

# Malaria

# HISTORY

- ▶ Malaria has been known to mankind for thousands of years.
- ▶ Increase in temperatures in Africa, rise in humidity creating new water sources and the start of agriculture in the Middle East and North East Africa
- ▶ favourable climate and area for breeding and transmission of malaria parasites and its carrier, the mosquito.



<http://www.un.org/africarenewal/sites/www.un.org/files/climate2.jpg>

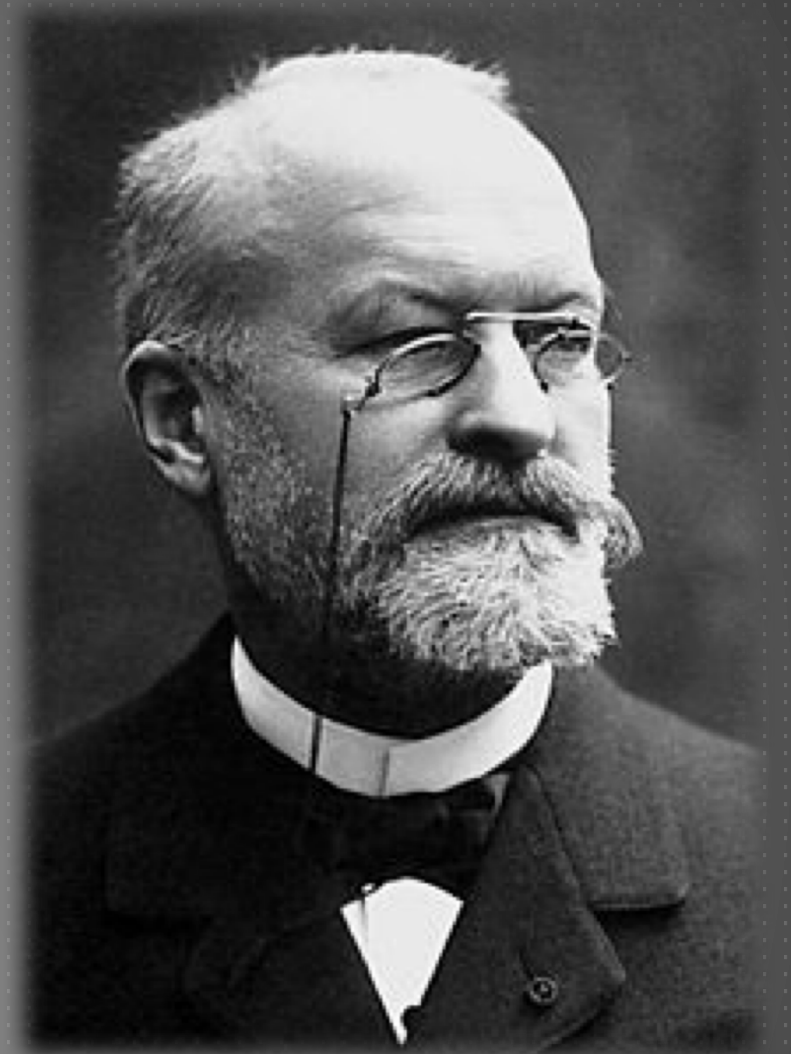
(Srinivas, 2016)

[http://www.unocha.org/sites/default/files/OCHA\\_Category/story\\_crisis/Chad-floods\\_3.png](http://www.unocha.org/sites/default/files/OCHA_Category/story_crisis/Chad-floods_3.png)

# DISCOVERY OF THE MALARIA PARASITE (1880)

- ▶ Charles Louis Alphonse Laveran
  - ▶ French army surgeon stationed in Constantine, Algeria
- ▶ First to notice parasites in the blood of a patient suffering from Malaria
- ▶ 6th of November 1880
- ▶ Awarded the Nobel Prize in 1907

(Lambert, 2016)



[http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1907/laveran.jpg](http://www.nobelprize.org/nobel_prizes/medicine/laureates/1907/laveran.jpg)

# NAMING OF HUMAN MALARIA PARASITES (1890, 1897)

- ▶ Giovanni Batista Grassi and Raimondo Filetti
  - ▶ Italian investigators
- ▶ First introduced the names *Plasmodium vivax* and *P. malariae* for two of the malaria parasites
- ▶ An American, William H. Welch, reviewed the subject and, in 1897, he named the malignant tertian malaria parasite *P. falciparum*.



<http://www.famousbirthdays.com/thumbnails/grassi-giovanni-large.jpg>



<http://www.malariasite.com/wp-content/uploads/2015/02/sternberg.gif>

# DISCOVERY THAT MOSQUITOES TRANSMIT MALARIA PARASITES (1897-1898)



- ▶ August 20th, 1897
- ▶ Ronald Ross
  - ▶ a British officer in the Indian Medical Service
- ▶ First to demonstrate that malaria parasites could be transmitted from infected patients to mosquitoes
- ▶ Awarded the Nobel Prize in 1902

(Lambert, 2016)



<http://www.sciencemuseum.org.uk/hommedia.ashx?id=10252&size=Small>

# TRANSMISSION AND MECHANISM OF ACTION

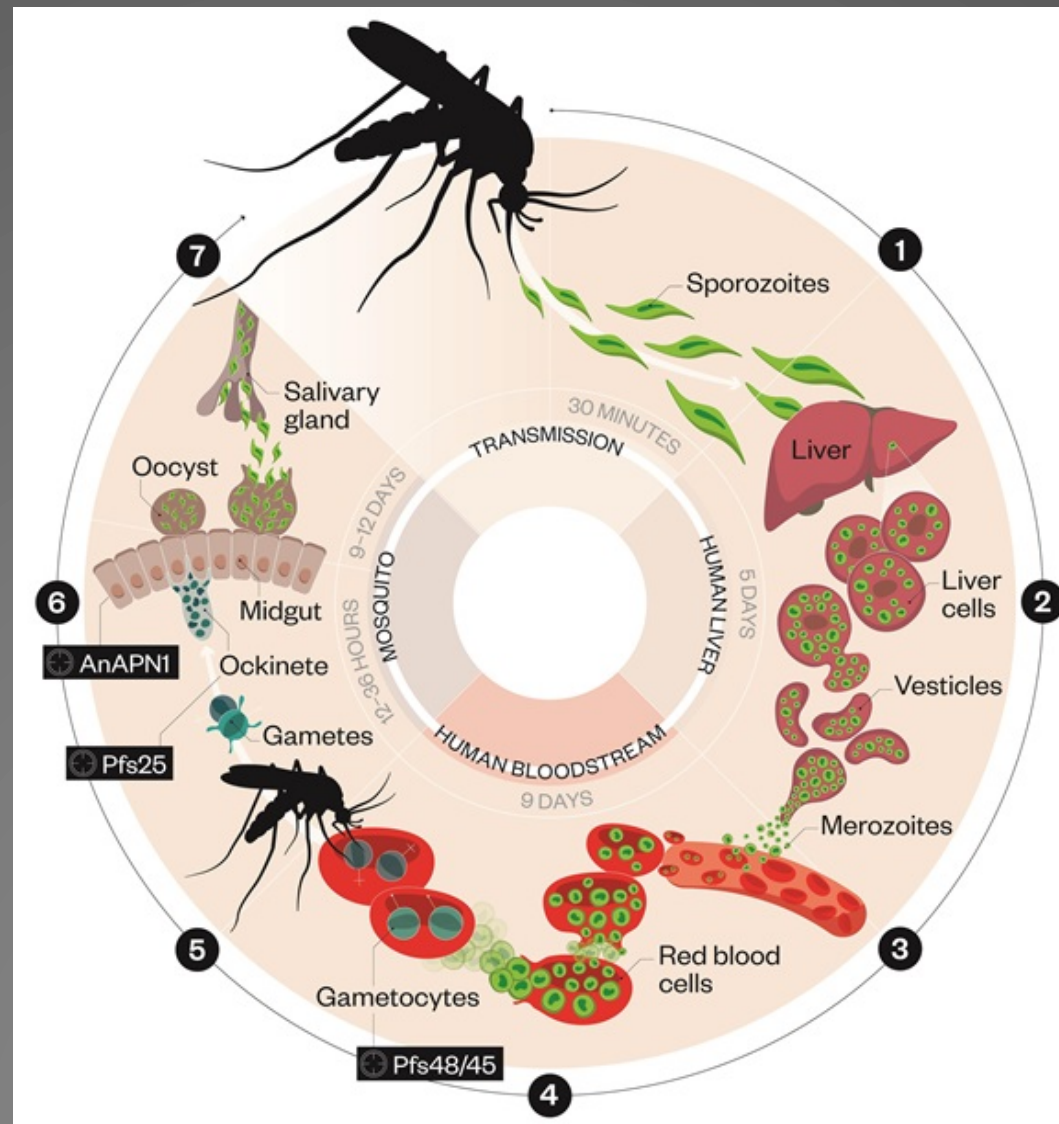
## Female Anopheles Mosquito

- ▶ Spotted wings
- ▶ 45 degrees
- ▶ No buzzing sound



<http://internationalmedicalcorps.org/page.aspx?pid=501>

# LIFE CYCLE



• <http://dx.doi.org/10.1211/pj.2015.20067483>

# TRANSMISSION

- ▶ Blood Transfusions
- ▶ Organ Transplants
- ▶ Shared needles
- ▶ fetal transmission



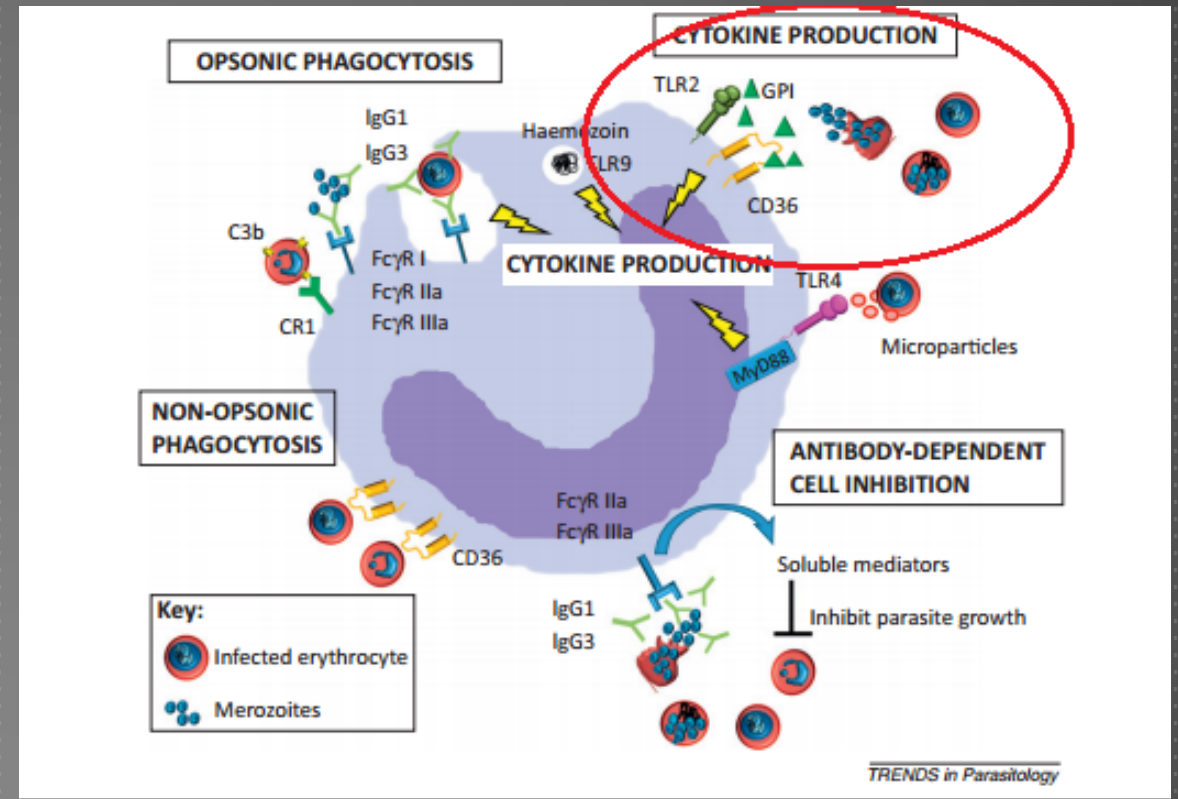
<http://www.wisegeekhealth.com/what-is-a-homologous-blood-transfusion.htm>

<http://celltrials.info/2009/10/25/fetal-maternal-cell-trafficking-microchimerism-and-cancer/>

# SYMPTOMATOLOGY

# CAUSE OF SYMPTOMS

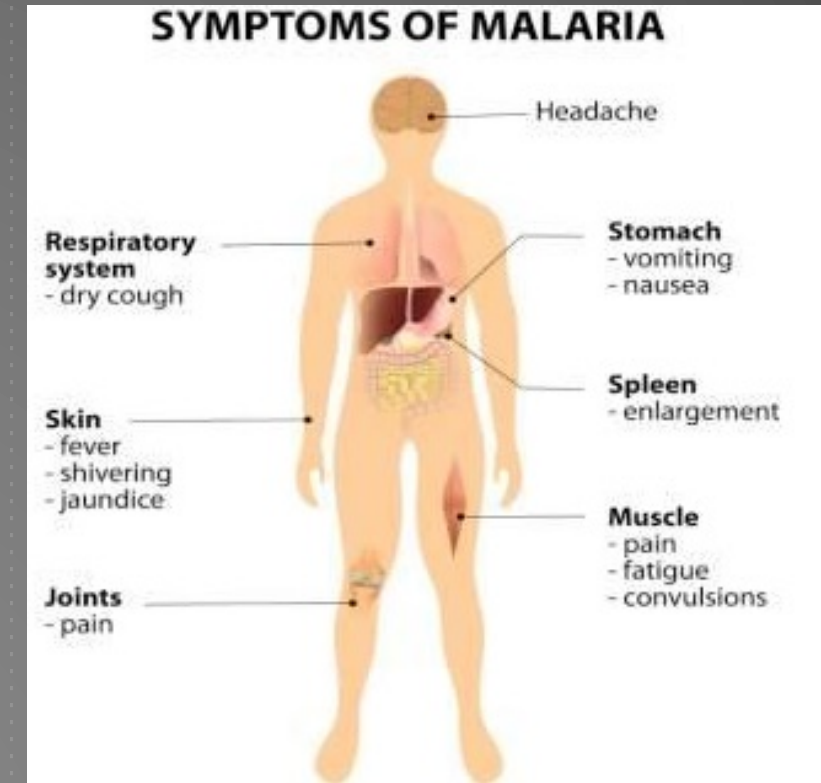
- ▶ Arise during blood cell infection stage
- ▶ Parasite-associated products released:
  - ▶ glycoposphatidylinositol (GPI)
  - ▶ haemozoin
- ▶ Release of inflammatory cytokines
- ▶ Lead to symptoms:
  - ▶ Fever
  - ▶ Chills
  - ▶ Aches
  - ▶ Vomiting



Adapted from Chua et al., 2013

# STAGES AND SYMPTOMS OF MALARIAL INFECTION

- ▶ Initial symptoms begin 7 days after infection
- ▶ Three stages of malarial infection
  1. Cold stage
  2. Hot stage
  3. Sweating stage
- ▶ Symptoms last 6-10 hours
- ▶ Very difficult to diagnose
- ▶ If not treated, could worsen and lead to death



<http://www.thehealthsite.com/diseases-conditions/malaria/001/>

(WHO, 2016)



# SEVERE MALARIA INFECTIONS



[http://cdn.orkin.com/images/mosquitoes/mosquito-illustration\\_360x286.jpg](http://cdn.orkin.com/images/mosquitoes/mosquito-illustration_360x286.jpg)

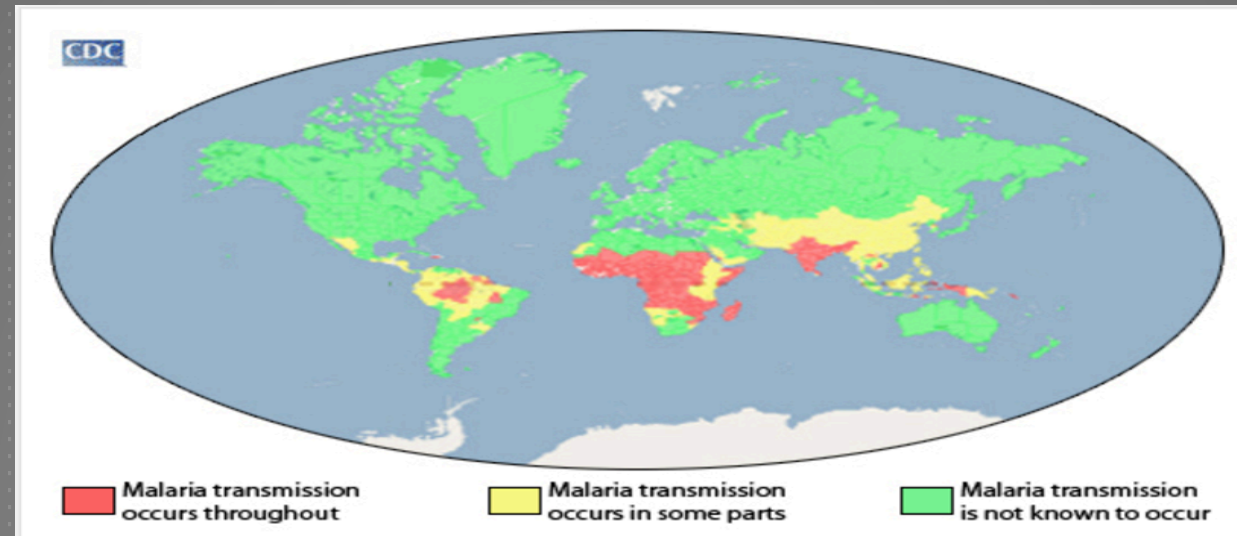
- ▶ Patient experiences serious organ failure or blood abnormalities
- ▶ Cerebral malaria → may fall into coma
- ▶ Hemolysis → severe anemia
- ▶ Hyperparasitemia: >5% of erythrocytes infected
- ▶ Acute Respiratory Distress Syndrome: fluid buildup in alveoli

(CDC, 2015)

# DEMOGRAPHICS

# GEOGRAPHY

- ▶ Tropical
- ▶ Impoverished areas
- ▶ Highest in Africa and South East Asia

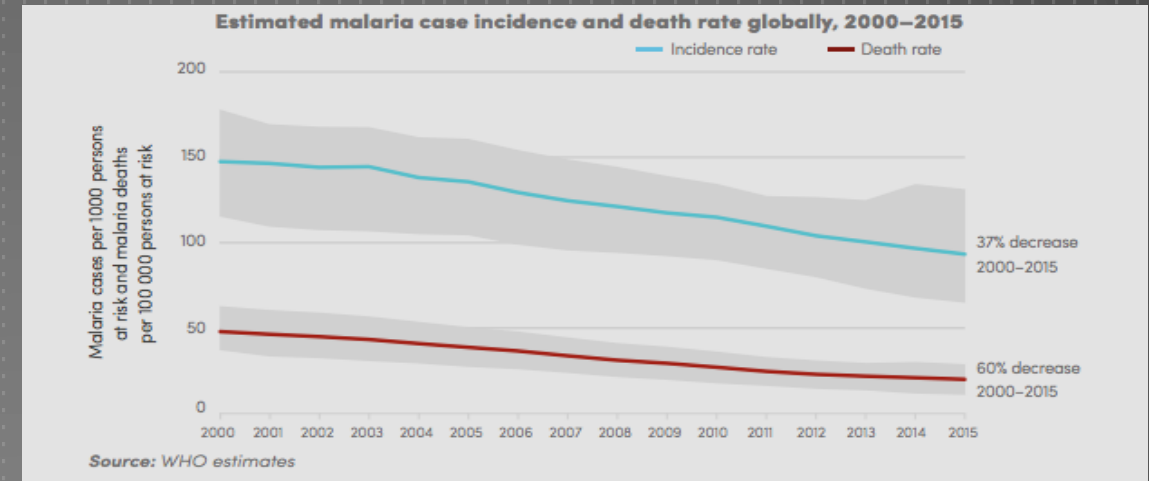


CDC (2016)

Retrieved from [https://www.cdc.gov/malaria/malaria\\_worldwide/impact.html](https://www.cdc.gov/malaria/malaria_worldwide/impact.html)

# STATISTICS

- ▶ 37% decrease in those affected globally
- ▶ 60% decrease in number of deaths
- ▶ 2015
  - ▶ 3.2 billion people at risk
  - ▶ 214 million people infected
  - ▶ 438,000 deaths
- ▶ 3<sup>rd</sup> leading cause of death in Africa



**Estimated malaria cases and deaths, by WHO region, 2000–2015**

WHO region	Estimated number of malaria cases (000's)				Change 2000–2015	Estimated number of malaria deaths				Change 2000–2015
	2000	2005	2010	2015		2000	2005	2010	2015	
African	214 000	217 000	209 000	188 000	-12%	764 000	670 000	499 000	395 000	-48%
Americas	2 500	1 800	1 100	660	-74%	1 600	1 200	1 100	500	-69%
Eastern Mediterranean	9 100	8 600	4 000	3 900	-57%	15 000	15 000	7 000	7 000	-51%
European*	36	5.6	0.2	0	-100%	0	0	0	0	
South-East Asia	33 000	34 000	28 000	20 000	-39%	51 000	48 000	44 000	32 000	-37%
Western Pacific	3 700	2 300	1 700	1 500	-59%	8 100	4 200	3 500	3 200	-60%
<b>World</b>	<b>262 000</b>	<b>264 000</b>	<b>243 000</b>	<b>214 000</b>	<b>-18%</b>	<b>839 000</b>	<b>738 000</b>	<b>554 000</b>	<b>438 000</b>	<b>-48%</b>
Lower bound	205 000	203 000	190 000	149 000		653 000	522 000	362 000	236 000	
Upper bound	316 000	313 000	285 000	303 000		1 099 000	961 000	741 000	635 000	

\* There were no recorded deaths among indigenous cases in the WHO European Region for the years shown.  
Source: WHO estimates

Retrieved from: [http://apps.who.int/iris/bitstream/10665/205224/1/WHO\\_HTM\\_GMP\\_2016.2\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/205224/1/WHO_HTM_GMP_2016.2_eng.pdf?ua=1)

# HIGH RISK

- ▶ Children
- ▶ Women
- ▶ Traveler
- ▶ HIV/AIDS Patients



Retrieved from: <http://www.shutterstock.com/pic-161043503/stock-vector-pregnant-woman-cartoon.html>

CDC (2016)

# TREATMENTS

### 3 General Classes of Treatment:

1. Pre-exposure Prophylaxis
2. Fast-Acting Antimalarials
3. Slow-acting Antimalarials

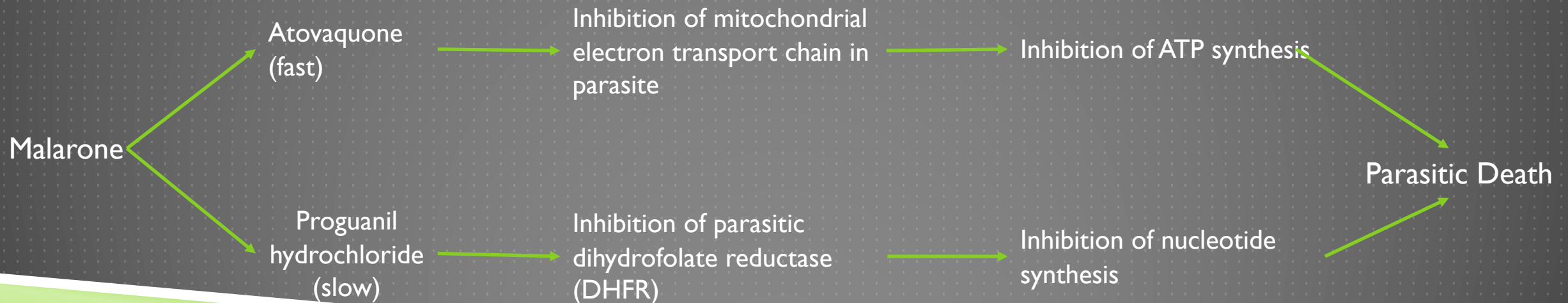
# PRE-EXPOSURE PROPHYLAXIS

Malarone: Atovaquone + Proguanil Hydrochloride

Administration:

- ▶ For travelers going to areas of high transmission (ex. India, African countries)
- ▶ Given as a pill, to be taken once a day

Mechanism of Action:





# FAST-ACTING ANTIMALARIALS: ACT AND CHLOROQUINE

Artemisinin: used in Artemisinin-based  
Combination Therapy

- Treatment for uncomplicated *P. Falciparum*  
Malaria
- Discovered by Chinese Scientist, **Tu Youyou**  
(Winner of Nobel Prize in Medicine, 2015)

Chloroquine:

- Treatment for *P.vivax*

Meshnick, 2002; Tripathi, 2002

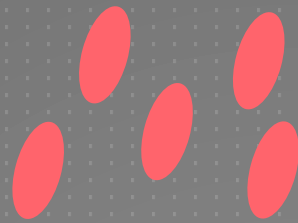


Image retrieved from: <http://www.xrapid.org/tu-youyou-wins-the-2015-nobel-prize-for-medicine/>

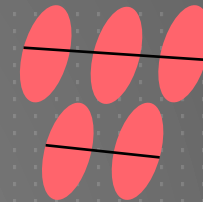
# NORMAL PARASITIC PATHWAY



Host hemoglobin  
breakdown by  
parasite



Heme (toxic)



Hemozoin (polymer, non-toxic)

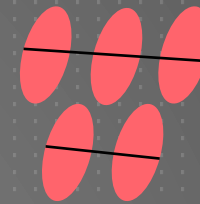
# FAST-ACTING ANTIMALARIALS: ARTEMISININ



Host hemoglobin  
breakdown by  
parasite



Heme (toxic)



Hemozoin (polymer, non-toxic)

Artemisinin Free Radicals

R = Artemisinin

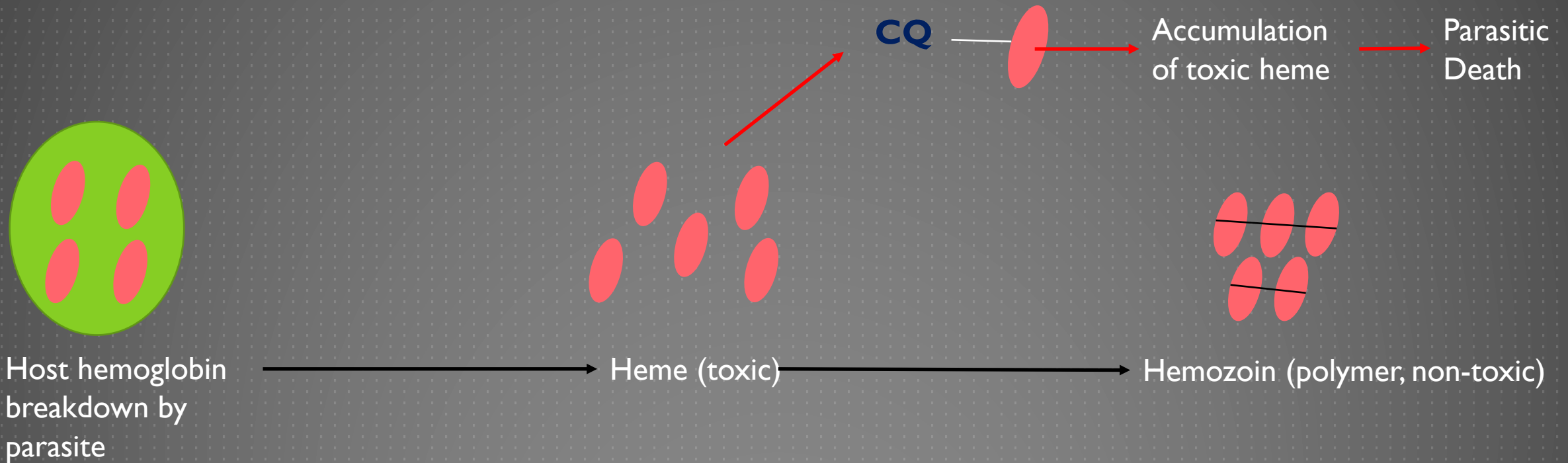


Alkylation of Heme

Porphyrin Degradation

Parasitic Death

# FAST-ACTING ANTIMALARIALS: CHLOROQUINE

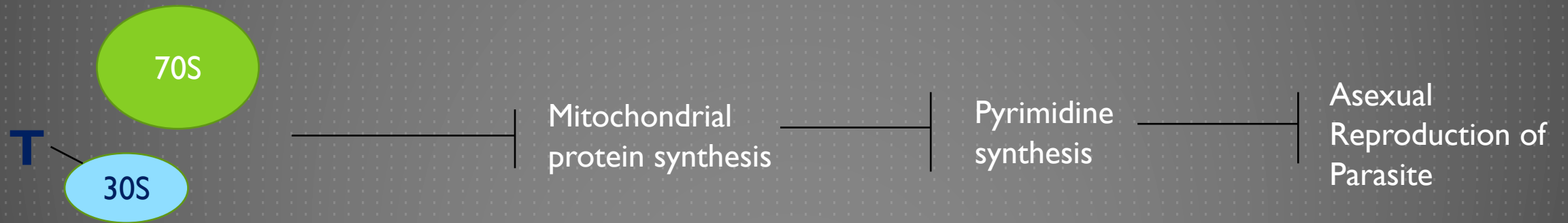


CQ = Chloroquine

# SLOW-ACTING ANTIMALARIALS - TETRACYCLINE

- ▶ Slow-acting Drug → used in combination with fast-acting drugs

Mechanism: inhibits mitochondrial protein synthesis



# CONCLUSION

# FUTURE RESEARCH

- ▶ Researchers are contemplating new interventions or updating previously used malaria control interventions.
  - ▶ New drugs and vaccines for treatment and prevention
  - ▶ New diagnostic tests
  - ▶ Innovative insecticide-treated materials
  - ▶ Revised systems for delivering and evaluating malaria control



Retrieved from: <http://www.greens-efa.eu/typo3temp/pics/8c5394b60d.jpg>

# VACCINES

- ▶ Development of an effective malaria vaccine faces major challenges
- ▶ Targeted against *Plasmodium falciparum*
- ▶ Genetic diversity of both the parasite and the human host
- ▶ Produce vaccines that target *P. vivax*
- ▶ Take into consideration features such as relapses and hypnozoite stages



Retrieved from: <http://cliparts.co/cliparts/dc9/K79/dc9K79Lc7.jpg>



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