

# Chaga's Disease

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# Trypanosomiasis

## ▶ African trypanosomiasis

- *Trypanosoma brucei gambiense*
- *Trypanosoma brucei rhodesiense*

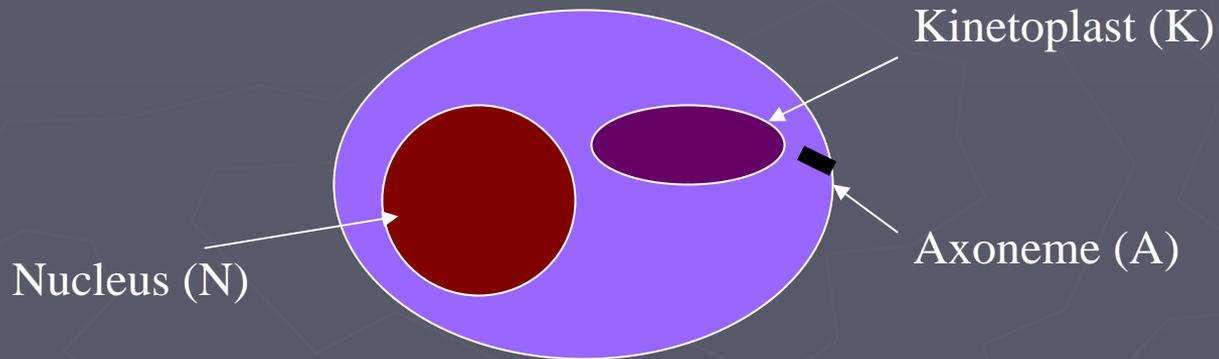
## ▶ American trypanosomiasis

- *Trypanosoma cruzi*
- *Trypanosoma rangeli*

# Basic Hemoflaggelatology

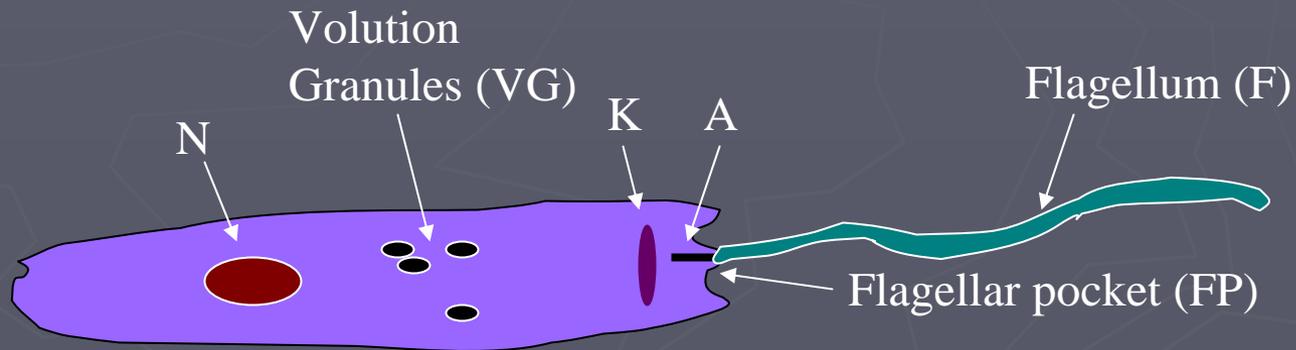
- ▶ Found in the blood
- ▶ They are also called kinitoplastida (contain kinetoplasts or modified mitochondria)
- ▶ Basic forms
  - Amastigotes
  - Promastigotes
  - Epimastigotes
  - Trypomastigotes
  - Metacyclic trypomastigotes

# Amastigote (old Leishmania stage)



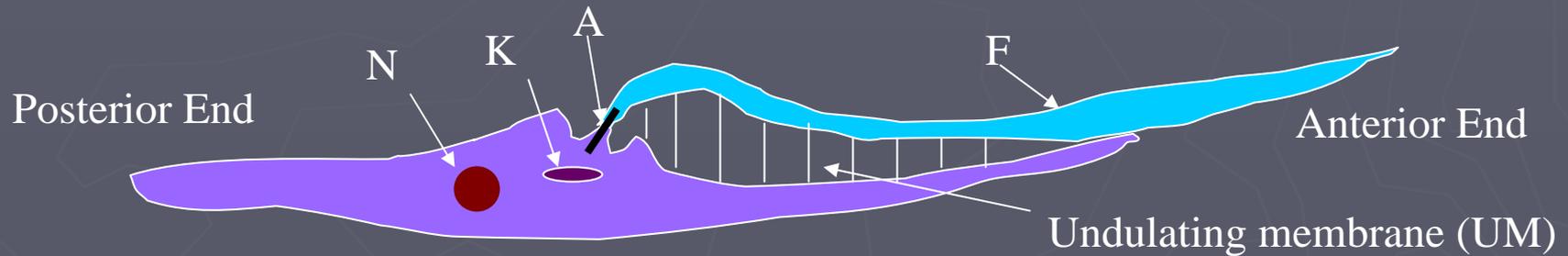
- ▶ Slightly oval (2-3 X 3-4 microns)
- ▶ Axonemes are like microtubules that are associated with future flagellate motility
- ▶ Found inside reticuloendothelial cells
- ▶ Multiplies by longitudinal binary fission
- ▶ There is generally a small zone between the K and A

# Promastigote (old leptomonas stage)



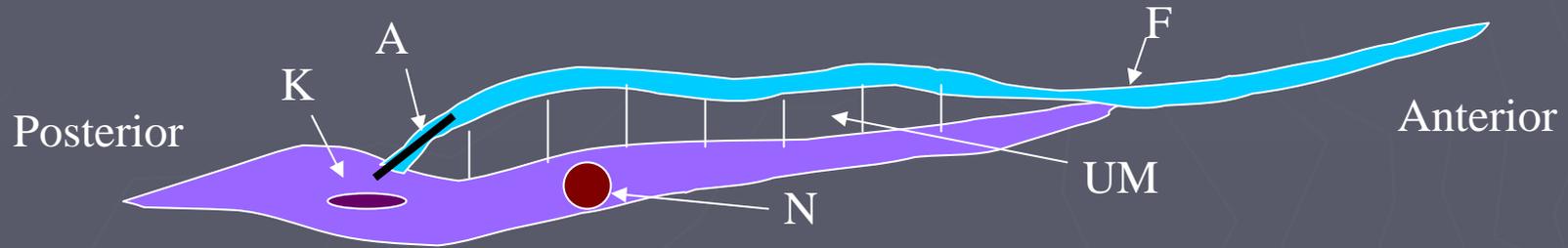
- ▶ May have various shapes from short and fat to long and thin
- ▶ Occasionally see volutin granules (VG) that represent waste products in the cytoplasm

# Epimastigote (old crithidia stage)



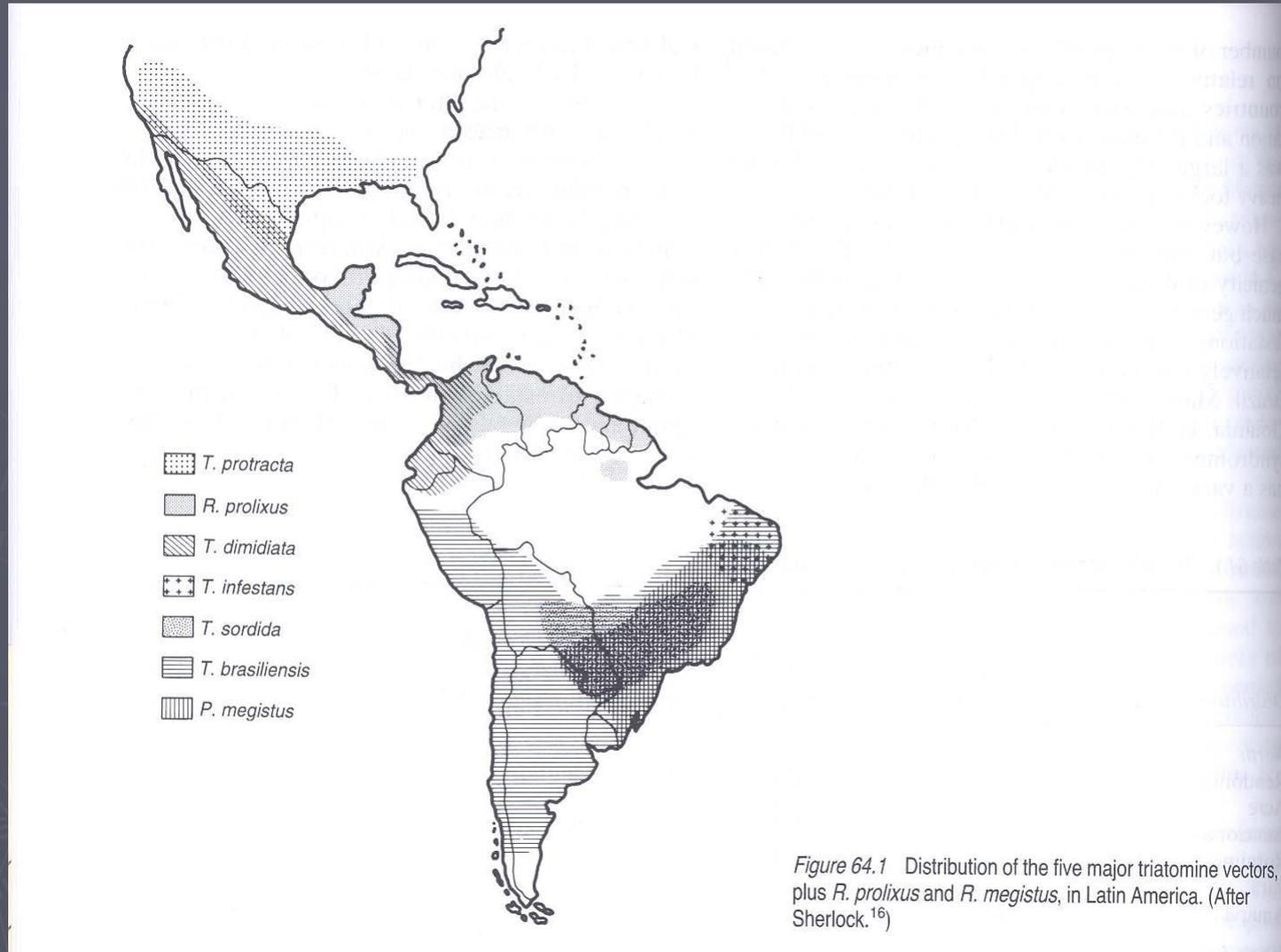
- ▶ Varies in length (12-75 microns)
- ▶ K is always anterior to the nucleus
- ▶ F pulls the body through tissues
- ▶ Epimastigote has an undulating membrane where the promastigote doesn't
- ▶ The undulating membrane causes the body to undulate

# Trypomastigote and Metacyclic Trypomastigote



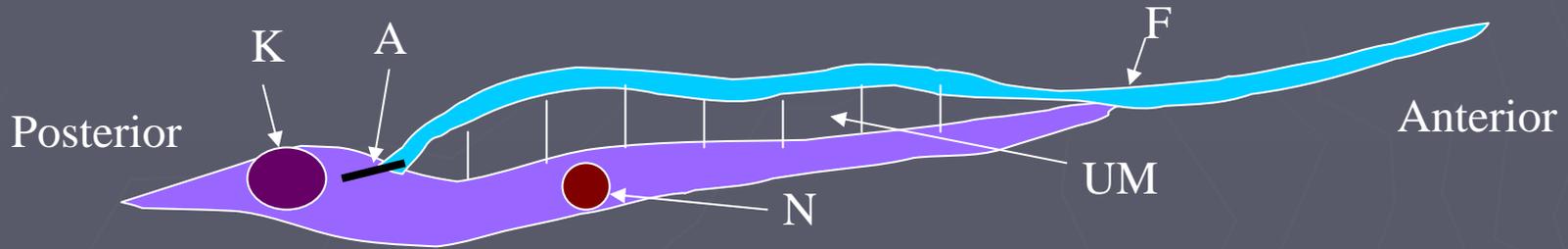
- ▶ This is the Trypanosome
- ▶ The K is posterior to the N vs the Epimastigote with the N posterior to the K
- ▶ Binary fission of the Promastigote, Epimastigote and Trypomastigote are the same (K first followed by the A, F, the N and then the cell)
- ▶ Metacyclic Trypomastigote is the same as the trypomastigote but is the infectious stage in the vector

# American Trypanosomiasis

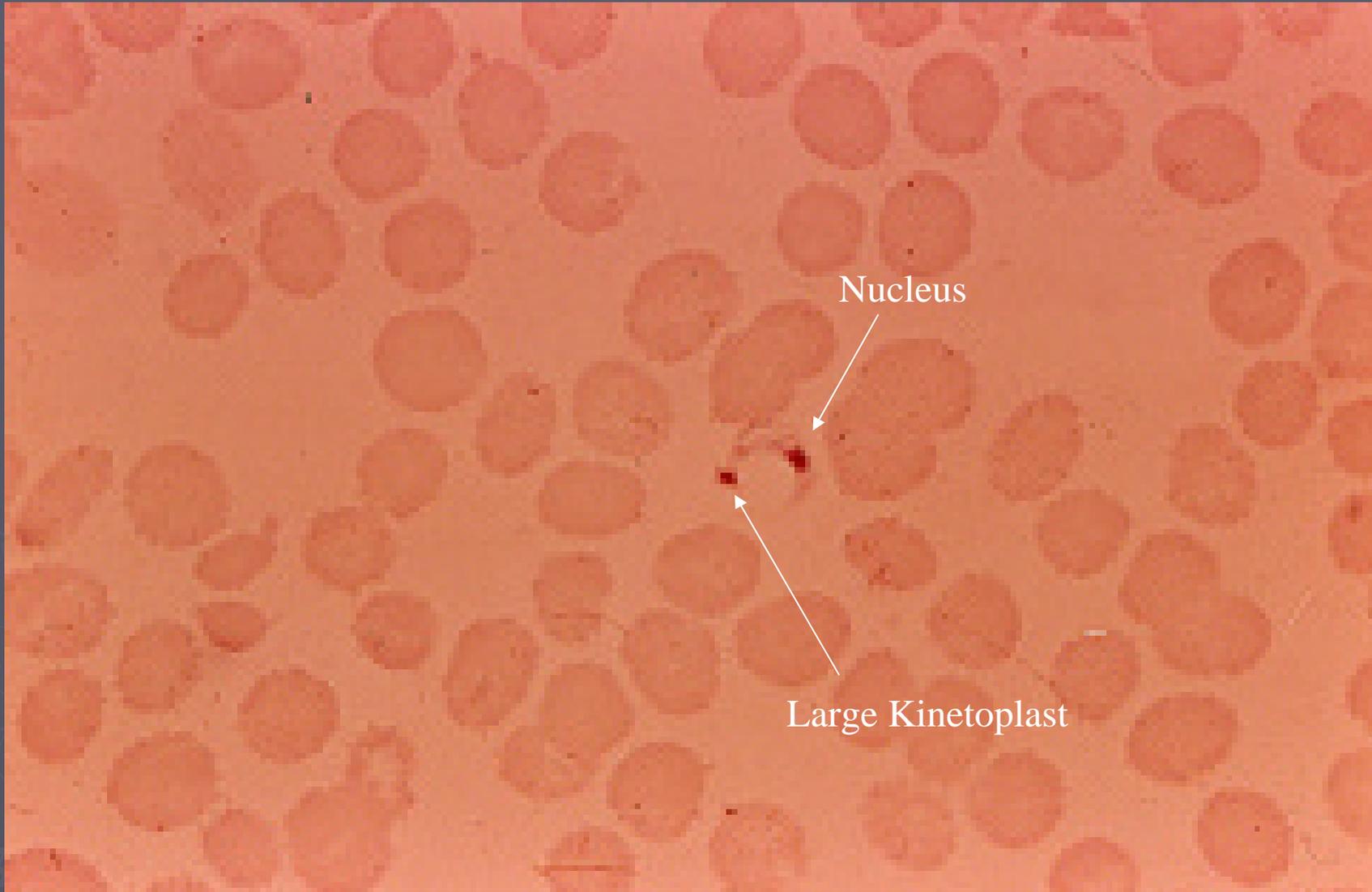


From Manson's Tropical Diseases, pp 1200, Saunder's 1996.

# Trypomastigote of Trypanosoma Cruzi



- ▶ 20 micrometers long
- ▶ Larger kinetoplast than Trypanosoma Rhodesiense or Gambiense
- ▶ 3 zymodeme profiles – all produce human infections
  - Z1 and Z2 – arboreal and terrestrial mammalian transmission
  - Z3 – domiciliary parasites



Nucleus

Large Kinetoplast

# Life Cycle

Insect Vector

Binary Fission of Amastigotes and Epimastigotes

M. Trypomastigotes (30 days)

Bug (bite site, mucous membrane, GI)

Metacyclic Trypomastigote

Bug bite

Macrophages

M. Trypomastigote

Amastigotes

4-5 days of binary fission

Trypomastigote

(5-12 days)

Blood Stream

Pseudocyst ruptures

Trypomastigote

Amastigotes

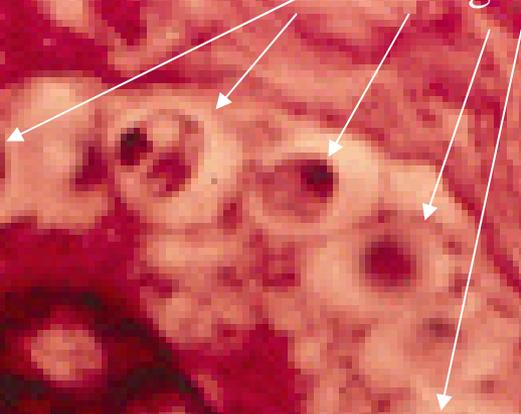
Trypomastigote

Other cells (heart, skeletal muscle, neuroglia, etc)

Acute Symptoms 2-3 weeks



Amastigotes

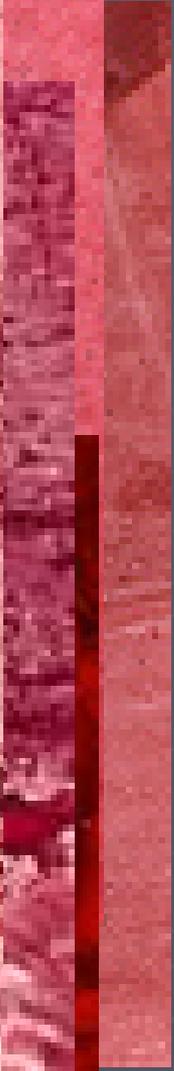


# Transmission Factors

- ▶ Vector exposure
- ▶ Blood transfusions
- ▶ Vertical transmission
- ▶ Trans-mammary transmission
- ▶ Infected food or meat
- ▶ Laboratory accidents
- ▶ Land colonization
- ▶ Quality of human dwellings

# Vector

- ▶ Adult insects can fly.
- ▶ Feed at night
- ▶ Live in holes, like dark, humid sites



# Chagas' Disease

## Acute

Entry site lesions

Systemic signs and symptoms

Organ involvement

## Chronic

Dilation of hollow viscera including the heart

# Acute phase

- ▶ 95% have no acute phase
- ▶ Children have more symptoms
- ▶ Acute phase is often followed by a life-long asymptomatic period (70-90% of those infected)
- ▶ Some patients experience a subacute progression of illness that can result in a rapid demise.
- ▶ 10% fatality rate in the acute phase

# Portals of Entry

- ▶ Ocular – 48%
- ▶ Skin – 24%
- ▶ Other / Inapparent – 28%

# Entry site lesions

## ▶ Romana's sign

- Unilateral, painless, erythematous palpebral edema
- Occasional swelling of the entire side of the face
- Preauricular or submaxillary adenopathy
- Conjunctivitis
- Dacryoadenitis

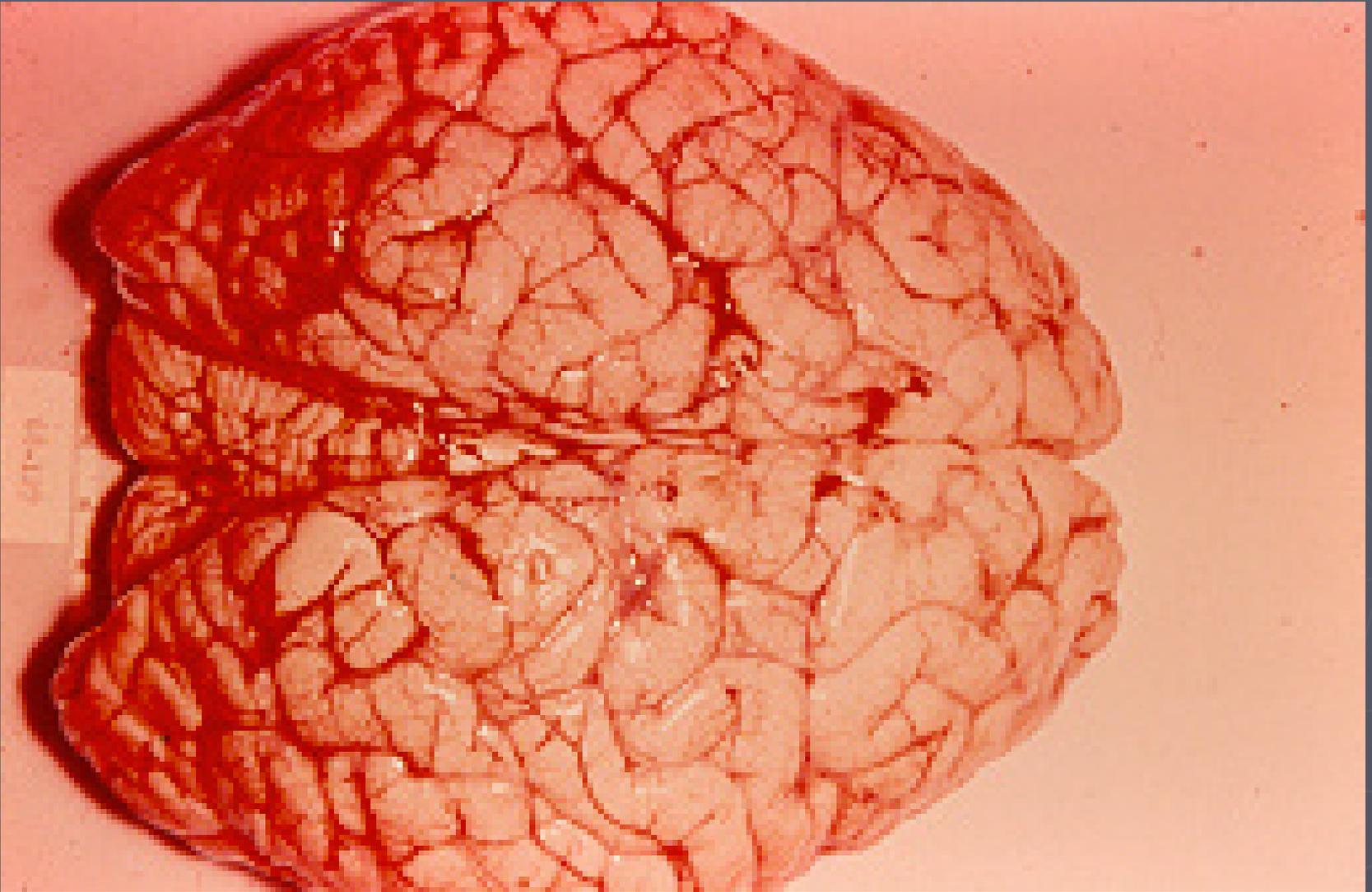
## ▶ Chagoma

- Erythema, prurritus, painless infiltration of the dermis
- Central desquamation with rare ulceration
- Exposed parts of a sleeping person
- Last for weeks



# Organ Involvement

- ▶ Hepatosplenomegaly
- ▶ Lymphadenopathy
- ▶ Muscles
- ▶ GI
- ▶ Pulmonary
- ▶ Heart
- ▶ CNS – meningoencephalitis
- ▶ Bone marrow
- ▶ Skin



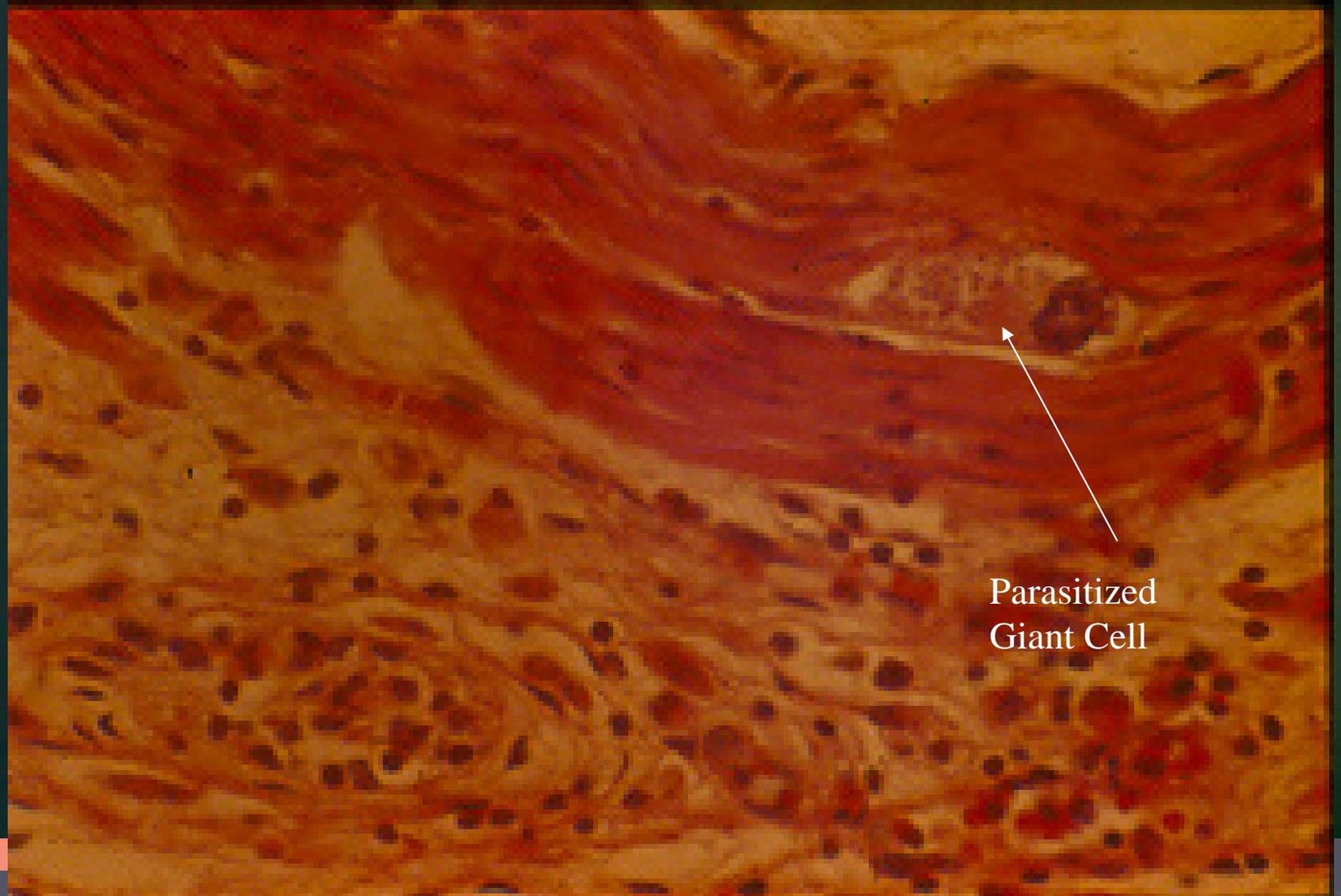
# Congenital Chagas' Disease

- ▶ Low birth weight
- ▶ Hepatomegaly
- ▶ Meningoencephalitis with seizures and tremors

# Chronic Chagas Disease

- ▶ Often seen at 30-40 years old
- ▶ Occurs in 10-30% of those infected
- ▶ Chronic myocarditis is most common
  - Diffuse multifocal myocarditis with edema and fibrosis
  - Increased thrombosis seen in the heart wall
  - Apical aneurysms occasionally seen
  - EKG is the 1<sup>st</sup> manifestation (RBBB, PVC's)
  - Sudden death is common
  - May present with CHF, embolism, ruptured aneurysm, vent. fibrillation
- ▶ Can see dilation of other hollow viscera
  - Esophagus
  - Colon with megacolon
  - Ureter

5 2 4 6 8 10  
Lymphocytic myocarditis



Parasitized  
Giant Cell

# Laboratory Diagnosis

## ▶ Acute phase

- Giemsa stained buffy coat blood smear
- Biopsy specimen – find Trypomastigotes and Amastigotes

## ▶ Chronic phase

- Culture on NNN media
- Xenodiagnosis
- Serology – CF, IHA, IFAT, ELISA, RIPA, Latex Agglutination, Direct Agglutination Tests

# Clinical Diagnosis

- ▶ No single laboratory test is adequately sensitive and specific to diagnose Chaga's disease
- ▶ Generally the diagnosis is made by at least 2 different serologic tests (ELISA, immunofluorescence, indirect hemagglutination) along with clinical and exposure history.



# Treatment

Drug	Adult	Child
Benznidazole (not available in the US)	5-7 mg/kg/day in 2 div doses X 30-90 days	$\leq 12$ yo: 10 mg/kg/day div in 2 doses X 30-90 days
Nifurtimox* (consider with gamma interferon X 20 days)	8-10 mg/kg/day div in 3-4 doses X 90-120 days	1-10 yo: 15-20 mg/kg/day div in 4 doses X 90 days 11-16 yo: 12.5-15 mg/kg/day div in 4 doses X 90 days

\*Nifurtimox (Lampit, Bayer, Germany). It is only available under the Investigational New Drug (IND) protocol from CDC Drug Service, CDC, 404-639-3670 (evenings, weekends, or holidays: 404-639-2888).

# Control Measures

- ▶ Avoid habitation in buildings infested with reduviid bugs (constructed of mud, palm thatch, adobe brick especially those with cracks in walls or roofs)
- ▶ Use insecticide impregnated bed nets
- ▶ Don't sleep or camp outdoors in highly endemic areas
- ▶ Blood and serologic screening of household members of infected patients with common exposure histories
- ▶ Serologic screening before and after travel if exposure to the vector is unavoidable
- ▶ Eliminate vectors in homes
- ▶ Blood and organ donor screening by serology
- ▶ Treat donated blood in endemic areas with gentian violet (diluted 1:4000)
- ▶ Treat infected (acute and chronic) to prevent progression to cardiac morbidity and congenital infection

# Blood Donor Screening for Chagas in the US, 2006-2007

- ▶ American Red Cross screened 148,969 blood samples at three collection centers, Los Angeles, Oakland, and Tucson.
- ▶ Initial screen with ELISA. If positive it is repeated twice. If the second or third test is positive a RIPA (radioimmunoprecipitation assay) is completed. If the RIPA is positive the specimen is considered positive.
- ▶ 63 specimens from 61 donors were ELISA repeat positive. 32 were RIPA positive (51%).
- ▶ Prevalence 1/4655.
- ▶ On December 13, 2006 the FDA licensed the Ortho T cruzi ELISA test to screen blood donors in the US. It is labeled for testing plasma and serum samples from living cell and tissue donors and from heart beating organ donors but not labeled for general clinical diagnostic use.
- ▶ US blood supply began screening all donations for T cruzi on January 29, 2007 and providing testing services for smaller blood collection centers and hospitals that request testing.

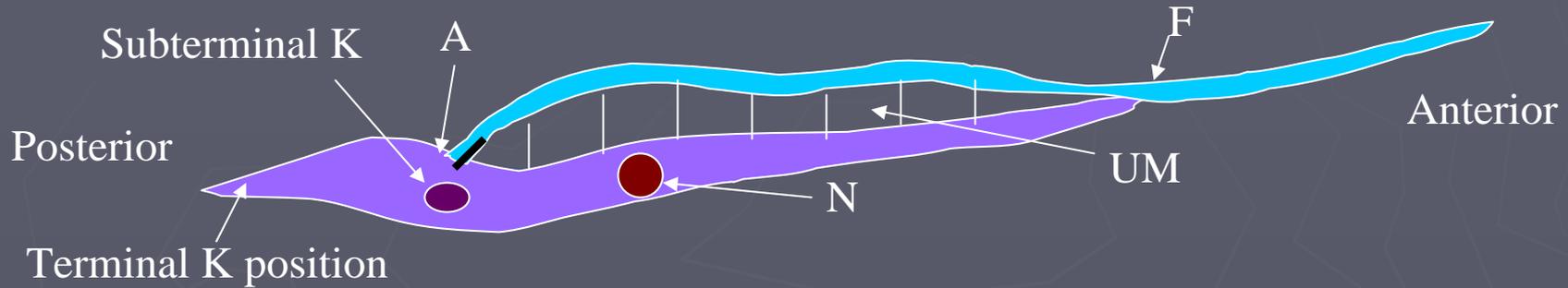
# American Association of Blood Banks

- ▶ All components from blood donations that are repeat reactive by ELISA should be quarantined and removed from distribution
- ▶ Donor should be deferred from making donations indefinitely
- ▶ Recipient tracing should be done on those specimens repeat positive by ELISA and confirmed with RIPA
- ▶ Test at risk family members of confirmed positives with a similar history of exposure to Chaga vectors in an endemic area
- ▶ Deferred donors, at risk family members, and potentially infected recipients should be referred to health care providers

# Trypanosome Rangeli

- ▶ Historically known as T. Ariari
- ▶ Seen in Uruguay, Chile, Honduras, Guatemala, Southern Mexico to Brazil where Rhodnius is present
- ▶ Larger and more slender than T. Cruzi (26-34 micrometers)
- ▶ Has a subterminal kinetoplast
- ▶ Host – animals and occasionally man
- ▶ Does not cause disease
- ▶ Life cycle – similar to T. Cruzi except for method of transmission to humans
- ▶ Transmitted by bug bite (anterior inoculative transmission) not from bug feces
- ▶ Diagnosis – Blood smear, Culture of blood
- ▶ Problem – may be confused with T. Cruzi

# Trypomastigote of *Trypanosoma Rangeli*



- ▶ 26-34 micrometers long
- ▶ Subterminal kinetoplast vs *T. Cruzi*, *T. Rhodesiense* or *T. Gambiense*



Subterminal Kinetoplast