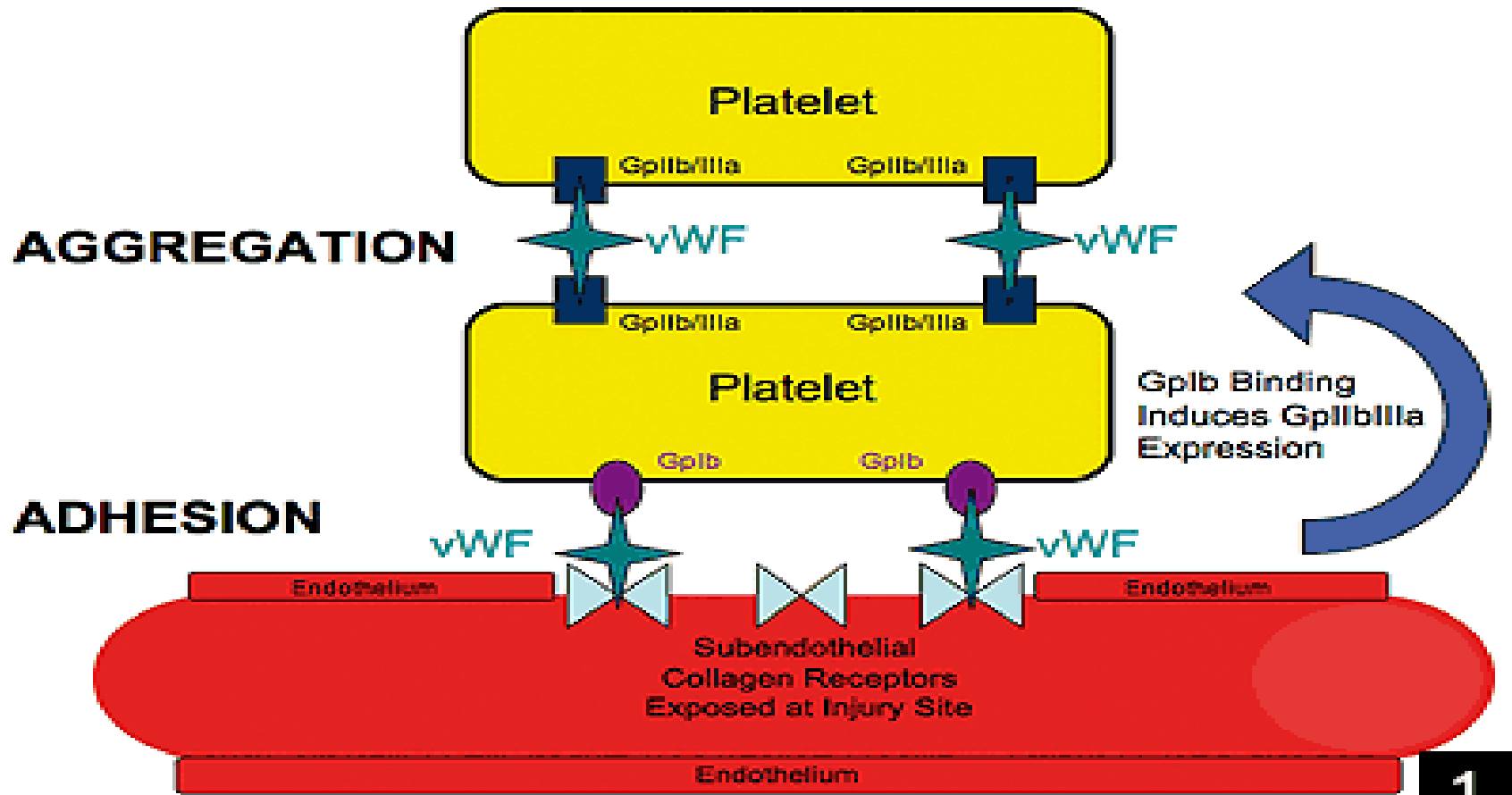


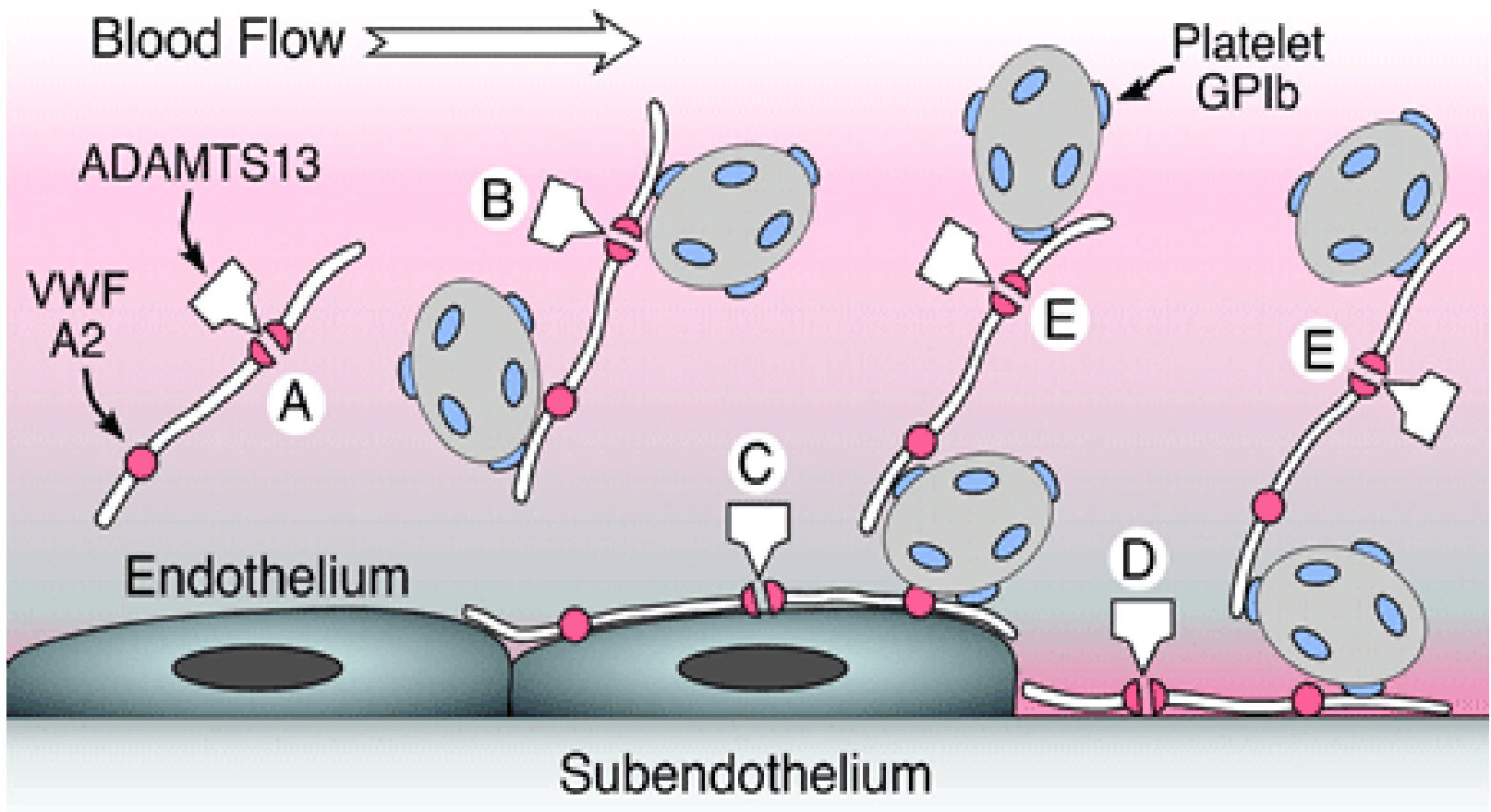
Mphahlele BJ

Infectious Diseases

UP

TTP





TTP

- ~ deficiency of protease that lyses vWF
 - ADAMTS 13
 - *A Disintegrin And Metalloproteinase with A Thrombospondin member 13*—also known as *von Willebrand factor-cleaving protease* (VWFCP)
- Strands of (vWF) → platelets to aggregate → thrombi
- ↓ platelets and RBC destruction → anemia.
- Diagnosis
 - Previously pentad
 - Fever
 - Renal failure
 - Neurological abnormalities.
 - Thrombocytopenia
 - Non-immune microangiopathic haemolytic anaemia

- Current guidelines for diagnosis:
 - American Associations of Blood Banks,
 - The American Society of Apheresis
 - British Committee for Standards in Haematology:
 - Yard stick
 - Thrombocytopaenia
 - Non-immune microangiopathic haemolytic anaemia
 - » Neg Coombs haemolytic anaemia
 - Rule out conditions that present similarly:
 - Sepsis
 - Malignancy
 - HELLP Syndrome

Treatment

- Plasma exchange (P/E)
 - Until platelets are normal and continue for 2 more days after normalisation
- Use plasma transfusion while waiting
- Glucocorticoids
 - Indication
 - Worsening condition when P/E is stopped
 - Relapse
- Platelet transfusion contraindicated

TTP in HIV

- Relative common
- Not an AIDS-defining condition
- Life threatening
- Thought to be d/t ab against ADAMTS13
- Indication to fast track patient on ARV
 - In spite of CD4
- Plasma exchange treatment of choice
- Temporise with plasma infusion

Presentation

- 49 yr old gentleman.
- Presented with fever and drowsiness
- Admitted with fever and drowsiness
 - Meningo-encephalitis
- Treated with antibiotics.
 - Rocephin 2g ivi 12hly
 - Ampicillin
- Referred to ID for failure to respond.

- Seen by ID 3 days on AB
- Have a positive history of travel to Zambia
- Not taken any prophylaxis for malaria
- Was vaccinated against
 - Typhoid
 - Rabies
 - Hepatitis B
 - DT

- Further hx: he had Barlow syndrome
 - Chickened out of θ for MV repair 1 year back
- Never ill apart from tonsillectomy at 7 yrs
 - Indication: Quinsey abscess
- 1st hospital admission
- Had had painful insect bites Zambia

On Examination

- Extremely sleepy gentleman
- Haggard looking
- Generally
 - Not in respiratory distress
 - Slightly pale + tinge of jaundice
 - Slightly dehydrated with ↓ skin turgor
 - (L) significant axillary LN
 - No clubbing or cyanosis
 - No peripheral oedema

Clinical examination

- Peripheral signs
 - T 39.1°C
 - RR20 breaths/min
 - P108 beats/min
- BP 110/80 mmHg.
- GCS 12/15
- Chest clinically clear
- CVS- grade 3/6 pan sys murmur apex → axilla
- ABD- SNT HSM moderate
- Extremities (N)



- Urinalysis
 - Ph 5
 - Specific gravity 1030
 - 2+ protein
 - 2+ red cells
 - Leucocytes esterase
 - Some hyaline casts

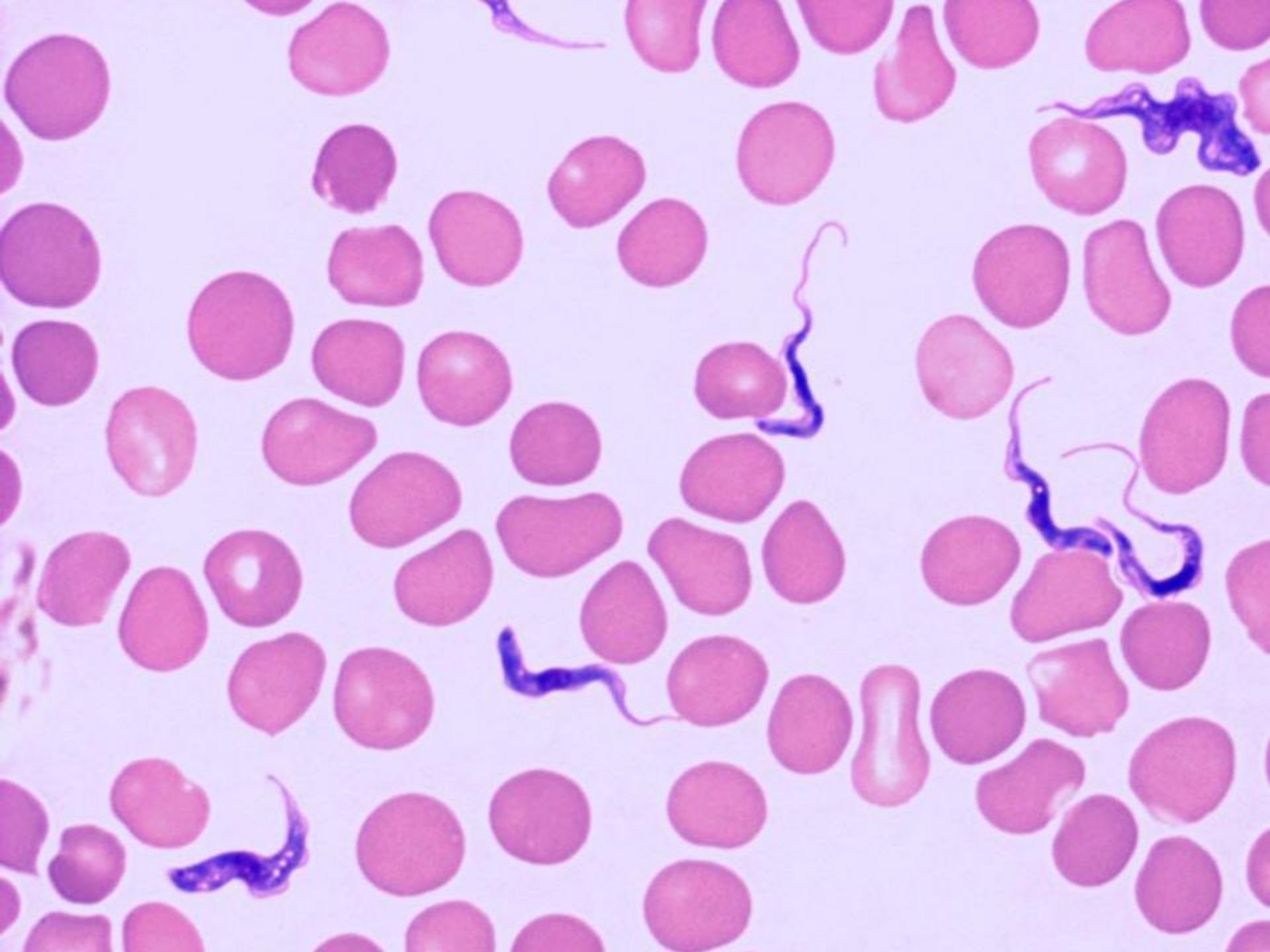
Differential diagnoses

- Malaria
- Enteric fever
- Meningitis
- Trypanosomiasis
- Schistosomiasis
- Infective Endocarditis
- UTI
- RVD

Blood tests

- Haemoglobin 11,3g/dL
- WBC 4.8
 - Diff count
 - lymphocytes 0.2 L
 - neutrophils 0.84 (0.50-0.75)
 - platelets 40
 - C reactive protein 1113 $\mu\text{mol/L}$ (8-31),
- LFT
 - Tot bil 41.85 $\mu\text{mol/L}$
 - Direct 13
 - AST 161 U/L
 - ALT 212 U/L (<45),
 - GGT274 (<55) U/L,
 - S-creat 477.36 $\mu\text{mol/L}$
 - eGFR 14
 - Na 133 and K 4.5

- LP protein slightly elevated at 0.51
 - No glycorrhagia
 - No pleocytosis
 - ADA 2
- Malaria test
 - Rapid test
 - Negative
 - Blood films negative for malaria
 - Blood cultures were done and still pending
 - Extracellular structures were seen



- Imaging NAD

Diagnosis?

Human African Trypanosomiasis

- **Trypanosomiasis** is diseases caused by trypanosomes:
 - *Trypanosoma brucei gambiense* or
 - *Trypanosoma brucei rhodesiense*
 - *Human African trypanosomiasis* (HAT)

- Trypanosoma cruzi causes Chagas
- Common in South America
- Responsible for DCMO
- Can cause GIT abnormalities

HAT

- 60 million people at risk
- Approximately 500,000 people in SSA have HAT.
- 48,000 people died of it in 2008
- Four major epidemics in the past
 - 1896–1906 primarily in Uganda and Congo Basin
 - Epidemic in 1920
 - Epidemic in 1970 Malawi and Zambia, Congo and upper Zimbabwe
 - 2008 epidemic in Uganda

- Neglected tropical disease
- Tsetse fly a vector
- Common in SSA
- Risks enhanced by
 - War
 - Hunting
 - Etc.



- Tsetse fly differs from house fly:
 - Wings rest one atop the other on the abdomen
 - Long proboscis attached to bottom of head
- Both female and male species bite

Parasites

- Tsetse fly acquire ~ the when feeding on an infected host
- multiply in the gut of fly
 - Binary fission
- ~ transmitted to mammalian host in next tsetse feeding
- ~ multiply in blood and evade immunity
 - ~ undergo antigenic switching to stay ahead of immunity
 - Gene switching of antigenic structure changing parasitic glycoprotein cell wall (variant antigenic types VATs)
- After inoculation parasite expresses VATs for 5 days and then switches to another

Animal reservoirs

- Rhodiense

- Domesticated animals

- Cattle
 - Sheep
 - Goats
 - Dogs

- Wild animals

- Hypos
 - Giraffes
 - Lions
 - Hyenas
 - Warthogs

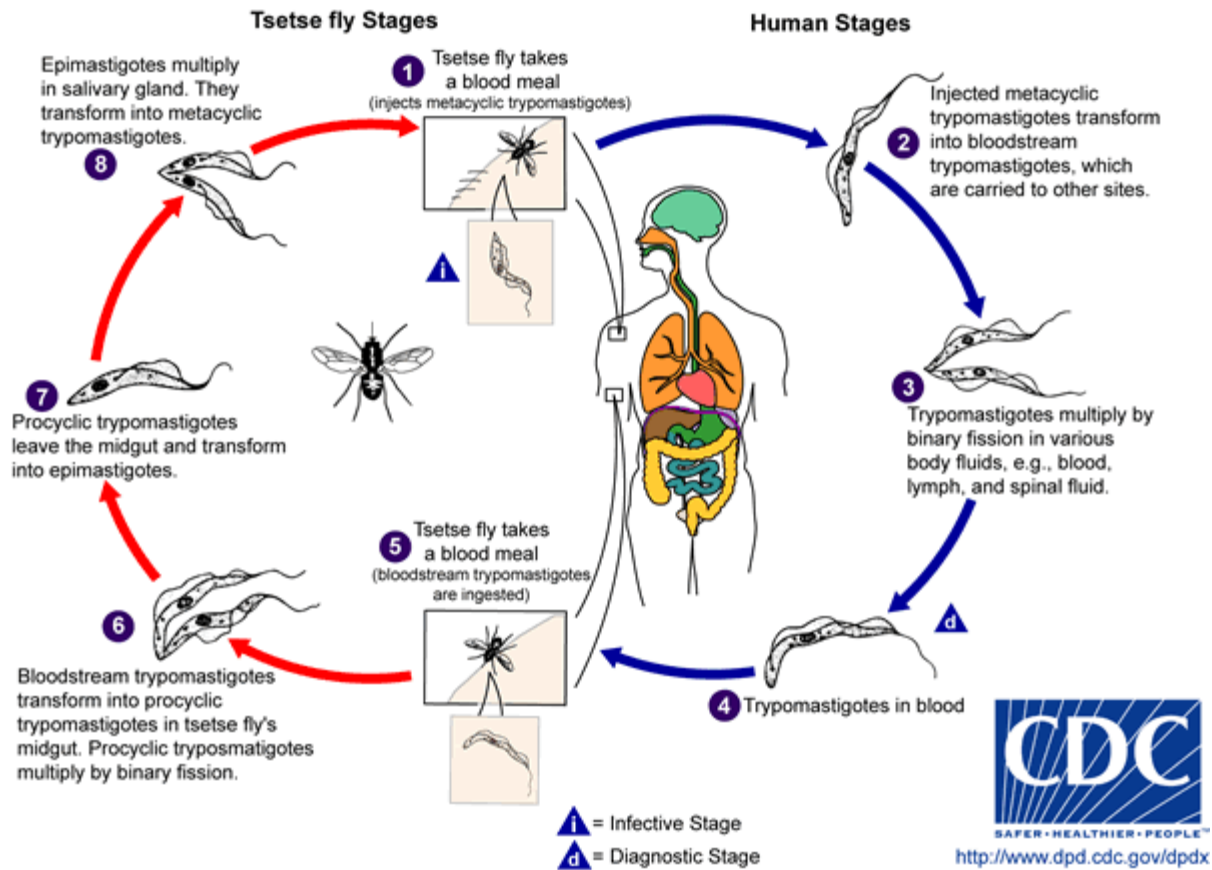
- Gambiense

- Domesticated animal

- Pigs
 - Cattle
 - Sheep
 - Cats

- Wild animals

- kob



Pathology and pathogenesis

- After a bite chancre appears & resolves over weeks
- Parasite evades immunity
- Disseminate to regional LN then blood stream
- ↑ capillary permeability → ↑ inflam resp with 2nd fibrosis.
- Rhodiense → pancarditis and involvement of cardiac conduction system.

Clinical picture

- Looks like malaria
- Has 2 stages
 - Haemolympathic
 - Meningo-encephalitic
- Rhodensie more acute than gambiense

1st stage

- Haemo-lymphatic phase:
 - Chancre (self limiting)
 - headaches and fever
 - joint pains and itching.
 - Big LN posterior Δ of neck
 - Winterbottom's sign
 - Myocarditis (especially in T.b. Rhodesiense)
 - Pallor
 - HSM
 - No neurological involvement

Haematology

- Leukocytosis
- Thrombocytopaenia
- Normocytic anaemia
- ↑ polyclonal Ig esp IgM
- ESR is also elevated
- Expression of auto-antibodies
 - RF+
 - Heterophilic antibodies
 - Anti-DNA antibodies
 - CSF > Pleocytosis, ↑ protein & Id of parasites

2nd phase

- Neurological phase
- Reaches the brain via bloodstream
- Causes meningoencephalitis or meningomyelitis or both

- Sleeping sickness
 - (production of tryptaphol from tryptanol)
 - Confusion
 - In-coordination and slurring of speech
 - Easy fatigability
 - Mania
 - Daytime slumber and night-time insomnia
 - May have parkinsonism and cerebellar signs
 - Coma and death

Transmission

- MTCT
 - Child presenting with 2nd stage disease
- Laboratories
 - through the handling of infected blood
- Blood transfusion
- Sexual contact
 - rare

Mechanism of narcolepsy

- ↑ production of tryptophol by parasite
- Tryptophol induces narcolepsy
- Derived from conversion of tryptophan
 - OH substitution of CO in position 8 of C=C chain
- Same as derived from disulphuram and wine
- High doses of tryptophol → drowsiness and suppression of brain stem reflexes
 - Coma and death

Difference between R and G

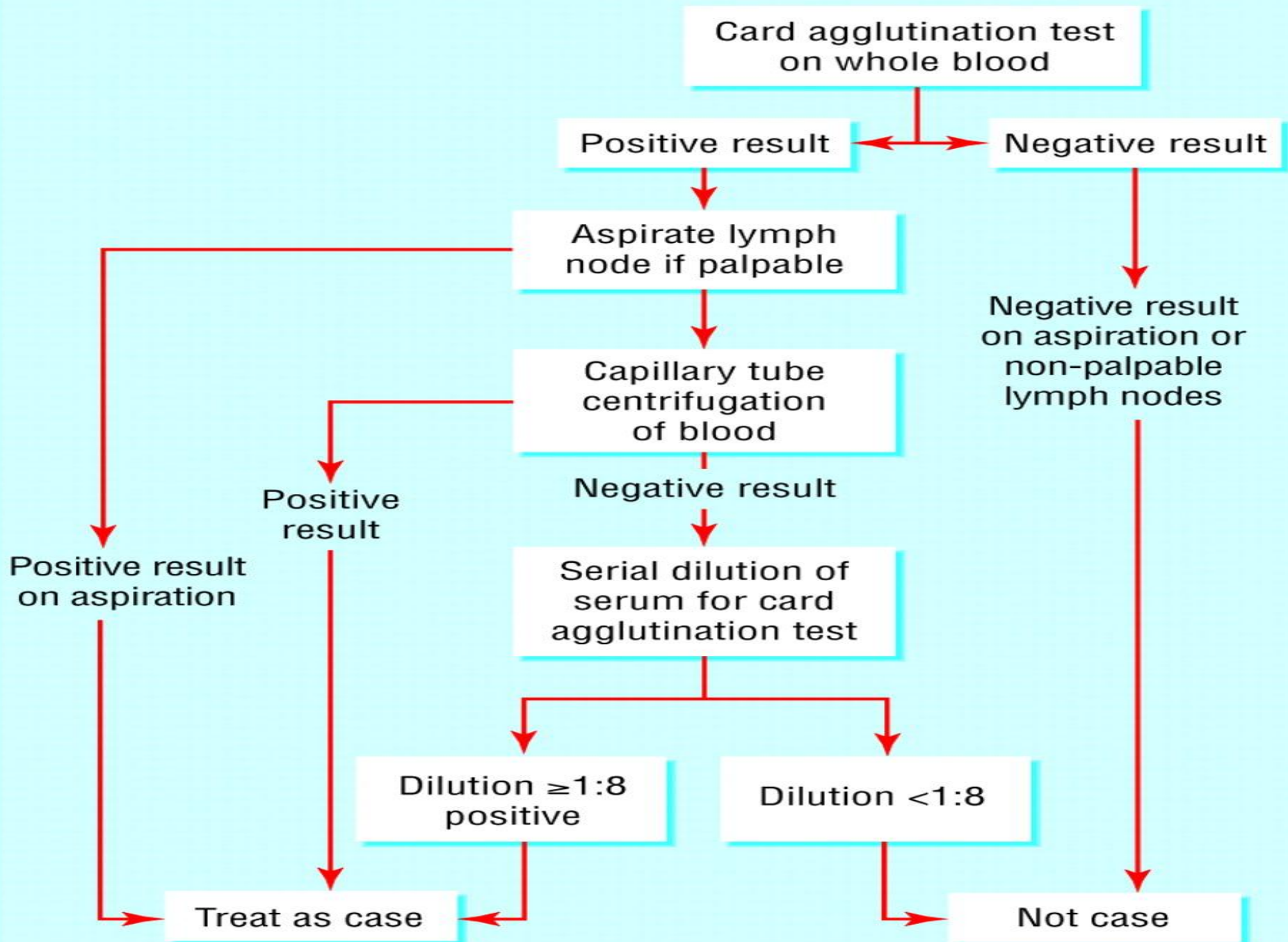
- Rhodesiense
 - Acute illness.
 - Tachycardia out of proportion with fever
 - Can cause myocarditis and CMO
 - Kills quickly
- Gambiense
 - Chronic illness

Diagnosis

- High index of suspicion in a traveller
- Demonstration of parasites
- Fresh wet preparations easier
 - May demonstrate life parasites:
 - the trypanosomes are motile and attract the eye
 - Blood
 - CFS
 - Chancre
 - Tissue
- Giemsa stain can be used

CATT

- Card agglutination test for trypanosomiasis
- Antibody detection test
 - Used as a screening test only
 - 95% sensitive for gambiense
 - Not sensitive for rhodesiense
 - The higher the dilution the more likely true +
 - + CATT may be confirmed using microscopy



- Every patient diagnosed with HAT must have LP.
- CSF WCC of 6 or $>$ means 2nd stage disease

Treatment

- Pt treated with Suramin
- Took 3 days to arrive
- Test dose should be given
- MOA
 - Inhibition of enz in energy production
 - Eg glycerol phosphate dehydrogenase
 - Binds to plasma proteins & accumulates in plasma for long
- Adverse reactions include:
 - Severe hypersensitivity
 - Nephrotoxicity and peripheral neuropathy.
 - U & E should be done before each dose
- Rx on day 1, then 5, 8, 12 and 26.

Other drugs

- Pentamidine
 - MOA
 - Concentrates in pcell and binds to pDNA and interferes with DNA synthesis
 - T cruzi cant concentrate Penta → resistant
 - Poor CNS penetration
 - Effective for HL stage
 - Painful injection
 - Can cause sterile abscess
- Eflornithin
 - Effective in both HL and CNS stages
- Melarsoprol
 - Highly toxic drug

SPECIES	DRUG OF CHOICE
T.RHODESIENSE – HL STAGE	SURAMIN
T RHODESIENSE CNS	MELARSOPROL
T GAMBIENSE – HL STAGE	PENTAMINIDE
T GAMBIENSE CNS	EFLORNITHINE

- THERE IS NO CURE TEST FOR HAT
- LP MUST BE DONE EVERY 6 MONTH FOR 2YRS
- PATIENT DETERIORATING MUST BE RE-LP
 - RE-RX IF NECESSARY
- OUR PATIENT FOLLOWED UP FOR 2 YEARS AND WAS SYMPTOMS FREE
- NEVER TO GO TO AFRICA AGAIN

Prevention

- Avoidance of areas afflicted with disease
- Avoidance of colour blue
- Use of net impregnated with Dichloro-Diphenyl-Trichloroethane
- Wearing of long sleeved clothes
- Use of insect repellants
- etc