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A VACCINE TO PREVENT MALARIA

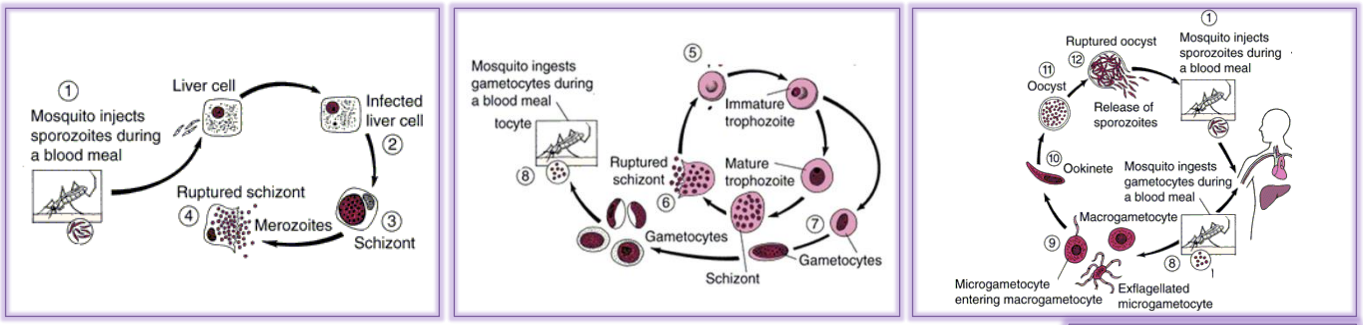
Malaria is a potentially mortal disease caused by four different species of the parasite *Plasmodium*, which are transmitted by the bite of *Anofeles* mosquitoes infected by the parasite[1]. According to the World Organization Of Health (WHO), mortality is about 1.1 million of people every year. Despite of it, between 2000 and 2012, it was estimated that 3.3 million lives had been saved thanks to different treatments to control Malaria in Sub-Saharan Africa[2,3].

Vaccines which are well known nowadays allow a certain control of the illness, but not its eradication by the total elimination of the parasite[4].

OBJECTIVES

This study revises the recent state of Malaria vaccine handled to control the disease in countries with a major incidence. With this information, it tries to infer which vaccine would be the appropriate one to prevent Malaria.

Human Stages[5]		Mosquito Stage[5]
Exo-erythrocytic stage	Erythrocytic Stage	Sexual Stage
1) A Malaria-infected mosquito inoculates the sporozoites into a human host and they are transported through out the blood till the liver. 2) Sporozoites infect liver cells. 3) Formation of schizonts. 4) Rupture of liver cell membranes and release of the merozoites.	5) Merozoites infect erythrocytes and suffer multiples rounds of nuclear division without cytokinesis. 6) Rupture of the erythrocyte. Merozoites are able to infect other erythrocytes. 7) Merozoits can differentiate into sexual forms known as gametocytes (macrogametocytes and microgametocytes). 8) Ingestion of gametocytes by the mosquito vector *Anofeles*.	9) Mosquito vector induces gametogenesis: production of gametes. Microgametes fertilize macrogametes, leading a zygote. 10)Zygote develops into a motile ookinete. 11)The ookinete penetrates into the gut cells and it develops into an oocyst. 12)Rupture of the oocyst and release of the sporozoites, which migrate to the salivary glands of the mosquito.



Plasmodium falciparum life cycle (modified image)[1]

	RTS,S	MSP3-LSP	Pfs25-CP VLP
Action	Protection against the invasion of sporozoits. Inhibition of the development of the parasite in liver cells[4].	Prevent merozoit multiplication and invasion of erythrocytes[8]	Prevent the transmission, gametocytes could not produce sporozoits[8]
Target	*Plasmodium falciparum* circumsporozoite protein (CSP)[6]	Surface protein of merozoit *Plasmodium falciparum* (MSP-3)[8]	Specie-specific gametocytes of *Plasmodium falciparum* (Pfs25)[4]
Adyuvants	AS01 and AS02, AS01 more immunogenic[6,7]	Alum and Montanide ISA720[9]	
Effects	Antibodies anti-CSP IgG Lymphocytes T $CD4^+$ and $CD8^+$ proliferation → block the invasion into the liver cells IFN-γ production → macrophages activation → parasite decreases [4,6]	Trials: • Induction of B and T cell responses • IFN-γ and antibody secretion Similar effects to the natural immunity, except: • IgG1 > IgG3 • Faster[10]	Induction of an antibody serum which blocks the transmission[11]
Response	Humoral > Cellular[7]	Humoral and cellular[9]	
Last	Short term, keep IFN-γ levels[7]	12 months[9]	6 months (study time) [11]
Efficacy	AS01 → 53% (5-17 months) AS02 → 31% (6-12 weeks) and 50% (5-10 months)[4,7]	60% presented immunity 70% of volunteers reacted to the vaccine Adjuvant Alum has an advantage[9]	
Adverse effects	No[4,7]	Alum is more tolerable[9]	
Phase	Phase III	Phase I	Previous studies of Phase I[11]
Conclusion	RTS,S/AS01 is an appropriate candidate, it allows continuing with Phase III of vaccination[7]	The results encourage to continue with the studies	Satisfactory results, in 2011 starts the Phase I[11]

CONCLUSIONS

- RTS,S is the only candidate vaccine in Phase III of the studies. The results analysed in this review show that it could be a good vaccine for preventing Malaria. It shows 53% efficacy in children between 5 and 7 months and it does not present adverse effects.
- MSP3-LSP and Psf-CP VLP could also be considered good vaccines, despite they are on the first phases of the studies.
  - In Phase I of MSP3-LPS it was shown 77% efficacy, which encourages to continue the studies.
  - Studies based on Psf-CP VLP show an induction of antibodies with the total block of the transmission activity. Those results allow the beginning of Phase I.

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