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The *Leishmania* Years at UNL (Or, My Life as a Cell Biologist, 1966-1981)

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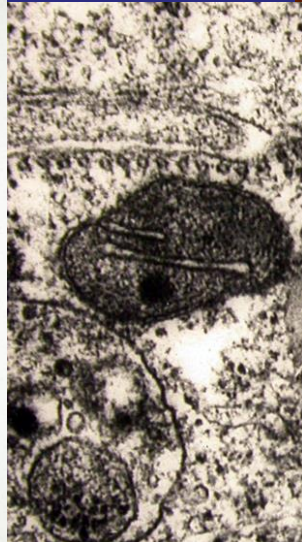
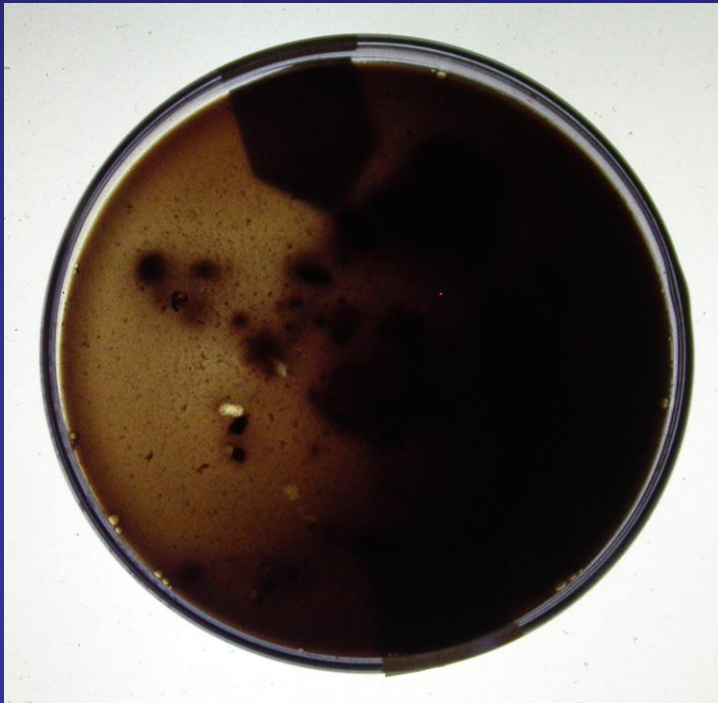
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The *Leishmania* years at UNL (or, my life as a cell biologist, 1966- 1981)

John Janovy, Jr.

BIOS 915P 012215



Sandfly Stages

Human Stages

1 Sandfly takes a blood meal (injects promastigote stage into the skin)

2 Promastigotes are phagocytized by macrophages

8 Divide in midgut and migrate to proboscis

3 Promastigotes transform into amastigotes inside macrophages

7 Amastigotes transform into promastigote stage in midgut

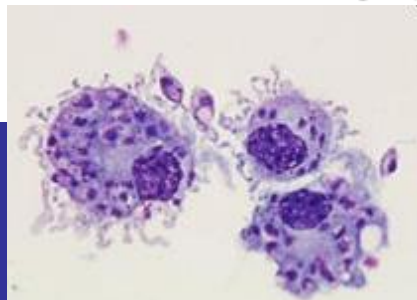
4 Amastigotes multiply in cells (including macrophages) of various tissues

6 Ingestion of parasitized cell

5 Sandfly takes a blood meal (ingests macrophages infected with amastigotes)

i = Infective Stage

d = Diagnostic Stage



<http://www.dpd.cdc.gov/dpdx>

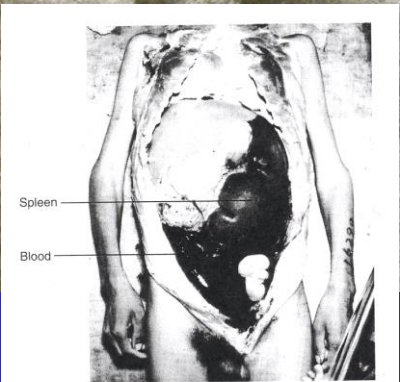
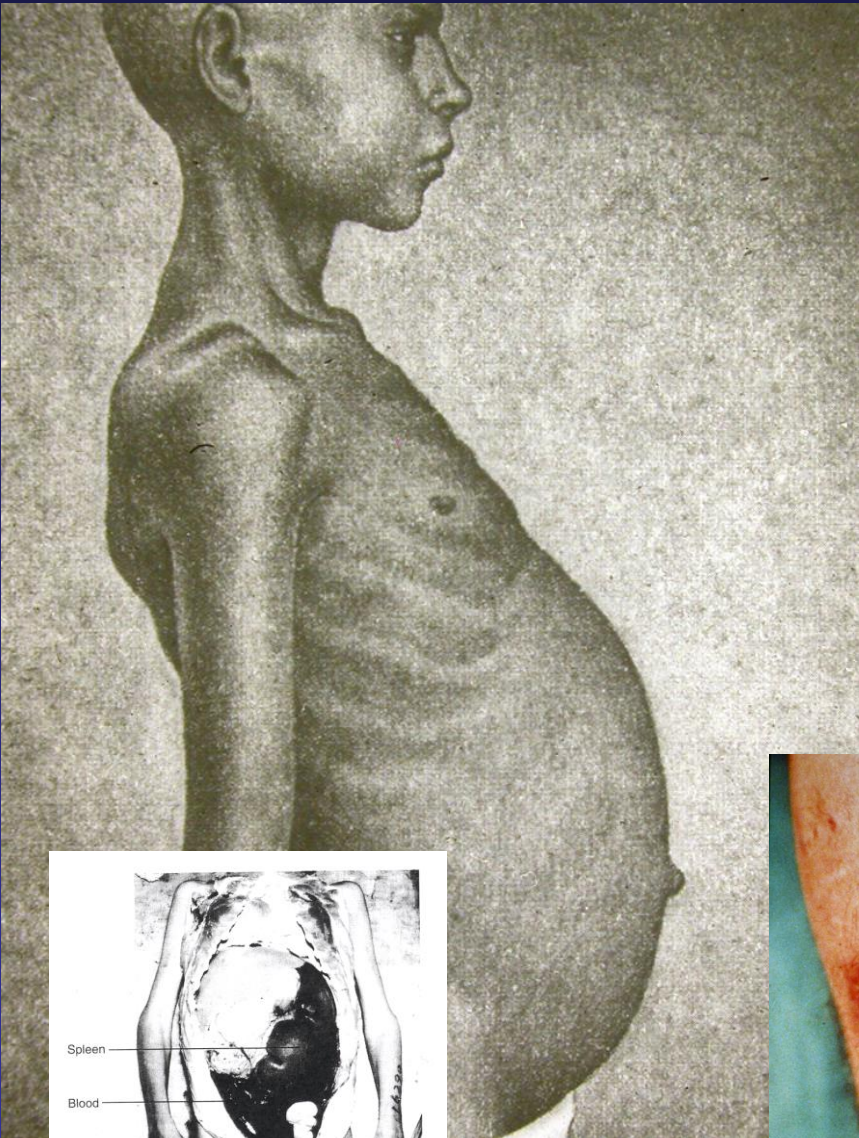


Figure 5.21 A patient with kala-azar who died of hemorrhage after a spleen biopsy.
Note the greatly enlarged spleen. (The dark matter in the lower abdominal cavity is blood.)

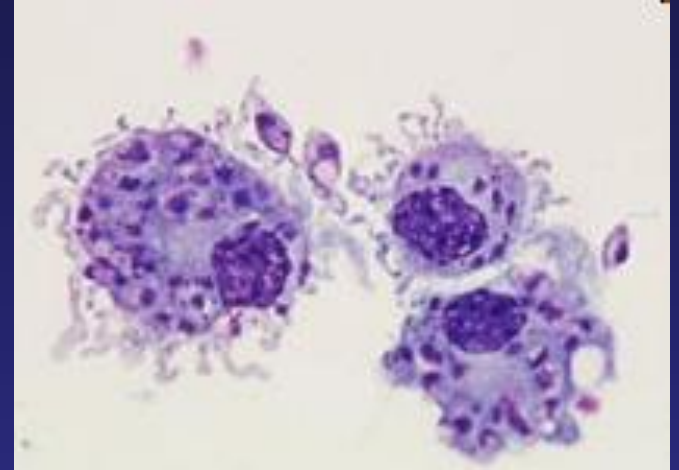
AFIP neg. no. A-45364.



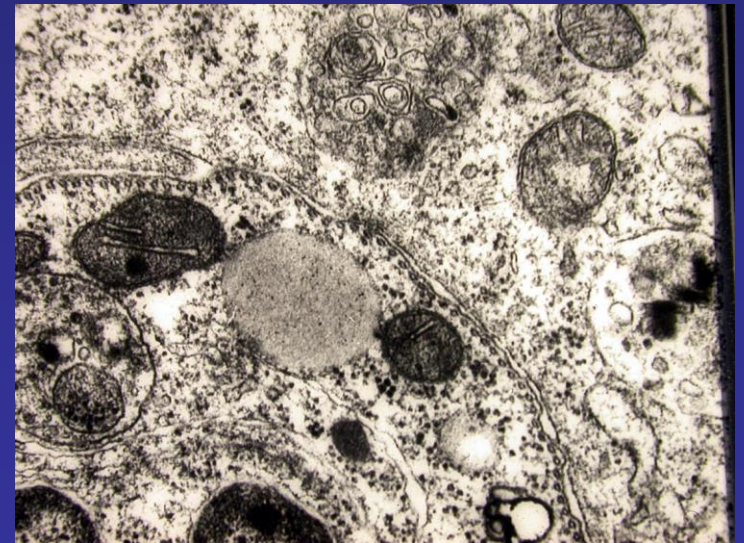
Zaiman slides

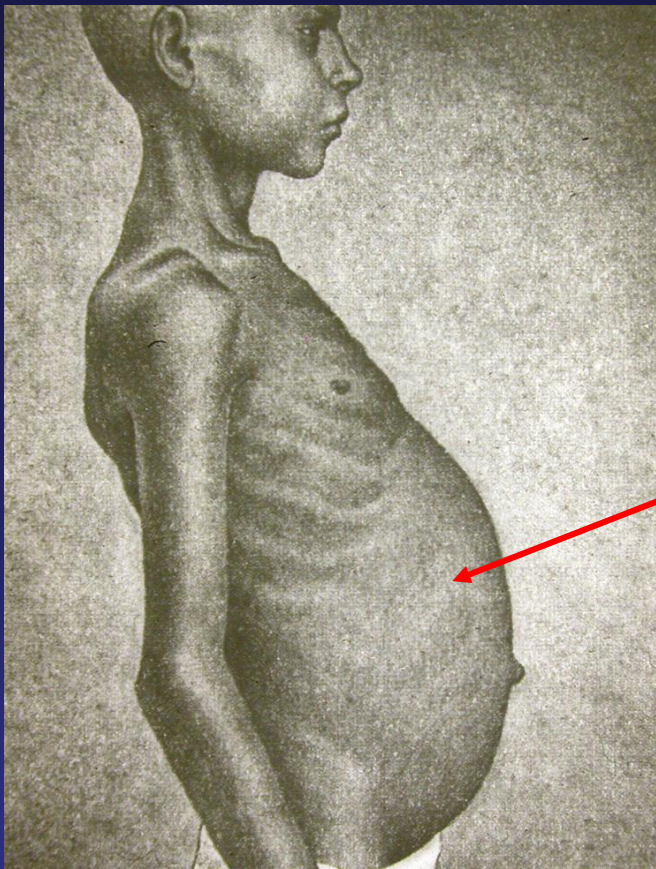
The Three Big Problems:

- The physiological basis for infection site specificity.
- The evolution of infectivity.
- Relationships between intracellular parasites and their host cells.

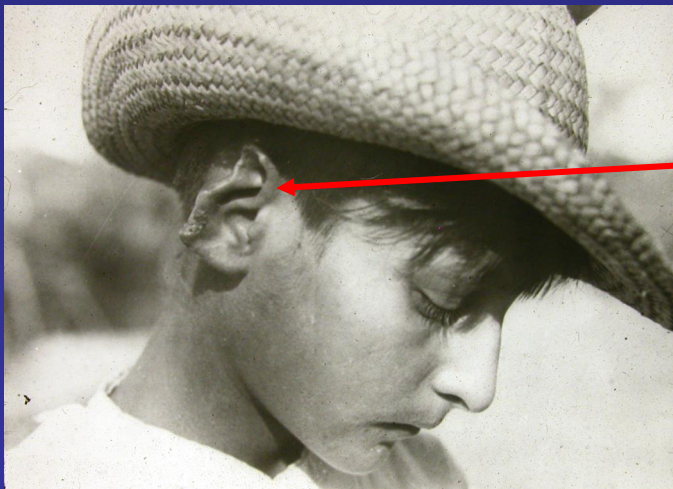


bakerinstitute.vet.cornell.edu





Do the parasites that cause **this** disease differ in their physiological responses to elevated temperature from the parasites that cause **this** disease?



Stauber, L. A. 1958.
Host resistance to the
Khartoum strain of
Leishmania donovani.
Rice Institute
Pamphlet 45:80-96.

This work is what
really enabled the
entire field of
experimental
leishmaniasis,
including drug
screening,
immunology, etc.

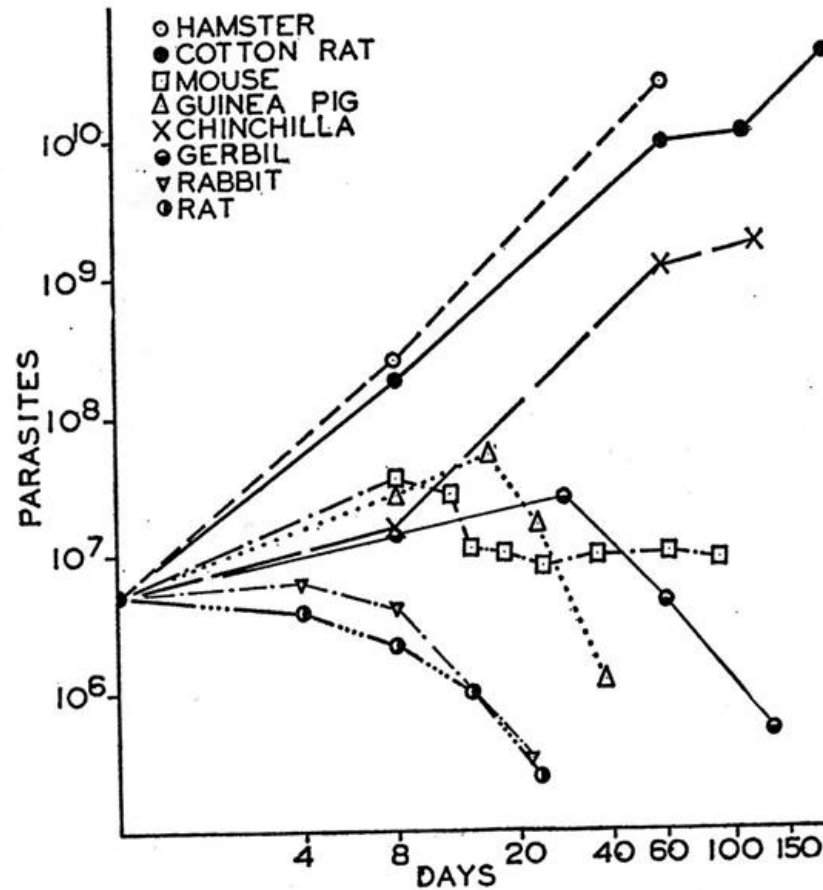


Fig. 3. Representative courses of infection in eight species of small mammals as determined from parasite counts in the liver on various days after inoculation with *L. donovani*. All data adjusted to approximately the same initial density of parasites in the liver at 1 to 2 hours after inoculation. The threshold of patency for these conditions lies close to the axis for 1×10^6 parasites.

What do you need in order to do this work?

- Sterile blood
- Culture medium ingredients
- Autoclave
- Culture tubes
- Pipets (various)
- Rabbits and hamsters
- Autoclave envelopes
- A great big fire
- Haemocytometer
- Lots of 70% EtOH
- Animal care facilities, feed, cages, etc.
- A great big incubator
- Pre-weighed glassware
- A good compound microscope
- Lots of slides
- Glass beads
- Counter

What do you need in order to do this work?

- Tissue grinder
- Screw-cap flasks
- 50 ml glass syringes
- 18-gauge needles
- 1ml syringes; 23 gauge needles
- Rabbit board
- Precision balance
- Weighing paper
- Lots of 70% EtOH
- A door you can close
- Your favorite loop
- Giemsa stain; methanol
- Petri dishes
- Beakers and Erlenmeyer flasks
- Lots of cover glasses



You need a supply of parasites, both amastigotes and promastigotes.

**The Golden Hamster – Leishmanial
workhorse**



wildnatureimages.org

Christmas break, 1966, four cotton rats trapped from Oklahoma City suburbs and brought back to Lincoln for breeding.

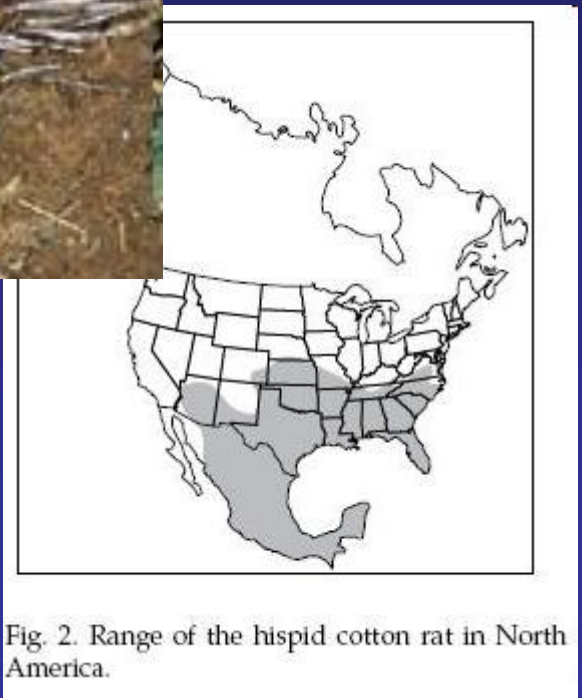
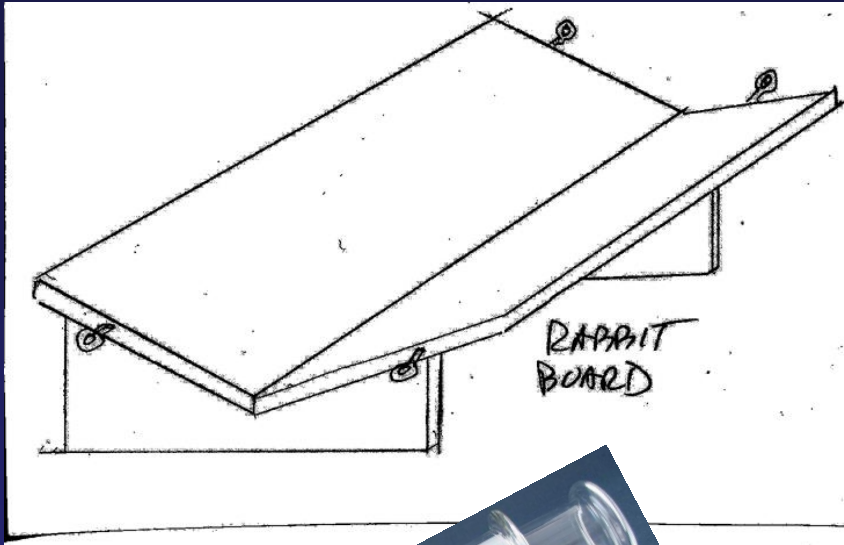
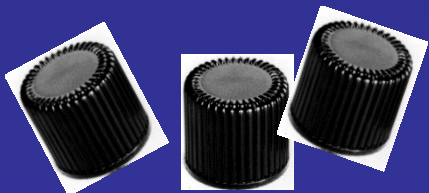
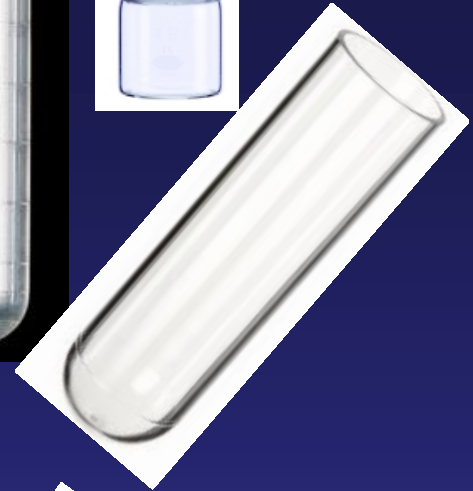


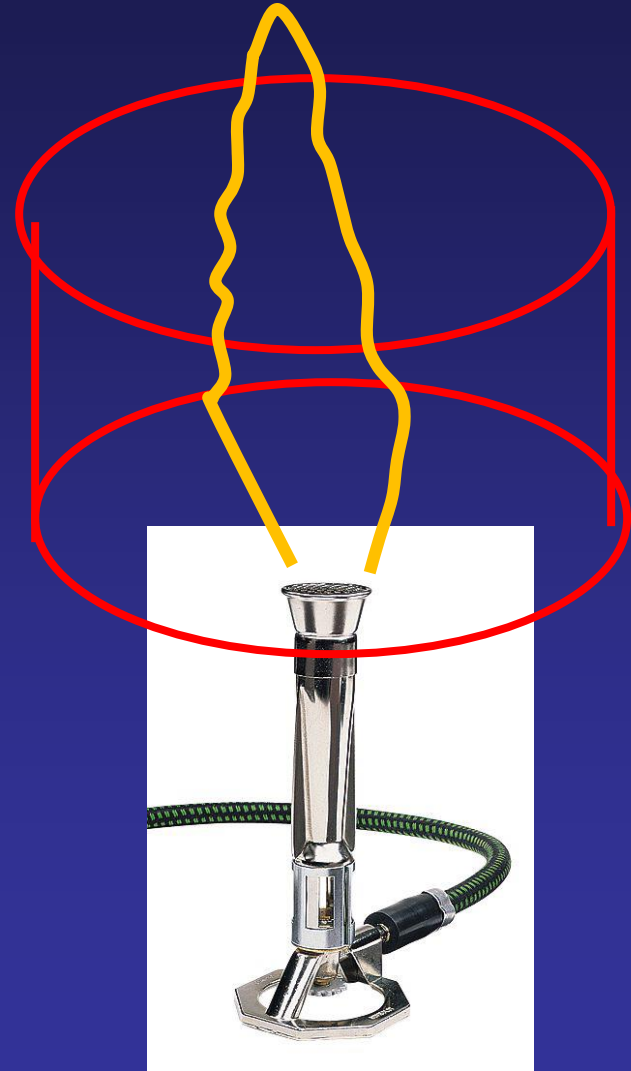
Fig. 2. Range of the hispid cotton rat in North America.

icwdm.org



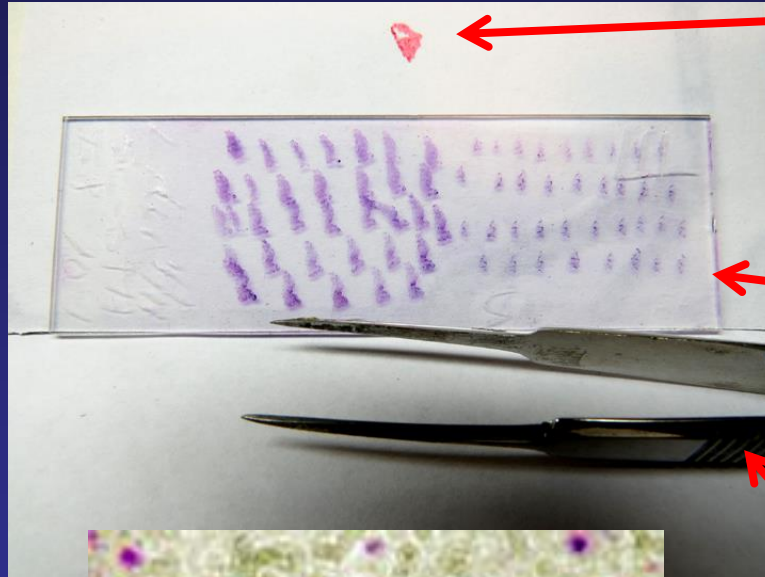
Sterile defibrinated rabbit blood, sodium citrate, glucose, liver digest, agar, KCl, $MgCl_2$, proteose peptone, NaCl, etc. – in various combinations.





“LDs per host cell nucleus”

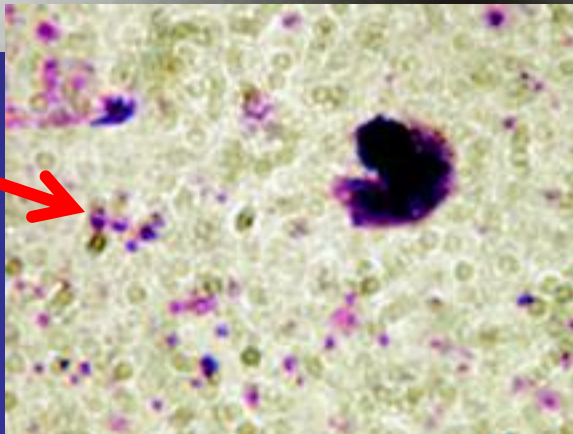
The liver and spleen imprint:



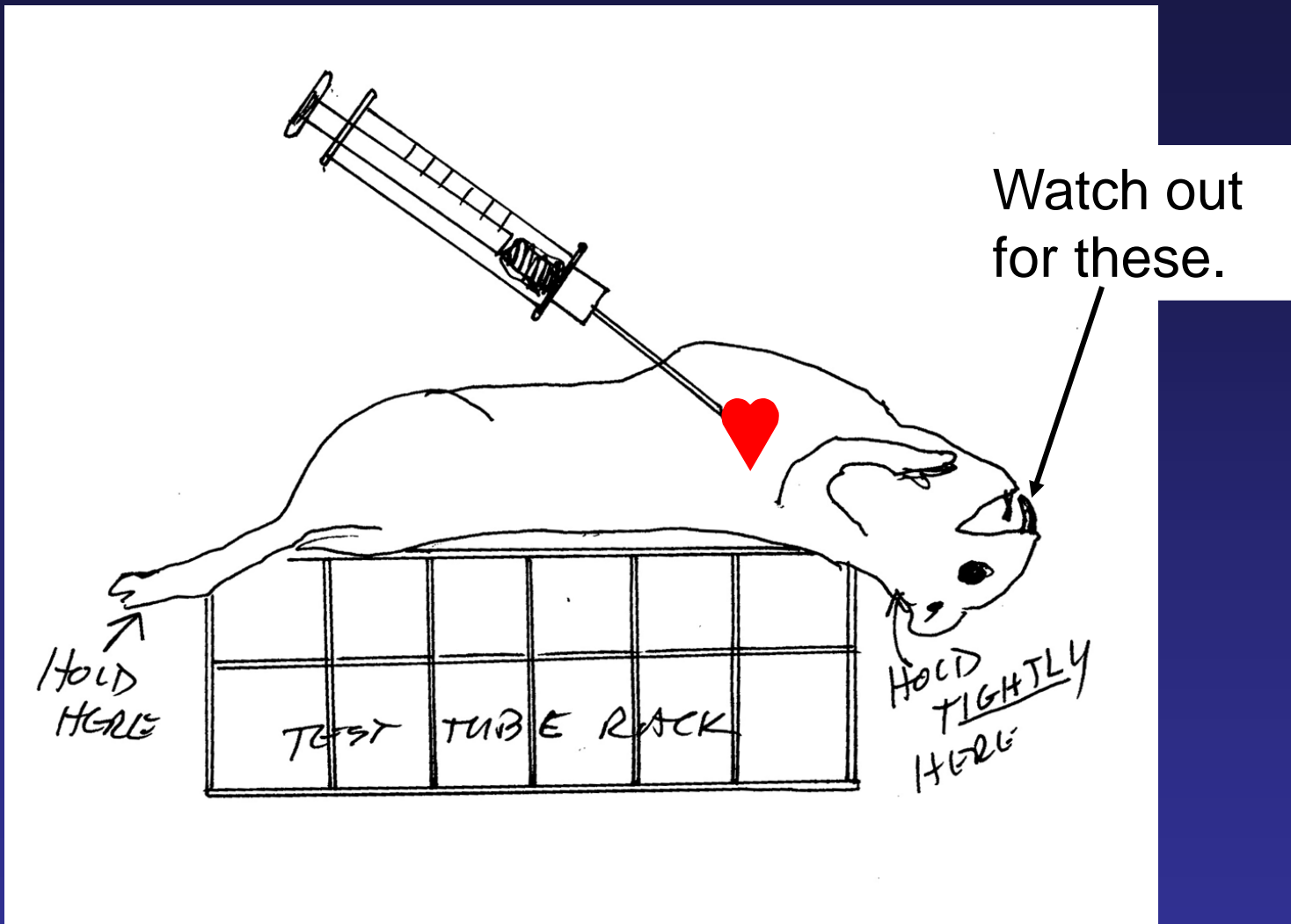
A piece of spleen or liver.

Slide.

Forceps



LDs per host cell nucleus x weight of spleen or liver gives a relative parasite burden per organ per animal.



The Stauber hamster technique for IC injection of leishmanial soup.



Uninfected hamster



Infected hamster



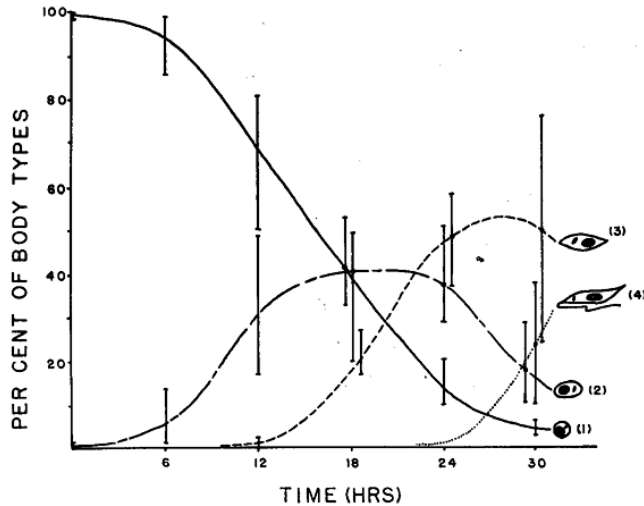


- Janovy, J. Jr. 1967. Respiratory changes accompanying leishmania to leptomonad transformation in *Leishmania donovani*. Exptl. Parasitol., 20:51-55.
- Janovy, J. Jr., and A. E. Poorman. 1969. Temperature and metabolism in *Leishmania*. I. respiration in *L. donovani*, *L. mexicana* and *L. tarentolae*. Exptl. Parasitol., 25:276-282.
- Poorman, A. E. and J. Janovy, Jr. 1969. Temperature and metabolism in *Leishmania*. II. Aldolase in *L. adleri*, *L. donovani*, *L. mexicana* and *L. tarentolae*. Exptl. Parasitol., 26:329-335.
- Janovy, J. Jr. 1972. Temperature and metabolism in *Leishmania*. III. Some dehydrogenases of *L. donovani*, *L. mexicana* and *L. tarentolae*. Exptl. Parasitol., 32:196-205.

The physiological basis for infection site specificity.

LEISHMANIA TO LEPTOMONAD TRANSFORMATION

53



1. Gross morphological composition of transforming populations of *Leishmania donovani* in Tanabe's Medium. Vertical bars represent the extent of individual variation in percentages for experiments.

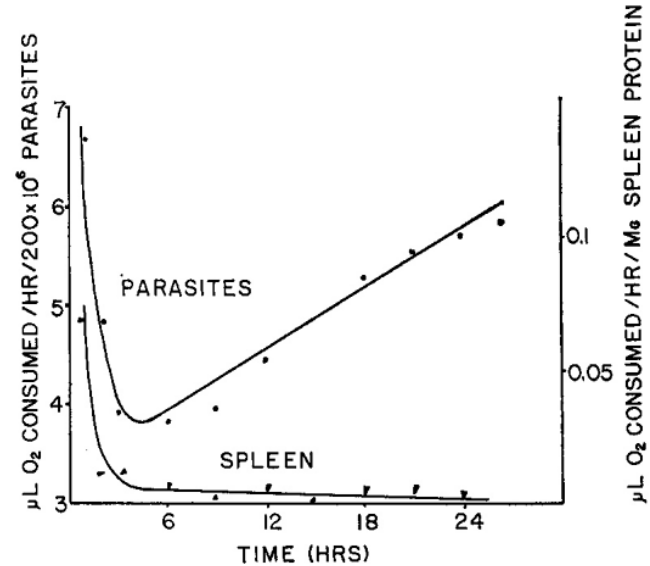


FIG. 2. Changing respiratory rates of leishmania and noninfected spleen preparations.



The physiological basis for infection site specificity (cont'd).

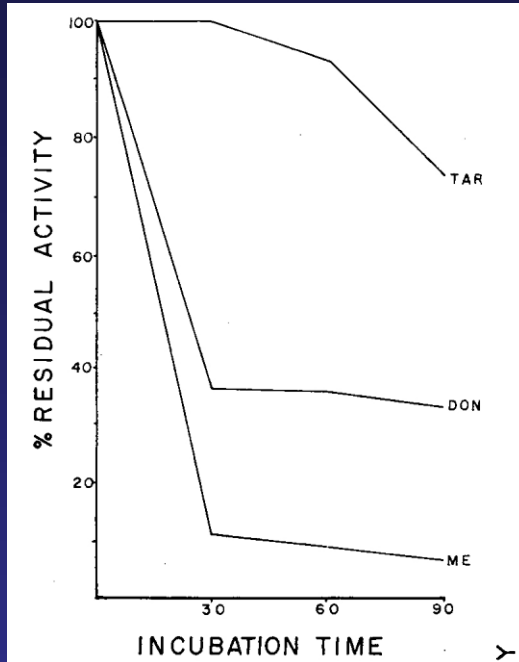
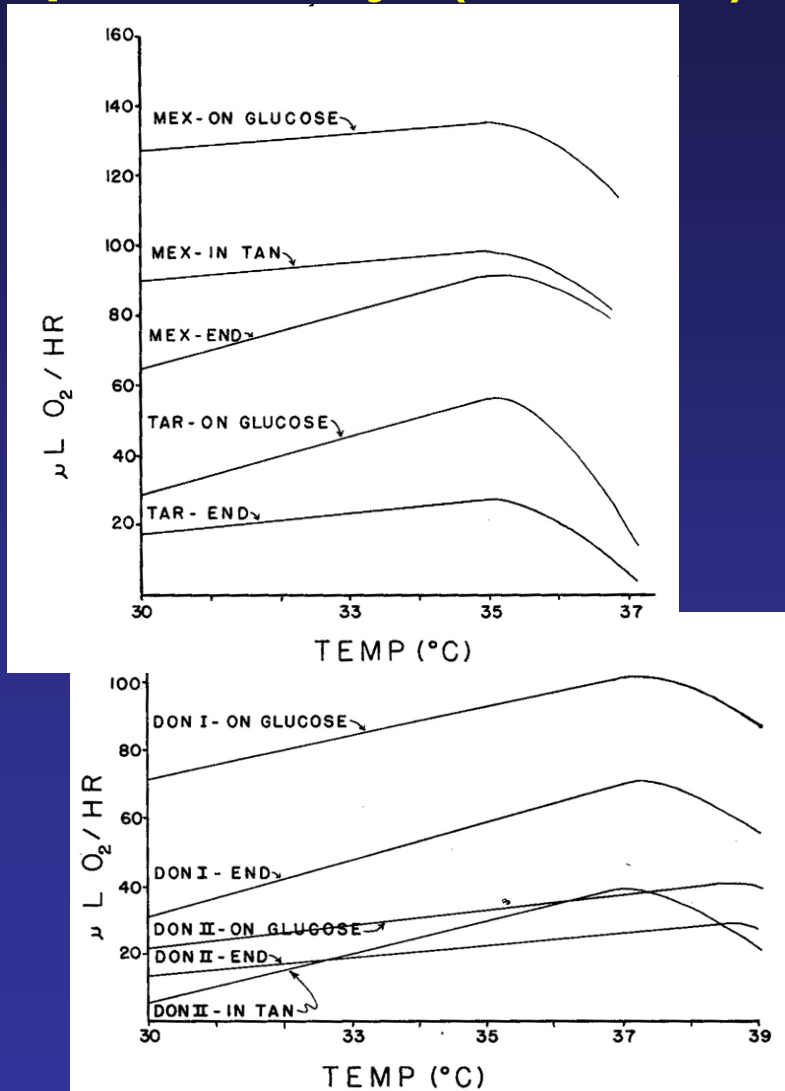


FIG. 6. Inactivation curves of GADP in *Leishmania*

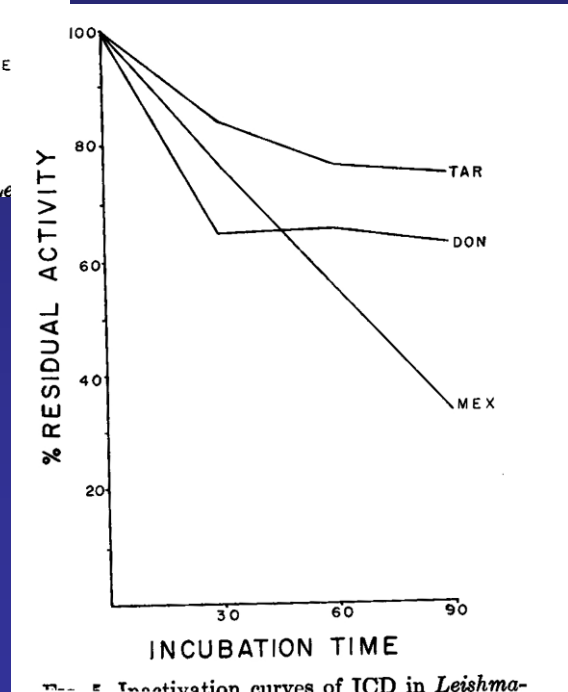
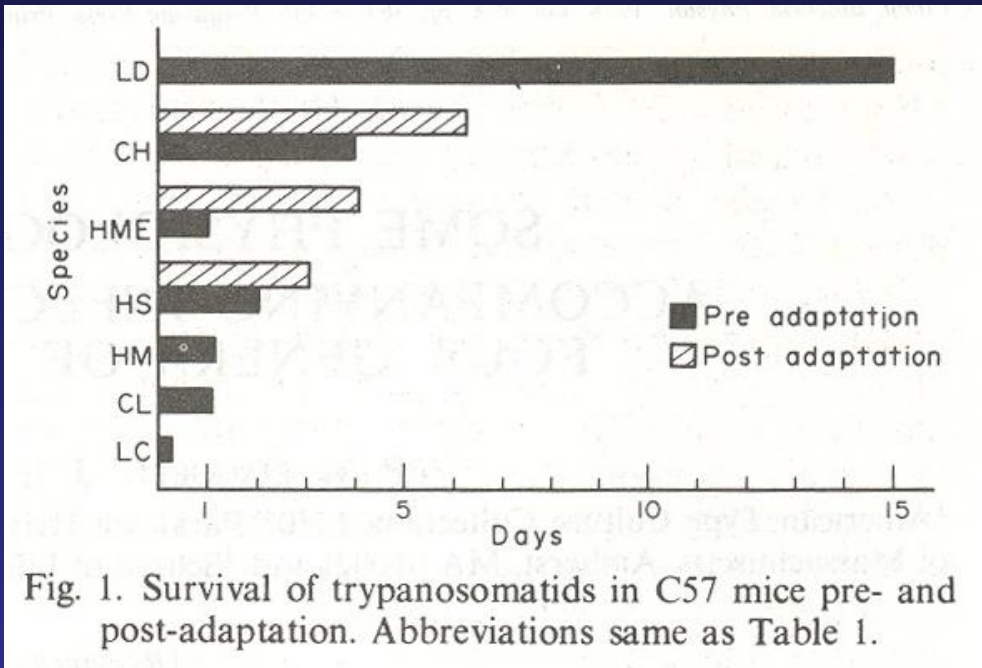


FIG. 5. Inactivation curves of ICD in *Leishmania*

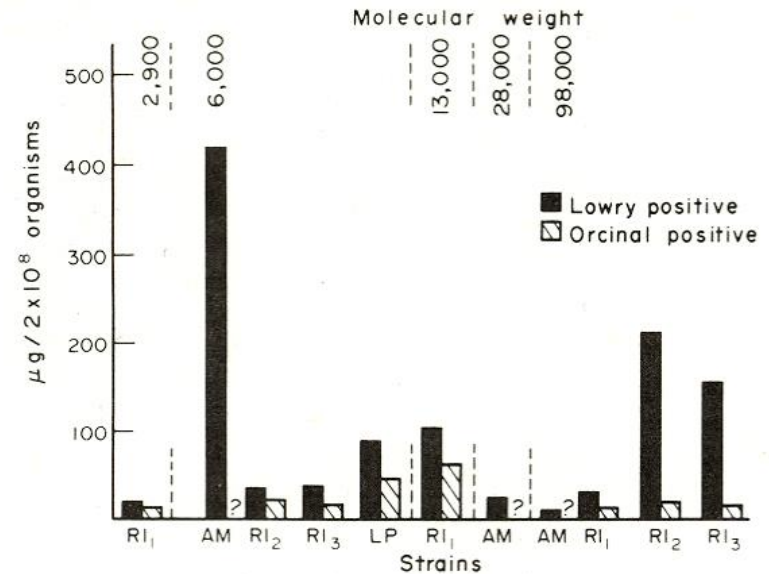
The evolution of infectivity.



The Daggett doctoral work.



The Decker doctoral work.



Graduate students with thesis or dissertation work on trypanosomatids:

Pierre Daggett

Amy Keppel

Joan Decker

Bob Fuchs

Moslih I. Moslih

Gerald Kutish (post-doc)

Bill Current

Steve Knight

Al Poorman

Amal Bhattacharya

Norman Dollahon



Steve Knight

Bob Fuchs

Gerald Kutish

Amy Keppel

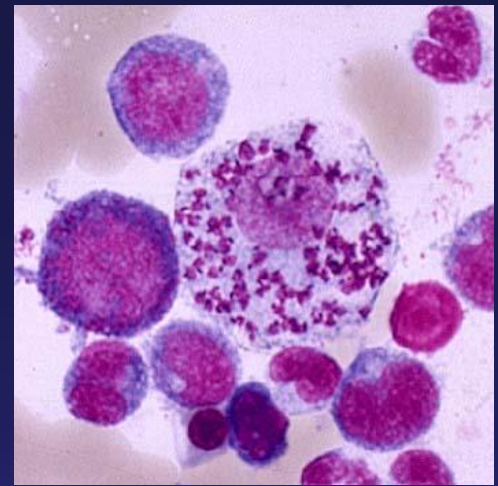
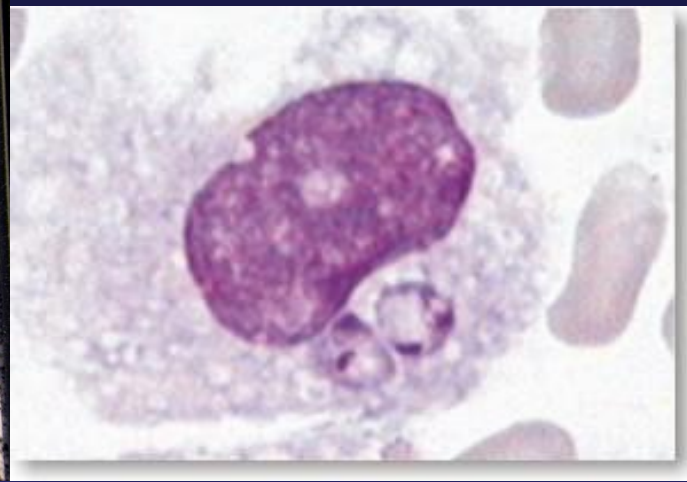
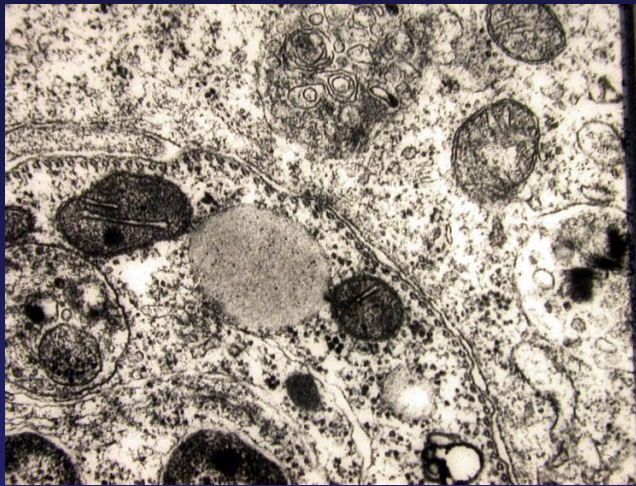


The problems:

- Knigh – Linkage of kinetoplast division with nuclear division.
- Moslih – Chromosome numbers and mitosis control.
- Bhattacharya – Molecular exchanges between parasites and host cells.
- Daggett – Infectivity series in flagellates from insects.

The problems:

- Decker – Excretion factor and its role in infectivity.
- Poorman – Thermosensitivity of enzymes.
- Dollahon – Infectivity of Old World lizard leishmanias for New World lizards.
- Keppel – Agar plate colony morphology among various species.
- Fuchs – Molecular effects of infection on macrophages.



Janovy, J. Jr., P. M. Daggett and K. W. Lee. 1974. *Herpetomonas megaseliae*: Architectural rearrangements during amastigote formation. J. Parasitol., 60:716-718.

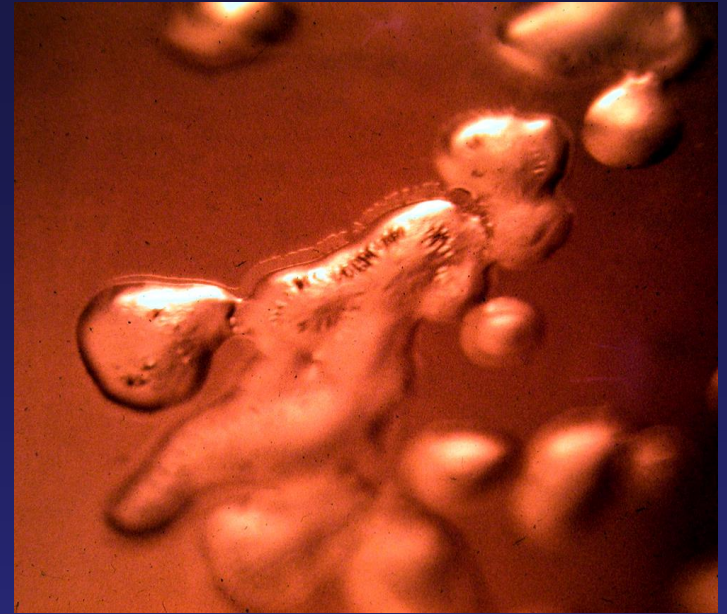
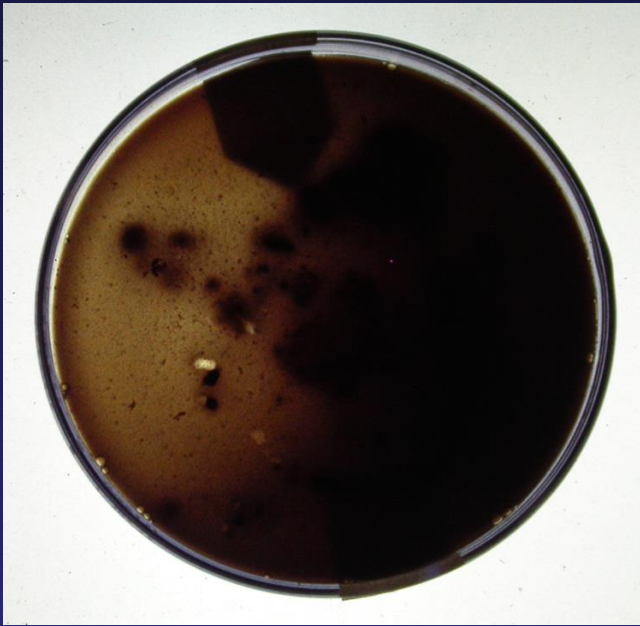
Janovy, J. Jr., P. M. Daggett, S. Knight and J. Gunderson 1975. Differentiation in *Herpetomonas megaseliae*: Population and physiological changes. Proc. Okla. Acad. Sci., 55:130-135. (J. T. Self retirement honor volume)

Janovy, J. Jr., K. W. Lee and J. A. Brumbaugh. 1974. Differentiation in *Herpetomonas megaseliae*: Ultrastructural observations. J. Protozool., 21:53-59.

Bhattacharya, A. and J. Janovy, Jr. 1975. *Leishmania donovani*: Autoradiographic evidence for molecular exchanges between parasite and host cell. Exptl. Parasitol., 37:353-360.



- Daggett, P. M., J. E. Decker, and J. Janovy, Jr. 1978. Some physiological alterations accompanying infectivity to mammals by four genera of Trypanosomatidae. *Comp. Biochem. Physiol.*, 59A:363-366.
- Daggett, P. M., N. R. Dollahon and J. Janovy, Jr. 1972. *Herpetomonas megaseliae* sp. n. (Protozoa: Trypanosomatidae) from *Megaselia scalaris* (Loew, 1866) Schmitz, 1929 (Diptera: Phoridae). *J. Parasitol.*, 58:946- 949.
- Decker, Joan E. and J. Janovy, Jr. 1974. *Leishmania donovani* and *Leishmania mexicana*: Production of the Excretion Factor. *Comp. Biochem. and Physiol.*, 49B:513-523.
- Dollahon, N. R. and J. Janovy, Jr. 1971. Insect flagellates from feces and gut contents of four genera of lizards. *J. Parasitol.*, 57:1130-1132.
- Dollahon, N. R. and J. Janovy, Jr. 1973. *Leishmania adleri* (Protozoa: Trypanosomatidae): In vitro phagocytosis by leucocytes of the iguanid lizards *Dipsosaurus dorsalis* and *Basiliscus vittatus*. *Exptl. Parasitol.*, 34:56-61.
- Dollahon, N. R. and J. Janovy, Jr. 1974. Experimental infection of New World lizards with Old World lizard *Leishmania* species. *Exptl. Parasitol.*, 36:253-260.



Keppel, Amy Doran and J. Janovy, Jr. 1977. *Herpetomonas megaseliae* and *Crithidia hamosa*: Growth on blood agar plates. *J. Parasitol.*, 63:879-882.

Keppel, Amy Doran and J. Janovy, Jr. 1980. *Leishmania donovani*: Structure of agar plate grown colonies. *J. Parasitol.*, 66:849-851.

Relationships between intracellular parasites and their host cells.

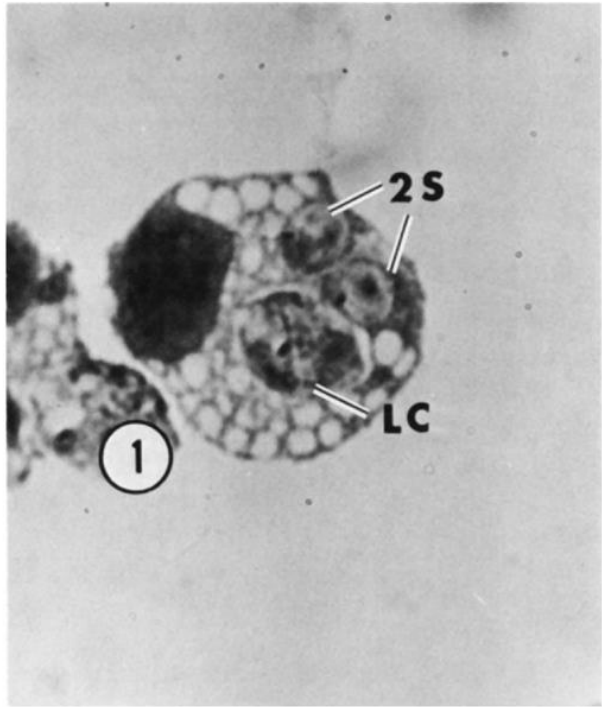


FIGURE 1. Typical macrophage in vitro infected with *Leishmania donovani* 2S strain and subsequently with *Leptomonas costoris* (LC). Giemsa, $\times 1,200$. Differences in size and granulation are seen between the two species of parasites.

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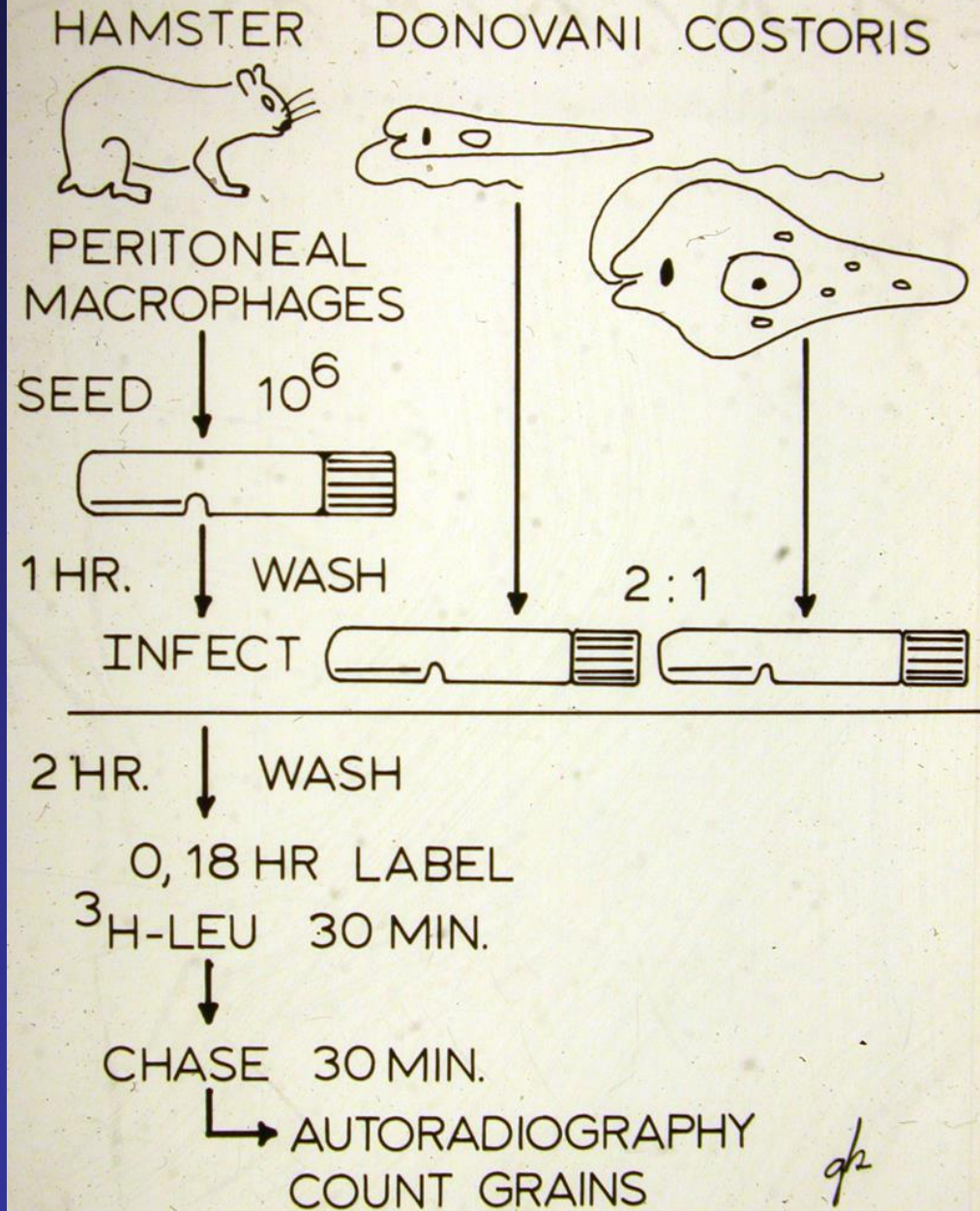
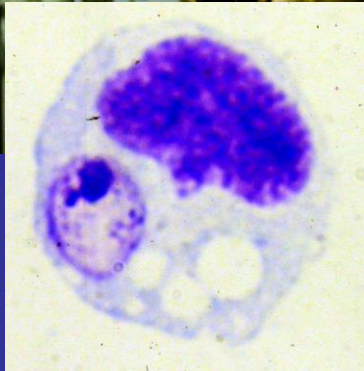
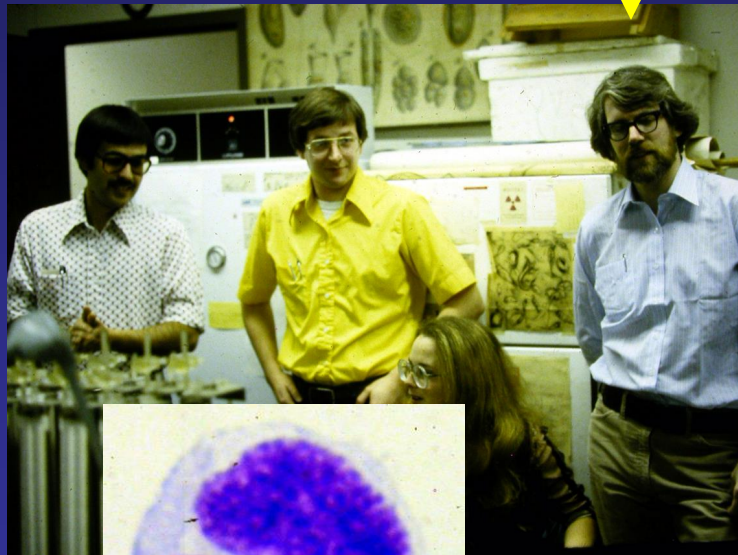
J. Parasitol., 67(4), 1981, pp. 457-462
© American Society of Parasitologists 1981

INHIBITION OF IN VITRO MACROPHAGE DIGESTION CAPACITY BY INFECTION WITH *LEISHMANIA DONOVANI* (PROTOZOA: KINETOPLASTIDA)

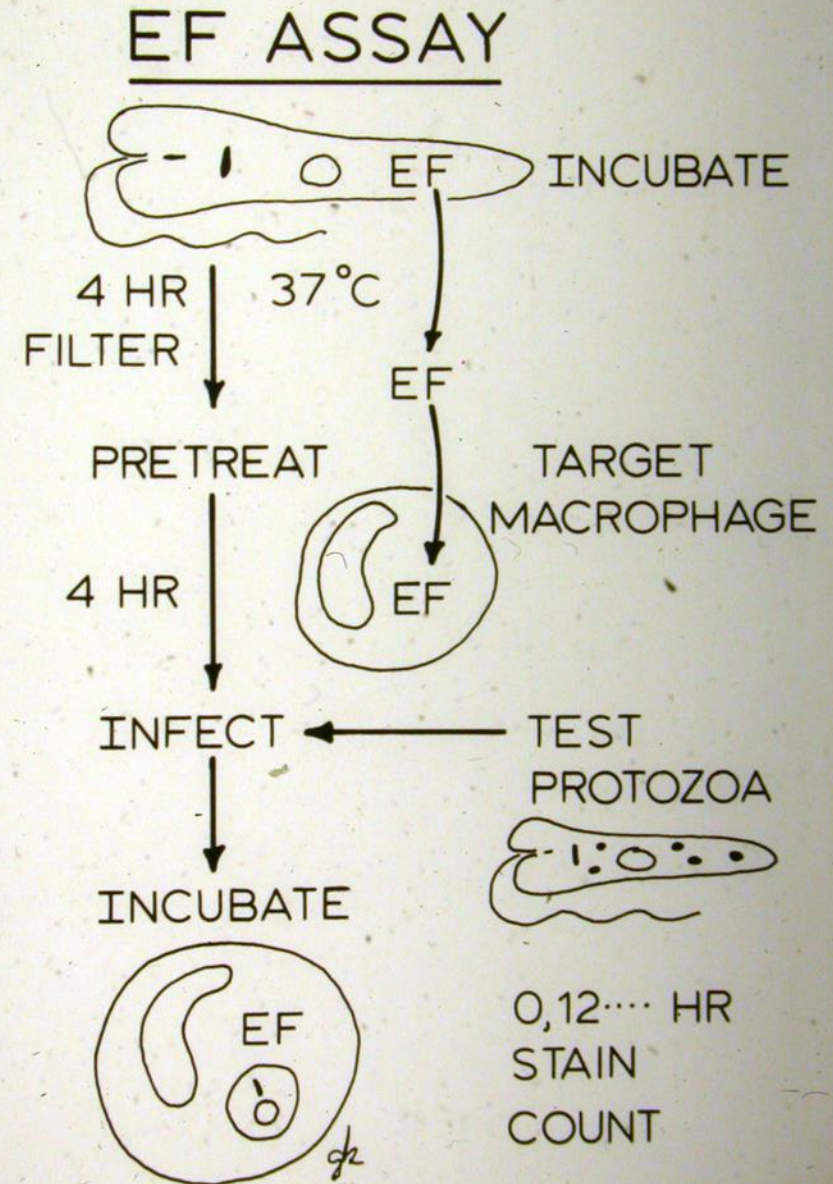
Gerald F. Kutish and J. Janovy, Jr.

School of Life Sciences, University of Nebraska, Lincoln, Nebraska 68588

The infamous Gerald Kutish experiments:



The infamous Gerald Kutish experiments (cont'd):



Take-home messages:

- **Some parasites (organisms) are very easy to manipulate in the lab, whereas others are not.**

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Take-home messages:

- Some parasites (organisms) are very easy to manipulate in the lab, whereas others are not.
- Ease of manipulation is the reason why the vast majority of biological research is done on a relatively small minority of species.
- Nobody needs to tell a bunch of parasitologists this obvious fact of life in the lab vs. life in the field.
- **Finally, the large philosophical question, concerns the influence of a species on the way we study it = The Parasitologist's Dilemma.**

Still more take-home messages:

- **The logistical burden of doing science needs to be understood, and learned, by all glory seekers, especially young ones.**

Still more take-home messages:

- The logistical burden of doing science needs to be understood, and learned, by all glory seekers, especially young ones.
- **The titles of published scientific papers tend to mask all the hassle and interpersonal conflict often associated with the research.**

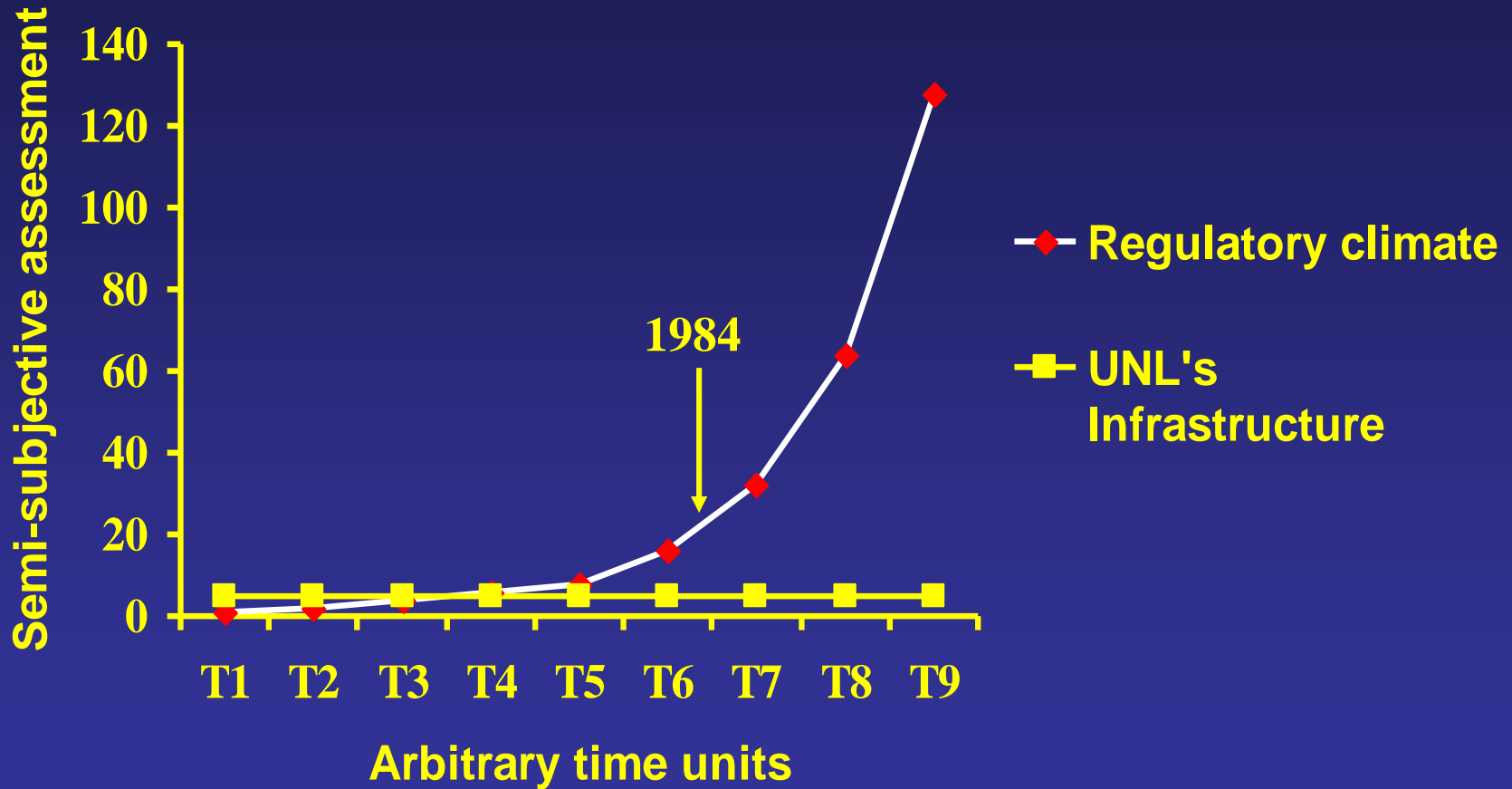
The Three Biggies:

Bhattacharya, A., and J. Janovy, Jr. 1975. *Leishmania donovani*: autoradiographic evidence for molecular exchanges between parasite and host cell. *Exptl. Parasitol.* 37:353-360.

Daggett, P.-M., J. E. Decker, and J. Janovy, Jr. 1978. Some physiological alterations accompanying infectivity to mammals by four genera of Trypanosomatidae. *Comp. Biochem. Physiol.* 59A:363-366.

Kutish, G. F., and J. Janovy, Jr. 1981. Inhibition of in vitro macrophage digestion capacity by infection with *Leishmania donovani* (Protozoa: Kinetoplastida). *J. Parasitol.* 67:457-462.

JJ's impression of his future (1981):



**What do you do to
maintain an interesting
research program if all you
have is a microscope and
your VISA card?**



What do you do to maintain an interesting research program if all you have is a microscope and your VISA card?



A: Work on gregarines.



Manter Hall
under
construction –
1974.

I don't know
why I put this
one in except
that it was in a
pile of slides I
was digitizing.