
下午2時10分	情況轉差，失去知覺，需要急救及插喉協助呼吸，出現腦水腫。血液報告證實感染瘧疾
下午4時30分	轉往深切治療部，開始瘧疾的藥物治療，現仍留醫，情況危殆

Hong Kong situation



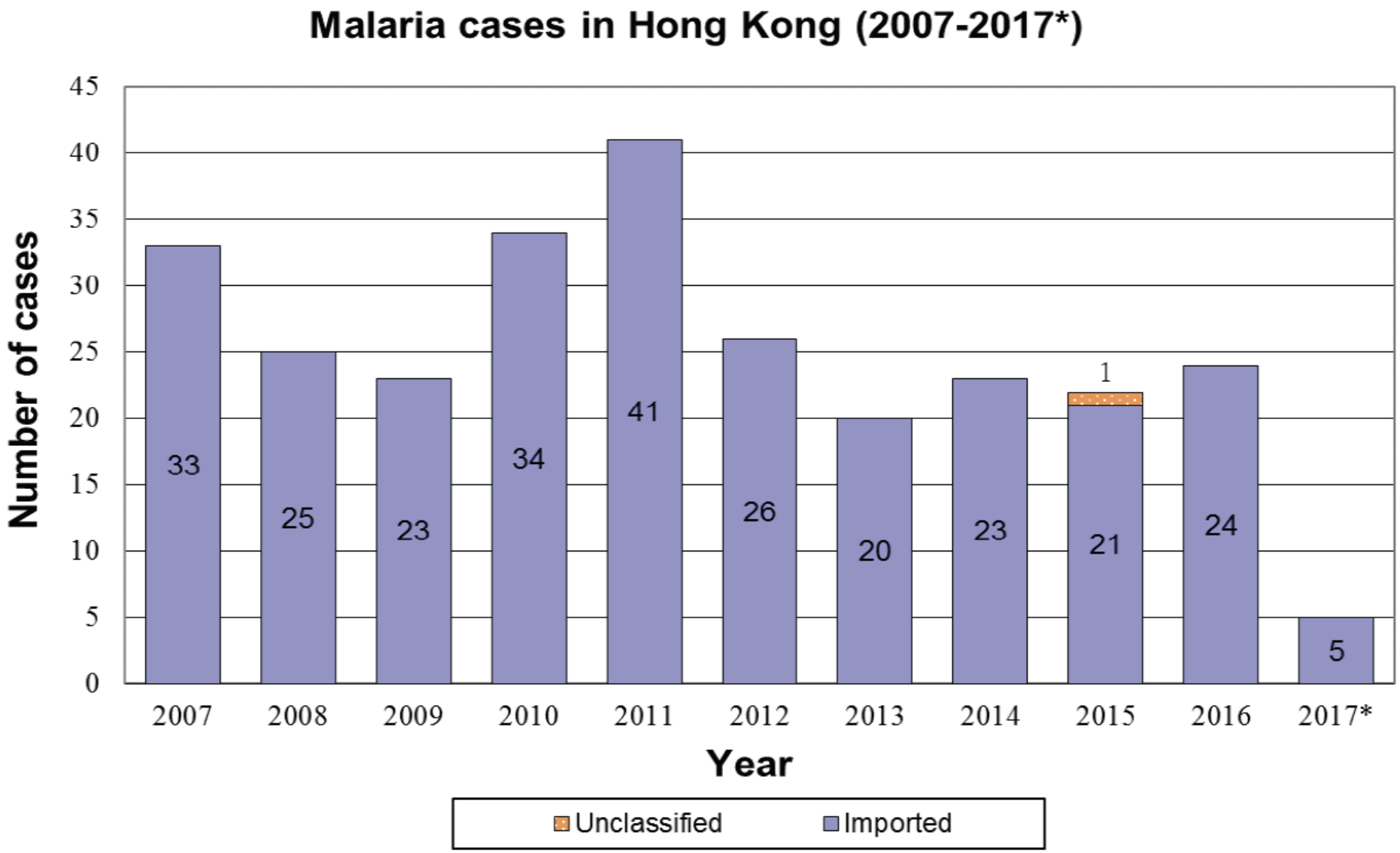
Ma SKE, et al. Travel Med Infect Dis 2011; 9: 95-105

Place of origin of imported malaria cases (1999 – 2008)

From 1999-2008:

- **Case fatality 2% (6 cases)**
- **PF: 5; PM:1**
- **Age 32 – 73**
- **3 cerebral malaria, 2 bacterial pneumonia, 1 GN**

Ma SKE, et al. Travel Med Infect Dis 2011; 9: 95-105



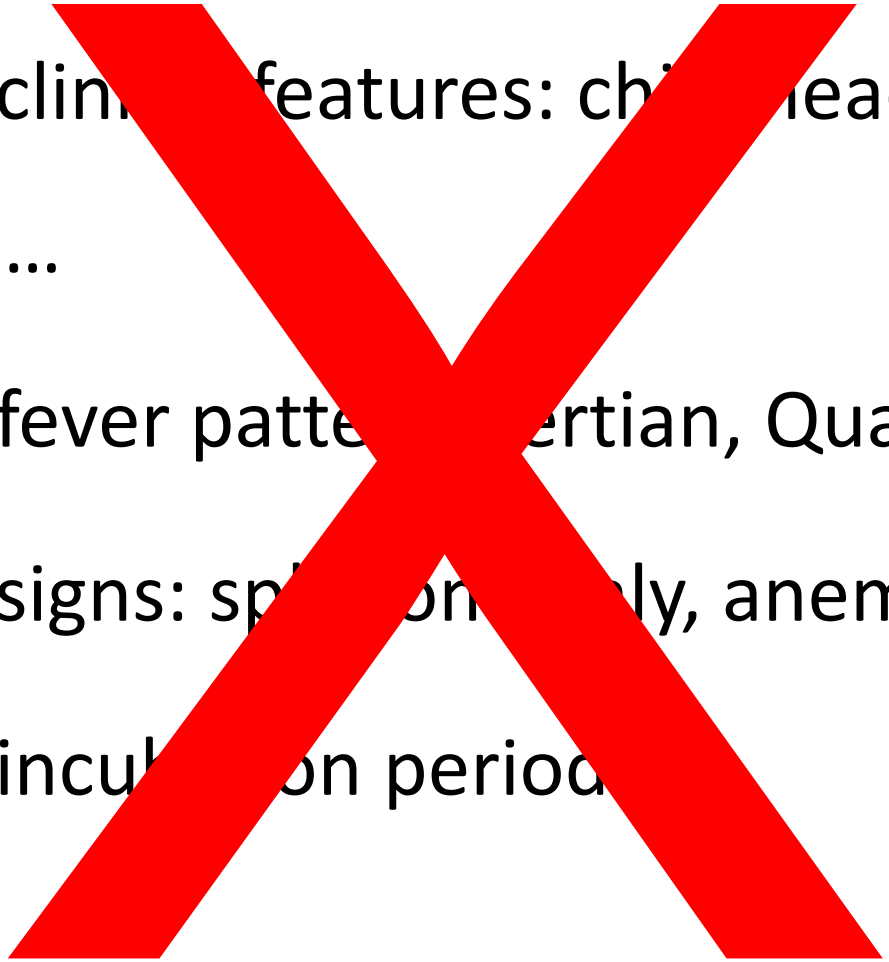
Terence Lam, et al. Communicable Disease Watch 2017;14 (7):29-31

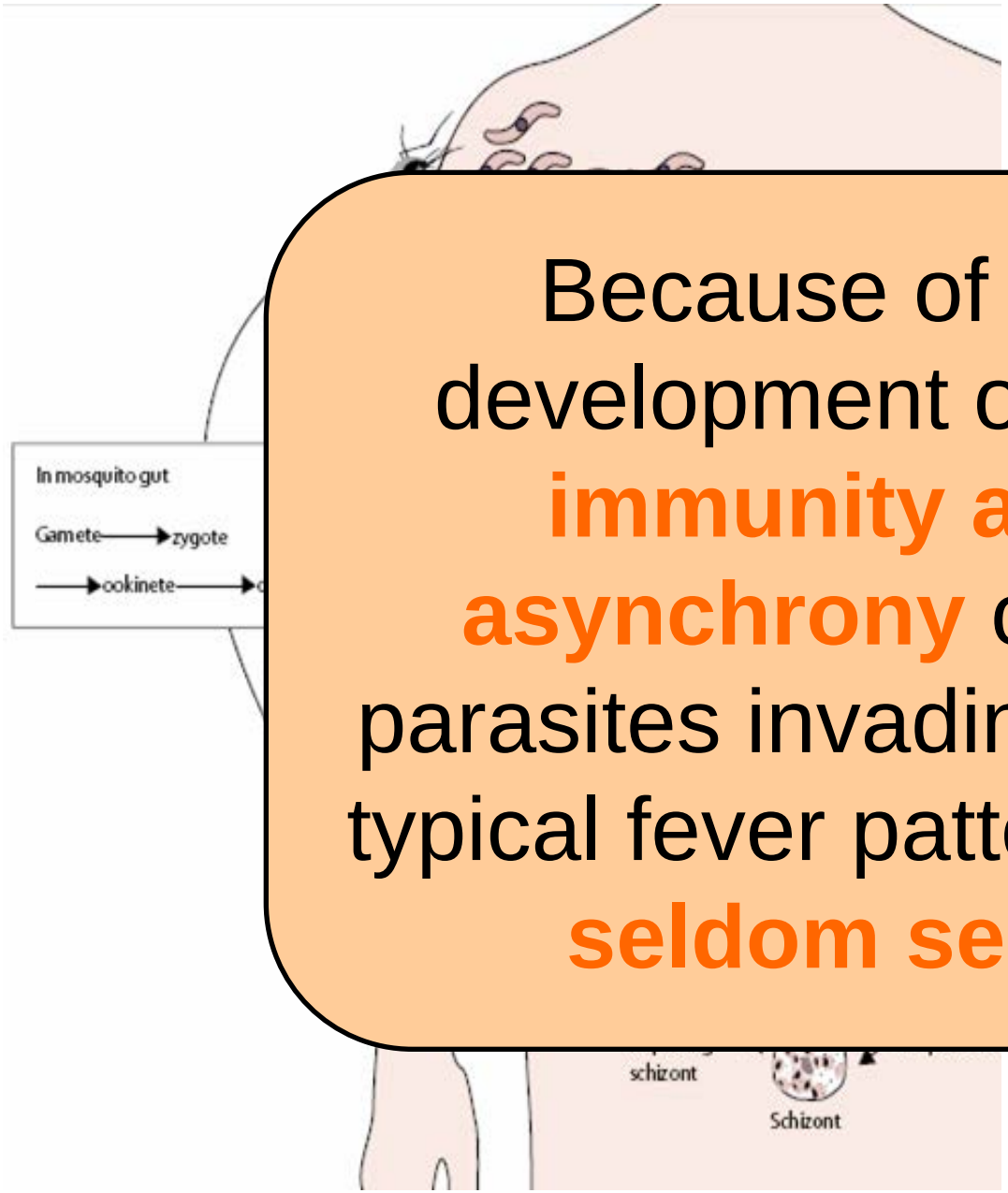
Difficult to make a diagnosis of malaria?

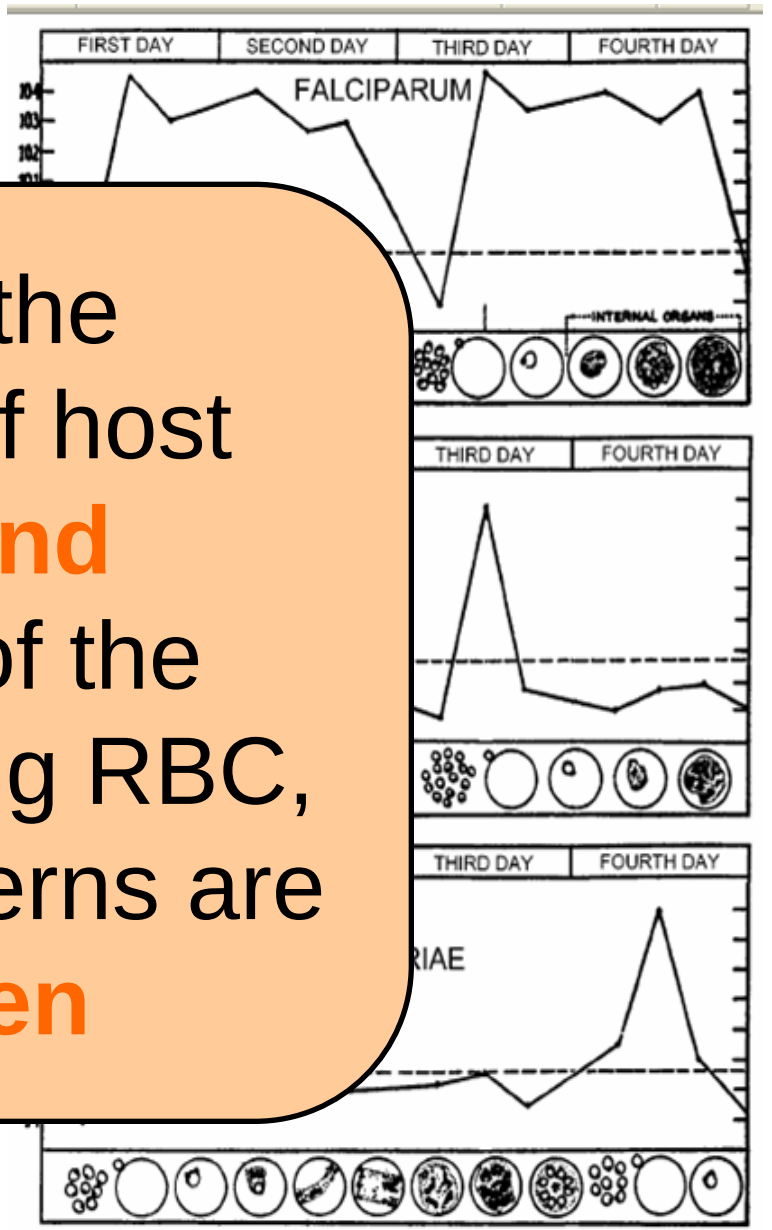
Yes or No

History and physical examination

- Typical clinical features: chills, headache, malaise…
- Typical fever pattern: Tertian, Quantan
- Typical signs: splenomegaly, anemia
- Typical incubation period







Because of the development of host **immunity and asynchrony** of the parasites invading RBC, typical fever patterns are **seldom seen**

Greenwood BM, et al. ***Lancet*** *2005; 365: 1487–98*

Medium (11–21 days)

- Malaria (especially *P falciparum*)
- Leptospirosis
- Typhoid fever
- Rickettsioses: scrub typhus, spotted fever group, Q fever

Incub

per

Difficult to predict malaria from the incubation period

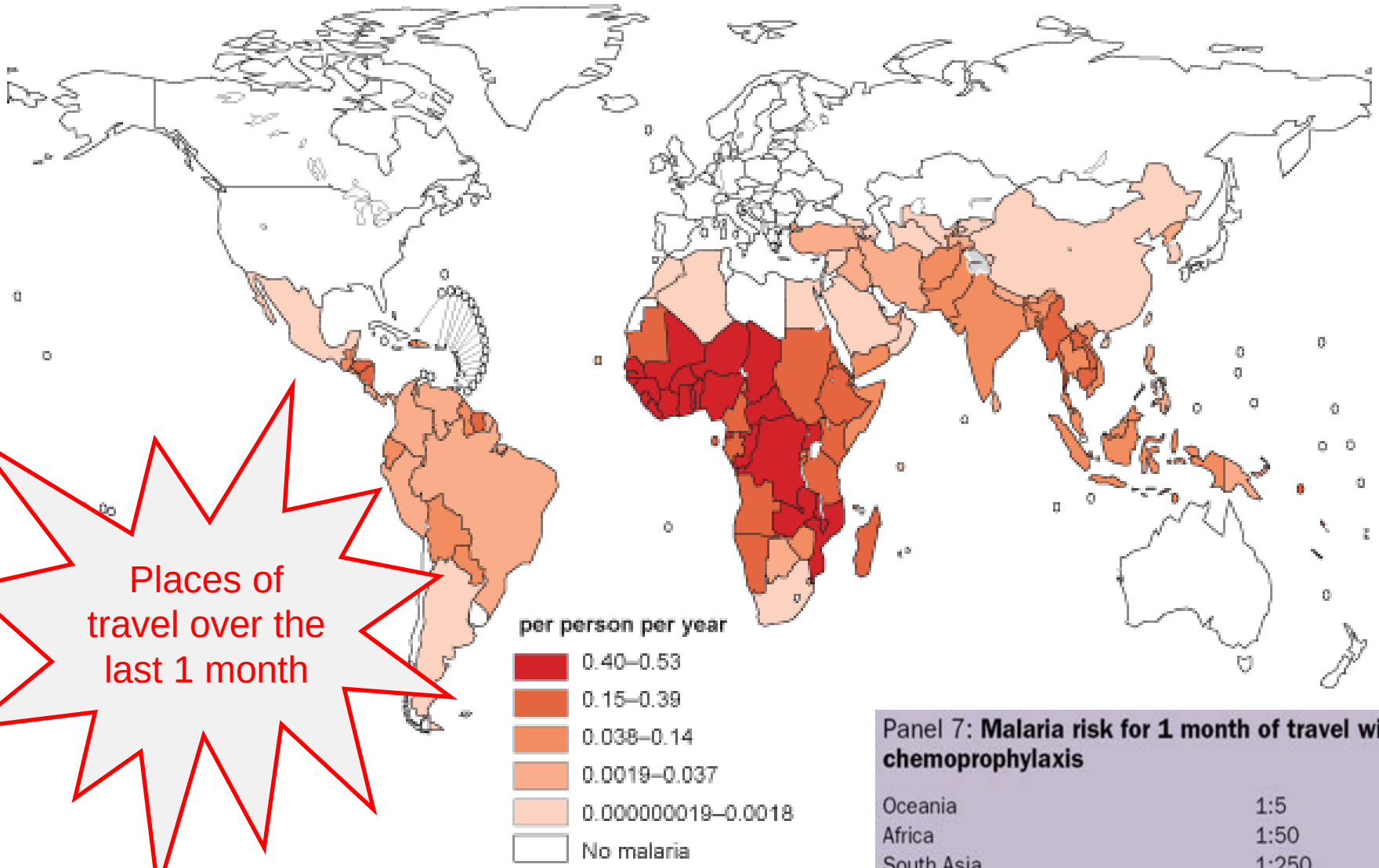
- Amoebic liver abscess
- Leishmaniasis
- American trypanosomiasis

Spira AM. ***Lancet*** *2003;361:1459-69*

Disease Severity and Duration

	vivax	ovale	malariae	falciparum
Prepatent Period (days)	8-12	8-12	15-18	6-9
Incubation Period (days)	8-27	8-27	16->40	6-25
Severity of Initial Paroxysms	moderate to severe	mild	mild to moderate	severe
Average Parasitemia (per mm^3)	20,000	9,000	6,000	50,000-500,000
Maximum Parasitemia (per mm^3)	50,000	30,000	20,000	2,500,000
Typical Symptom Duration (untreated)	3-8 weeks	2-3 weeks	3-24 weeks	2-3 weeks
Maximum Infection Duration (untreated)	5-8 years*	12-20 months*	20-50 years	6-17 months
Anemia	++	+	++	++++
Other Complications			renal	cerebral

*Includes relapses



Panel 7: **Malaria risk for 1 month of travel without chemoprophylaxis**

Oceania	1:5
Africa	1:50
South Asia	1:250
Southeast Asia	1:2500
South America	1:5000
Mexico and Central America	1:10 000

Spira AM. ***Lancet*** *2003;361:1459-69*

Clinical

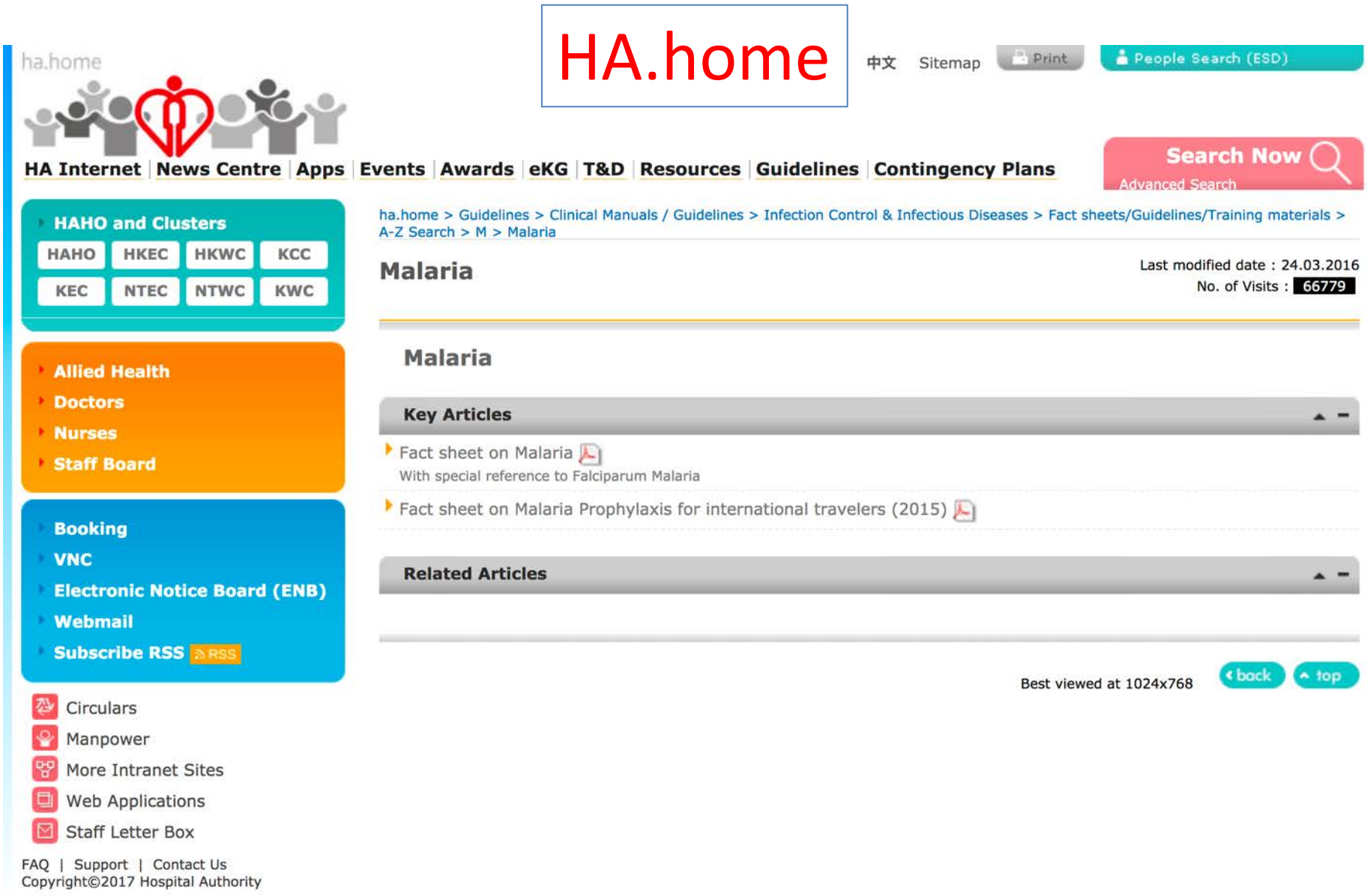
	Uncomplicated	Complicated
Species	Any	Falciparum mostly
Symptoms	Non-specific	Organs specific symptoms
P/E	Mild anemia, Mild splenomegaly	ARDS, circulatory collapse, renal failure, liver failure, metabolic acidosis, hypoglycemia, DIC, severe anemia
Parasitemia	< 5 parasites/ml of blood < 0.1% parasitized RBC	Hyperparasitemia: ≥ 1000 parasites/ml ≥ 5-10% parasitized RBC In Low transmission region: 5% In high transmission region: 10%
Cytoadherence	No	Yes
Cerebral malaria	Low risk	High risk
Mortality	Low	Severe anemia: 1% Metabolic acidosis: 15% Coma: 18%

Severe Falciparum malaria

≥ 1 of the following, in the presence of P. falciparum asexual parasitaemia & after excluding other causes	
Impaired consciousness	GCS < 11 in adults or a Blantyre coma score < 3 in children
Prostration	unable to sit, stand or walk without assistance
Convulsions	> 2 episodes within 24 h
Acidosis	BE > 8 mEq/L, bicarbonate < 15 mmol/L or venous lactate ≥ 5 mmol/L.
Hypoglycaemia	Blood or plasma glucose < 2.2 mmol/L (< 40 mg/dL)
Severe anaemia	Hb ≤ 5 g/dL or a HCT ≤ 15% in children < 12 years of age (< 7 g/dL and < 20%, respectively, in adults) with a parasite count > 10 000/µL
Renal impairment	Cr > 265 µmol/L (3 mg/dL) or blood urea > 20 mmol/L
Jaundice	bilirubin > 50 µmol/L (3 mg/dL) with a parasite count > 100 000/ µL
Pulmonary oedema	Radiologically confirmed or SaO2 < 92% on RA with RR > 30/min
Significant bleeding	Recurrent or prolonged bleeding
Shock	Compensated shock: capillary refill ≥ 3 s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock: systolic BP < 70 mm Hg in children or < 80 mm Hg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).
Hyperparasitaemia	P. falciparum parasitaemia **> 10%**

WHO. Guideline for treatment of malaria (3rd) 2015

Treatment


HA.home
ha.home
中文 Sitemap Print People Search (ESD)
HA Internet | News Centre | Apps | Events | Awards | eKG | T&D | Resources | Guidelines | Contingency Plans
Search Now
Advanced Search
HAHO and Clusters
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KEC NTEC NTWC KWC
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Malaria
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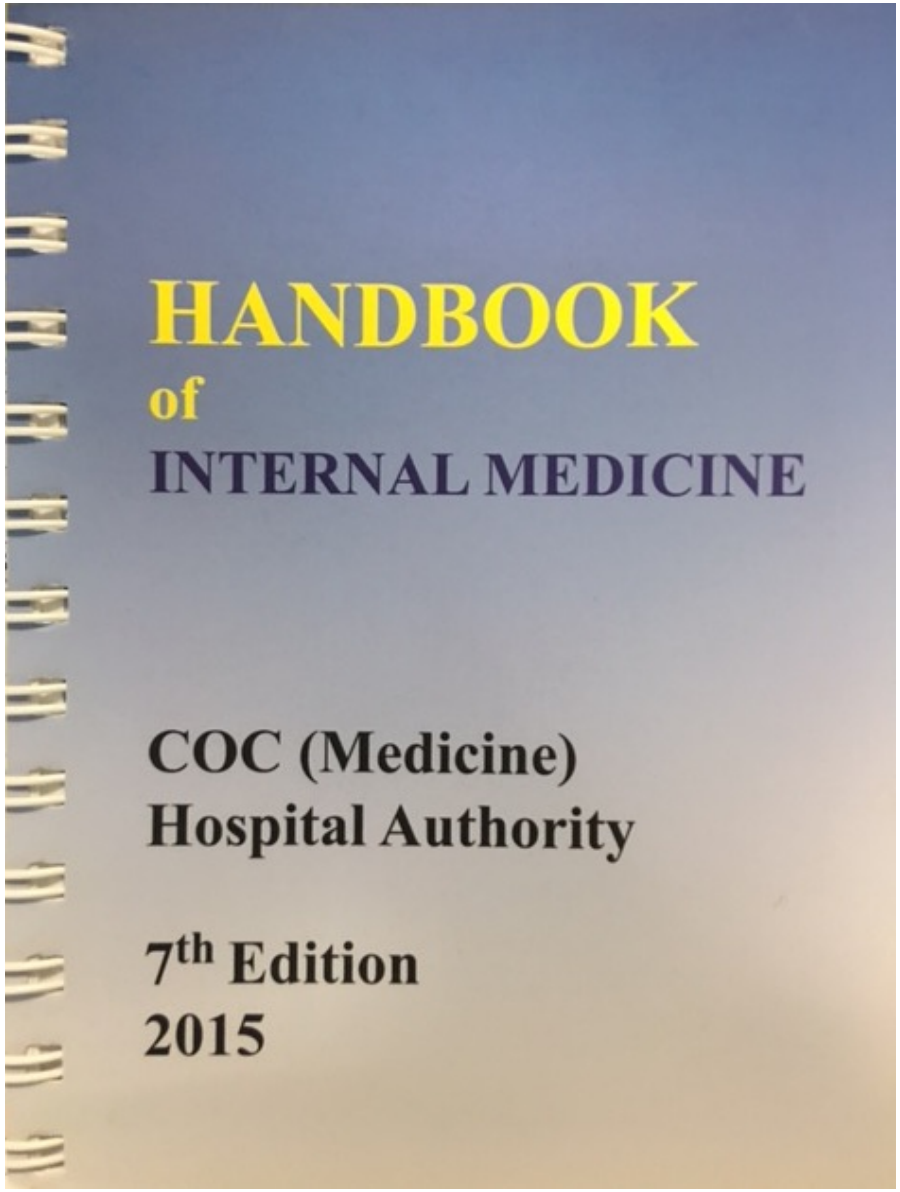
Malaria
Key Articles
Fact sheet on Malaria
With special reference to Falciparum Malaria
Fact sheet on Malaria Prophylaxis for international travelers (2015)
Related Articles
Best viewed at 1024x768
back top

Fact Sheet on Malaria

(with special reference to Falciparum Malaria)



MALARIA

Management of Acute Attack

1. Anti-malarial chemotherapy should be administered as soon as the diagnosis is made
2. Monitor blood for parasites and repeat testing is needed if the diagnosis is strongly suspected
3. Maintain fluid and electrolytes balance; avoid over-hydration
4. Renal failure regime for blackwater fever; treat hypoglycaemia and/or shock if present
5. Pulmonary oedema may develop, treated by prop up, oxygen, loop diuretic, veno-dilator; if hypoxic may need positive pressure ventilation
6. Avoid sedatives and corticosteroids
7. Watch for relapse (usually within 2 months) and signs of peritoneal irritation (splenic rupture).

Anti-malarial Chemotherapy

A. Uncomplicated P. vivax, P. malariae and P. ovale

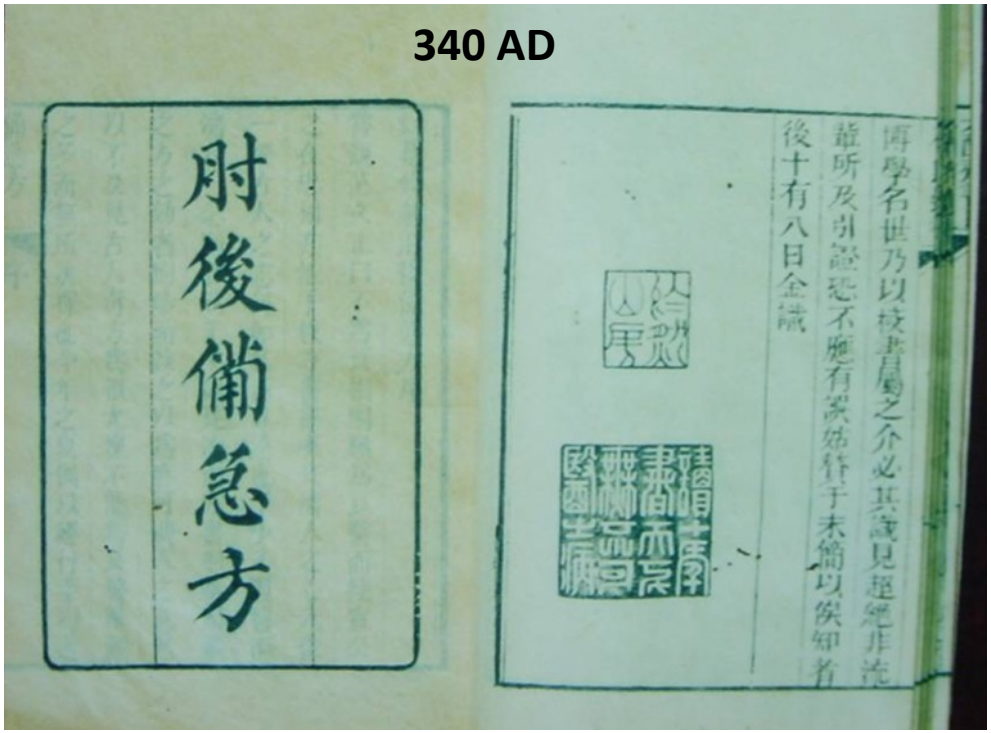
Chloroquine 600 mg base po stat
and 300 mg base 6 hours later
then 300 mg base daily for 2 more days
plus *Primaquine* 15 mg base (0.25 mg/kg) po daily taken with food for 14 days in *P. vivax* and *P. ovale* infection to eradicate hypnozoites in the liver.

NOTE 1 Chloroquine-resistant *P. vivax* reported from Oceania, Indonesia and South America, treatment similar to that of *P. falciparum* malaria is required.

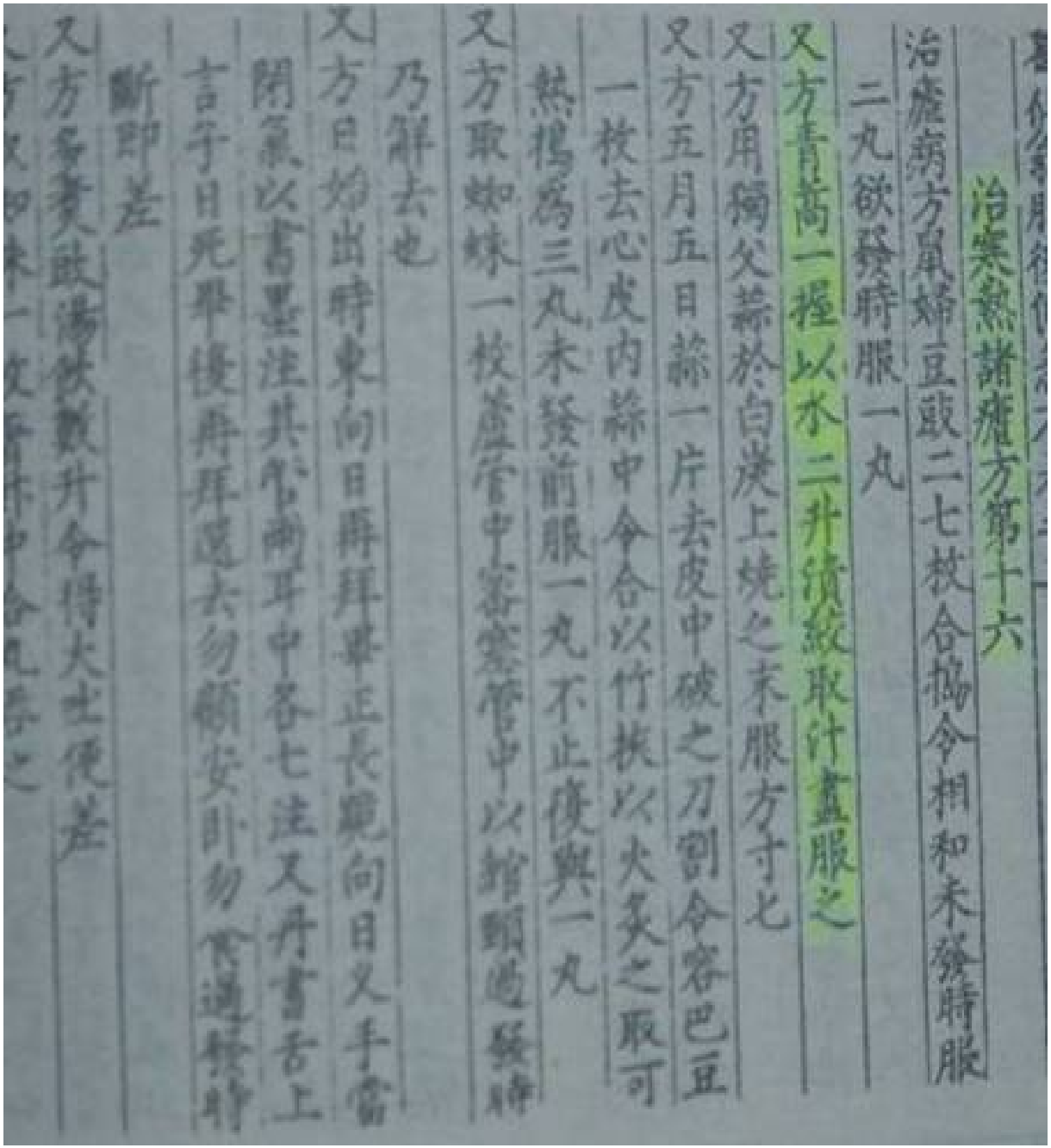
NOTE 2 Primaquine-resistant *P. vivax* reported in South-east Asia and Western Pacific. An increased of the dose to 22.5 – 30 mg daily (or 0.5 mg/kg) is effective

NOTE 3 Primaquine is contraindicated in pregnancy. In G6PD deficiency, primaquine is safe in dosage of 0.75mg/kg once a week for 8 weeks. Monitor Hb level.

History of Artemisinin



Emergency medicine



治瘧熱諸瘧方第十六

治瘧病方鼠婦豆豉二七枚合搗令相和未發時服三丸欲發時服一丸

又方青蒿一握以水二升漬絞取汁盡服之

又方用獨父絲於白炭上燒之末服方寸匕

又方五月五日絲一斤去皮中破之刀割令容巴豆一枚去心皮內絲中令合以竹挾以火炙之取可熱稍為三丸未發前服一丸不止復與一丸

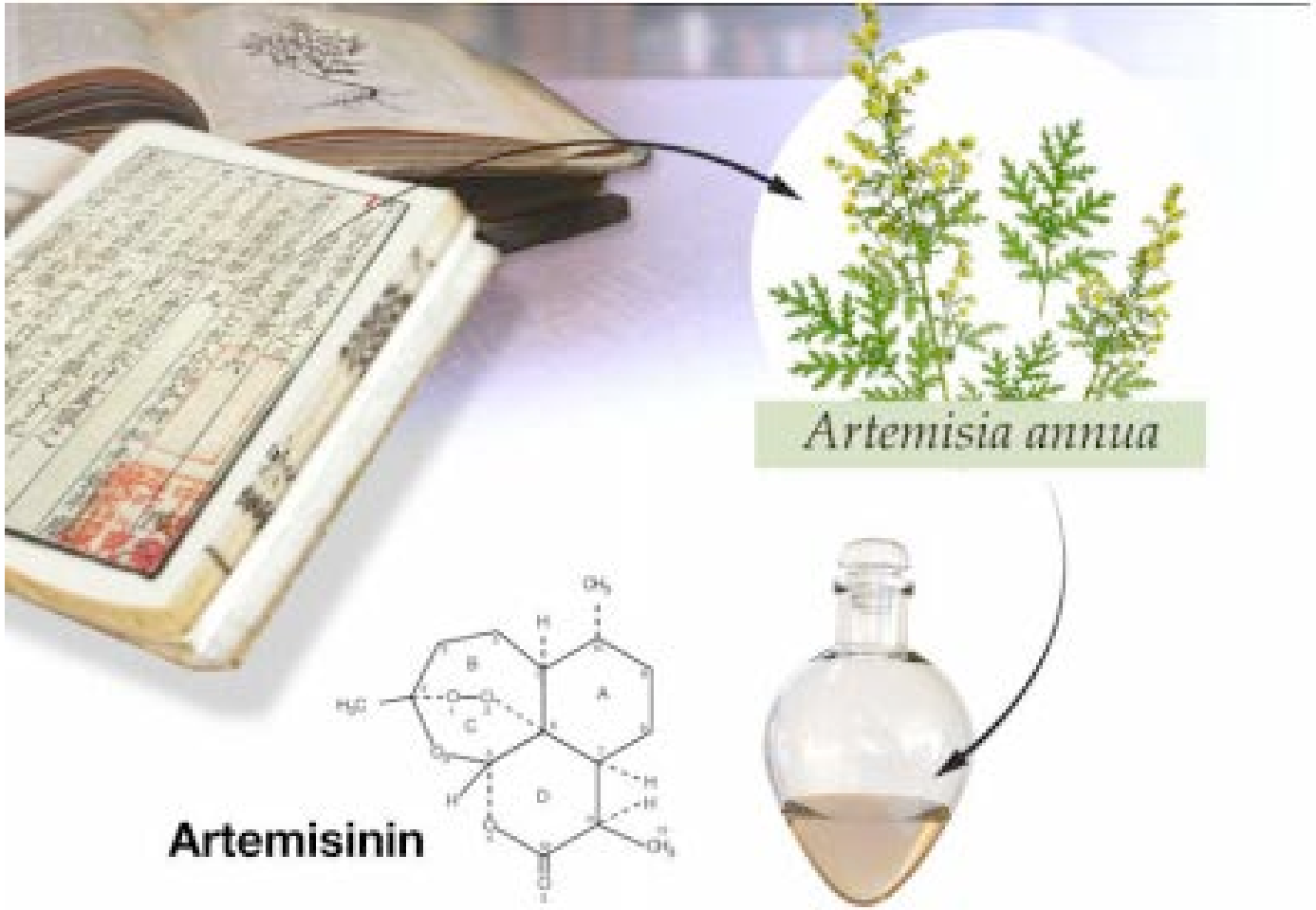
又方取蜘蛛一枚盛管中塞管中以綿頭過發時乃解去也

又方日始出時東向日再拜畢正長跪向日又手當閉氣以書墨注其兩耳中各七注又丹書舌上言千日死畢後再拜還去勿顧安卧勿食過發時斷即差

又方桑根煎湯飲數升令病人吐便差

青蒿素

History of Artemisinin



Timeline

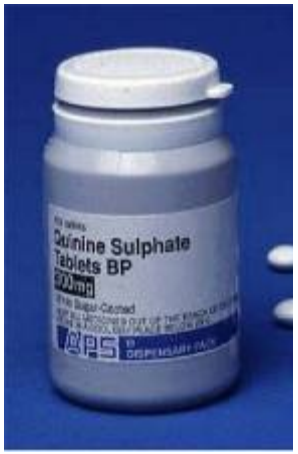
340 AD: Qinghao

1630: Cinchona bark

1820: **Quinine** isolated from Cinchona bark

1934: **Chloroquine**

1844: Sporadic resistance to Quinine reported



1944: Proguanil

1945: Amodiaquin, **Primaquine**

1952: Pyrimethamine

1974 - 75: **Mefloquine**

1972: **Artemisinin** isolated in China

1998: **Malarone** (Atovaquone + Proguanil)

1992: Atovaquone

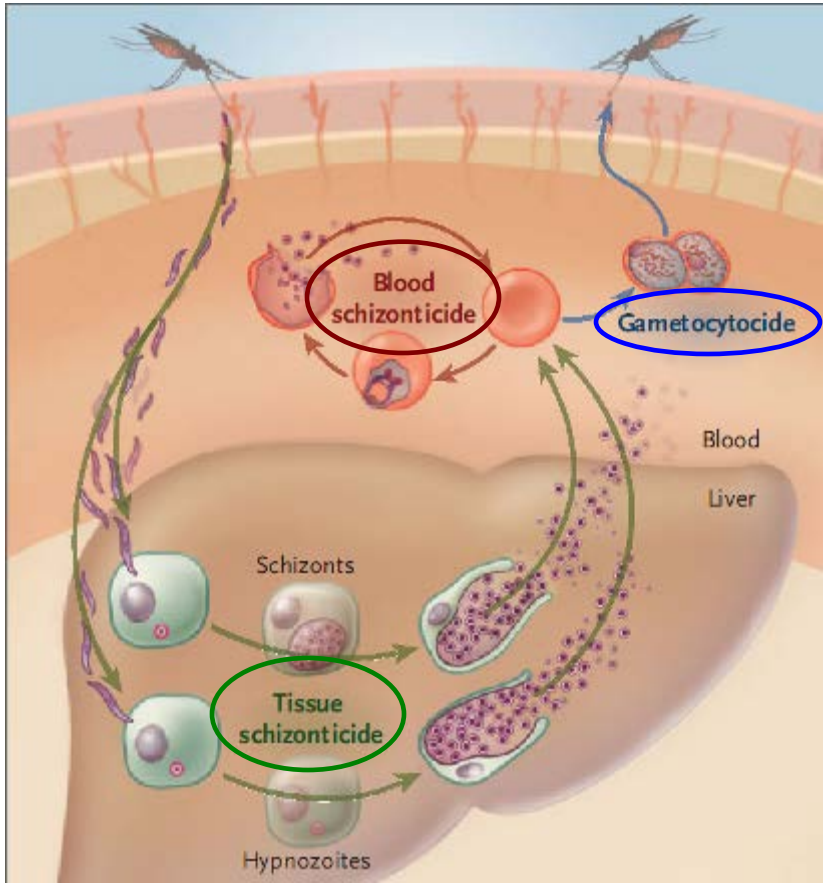
2009-2012: Launching of artemisinin fixed dose combination

2006: **Artemisinin combination therapy recommended by WHO**

2010: Artesunate Injection by Guilin company

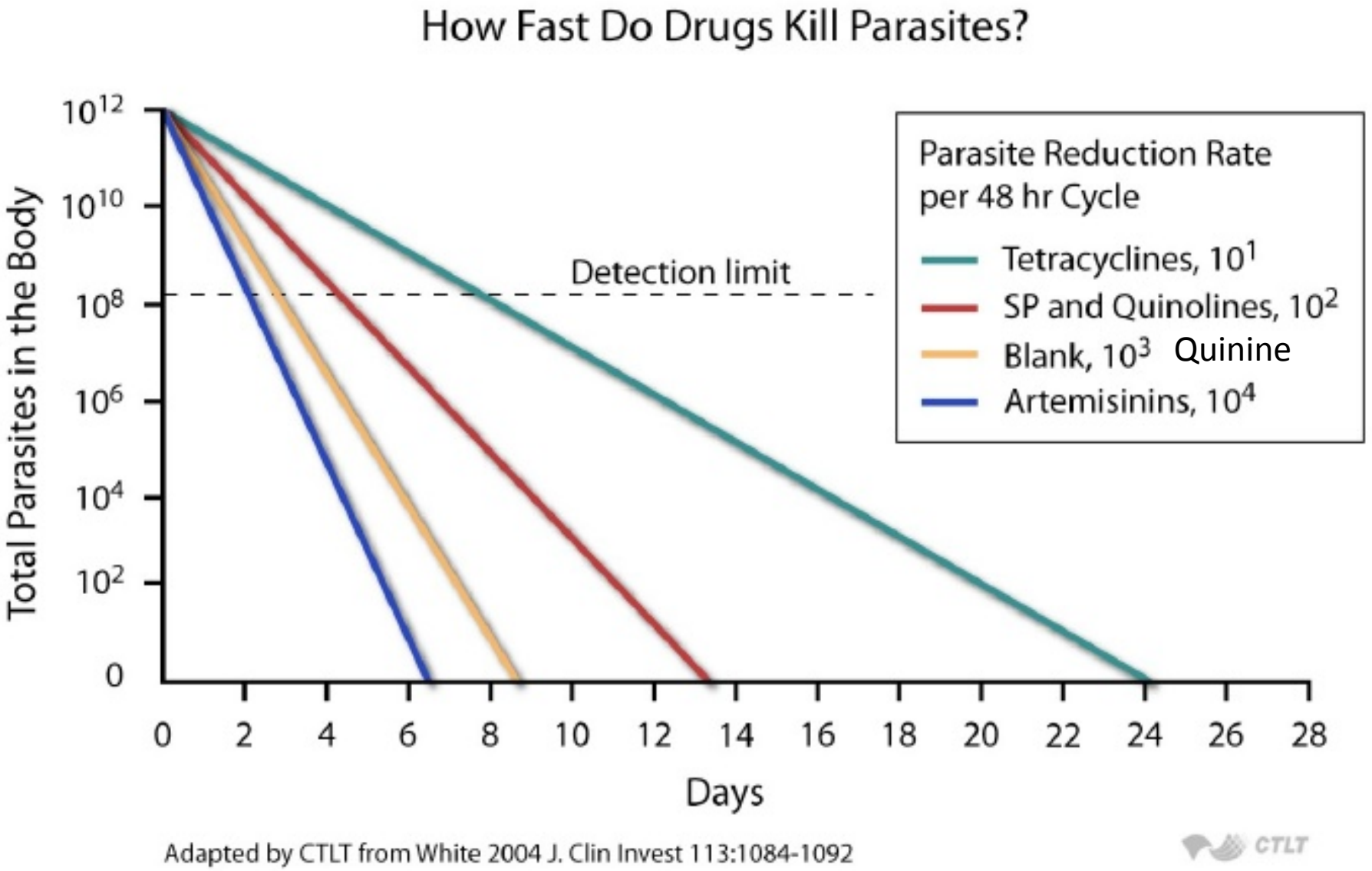
2015: 4 new molecules PII trial: OZ439, KAE609, KAF156, DSM265

Mechanism of actions of anti-malarials



- Blood schizonticide:
  - Chloroquine,
  - Quinine,
  - Pyrimethamine/sulfadoxine,
  - Artemisinin,
  - Doxycycline
  - Mefloquine
  - Proguanil
  - Halofantrine
  - Lumefantrine
- Tissue schizonticide:
  - Primaquine
  - Proguanil
- Gametocytocide:
  - All species: Artemisinin, Primaquine
  - PV: Chloroquine, Quinine

Baird JK. ***N Engl J Med*** *2005;352:1565-77.*


How Fast Do Drugs Kill Parasites?
Total Parasites in the Body
10^{12}
10^{10}
10^{8}
10^{6}
10^{4}
10^{2}
0
Detection limit
Parasite Reduction Rate per 48 hr Cycle
Tetracyclines, 10^{1}
SP and Quinolines, 10^{2}
Blank, 10^{3} Quinine
Artemisinins, 10^{4}
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
Days
Adapted by CTLT from White 2004 J. Clin Invest 113:1084-1092
CTLT

WHO guideline 2015

Condition	Treatment
Uncomplicated PF	Artemisinin-based combination therapies (ACT) x 3d + 1 dose or primaquine
Uncomplicated PF in Pregnancy	1st trimester: Quinine + clindamycin x 7d 2nd or 3rd trimester: ACT
Uncomplicated PF in HIV	Avoid Sulfadoxine (if Rx with septrin) & amodiqauine (interaction with EFV or AZT
Uncomplicated PV, PO, PM, PK	Chloroquine sensitive: ACT or Chloroquine Chloroquine resistant: ACT + Primaquine 0.25 – 0.5mg/kg x 14d or 0.75mg/kg QW x 8w (G6PD deficiency)
Severe malaria	IV or IM Artesunate x at least 24h until PO is tolerated, Rx x 3d

WHO. Guideline for treatment of malaria (3rd) 2015

ACT

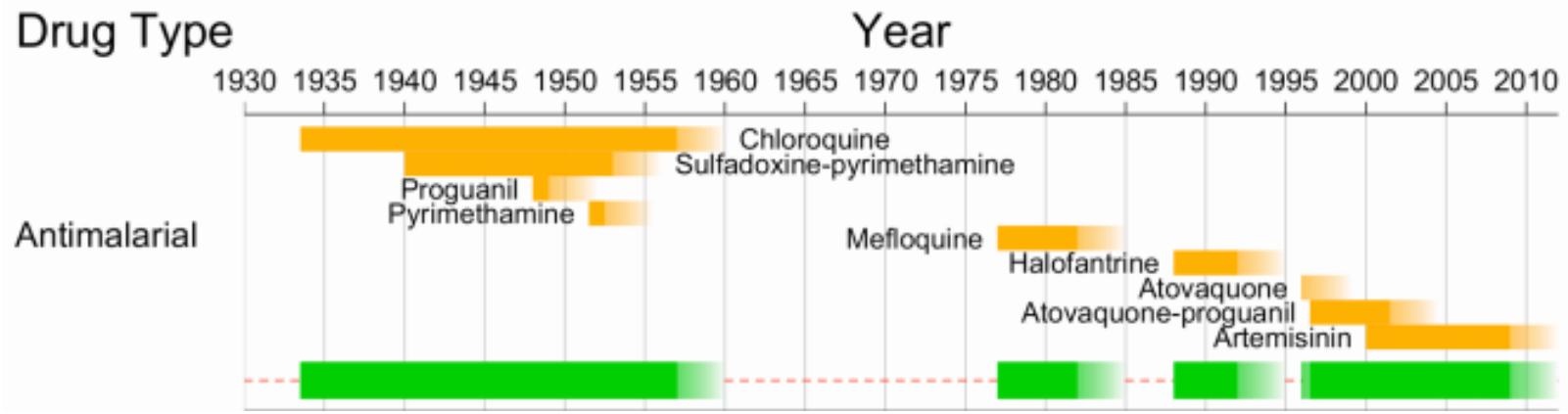
Table 1 | Plasma half-lives of drugs used in artemisinin-based combination therapies

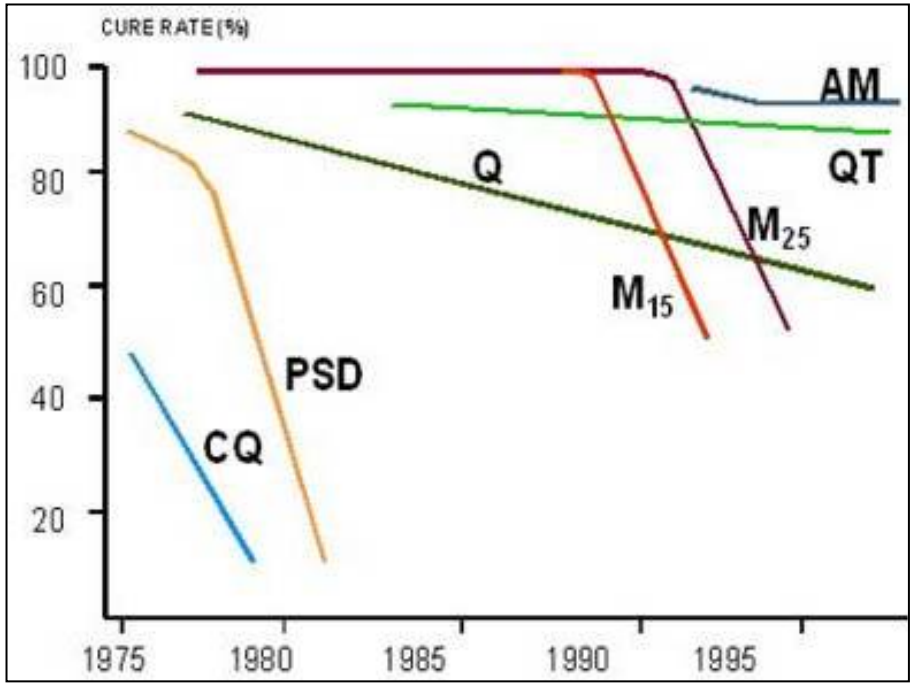
Antimalarial	$t_{1/2}$ of artemisinin derivative	$t_{1/2}$ of partner drug	Regions currently in use*
Artemether–lumefantrine	~3 hr	4–5 days	Africa, EM, SE Asia, WP and SA
Artesunate–mefloquine	<1 hr	14–21 days	Africa, SE Asia, WP and SA
Artesunate–amodiaquine	<1 hr	9–18 days‡	Africa and EM
Dihydroartemisinin–piperaquine	45 min	~5 weeks	SE Asia
Artesunate–pyronaridine§	<1 hr	16 days	NA
Chloroquine‖	NA	1–2 months	Africa, EM, SE Asia, WP and SA
Sulphadoxine–pyrimethamine‖	NA	~4 days (S) or ~8 days (P)	Africa, EM (IPT in Africa, EM and WP)

Eastman RD & Fidock DA. Nat Rev Microbiol 2009;7:864-74

Anti-malarial resistance

Anti-malarials resistance

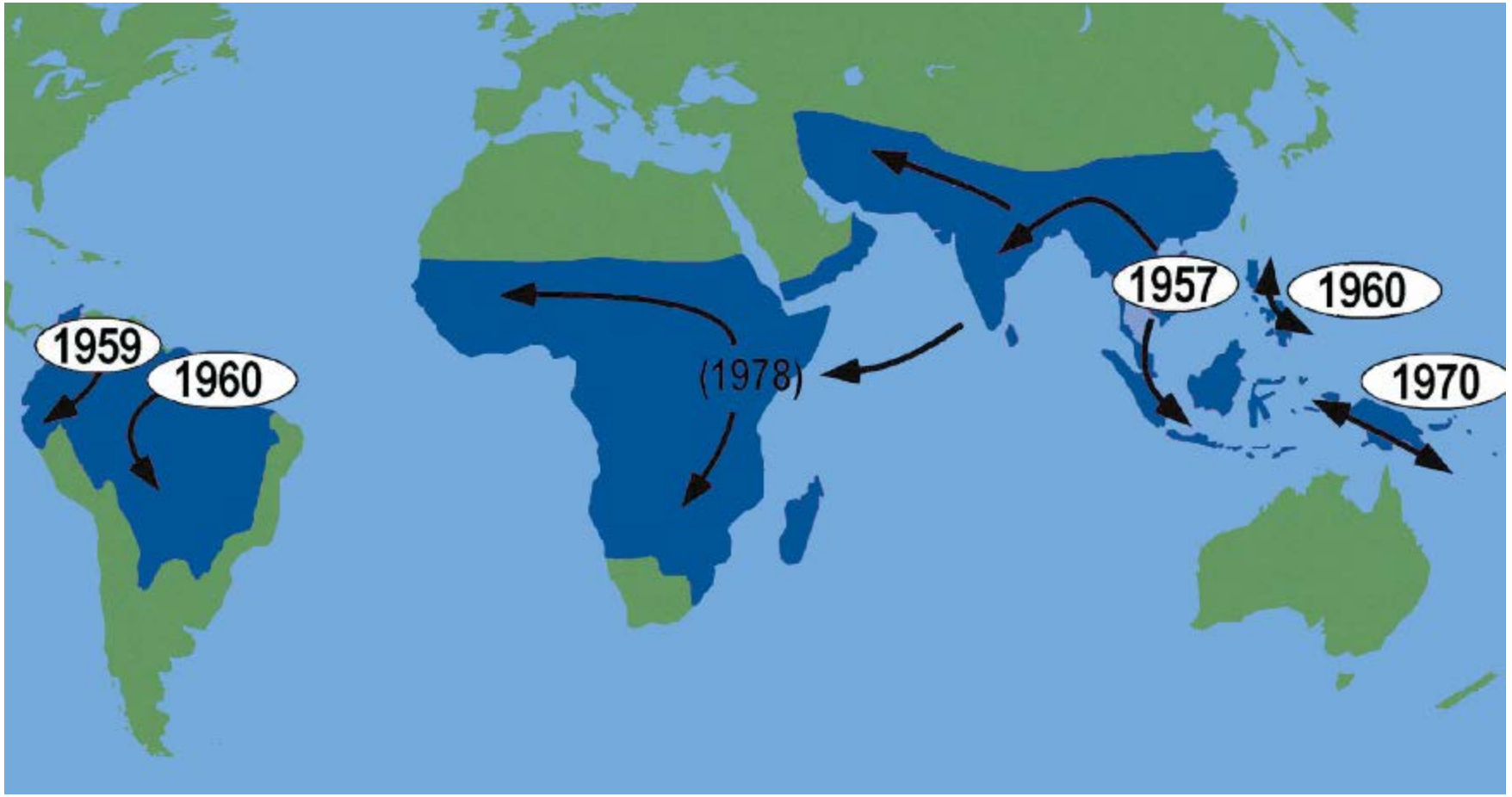




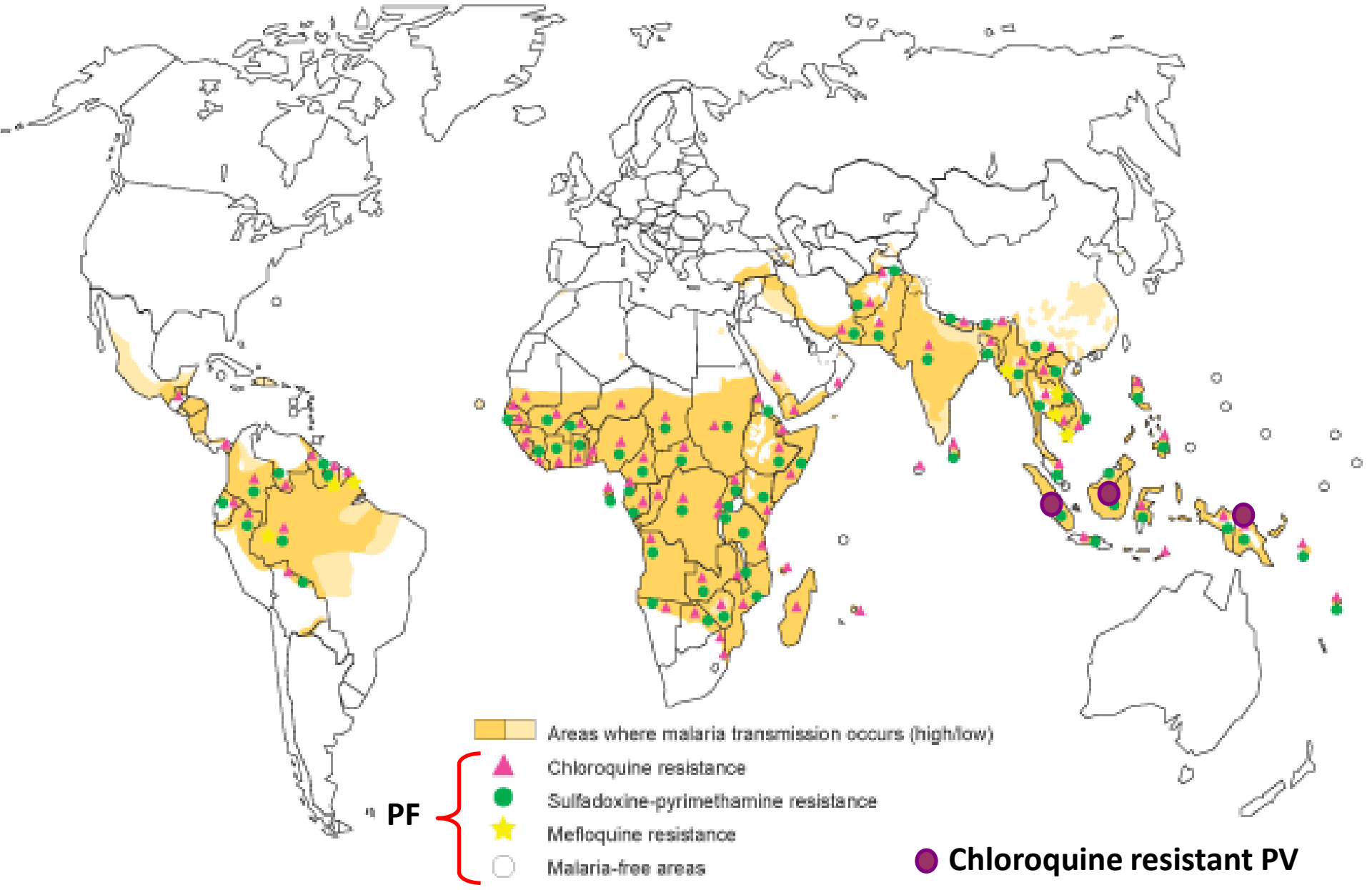
AM: Artemisinin + Mefloquine
QT: Quinine + tetracycline
M_{15}: Mefloquine 15mg/kg
M_{25}: Mefloquine 25mg/kg
PSD: Pyrimethamine + Sulfadoxine
CQ: Chloroquine

http://www.technologyreview.com/view/517126/mathematical-model-reveals-counterintuitive-way-to-beat-multidrug-resistance/

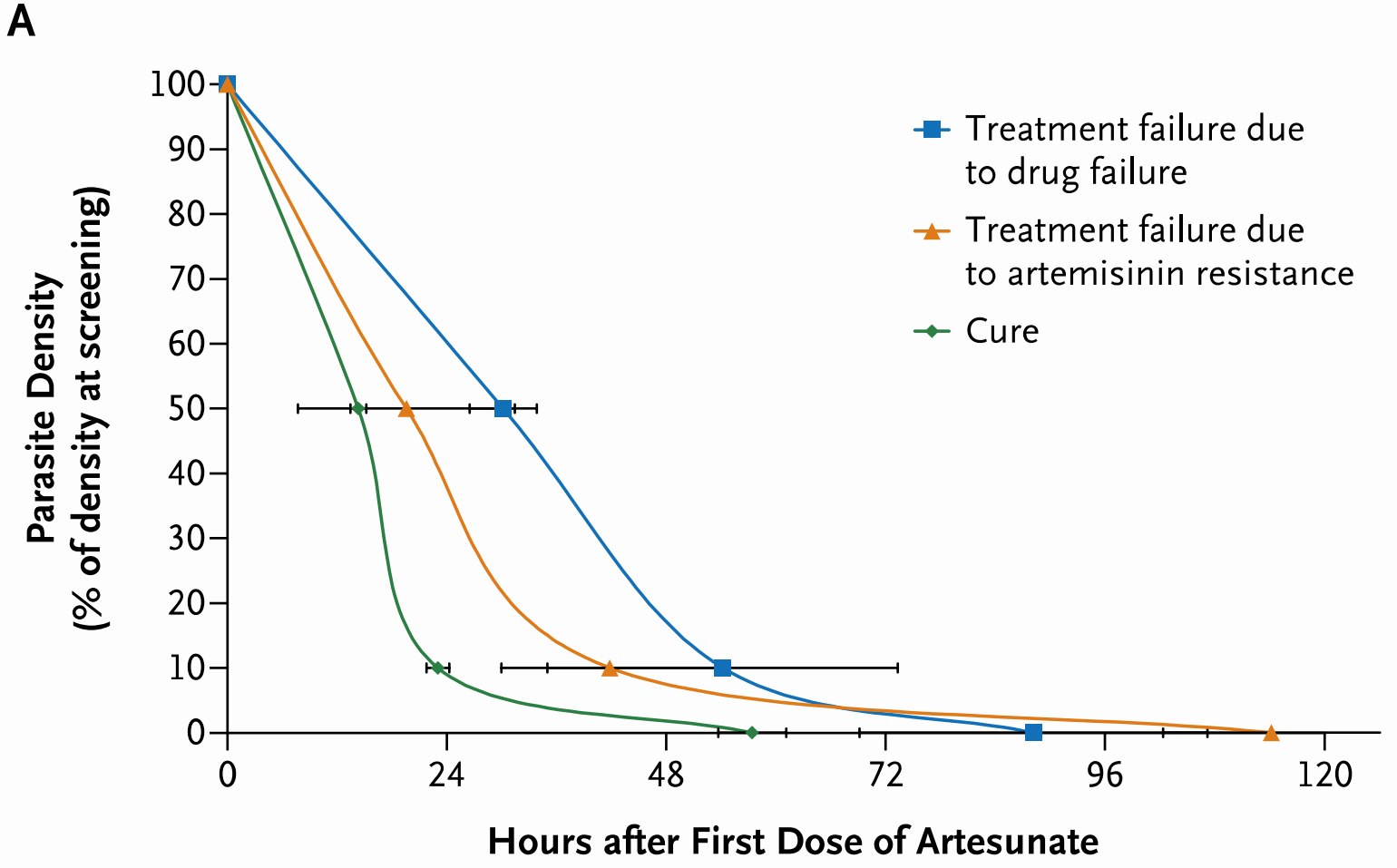
Spread of Chloroquine Resistant Malaria



Wellems. ***Nat Med*** *2004;10:1169-71*

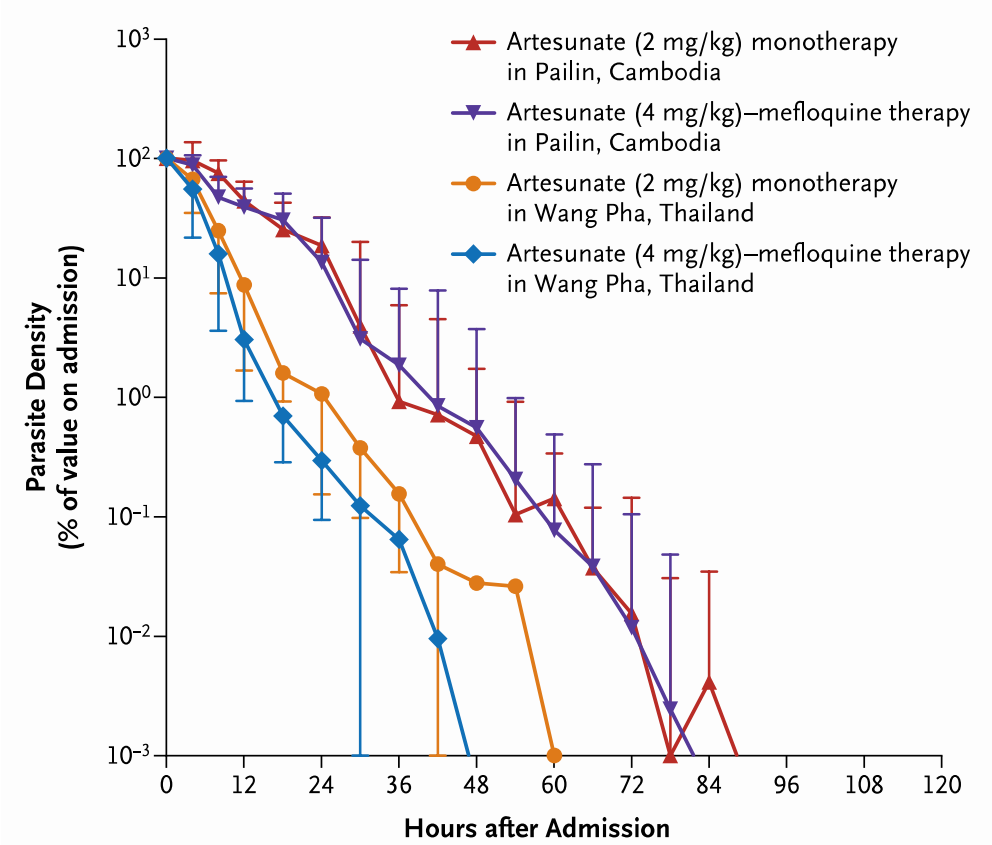

Areas where malaria transmission occurs (high/low)
Chloroquine resistance
Sulfadoxine-pyrimethamine resistance
Mefloquine resistance
Malaria-free areas
PF
Chloroquine resistant PV

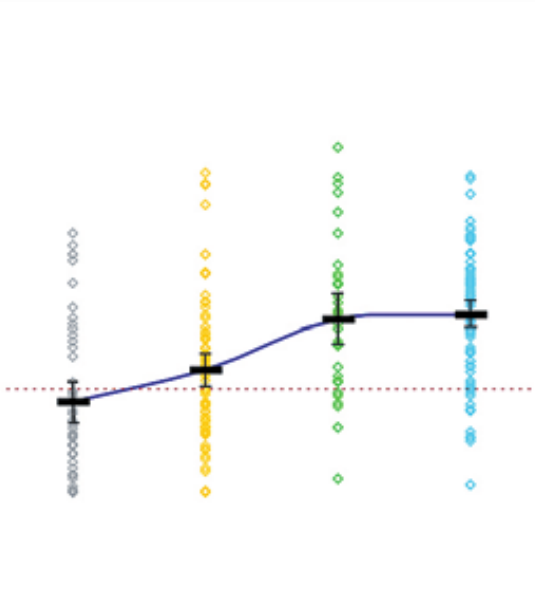
Artemisinin-Resistant Malaria in Western Cambodia



Noedl H, et al. N Eng J Med 2008;359:2619-20

Artemisinin-Resistant in West Cambodia

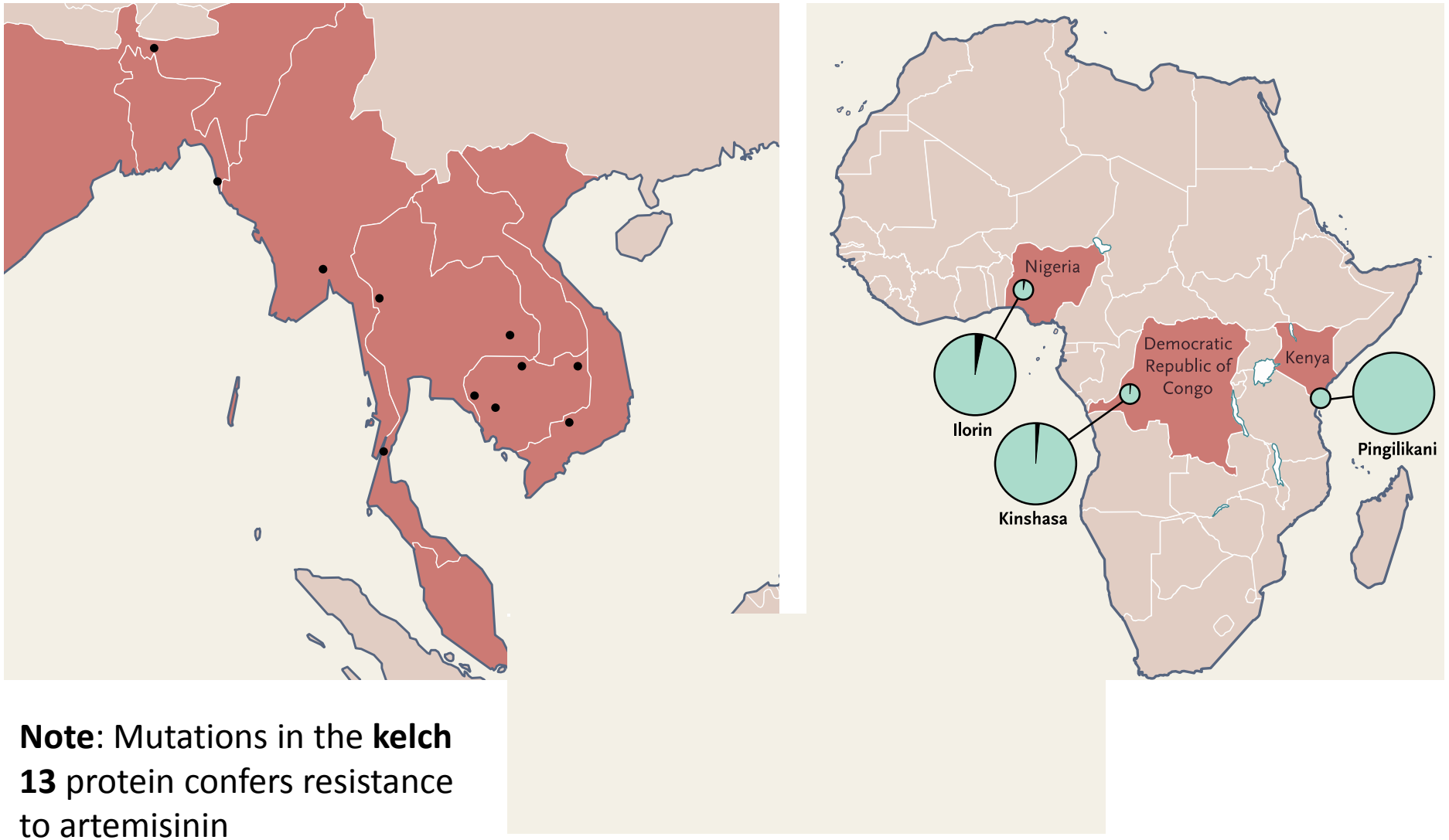




Dondorp AM, et al. N Engl J Med 2009;361:455-67.

Noedl H, et al. N Eng J Med 2009;361:540-1

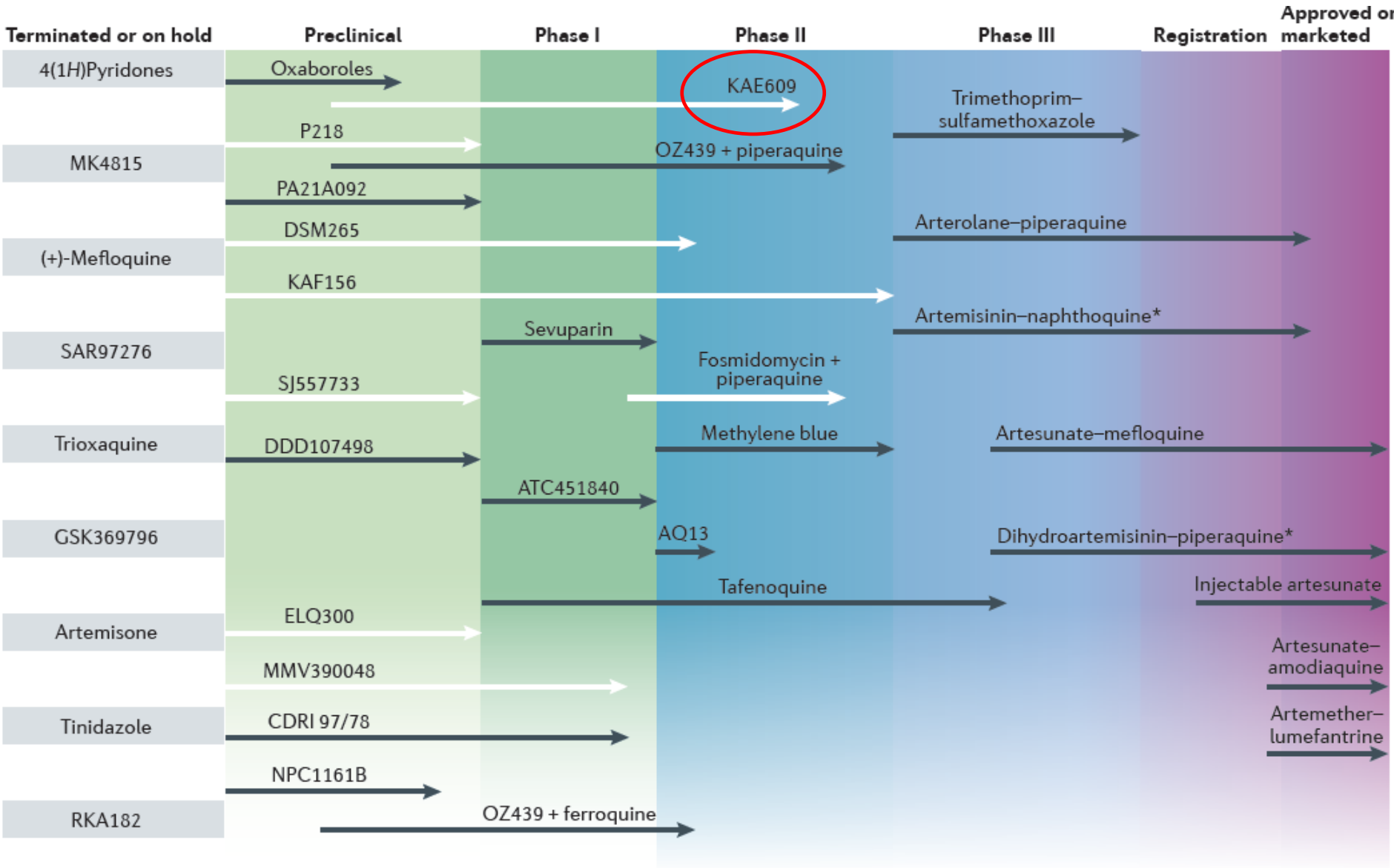
Artemisinin resistance has spread



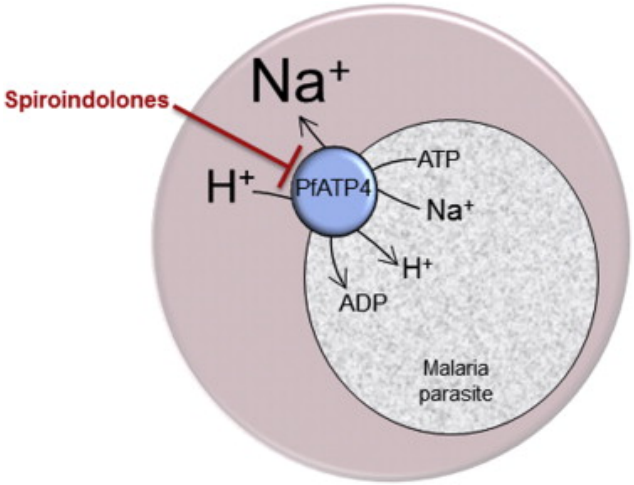
Note: Mutations in the **kelch 13** protein confers resistance to artemisinin

Ashley EA, et al. N Engl J Med 2014;371:411-23.

New medications for malaria



Wells TNC, et al. Nat Rev Drug Discov. 2015 Jun;14(6):424-42



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 31, 2014 VOL. 371 NO. 5

Spiroindolone KAE609 for Falciparum and Vivax Malaria

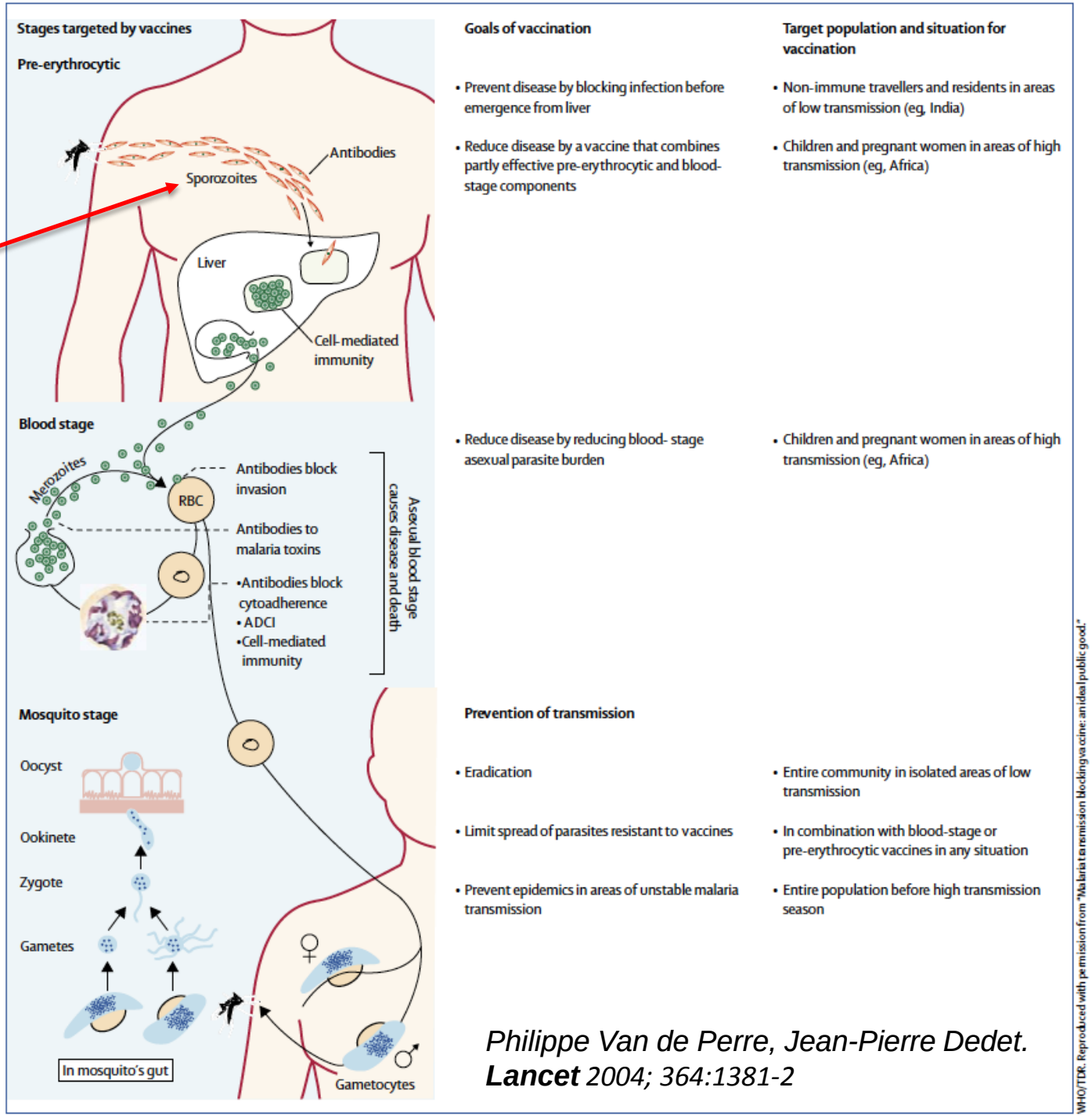
Nicholas J. White, F.R.S., Sasithon Pukrittayakamee, M.B., B.S., D.Phil., Aung Pyae Phyo, M.D., Ronnatrai Rueangweerayut, M.D., François Nosten, M.D., Podjanee Jittamala, M.D., Atthanee Jeeyapant, M.Sc., Jay Prakash Jain, Ph.D., Gilbert Lefèvre, Ph.D., Ruobing Li, M.D., Baldur Magnusson, Ph.D., Thierry T. Diagana, Ph.D., and F. Joel Leong, M.B., B.S., D.Phil.

- Inhibit PfATP4, ie parasite membrane NA-ATPase that regulate Na & osmotic homeostasis
- Vs **both sexual & asexual** forms
- Parasite clearance t1/2 for both Pf & Pv **within an hour**, only < 1% of Pf treated with artesunate can achieve that within an hour
- Reliable absorption and **T1/2 of 20.8h**, allowing QD dose
- Main S/E: nausea & vomiting, but not leading to discontinuation

Table 1. Parasite Clearance in Cohorts of Patients with *Plasmodium vivax* or *P. falciparum* Infection.

End Point	*P. vivax* Cohort (N=10)	*P. falciparum* Cohort (N=11)
	hours	
Time to clearance of asexual parasitemia		
50% clearance	8	12
99% clearance	12	16
100% clearance	30	16
Time to parasite clearance		
Median	12	12
Interquartile range	8–16	10–16
Parasite clearance half-life		
Median*	0.95	0.90
Interquartile range	0.85–1.14	0.78–1.07
Range	0.68–2.01	0.68–1.64

Malaria vaccine



Philippe Van de Perre, Jean-Pierre Dedet. ***Lancet*** *2004; 364:1381-2*

Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial

*RTS,S Clinical Trials Partnership**

Summary

Background The efficacy and safety of the RTS,S/AS01 candidate malaria vaccine during 18 months of follow-up have been published previously. Herein, we report the final results from the same trial, including the efficacy of a booster dose.

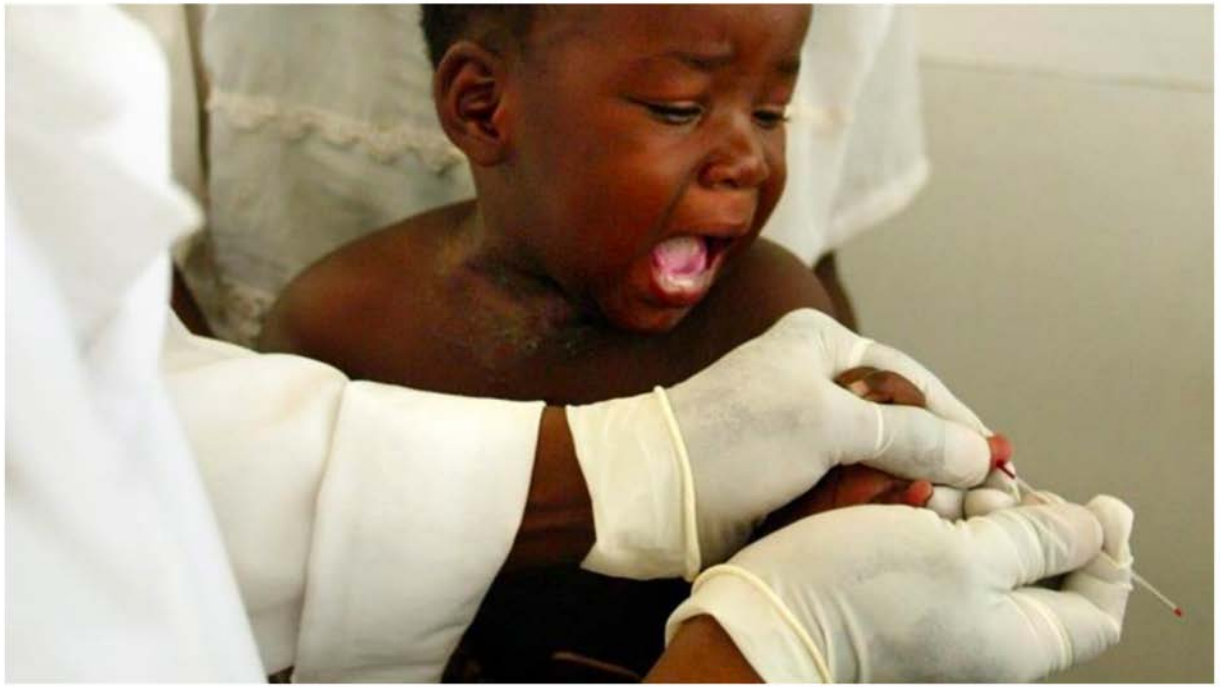
Lancet 2015; 386: 31–45
Published Online

- Vaccine efficacy was modest **32.2%** (95% CI 13.7–46.9)
- But efficacy was detected against:
  - Malaria hospital admission (**34.6%**, 22.5–44.9)
  - All-cause hospital admission (16.5%, 7.2–24.9).

NEWS | MALAWI 25 APRIL 2017

WHO: Malaria vaccine to be 'real life' tested in Africa

Ghana, Kenya and Malawi to start large scale trial of RTS,S injectable vaccine in 2018.



Africa suffers the most from malaria [File: Jon Hrusa/EPA]

The world's first malaria vaccine will be available in selected areas of Ghana, Kenya and Malawi from 2018, according to the World Health Organization (WHO).

The UN body's regional office for Africa said in a statement on Monday that RTS,S injectable vaccine was developed to protect young children from the deadliest form of malaria caused by Plasmodium falciparum.

Thanks