

## Navy logbooks, Malaria Prophylaxis and " Good Quinine Practice"

The heavy toll malaria took from the Europeans in Africa was reduced substantially in the 2nd half of the 19th century. It happened many decades before the plasmodia or the Anopheles vector were discovered. Malaria was still explained as a poisoning of putrid, miasma air. Statistical analyses of the health reports of the Navy and Troops led to wide use of malaria prophylaxis - and a practice that today we'd call Good Quinine Practice.

Standardization: a standard concentration quinine-wine was issued. Compliance: quinine-wine was more palatable easier, safer dosed –especially. Dose-finding: curative doses were determined and also ! duration of quinine treatment was extended in ague after fever was controlled. A „prophylactic“ quinine treatment was tested that protected from the poisonous miasma - for a period of 2 weeks, that is the incubation period of plasmodia. It resulted in stopping recurrence of bouts. Patient information: quinine-wine that was packed in the medicinal chest of the boats had a written instruction for use = PIL. SOP: navy surgeons were instructed ( SOP ) to register results, in other words to follow-up the cases. Validation: the surgeon of the Niger expedition in 1854 conducted a clinical trial and validated the prophylaxis concept. The measures mostly came from the analyses of the Navy (Troops ) reports – of the West African Squadron -and from other navy or troops sources. Hindsight may be misleading that we read 'into' the story something that was originally not there. But let us judge it after we have read this:

Europeans in Africa did not have the advantages of inherited immunity from genetic polymorphism ( e.g. Duffy-negativity or sickle-c. a. etc. ) or carried relative immunity that the individual acquires when spending long years in a „stable“ endemic region. (That relative immunity will be lost within a few months when reinfection stops - it seems to happen with the use of ITNs recently !) There were notorious fever coasts in the 19<sup>th</sup> century e.g. in Equatorial West Africa which the Portuguese called „The White Men's Grave“ in the Bight of Benin. Sources for statistical analyses of health reports: European presence in the West African region developed after the slave trade was banned at the early 19th century. The British West African Squadron ( W.A.S.) patrolled the African coasts and sea routes of the slavers. Annually that was a one thousand strong crew in the W.A.S. between 1825 and 1845. Total number was 20 604 marines.

For illustrations here is a text from the Journals of Laszlo Magyar ( 1818-1864 ).

Magyar was a Hungarian ex-navy officer Laszlo ( Ngana Komo by his African name ) served as the Admiral for the King of Calabar for two years. In 1848 he sailed up the estuary of the Kongo, crossed the Bahia dos Ingleses and reached Boma, the largest slave trade centre there. He moved south to Benguela where he married the daughter of a local king. As member of the royal family he could travel freely in today's Angola. In 1853 in Makolole crossed paths with Livingstone. Magyar died in 1864 – most probably of malaria.

He wrote in 16 May 1848 in his journal as he passed the Island of Coconuts:..."*This notorious settlement lies at some 70 miles from the delta (of River Congo). ..The climate is deadly miasma, steaming. ..no European can stand this for more than three years. The white slave traders only stick it because of their greed... ten per cent of these demoralised humans die every year My readers can imagine my position: I was alone, a Hungarian by nationality, who appeared unexpectedly through unknown routes among these piratical slave traders of some thirty nationalities, whose language mostly Spanish or Portuguese, I could speak. But I am a former naval officer, they regarded me as their sworn enemy . What does this Austro-Hungarian dog seek here, the ruder ones among them asked each other, others asserted that I must be the spy of some English cruiser and I wanted to ascertain the topography of their hideout, the number of the slaves they bought, the time and place of their embarkation, as a result of which it would be easy for the English not only to catch them on the high seas, but knowing the route up-river and the location of their depots, raid them there. ..From my own observations, I estimate the goods in the depots here are worth some two million Spanish Thalers and the number of slaves dispatched from here to diverse parts of the Americas at about 20.000 per annum.."*

Death rate was awfully high. The annual death rate among European settlers and troops was around 50 %, it was 20 % among sailors and merchants.

Therapy for fevers:

Fevers, like malaria in the early 19th century were explained by Galen's doctrine and it defined the therapy: The "poisoned" blood called for 1. blood letting or leeches 2. purging and emetics ( *Citrullus colocynthis*, *Jalap*, *Rhubarb*, *Seidlitz powder*, *Cascarilla* ), 3. mercury – kalomel /Hg Cl/ ( successful in syphilis) in doses up to 10-30 times of R.D.Ds. ), 4. Tonics :*Peruvian Bark-Quinine*, wine or champagne! Quinine administered usually in too low doses and discontinued too early ).

The (British ) Admiralty collected reports from 1816 from naval physicians, surgeons on the diseases in their service regions and of causes of deaths. In these reports fevers were identified by the name of a river or coast or jungle. Many of these were malaria but there were yellow fever or black vomit, vomiting fever, then typhoid and dysentery etc. The hope of many who moved to the new tropical regions that they may get used to the diseases,"seasoned" was an illusion. Geographic medicine used many names for the deadly fevers in tropical regions: Coimbatore fever, Guzzerat fever, Coromandel Fever, Mediterranean fever, Bengali fever, Roman fever, etc.. Actually far too many names for malaria.

Quinine :

Peruvian Bark was introduced into the Navy Medicine Chest in 1814 ( Article 9. ) and from 1830-ties it was quinine or amorphous quinine. Not as a drug of first choice! It was up to the navy physician to give it or not. The bark and the quinine powder were not very popular among the patients because of the bitter taste (a large amount of powdered bark was given which was disgusting even mixed in sweet wine. The officers and navy doctors doubted the effectiveness:

Counterfeits: the bark was expensive so quina was mixed or replaced with other barks ( e.g. cherry bark - similar colour, aloe was used to increase bitterness) . Alkaloid content varied between 1-15% in different *Cinchona* sub-species, depended on the area it was harvested. *C. succirubra* had 3 % while *C. calisaya* up to 15 % .

Quinine /bark was listed as a tonic in recuperation after the febrile period. It was administered late and then discontinued early. There was no standard dose regimen e.g. H.M. Stanley wrote he took quinine until tinnitus and blurred vision developed that is cinchonism but at least under dosage could not be a problem.

Statistics:

In the first half of the 19th century a huge amount of data were collected from different fields of human activities including the health reports from troops and navy stationed overseas in the tropical regions. The Statistical Section of British Association for the Advancement for Sciences was formed in 1831.

In the army health service Captain A.M. Tullock studied health reports and wrote in 1838 „ On Sickness and Mortality among Troops in the West Indies”. He made a study for the Navy after his analyses of reports from 1830-1836.

Log Books

In 1846 the Physician of the Navy from the R. Admiralty ordered Dr Alexander Bryson to compile a report to explain staggering high mortality. Dr Bryson himself was a Navy physician and served in West Africa in 1831-32. He studied Navy records, log-books between 1820 and 1846. During this period more than 20 000 marines served in the West African region. Bryson studied the routes of each ship, recorded the ports, anchorage, landings for water or wood etc. and the health status of the crews.

In his report he quoted from logbooks of the boats e.g.:

„...the crew including a marine obliged to remain in the bush drenched with rain until morning. 4 or 5 days afterwards...six of the men were attacked with fever of remittent form”

HMS Maidstone 1826 at St. Thomas

„...20 of the crew were employed on boats on the shore embarking provision. they had wine and bark as directed with the exception of lieutenant Boulton. he was the only one of the whole party who suffered from

HMS North star 1926 Sierra Leone

„... the boats crew that were most employed in the River Gambia, bark and port wine were administered and their immunity from the fever is to be attributed to their administration.”

HMS Etna 1834

Bryson's 250 pages report was published in 1847.

Conclusions: There are fever regions, spots, in estuaries, coasts, mangrove – marshes, fever seasons.

Boats should anchor in at least one nautical mile off the shore for the safety from the miasma poison of malaria. ( The flying range of Anopheles mosquito is 1500-2000 meters, same of Aedes aegypti - vector for yellow fever - only a few hundred meters )

Landing: crew should go on shore only when necessary e.g. for water, fuel wood. A written order should be issued with the reason for landing,

Staying on the land overnight or longer: it should be avoided if possible or reduce for the shortest stay.

If the crew was forced to spend the night on land overnight they should use oilskin cover and staying and sleeping in the boat was the safest during night. Even a mosquito net would prevent inhalation of miasma!!

Before Bryson's report Peruvian bark or quinine mixed in wine was given to the marines and it was repeated upon returning from the land. Bryson observed that fever developed usually 4-20 days after their return on board. He thought that it was an incubation period of the toxic miasma. He recommended that quinine should be continued for at least 14 days after the return from the land.( The estimated incubation period of : *P. falciparum*: 12 days, *P. Ovale* 17 days, *P. malariae* 18-40 days and *P. vivax* 15 days but can be as long as 6-12 months! )

Bryson suggested that quinine therapy should be based on new grounds: not as a tonic to strengthen the body but as a preventive or therapeutic agent that cures or prevents the toxic effect of the miasma.

By Bryson's report in 1847 quinine was introduced on all navy ships sailing in fever infested regions with instructions for the use ( SOP ).

Amorphous or pure quinine was dissolved in wine 4 grains/ 1 ounce ( 260 mg/ 30 ml ). This was a standardized medicine and this was a medicine that met patient compliance with the improved taste of the medicine. Quinine in a piece of paper could easily be blown in the wind, or spoiled by the seawater, humidity in a boat patrolling the coast. The wine tubes were packed into wine-chests that gave enough protection when handled from the ship onto barges or boats. A written instruction for use or a PIL was put into each wine-chest. Army and Navy medical staff had to report the effect of the Bryson project. Was it not the follow-up and a validation of incubation time?

Bryson's 1854 Navy Medical Report gave a summary of the results for prophylactic use and evaluated the feedback information e.g.:

..upon return on board " Immediately after they returned on board, the bark was discontinued. This was evidently wrong; for, although we know that both bark and quinine will prevent the occurrence of anguish paroxysm, and probably prevent the evolution of remitting fever, the influence of the bark or quinine had ceased...the evolution of the fever might take place at any time within twenty days from the day the persons were last exposed on shore..

The effectiveness of the bark or quinine were monitored.

" During our stay in the River Lagos quinine wine was regularly offered to the men morning and evening, - all took it, i believe, except two midshipmen and two seamen belonging to the galley. those four persons subsequently each suffered a severe attack of fever, while, in the whole force, consisting of upward 220 men, there occurred only a few other cases of trifling importance. „ by Mr. Heath, Navy Surgeon 1851

The proper doses of quinine were established in many steps:

Over-dosage and symptoms of cinchonism was an indicator, often however quinine was under-dosed. Pelletier studied cinchonine ( Gomez, 1816 ) and quinine( Pelletier, Caventou 1820) and compared the curative doses. Eliotson published in 1823 in England that 3grains of quinine were not effective, doses of 5 grains of 3 to 4 times daily ( 330 mg ) should be taken. Dr Thomson, a Navy surgeon published in 1845 that dose of 16 to 20 grains ( 1.0 – 1.26 g ) of quinine once or twice daily were effective. Dr Baikie preferred quinine to the Peruvian Bark, the latter was not standardized, the strength or effectiveness depended on the content of quinine ( and other alkaloids ) of the bark, the pure christalline quinine was dosed and administered easier and with accuracy.

#### Mortality of the British Troops between 1859-1875

Year	Death/ thousand		
1859	666.	1868	66.67
1861	181.80	1869	0.00
1862	n.a.	1870	n.a.
1863	n.a.	1871	250
1864	n.a.	1872	0.00
1865	66.67	1873	145.45
1866	66.67	1875	111.11
1867	133.33		

Mean value in this period 151.45

The story of the follow-up: Bryson summarized the results of the new policy in 1854.. Due to an apparent *success he recommended that merchant vessels should be provided with quinine wine*, too. The Admiralty ordered a scientific manual from Bryson – an SOP- on malaria prevention for the navy officers the „ *Medicine and Medical Statistics together with other papers* by scientists like J. Herschel and Ch. Darwin. A clinical trial on the River Kwora ( Niger ): Bryson sent a young physician Dr W.B..Baikie in 1854 to test the prophylaxis with the expedition of the River Niger. He proved that quinine taken for additional two weeks after leaving fever-land was effective. No (malaria) death occurred to this expedition. Baikie published his journals and drew a scientific report in 1857.He analysed fever reports from all over the world. „ The term 'fever' has been terribly abused'- he wrote. He distinguished remittent or intermittent fevers and continued fever, typhoid fever, brain fever etc. and differentiated malaria from other fevers e.g. thyphoid or yellow fever and suggested to use malaria for all the forms of intermittent, remittent fevers. He evaluated the chemical theories of production of miasma toxins that he thought were the causes of malaria. The observation that mosquito curtains proved to be useful as a protection against toxins he compared it's effect to that of the metal mesh in the safety-lamp ( *Davy's lamp* ) against deadly firedamp. Baikie discussed the co-medications in malaria, e.g. the use of emetics or opium before starting the quinine cure. For the side-effects of quinine therapy: ...'The only troublesome effect which I have observed from the continued administration of quinine is a tendency to rather obstinate constipation, that is easily guarded by the occasional use of a mild laxative such as *Seidlitz powder*". He recommended also jalap and rhuburb. For cerebral complications a topical treatment of cold lotions and in coma Liquor Lyttae or other fast vesuculant were applied onto the shaved head and the nape of the neck as a counter

irritant. Liberal, but carefully dosed champagne was also recommended. Baikie expressed that the mercurial treatment ( kalomel, HgCl, Mercurius Dulcis, Quicksilver Subchloride ) was „ irrational empiricism „ and only harmful. "When the body is struggling hard against the effects of one poison ... the chances are diminished if another and equally deadly poison is poured into his ( the patient) system. "For splenomegalia, a complication of the malaria he found that even the hardest ague-cake was reduced by the syrup of the iodine of iron, along with infusion of calumba or cassia . Another excellent remedy for the ague-cake according was citrate of quinine and iron, that is also effective in convalescence. Bitter taste of the quinine will easily be covered by a little syrup of orange peel will easily be covered. For dyspepsia he offered *Infusi Gentianae* ( *Gentianae radix* ), *Infusi cascarillae* ( *Cascarillae cortex* ) , *cusparia* ( *Galipeae cortex* ) , *calumba* ( *Colombo radix* ), *quassia* ( *Quassiae lignum* ) or a synonyme , *simaruba* ( *Simaruba amara, officinalis* or = *Quassia simaruba* !)

Writing about the improvement of health of the troops and marines in the tropical regions one has to add that it was due to many changes. There were better sanitary conditions in the Army and Navy e.g. piped water -,filtered ( porcelain filters ) or boiled - was made available. Drinking water was treated with potassium permanganate. Emetine ( Pelletier 1817 ) was successfully introduced against dysentery. Sewage disposal was introduced, sanitary conditions were better organized and also enforced. The success of quinine in the fever therapy brought a change in the medical thinking about fever. Galen's fever theory was defeated and a new approach of fever control emerged. Effective therapy of remittent fever and malaria prophylaxis with quinine were established led by the results of analysis of sheets of data. It was the age of positive natural sciences the 19th century. The Bryson-Baikie doctrine for the malaria treatment and prophylaxis were based on evidence from the health reports, the theory for infection and facts for it was yet in delay.

As I said that hindsight may deceive us, we interpret the past through the present. That concepts similar to today's GMP were there when quinine was introduced for a systematic use in therapy and in prophylaxis in the mid- 19th century. I hope I could establish that the development for a standard quinine practice happened just that way though. Sources:

*Bryson, A. Report on the Climate and Principal Diseases of the African Stations. 1847., Bryson. Navy medical report No. XV. On the prophylactic Influence of Quinine. Medicinal Times and Gazette, London 1854., Baikie, W.B.: Treatise on Quinine. Article III. On Remittent Fever Edinburgh Medical Journal. 1857., Baikie, W.B.: Narrative of an Exploring Voyage up The Rivers Kwora and Binue in 1854. Elibron Classics 2007., Magyar László dél-afrikai utazásai 1849-57. Szerk. Hunfalvy, J. 1859. Panoráma 1985. Curtin, P.D.: Disease and Empire. Cambridge University Press, 1998., Carlson, D.G. African Fever. Watson Publishing International 1984.*