

# The evidence base

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Pathophysiology

Diagnostics

Epidemiology

Drug Discovery

Clinical Trials

Meta-analyses

Optimum  
Therapy &  
National  
Policy

Prescribing  
Adherence  
Drug Quality



R<sub>x</sub>

Patient Use

# What do we know ?

1. Counterfeit medicines have a long, forgotten history
2. They have been reported from most countries, but very few accurate estimates
3. They must increase mortality and morbidity
4. Some contain diverse wrong active ingredients
5. Some contain subtherapeutic amounts of active ingredient – engendering drug resistance

# A forgotten history.....

[ 135 ]

it in substance, it has not always succeeded in stopping the fit in the first instance of its application, but when I have been able to prevail upon my patients to persevere in its use, in the same quantity, I have never known it fail to stop the fit after the second intermission, in which it has been taken. I should imagine there is no reason to believe that the common Bark, which has been used for some years past, is not the same with what was formerly in use, or with what was perhaps, originally introduced; as far as can be judged by its taste, and its appearance, either in the lump, in powder, in decoction, or in any of the other preparations.

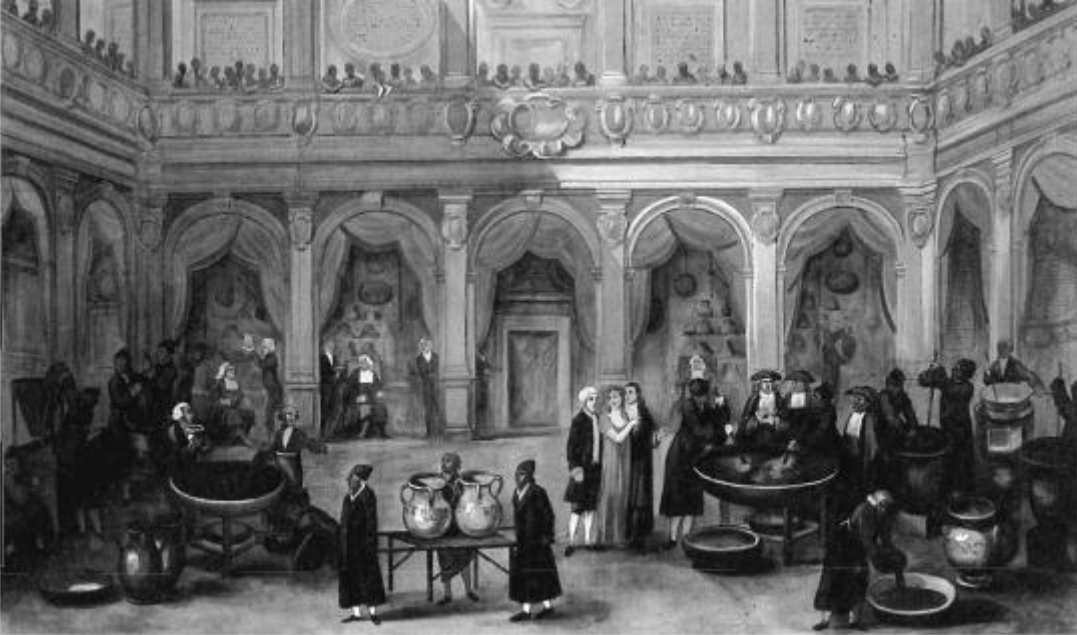
## Looking Back.

FROM

THE LANCET, SATURDAY, April 18th, 1829.

TESTS OF ADULTERATED QUININE.

THE adulteration of quinine is carried than is generally supposed, while the genuine is most important. The high renders it a source of successful imposture of corresponding disappointment to consumers most probably the cause of the various with which it has been used in the several adulterations most frequently used, a preparation of crystals of spermaceti gentianæ, a preparation partaking



# Recent Reports of Poor Quality Antimalarials

## Fakes

- ✧ Chloroquine
- ✧ Quinine
- ✧ Tetracycline/Doxycycline
- ✧ Sulphadoxine-pyrimethamine
- ✧ Sulphalene-pyrimethamine
- ✧ Mefloquine
- ✧ Halofantrine
- ✧ Primaquine
- ✧ Artesunate
- ✧ Intramuscular and oral artemether
- ✧ Dihydroartemisinin
- ✧ Dihydroartemisinin-piperaquine
- ✧ Artemether-lumefantrine

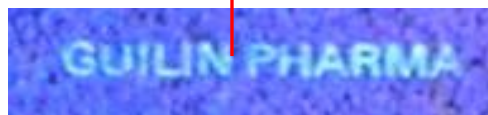
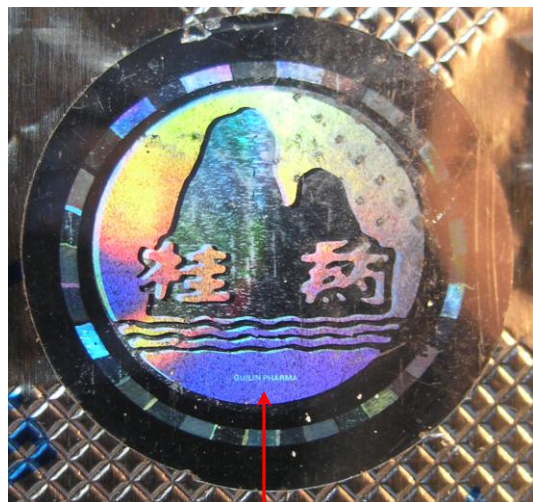
## Substandard

- ✧ Chloroquine
- ✧ Quinine
- ✧ Tetracycline/Doxycycline
- ✧ Sulphadoxine-pyrimethamine
- ✧ Primaquine
- ✧ Artesunate
- ✧ Intramuscular & oral artemether

Not faked ?

Atovaquone-proguanil and iv/im artesunate

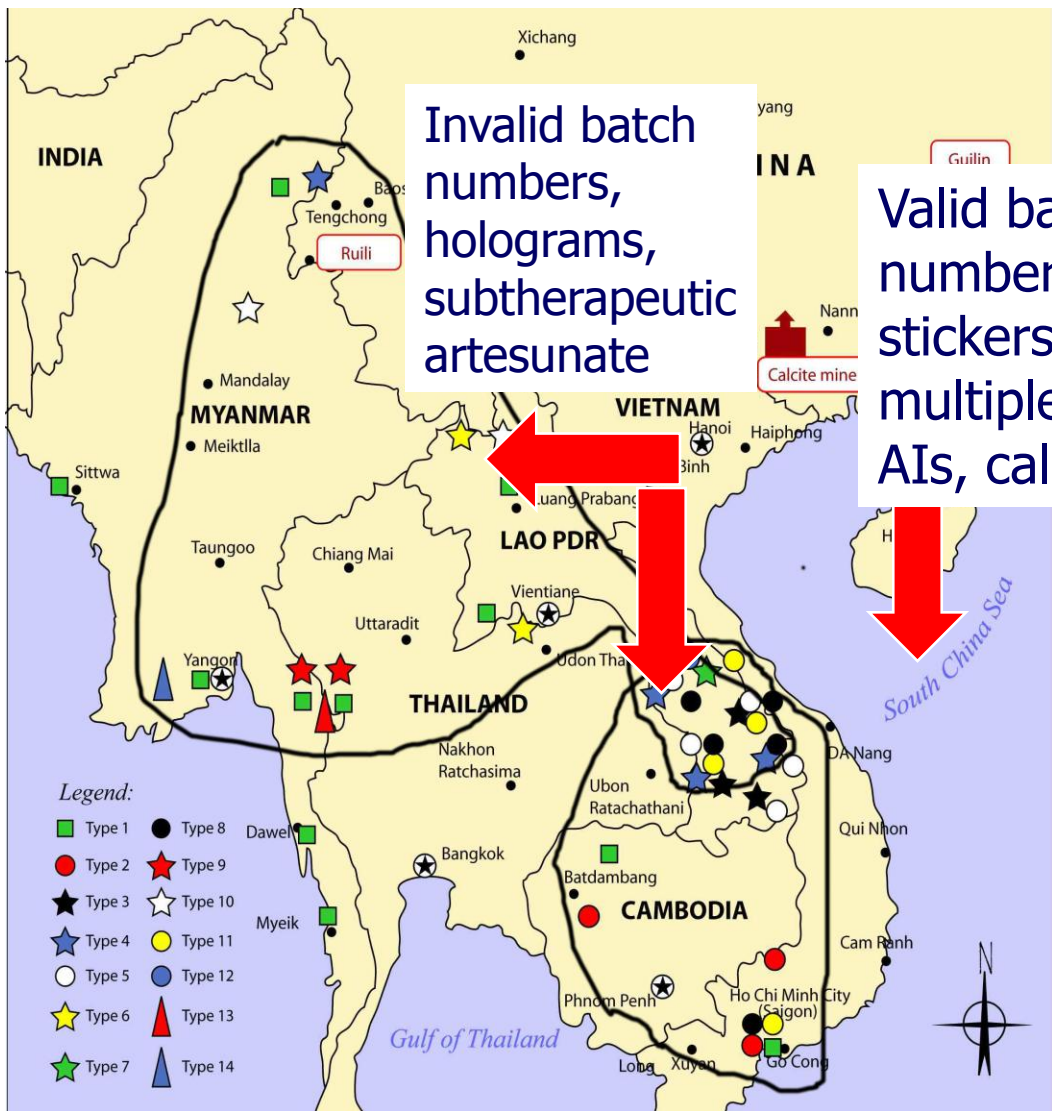
# Genuine



# Fake Artesunate 'Type 4'



- **2000-2001** - 38 % of shop bought artesunate counterfeit
- One NGO bought 100,000 tablets in one shop
- **2002-2003** - 53% of shop bought artesunate was counterfeit



Seized 24,000 of 240,000 blisterpacks traded by those arrested

# Fake artesunate 'wrong' ingredients

- Paracetamol
- Sulphadoxine
- Pyrimethamine
- Dimethylfumarate
- Erythromycin A-F
- Erucamide
- **Safrole**
- **Artemisinin**
- **Metamizole**
- Chloramphenicol
- Metronidazole
- Chloroquine
- Sulphamethoxazole



**Sildenafil** in fake DHA-  
piperazine in East Africa

**Chloroquine** in fake artesunate in  
Cameroon

# Sub-therapeutic artesunate/artemisinin in fakes

- Fake artesunate from Thai/Burma border contain 3-10 mg artesunate per tablet (genuine tablet ~ 50mg artesunate)
- Artemisinin in fake halofantrine in West Africa
- 15% of fake artesunate in Laos contained artemisinin ... 400km from the epicentre of artesunate resistance



# Substandard medicines

Genuine packaging but incorrect quantity of ingredient – due to poor production and quality assurance. Carelessness rather than criminality

- Different causes and solutions - but critical problem in treatment failure and drug resistance
- Probably more important than fakes in driving drug resistance

# How common are they ?

Using random sampling

- Nigeria – 48% of essential medicines from 35 pharmacies **poor quality**
- Tanzania – 12% of antimalarials collected across country **poor quality**
- Kenya – 49% SP and 31% amodiaquine **poor quality**
- Laos – 88 % artesunate were **fake**

# Impact

If those with a potentially fatal but curable disease are treated with medicine without active ingredient.....only guesses at **avoidable mortality & morbidity** available

**Economic losses** for patients, their families, the genuine pharmaceutical industry

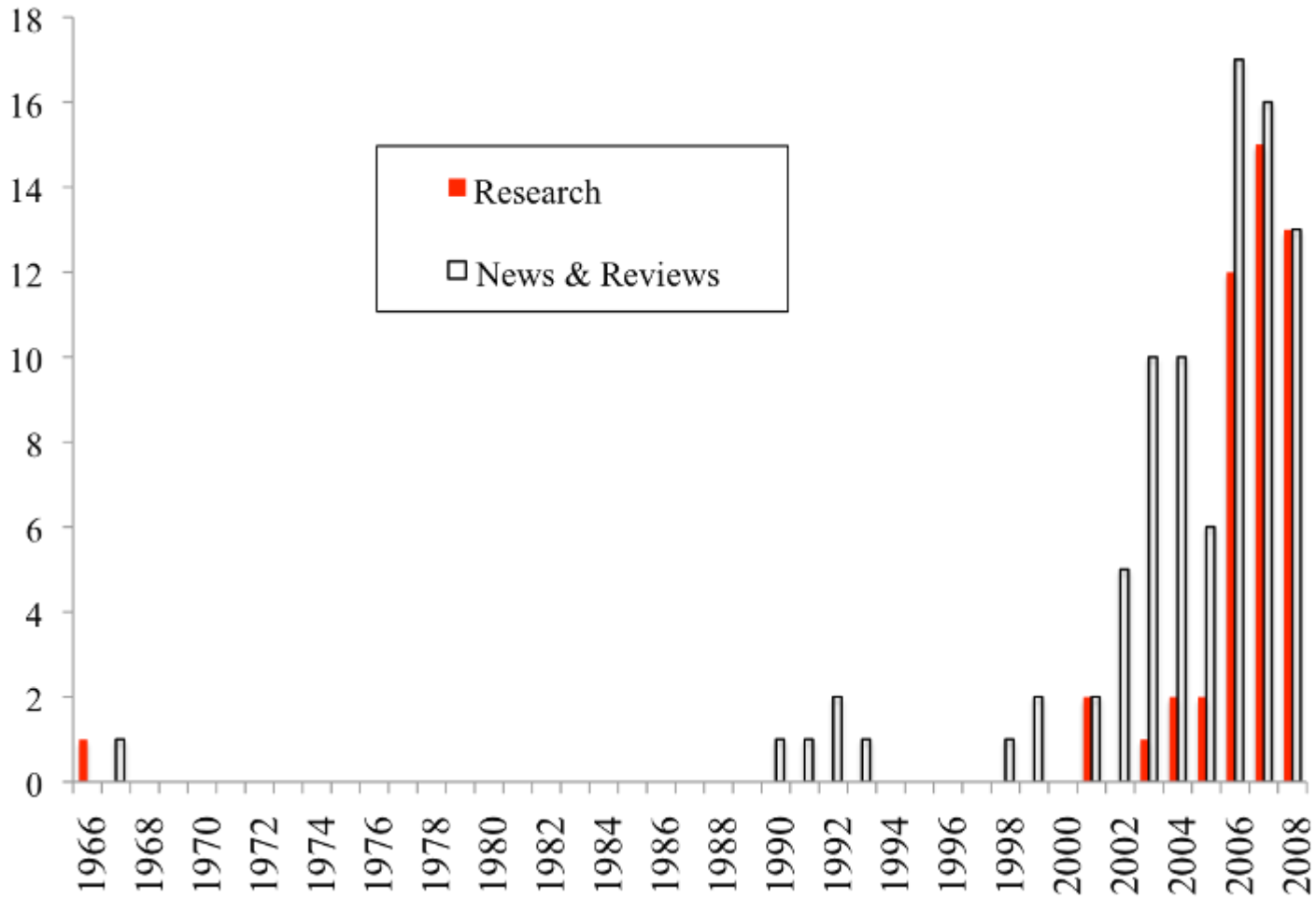
**Loss of faith** in medicines, health systems, MRAs and the pharmaceutical industry

**Drug resistance**

# We do not know

- The prevalence and geography of fake medicines
- Are counterfeit or substandard drugs the most significant in terms of public health ?
- Do health workers/patients know about them ?
- What are the most cost-effective accessible detection methods ?
- What are the most appropriate institutional, educational and enforcement interventions

# PubMed 'counterfeit drugs'



# Research Agenda ?

**To provide evidence** to support a surge in action to improve the quality of essential medicines, especially in the ‘developing world’

How common are they, what are the supply chains ?

What do people know about them ?

What are their public health & economic impact ?

Where do they come from ?

How can they be detected ?

What interventions work ?

# Prevalence ?

**Convenience** sampling – inherently prone to bias.  
Therefore, conventional or Lot Quality Assurance  
**random** sampling needed to obtain accurate  
estimates of the prevalence of counterfeit &  
substandard drugs in diverse areas, especially  
Africa

1. ACT Consortium – B & M Gates Foundation
2. ACT Watch - B & M Gates Foundation
3. US Pharmacopeia - USAID
4. WHO



# CODFIN - Counterfeit Drug Forensic Investigation Network



- a free forensic chemical/botanical analysis service for suspected poor quality antimalarials
- Build a web-based library of genuine and counterfeit medicines – packaging & chemistry

## IMPACT - International Medical Products Anti-Counterfeiting Taskforce

Coordinating international stakeholders in combating fake medicines . Bringing enforcement and regulators together – multiple collaborations leading to seizures and arrests

# Rapid assessment tools

Development and evaluation of rapid techniques for medicine quality assessment - to empower drug inspectors & police

Being used in China

No field research as to which is the most appropriate technology

Raman, NIR (ready to deploy), mass spec & ion-mobility (under development) ‘guns’ portable, battery powered, no consumables needed



# Interventions policy & practice

Difficult – networks need to be built

Still too much **secrecy**. Not enough **will**

Advocacy to raise awareness of importance for public health, increase political will and stimulate research

How to inform people of the problem - so that they can help demand better drug quality ?

- Multiple problems need action
- **30% of global drug regulatory authorities** have ‘no drug regulation or a capacity that hardly functions’ A major under recognised problem. How to support the keystones
- **Two** laboratories for drug analysis in malarious Africa are WHO pre-qualified
- Regional analysis laboratories needed
- Increased liaison between police and MRAs
- **No situational analysis** of what is being done and what needs to be done

# Thank you

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**wellcome**trust

