

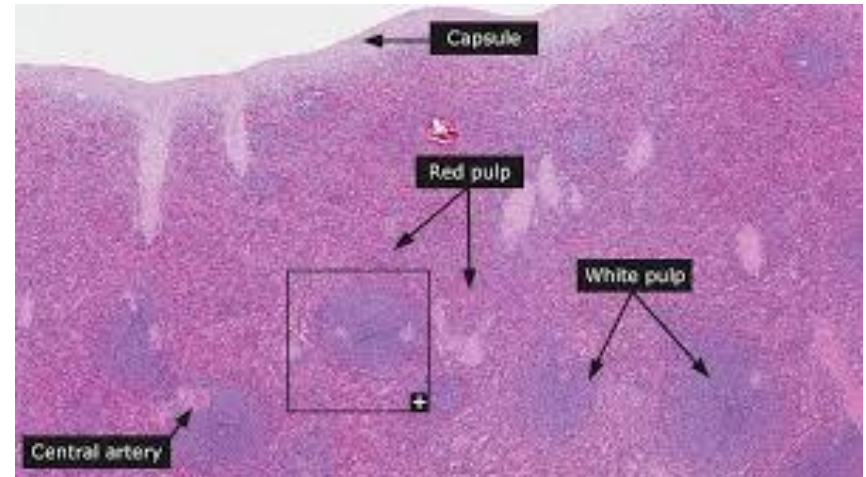
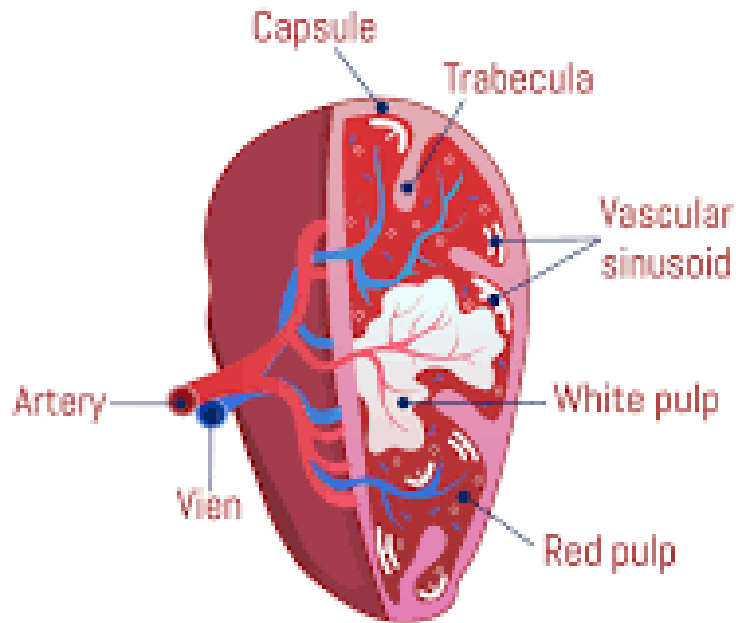


Focus op functie: De milt als filter

Perry JJ van Genderen, MD, PhD

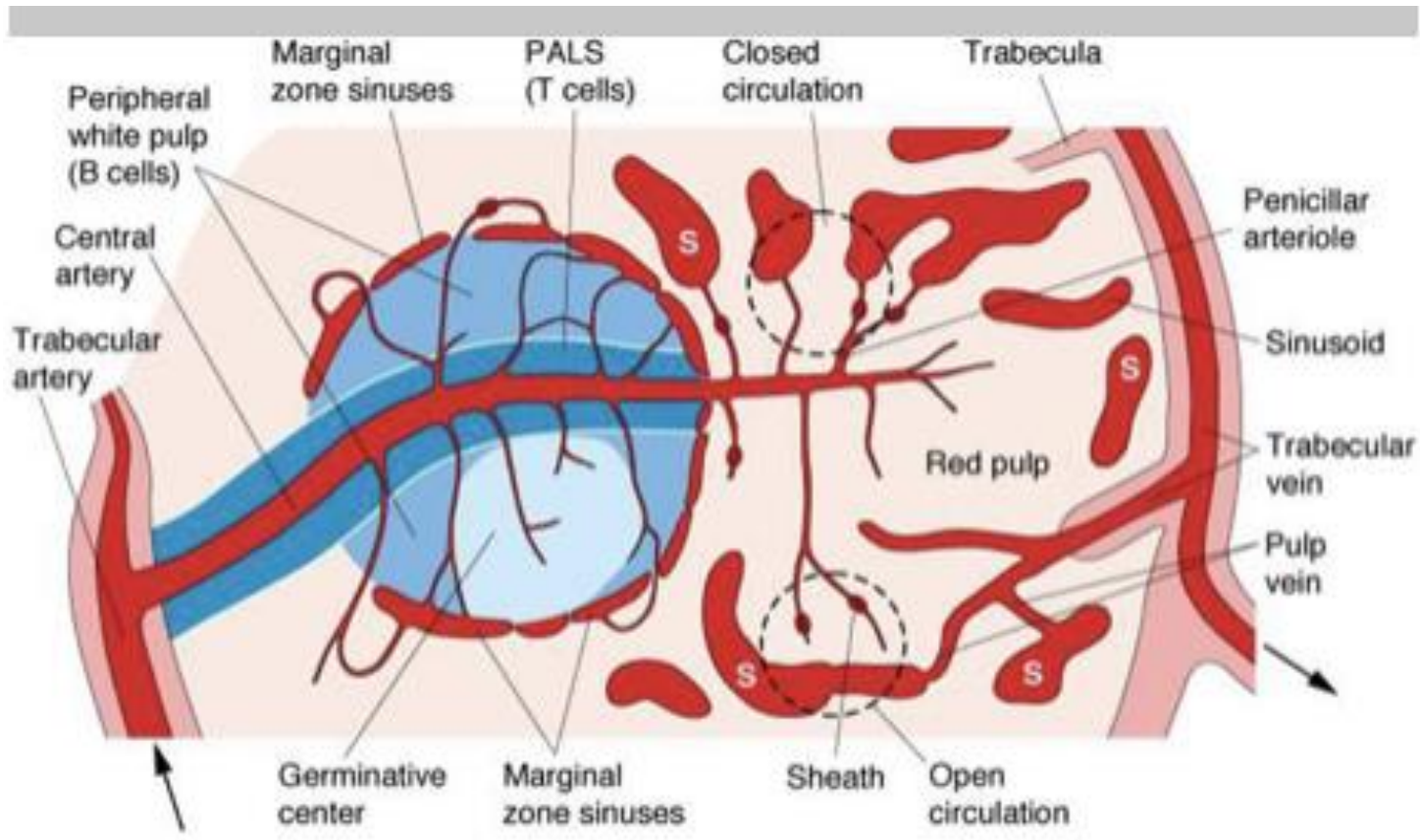
Havensymposium 2023

DE MILT | algemeen



1. WITTE PULPA = afweer | RODE PULPA = filter
2. Er zit geen kapsel om de witte pulpa dus er is GEEN scheiding van bloedstroom door rode en witte pulpa (interactie verschillende functies is dus optimaal)

DE MILT | circulatie van bloed



DE MILT | circulatie van bloed

Milt ontvangt 5% Cardiac output

90% Gesloten systeem = **SNELLE** circulatie

Elke **20 minuten** gaat RBC hier doorheen

→ Witte pulpa (deels in rode pulpa)

10% Open systeem = **LANGZAME** circulatie

Elke **4 uur** gaat RBC met check op

vervormbaarheid hier doorheen

→ Rode pulpa

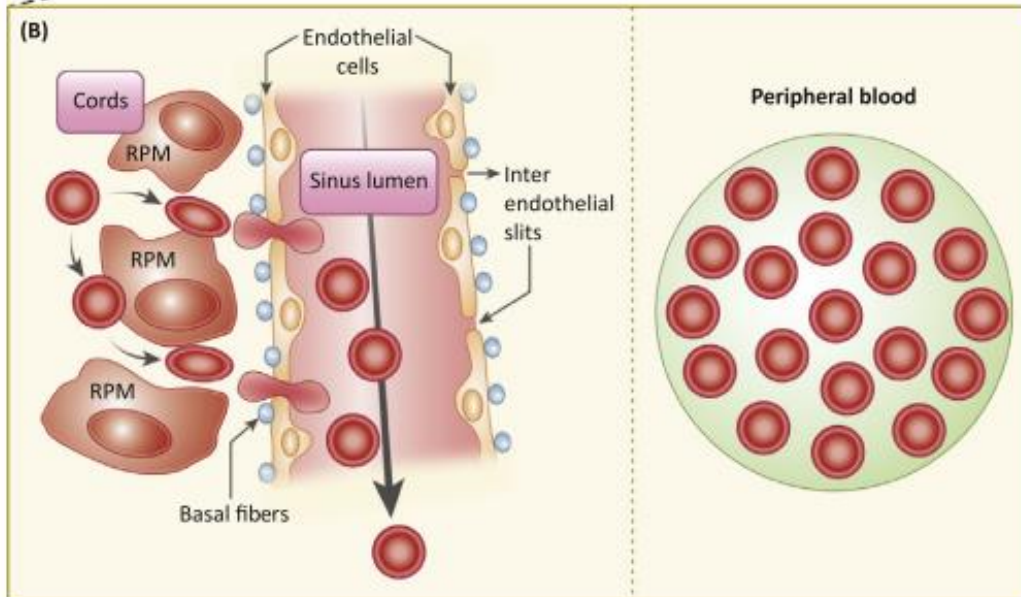
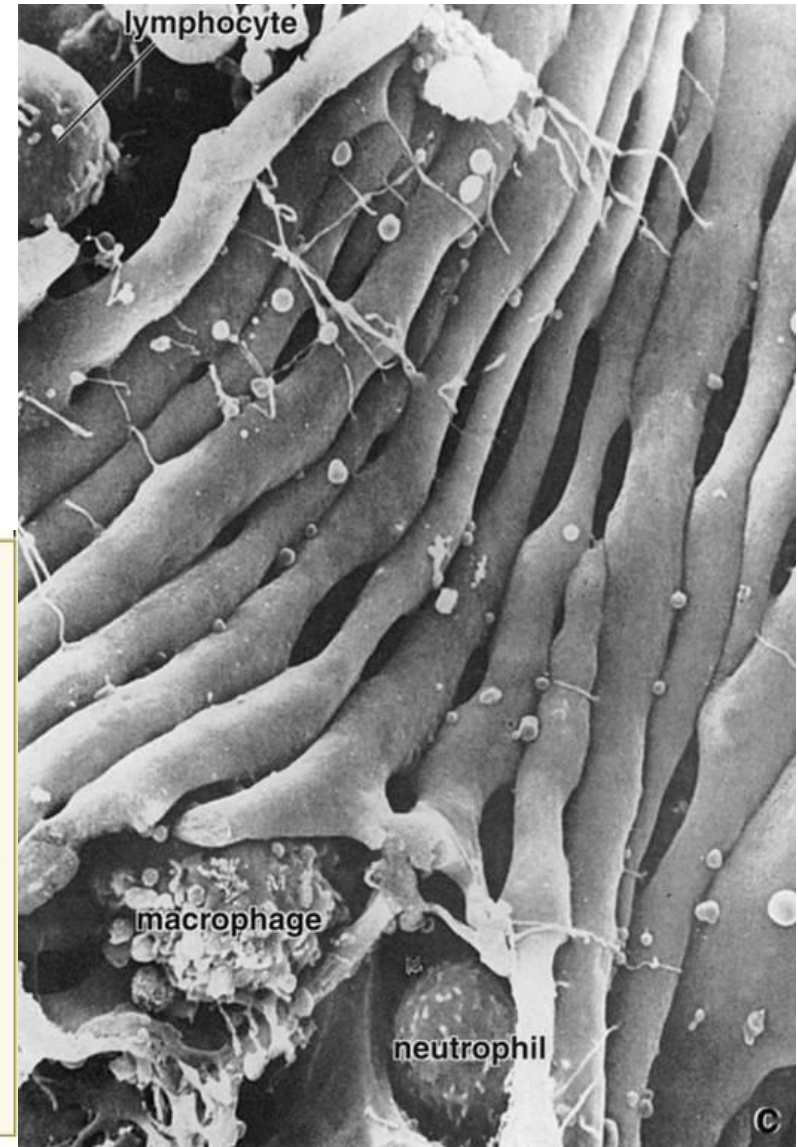
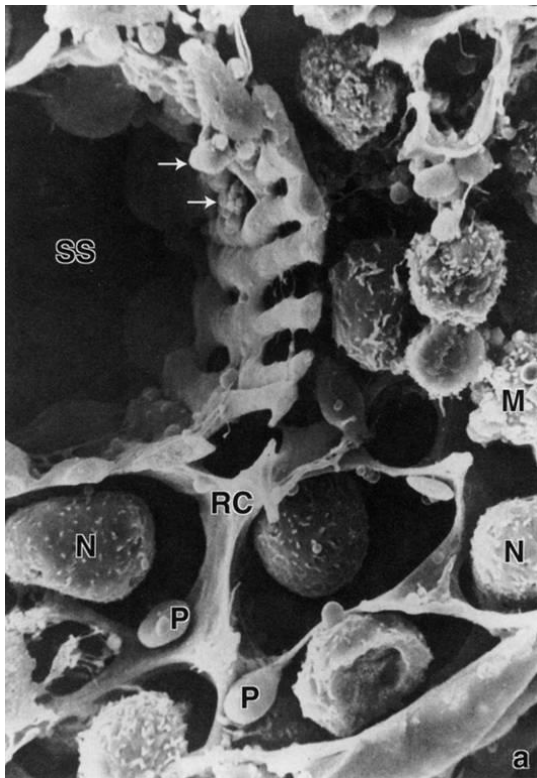
Pe
wh
(B
Cer
arte
Trabec
artery

center

zone sinuses

circulation

Hoe doet de milt dat?



DE MILT | rode pulpa

Filtering van 'alle' RBCs met afwijkende vorm of flexibiliteit

- Oude RBCs
- Geïnfecteerde RBCs
- Disfunctionele RBCs
- Opsonisatie door antistoffen of complement

Door macrofagen uit rode pulpa verwijderd waarbij ijzer gerecycled wordt

Wat gebeurt er dan bij malaria?

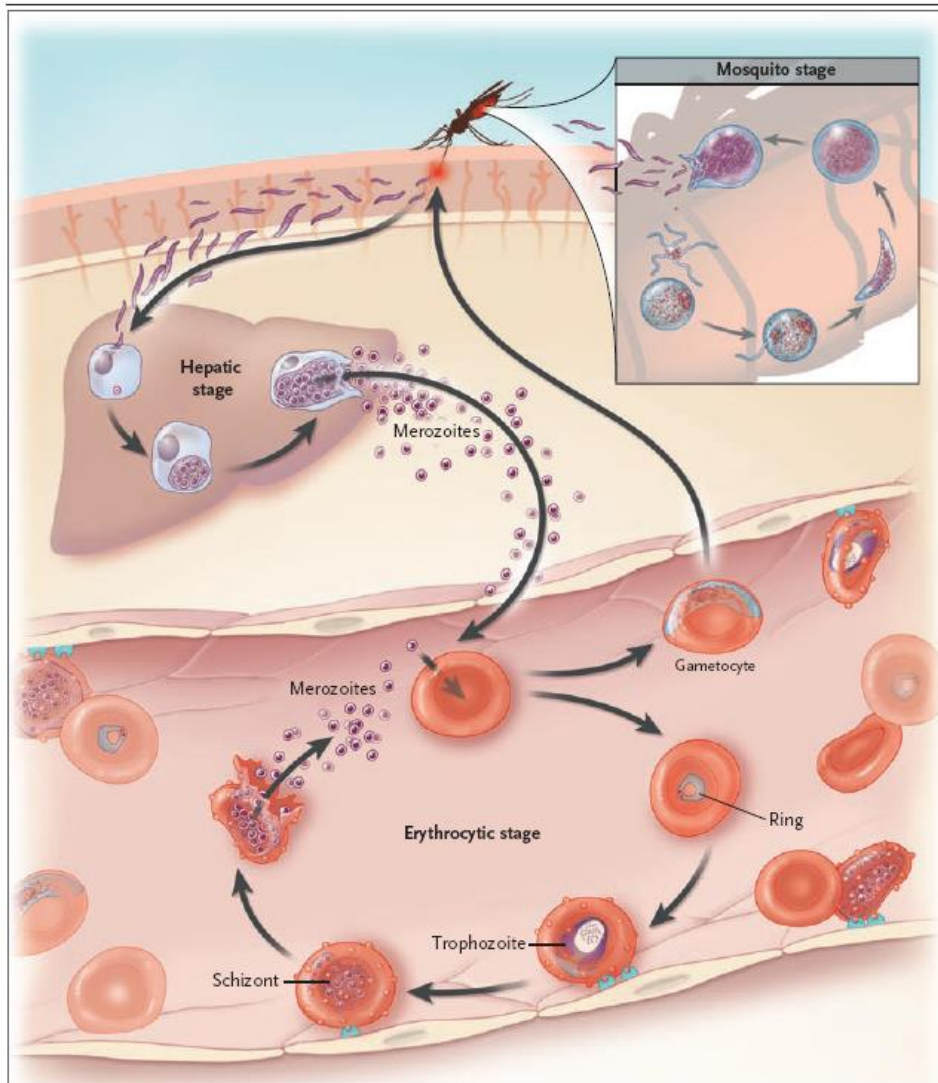
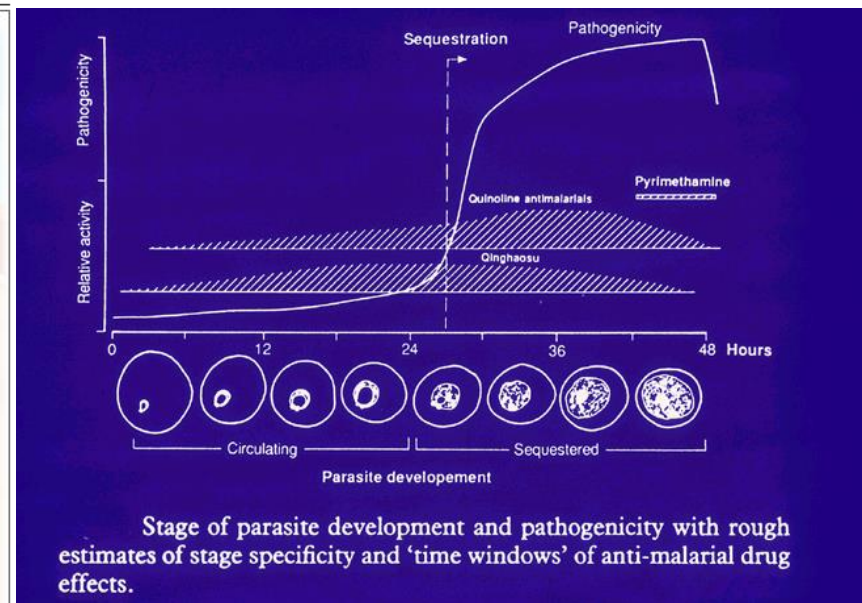


Figure 1. Life Cycle of *Plasmodium falciparum*.

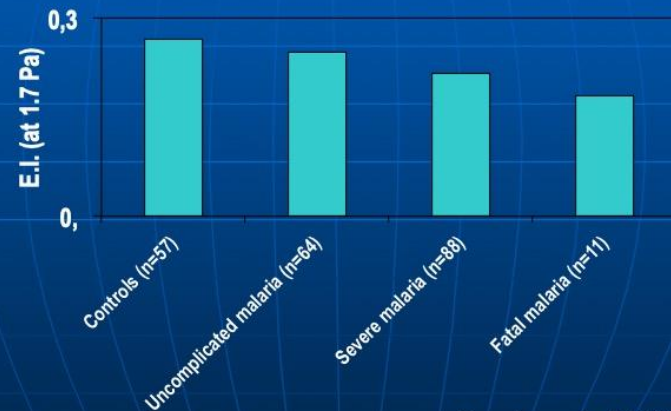
Elements that are important for the pathogenesis of severe malaria are shown. Erythrocytes containing *P. falciparum* in mature intraerythrocytic stages (trophozoites and schizonts) adhere to vascular endothelium, thereby avoiding clearance by the spleen. High numbers of circulating parasites and elaboration of host and parasite factors in the vasculature of various organs lead to the manifestations of severe malaria.



Stage of parasite development and pathogenicity with rough estimates of stage specificity and 'time windows' of anti-malarial drug effects.

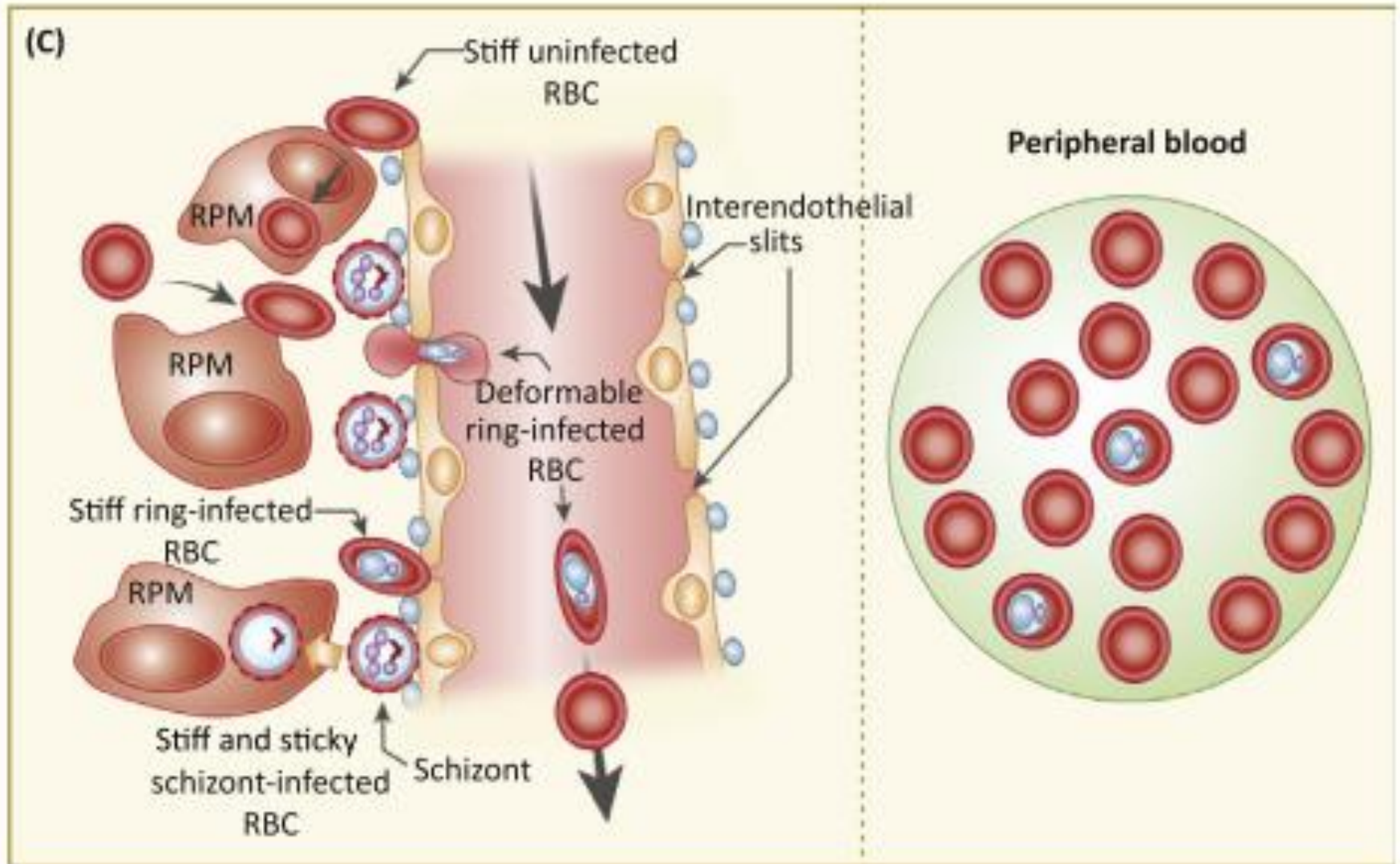
Reduced red blood cell deformability in malaria

Restoration by blood transfusion (+ 0,05 E.I.)

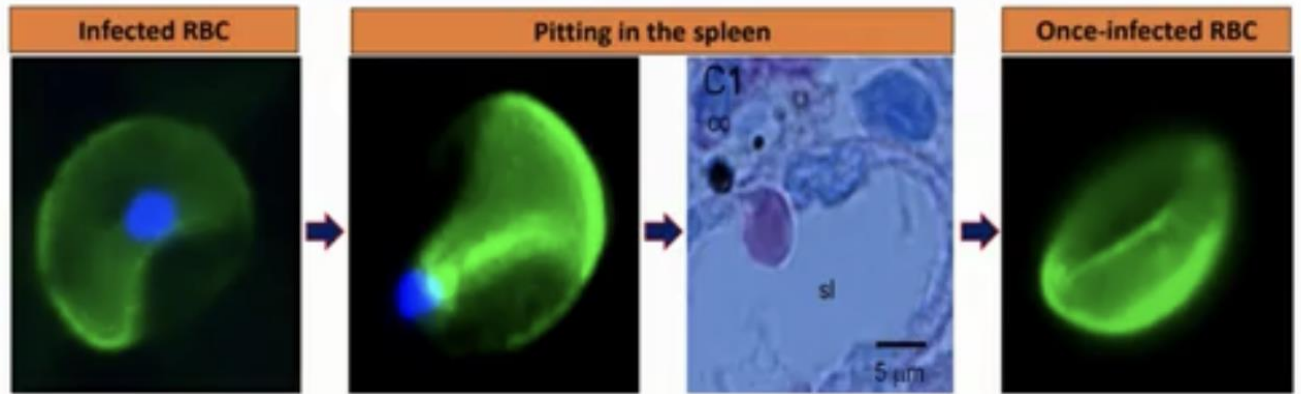
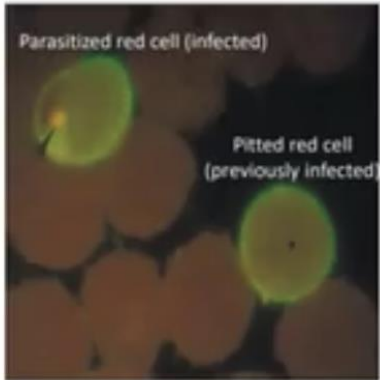
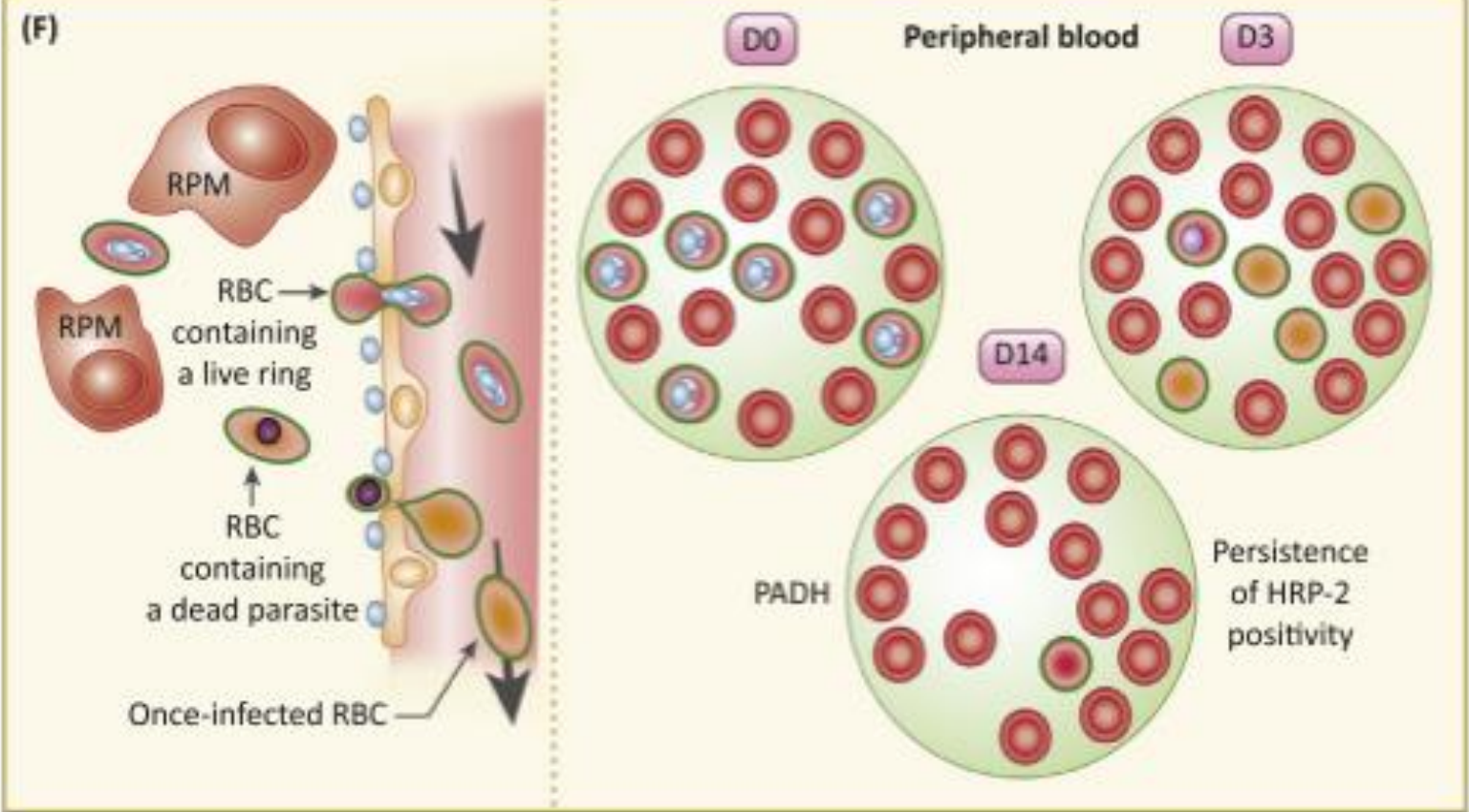


Dondorp et al (2002)

Alleen vervormbare RBC passeren filter



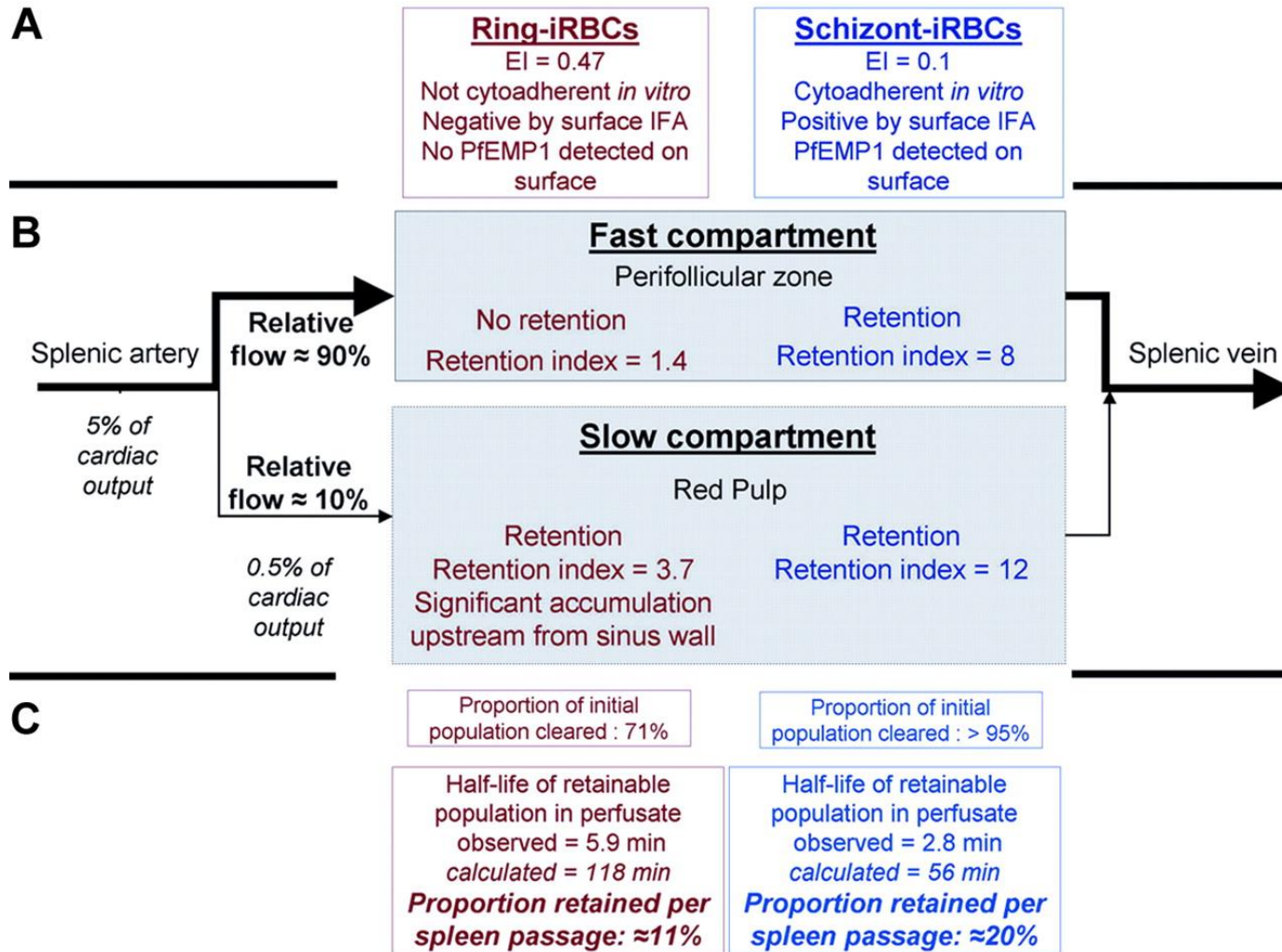
PITTING



■ Parasite DNA

■ RESA protein (from *P. falciparum*)

P falciparum–infected RBCs through the fast and slow circulatory compartments of the perfused human spleen



P falciparum–infected RBCs through the fast and slow circulatory compartments of the perfused human spleen

A

Ring-iRBCs

EI = 0.47

Not cytoadherent *in vitro*
Negative by surface IFA

Schizont-iRBCs

EI = 0.1

Cytoadherent *in vitro*
Positive by surface IFA

FILTRATIE door RODE PULPA van de milt

Verschillende stadia van malaria parasiet

- Ring-vormen > 70%
- Schizonten > 95%

cardiac
output

Retention index = 0.1
Significant accumulation
upstream from sinus wall

Retention index = 12

C

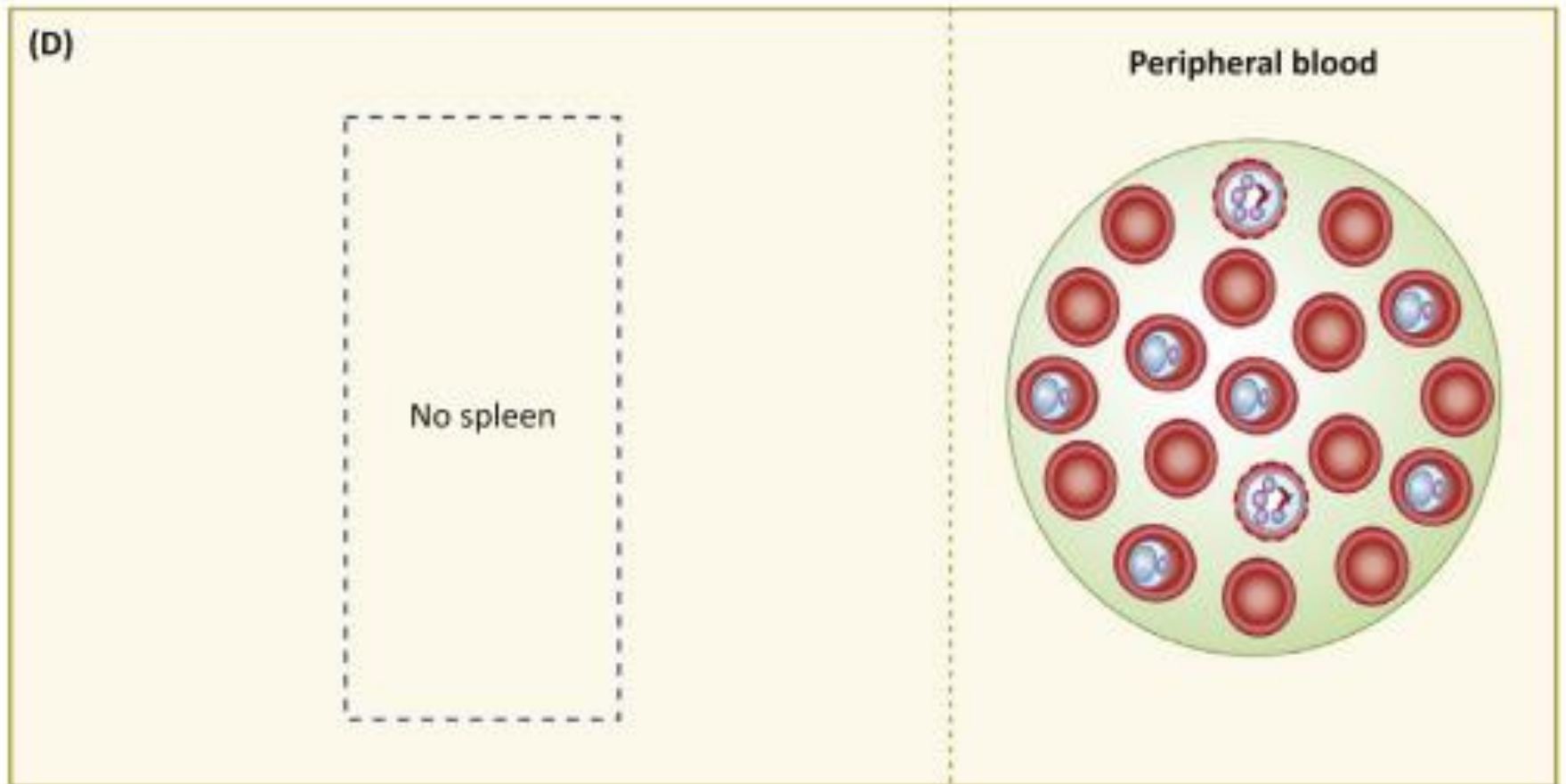
Proportion of initial
population cleared : 71%

Proportion of initial
population cleared : > 95%

Half-life of retainable
population in perfusate
observed = 5.9 min
calculated = 118 min
**Proportion retained per
spleen passage: ≈11%**

Half-life of retainable
population in perfusate
observed = 2.8 min
calculated = 56 min
**Proportion retained per
spleen passage: ≈20%**

Malaria en miltverwijdering



CONCLUSIE

Rode pulpa van milt zorgt voor continue surveillance van rode bloedcellen middels:

- I. Mechanische **filtratie** van rode bloedcellen op vorm-afwijkingen en vervormbaarheid
- II. Het verwijderen van geïnfecteerde rode bloedcellen en intra-erythrocytaire insluitels (**pitting**)