The dreadful Bight of Benin

Beware of the Bight of Benin
Few came out though many went in
Malaria

- WHO estimate:
  2-300 million deaths in 20th century
  = annual 3 million

Agriculture, irrigation, settlements, higher population density, like the Fertile crescent..

Female mosquitoes with human blood preference

Roman fever, King of fevers (Vedas), Alexander the Great (323 B.C. in Mesopotamia), Hippocrates (460-377 B.C.)

Marsh fever, tertian, quatrian, recurrent fever
The parazite and mala-aria

• The protozoan parazite - Alfons Laveran 1880
• The vector: ANOPHELES - Ronald Mosquito Ross 1900
• 4 types of plasmodia
• Rossi 1900
  P. vivax tertian (benign)
  P. ovale
  P. malariae (quartan) - may stay in host for decades>infect mosquito>
  \( P. falciparum \) (malignant tertian, tropical malaria) relatively new, Mediterranean region
  \textit{the distant relative of bird malaria,}
The name of the medicine, the bark of Loxa, the Legend

quina, ghina, guina = the bark (quechua-inka)

- Bado, Genoa 1653
- The miraculous recovery of Countess Chinchon wife if the Viceroy in Peru
- Linne: Cinchona officinalis 1742 (La Condamine)
The names of the bark

- From Loxa Protectorate>
  The Loxa bark
- Peruvian bark
- Jesuit’s Bark
- Cardinals Bark as champion for the use of the bark was Cardinal de Lugo as Director of Hospital Santo Spirito.
- Bark tested by the Pope’s physician Fonseca. It appeared in 1651 in Schedula Romana as “Corticus Peruvianus”
The meaning of the quinine/bark
Agustino Salumbrino 1630

- Different meaning of the bark in the Americas and for Europeans?
- San Pablo Hospital/Lima-Salumbrino
- Analogue symptoms: shaking, shivering from cold and in the fever attack of malaria
- 1492 and Genetic Polymorphism: P. falciparum and vivax probably not in the Americas < (No thalassemia, sickle cell anaemia, favism/ G6PH deficiency/, Baghdad fever, RBC Duffy negativity).
- Roman fever to be treated with Indian brew of bark against shivering?
- (Nocturnal) leg cramp
Semper aliquid novum ex Africa?

Galen and his teaching:
fever = mixing of bad biles in blood that causes boiling of it
Therapy: purging, bloodletting
no mention of the bark by Galen
The prestige, the authority

• Albrecht Durer in Zeeland (the Netherlands), 1520
England

„He had a fever when he was in Spain
And when the fit was on him
I did mark how he did shake”
Shakespeare Julius Caesar Act I. Scene 2,
Line 119

Daniel Defoe: .. the youth from London
return from Essex loaden with the kill
and ...of Essex Ague.
Robinson Crusoe...

The Jesuit Plot and CROMWELL
Jesuit’s or Cardinal’s bark suspicious
First advertisement for Peruvian Bark in 1658!
by Antwerp merchant

The Quack or Chevalier( 1678):
Robert Talbor: The PYRETIATRO
The English Remedy: Peruvian bark in Port Wine
The fever tree and the gunpowder

• Torti, 1711: the bark useful against certain fevers, but not all!
• Ramazzini 1700: the cortex is of similar importance than the invention of gunpowder in war
Bight of Benin

- Oil Rivers (Niger)
  - Palm oil for machinery as lubricant, soap, food
  - In 1810: 1,000 tons Palm oil
  - In 1855: 40,000 tons

Gold coast, Slave coast, Ivory coast…

Inland travel on rivers:
- Nile, Niger etc.
..few came out..

- 50% of soldiers died in a year (483 out of 1000)
- „a man of 25 after 2 years in this climate looks 10 years older, Europeans die here in 10-12 years” written by Magyar László (lived 1848-1856+ in Africa)
- carneirado, meat grinder carnivorous climate
The new meaning: Prevention
Dr. W. BAIKIE

- Mungo Park 1805 Gambia 2 survives of 46

- Baikie: **Narrative on the rivers Binue and Kwora** (Niger and Tsadda) 1854
  “a great modern discovery is that quinine not only cures but that actually prevents ..”
  “avoid night exposure sleeping in open air .. calomel has no real or curative effect” from his **Treatise of Quinine** 1856 – not published.
Pure Quinine

- 1816 Gomes, Portuguese naval surgeon isolated febrifuge Cinchonin
- 1820 Caventou and Pelletier: quinine
Travellers - and Scramble for Africa

Livingstone: "a dose of quinine was administered in cherry wine but before it a dose of calomel and a dose of jalap or rhubarb and 4 grains of chinin or larger doses in every two hours or so till the ears ring or deafness ensues, this last is the essential part of the cure". 1859 Zambesi Report

Stanley: "the Doctor’s prescription consists of 3 grains of resin of jalap, 3 grs of calomel with Tinct. cardamoms just to prevent irritation of the stomach. Quinine should be taken with this pills.. My stomach could never bear quinine unless subsequent to a cathartic... 3 grains of tartar emetic to eject bilious matter from the stomach. (How I found..1885)

Magyar: "I took a dose of castor oil and 12-16 grains of sulfate of quinine and repeated it 4, 8 hours"
Plantations: Quinine makes the Market

- The demand for quinine is soaring high
- Source was Spanish monopoly
- New plantations established by the English and Dutch in India and the Far East from middle of 19th century.
- Seeds, seedlings smuggled out from Spanish Americas: Spruce, Markham, Hasskarl (C. succirubra) and the best tree C. calisaya by Charles Ledger and Bolivian Manuel Incra Mamani +.
- Quinine content 2-3% vs 14%
- Price of calisaya (also called ledgeriana) bark 5x than price of succirubra bark
The Kinabureau

- Factories produce quinine from C. ledgeriana
- Amsterdam and Dutch Kininfabrik, Bandung Factory in the Far-East
- Amsterdam: the centre of quinine market: Kinabureau

Less potent C. succirubra mixture: totaquine

Sold in British India „one rupee one ounce” = poor men’s quinine.

Encouraged by the Secretary of State of India: the first „continental” size programme against a disease that killed millions in the Subcontinent.

The WWs caused quinine shortage and started research for quinine analogues Results: pamaquine, CHLOROQUINE, … artemisin derivates

Present: annual quinine production: 300-500 to (5,000-10,000 to bark)
Taste of Quinine

- Half of Quinine productuin used by food industry
- Indian Tonic Water
- (Dr Rozsnyai, Hungarian pharmacist: Chininum tannicum: a tastless salt (1863))
Eradication?

- The Vectors: DDT and insecticides
- Mosquito net (impregnated)
- Vaccines
- To fight the enzymes that help plasmodium resistency
Cinchona trees

- The latest plantation in Bakuvu, Rwanda.
- Quinine is used in resistant malaria in injections,
- The Arms of Peru with the Cinchona tree