



ESTRONGILOIDÍASE

Marcelo Andreetta Corral, PhD

2024

PLANO DE AULA - 2025

- ✓ Histórico e Epidemiologia da Estrongiloidíase
- ✓ O parasito *Strongyloides stercoralis*
 - Morfologia e Biologia
 - Ciclos Biológicos
- ✓ Relação Parasito-Hospedeiro
 - Patologia
- ✓ Diagnósticos
 - Aplicações

CLASSIFICAÇÃO TAXONÔMICA

- Domínio: Eucariota
- Reino: Metazoa
- Filo: Nematoda
- Classe: Chromadorea
- Ordem: Rhabditida
- Família: Strongyloididae
- Gênero: *Strongyloides*
- Espécie: *Strongyloides stercoralis*

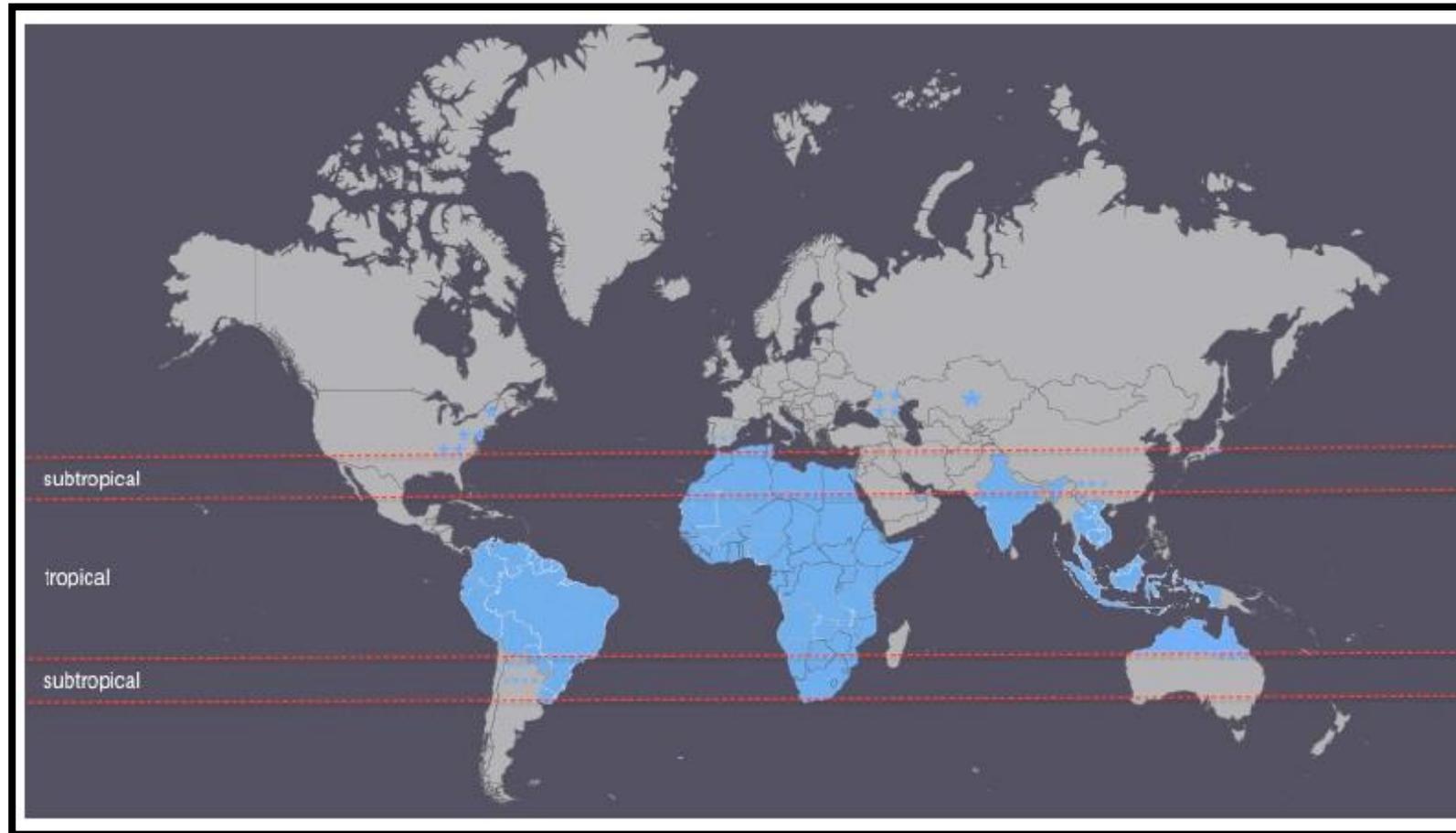
- Outras espécies: *Strongyloides fulleborni*
- *Strongyloides ratti*
- *Strongyloides venezuelensis*



EPIDEMIOLOGIA



DISTRIBUIÇÃO MUNDIAL DA ESTRONGILOIDÍASE

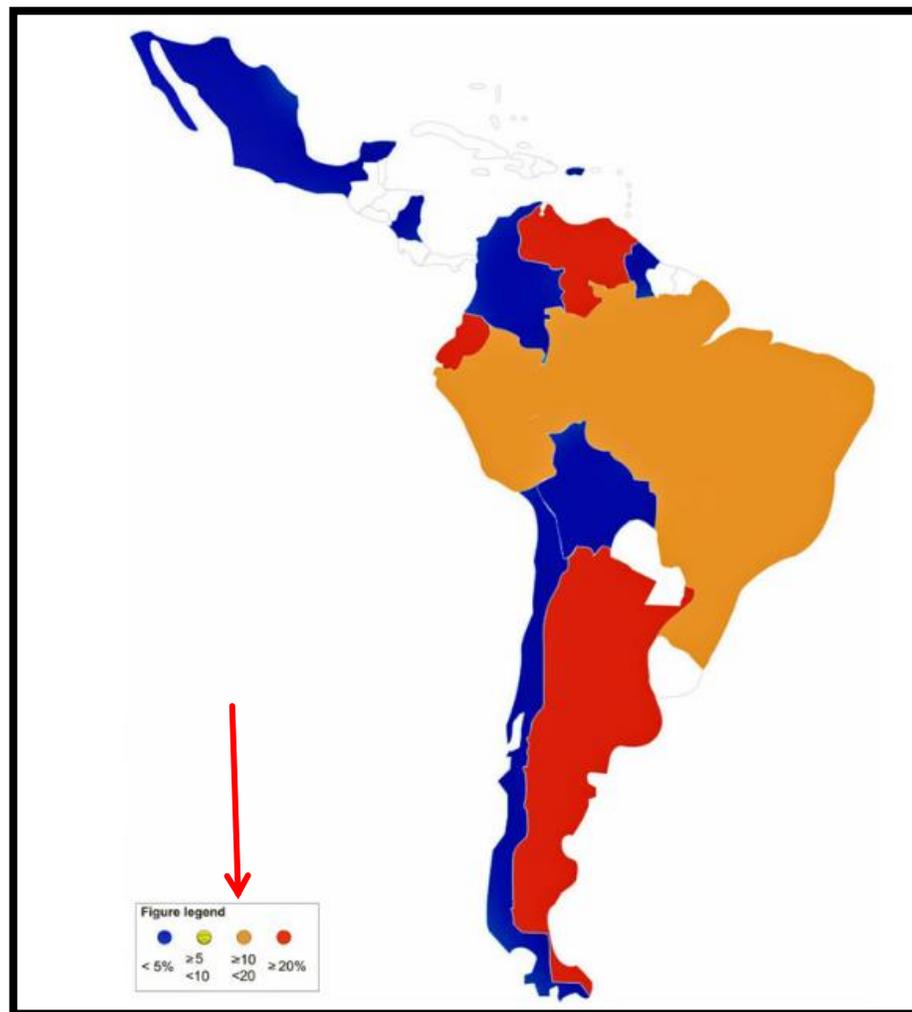


(Beknazarova et al., 2016)

DISTRIBUIÇÃO LATINO-AMERICANA DA ESTRONGILOIDÍASE

- 5,5% de ocorrência no Brasil.
- 3,9% na região Sudeste do país.

(Paula e Costa-Cruz, 2011)



(Buonfrate et al., 2014)

ESTRONGILOIDÍASE COMO ZONOSE?

Global prevalence of *Strongyloides stercoralis* in dogs: A systematic review and meta-analysis

Published online by Cambridge University Press: 21 February 2022

Tahmineh Gorgani-Firouzjaee , Narges Kalantari , Mohammad Chehrizi, Salman Ghaffari  and Shaysteh Shahdin

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Eslahi et al. *Parasites & Vectors* (2022) 15:21
<https://doi.org/10.1186/s13071-021-05135-0>

Parasites & Vectors

RESEARCH

Open Access

Global prevalence and epidemiology of *Strongyloides stercoralis* in dogs: a systematic review and meta-analysis

Aida Vafae Eslahi^{1†}, Sima Hashemipour^{2†}, Meysam Olfatifar^{1†}, Elham Houshmand³, Elham Hajjalilo^{4,5}, Razzagh Mahmoudi¹, Milad Badri^{1*} and Jennifer K. Ketzis^{6*} 

PLOS NEGLECTED TROPICAL DISEASES

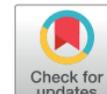
RESEARCH ARTICLE

A systematic review and meta-analysis of human and zoonotic dog soil-transmitted helminth infections in Australian Indigenous communities

Cameron Raw , Rebecca J. Traub, Patsy A. Zendejas-Heredia, Mark Stevenson, Anke Wiethoelter

Faculty of Veterinary and Agricultural Sciences, University of Melbourne, Parkville, Victoria, Australia

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MORFOLOGIA



OVOS

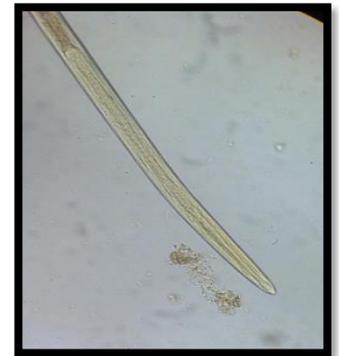


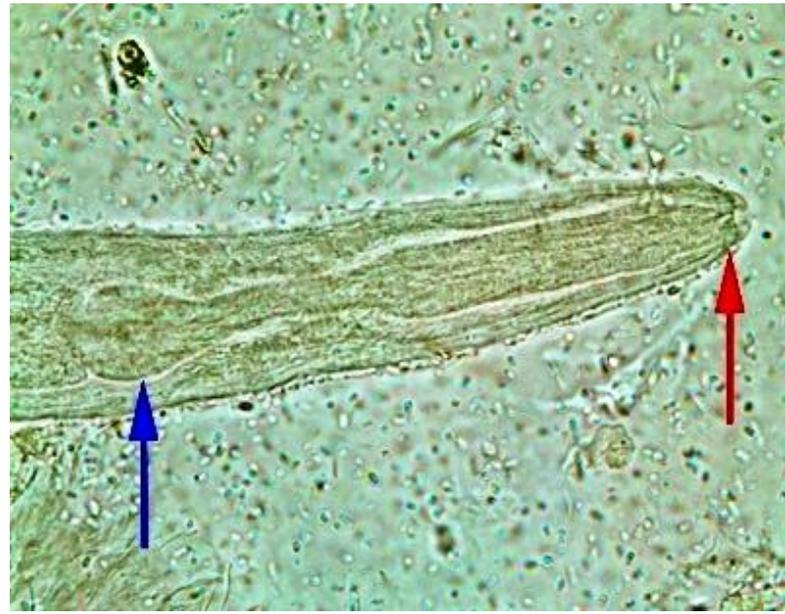
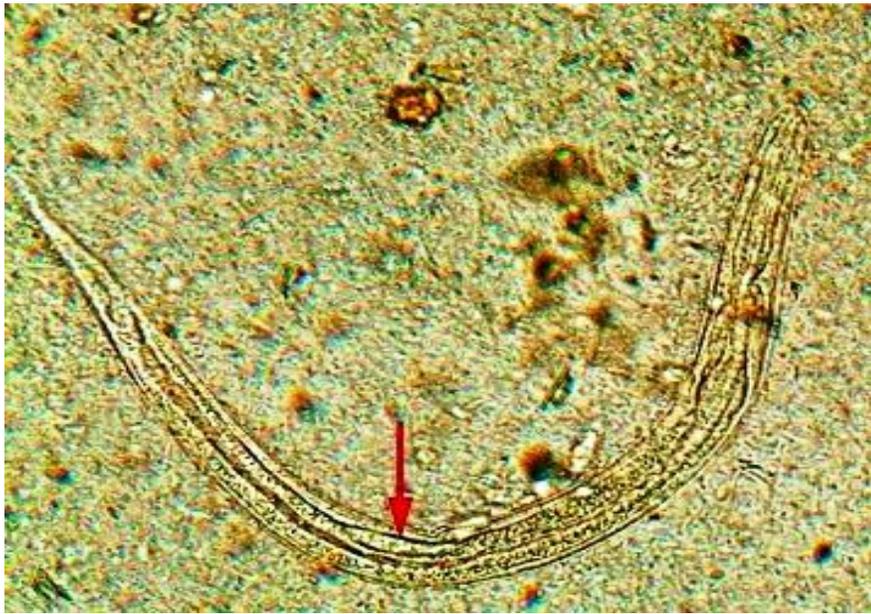
LARVAS

Larva rabditoide



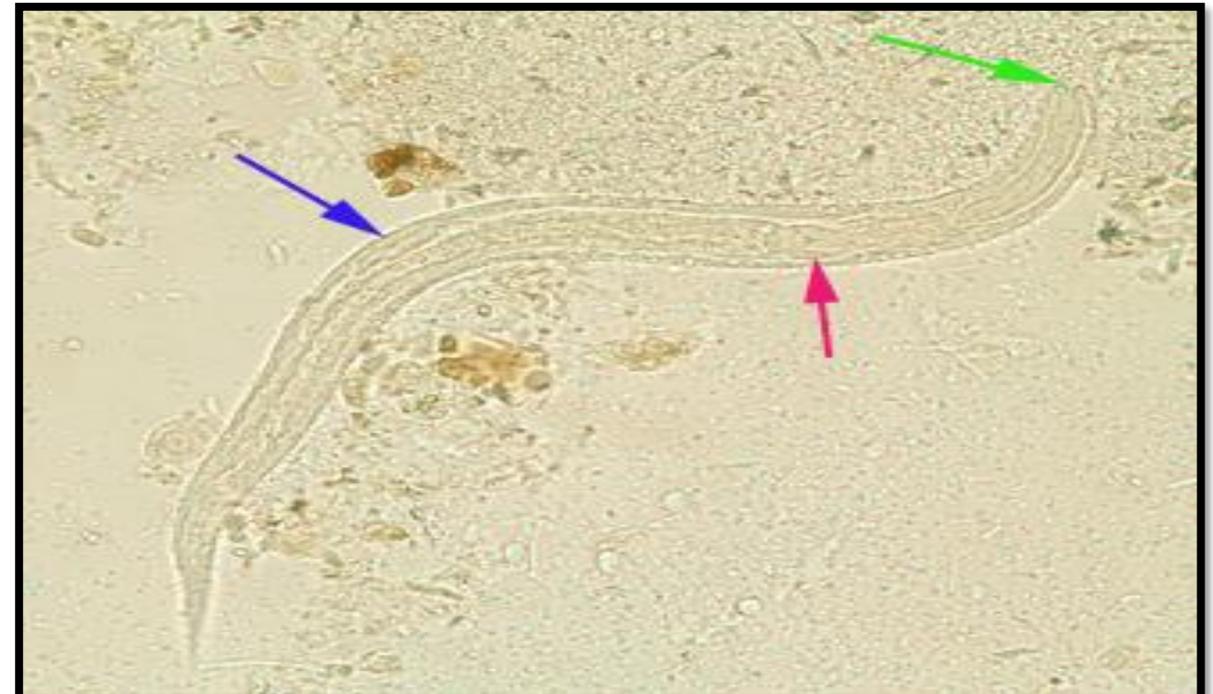
Larva filarioide





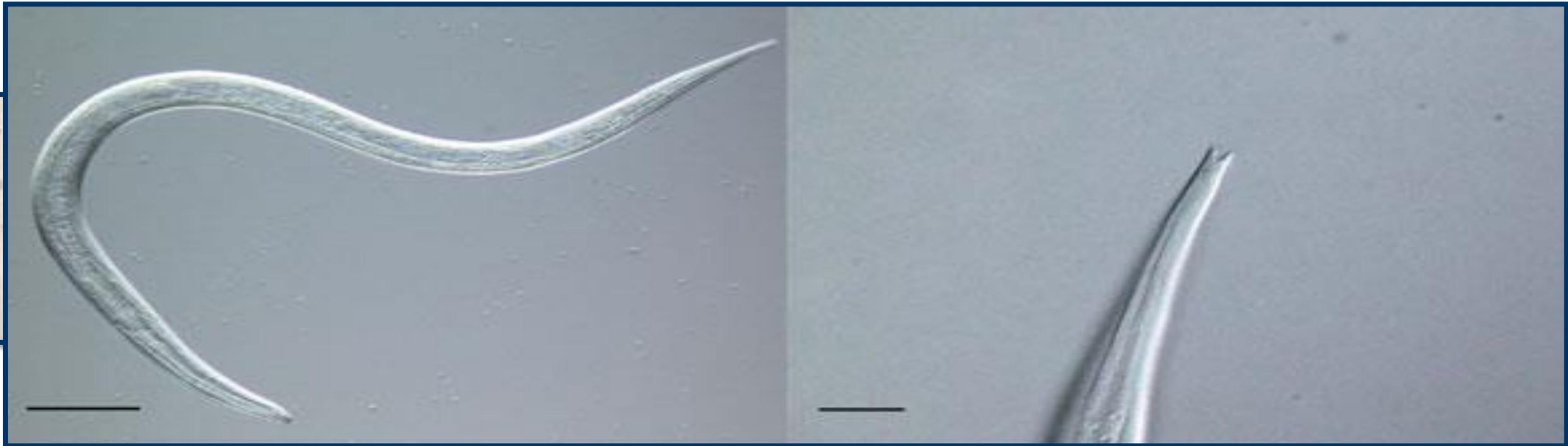
ASPECTOS BIOLÓGICOS: COMPARAÇÃO ENTRE LARVAS DE *STRONGYLOIDES STERCORALIS* E ANCILOSTOMÍDEOS

Larva Rabditoide	<i>S. stercoralis</i>	Ancilostomídeos
Primórdio genital	visível	Não visível
Vestíbulo bucal	curto	longo



ASPECTOS BIOLÓGICOS: COMPARAÇÃO ENTRE LARVAS DE *STRONGYLOIDES STERCORALIS* E ANCILOSTOMÍDEOS

Larva Filarioide	<i>S. stercoralis</i>	Ancilostomídeos
cauda	bifurcada	afilada



ADULTOS

Fêmea de Vida Livre

Macho de Vida Livre



FÊMEA PARASITA

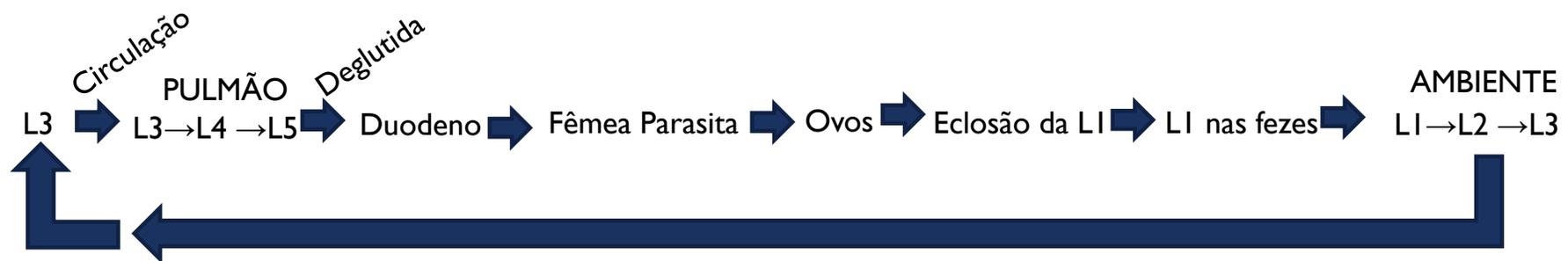




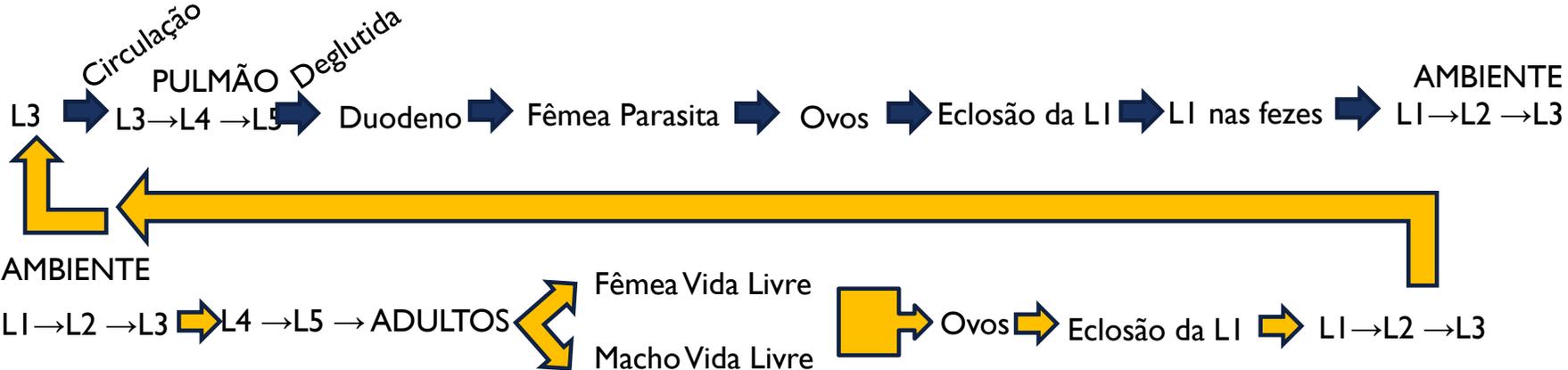
CICLOS BIOLÓGICOS



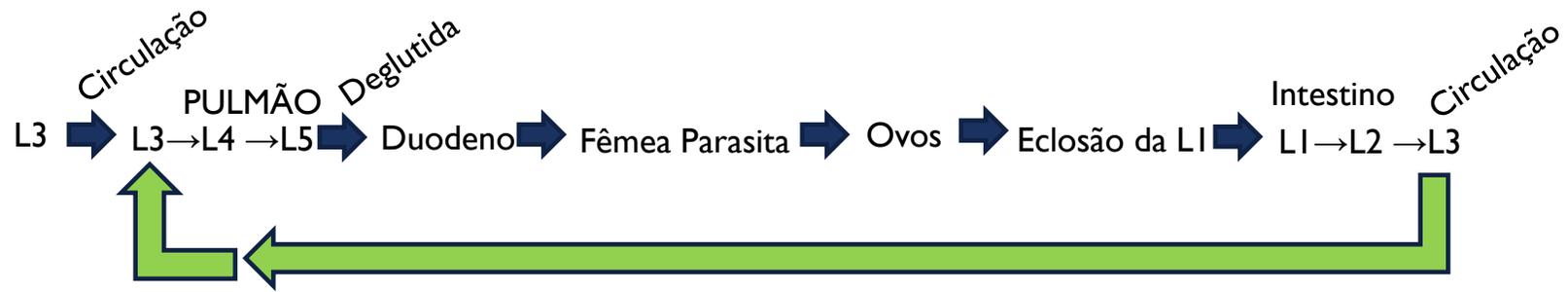
CICLO DIRETO



CICLO INDIRETO



CICLO AUTO INFECCÃO



HIPÓTESES PARA CICLOS

- Determinação do sexo durante a oogênese ou embriogênese (n , $2n$ e $3n$).
- Ambiente (Temperatura e umidade).

Triantaphyllou, Moncol, 1977

Viney, Lok, 2008

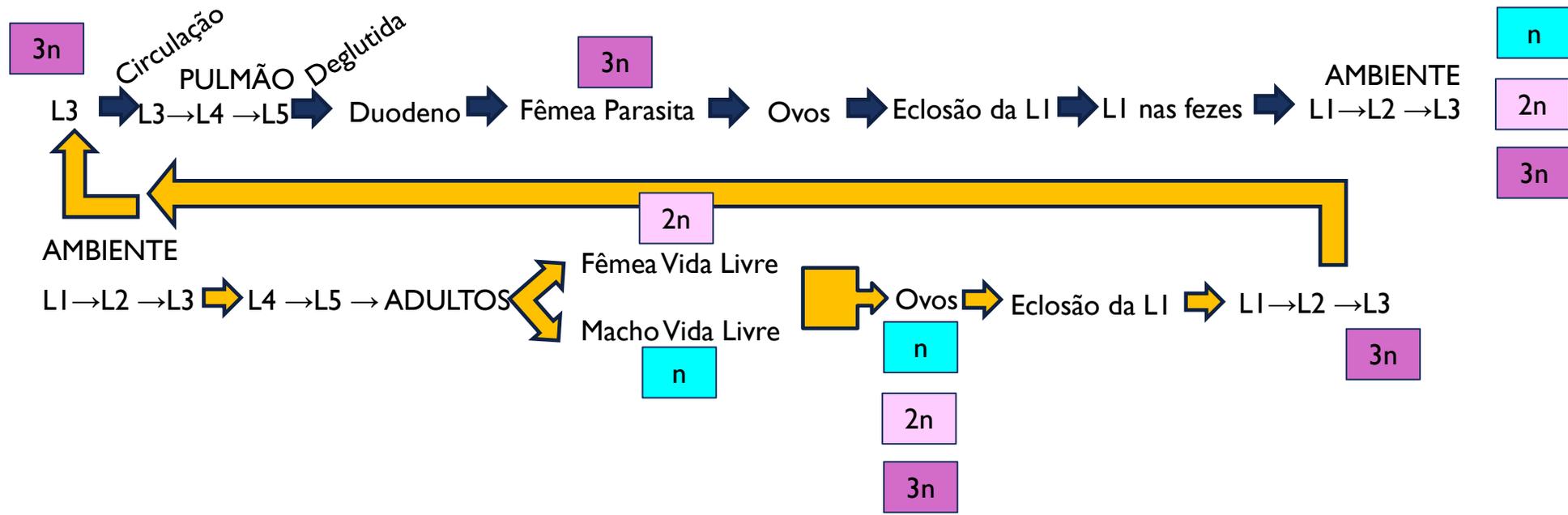
Nemetschke et al., 2010



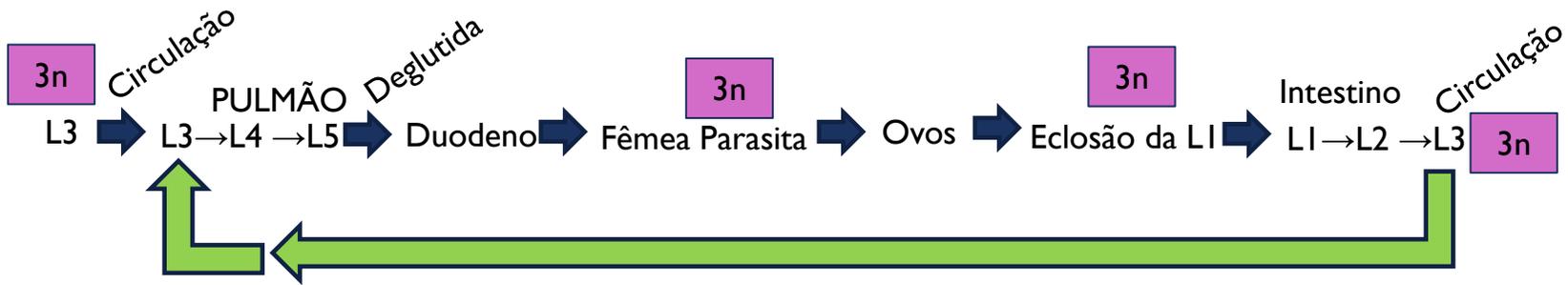
TEORIA DA CARGA GENÉTICA



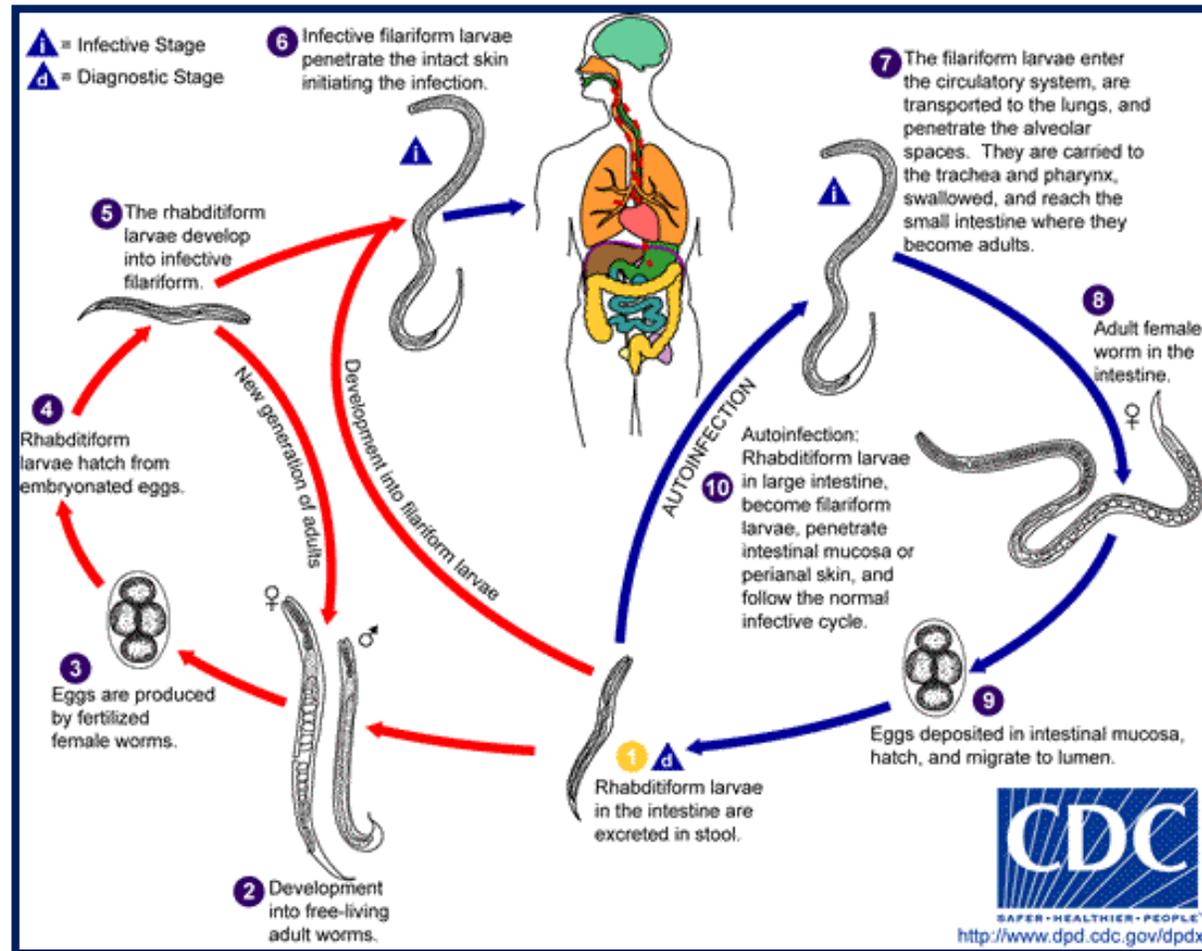
CICLO INDIRETO



CICLO AUTO INFECCÃO



CICLOS BIOLÓGICOS





IMUNIDADE



MECANISMOS

- ✓ Padrão de Resposta Imune **Th2** → **Helminto**
 - IL-3 → basófilos
 - IL-4 → basófilos, Linf. B produção IgE, IgG1, Eosinófilos, contração da musculatura lisa do intestino
 - IL-5 → Eosinófilos, IgA
 - IL-6 → Granulócitos e Linf. B e T
 - IL-10 e IL-13 → modulação negativa Th1

- ✓ Liberação histamina → Aumentam permeabilidade do epitélio intestinal
 - *Toll-like receptors* estimulam macrófagos que secretam moléculas pró-inflamatórias inespecíficas favorecendo o aumento na secreção de muco intestinal pelas células caliciformes



- Produção de anticorpos

- ✓ IgA

- ✓ IgE

- ✓ IgM

- ✓ IgG - IgG4: casos graves

INFECÇÕES GRAVES

- Comprometimento da imunidade mediada por células Th2
- Leucemias
- Carcinomas
- Etilismo
- Diabetes
- Candidatos a transplantes e transplantados
- Uso de corticoides
- HIV
- HTLV



PATOGENIA E SINTOMAS



ESTRONGILOIDÍASE

- Assintomática
- Sintomática:
 - ✓ Enterite
 - ✓ Enterocolite crônica

AÇÕES PATOGÊNICAS E SINTOMAS

1) Penetração no hospedeiro

- Lesões cutâneas decorrente da resposta do organismo frente as substâncias produzidas pelas larvas
- ✓ Pontos eritematosos
- ✓ Placas com prurido

- Assintomática
- Eritema
- Prurido
- edema

AÇÕES PATOGÊNICAS E SINTOMAS

2) Migração Pulmonar

- Lesões pulmonares
 - ✓ Hemorragias petequiais e profusas
 - ✓ Pneumonite difusa → Síndrome de Loeffler
 - ✓ Presença de larvas no escarro, derrames pleurais e pericárdio
-
- Assintomático
 - Tosse
 - Expectoração
 - Febre
 - Mal-estar

AÇÕES PATOGÊNICAS E SINTOMAS

3) Lesões de Permanência e multiplicação no intestino

- Lesões intestinais
 - ✓ Duodeno e jejuno
 - ✓ Lesões mecânicas, histolíticas e irritativas
 - ✓ Inflamação catarral → aumento do peristaltismo
 - ✓ Pontos hemorrágicos e ulcerções
 - ✓ Evacuações diarreicas a muco sanguinolentas
-
- Diarreia
 - Desconforto abdominal
 - Cólicas
 - Dor epigástrica

AÇÕES PATOGÊNICAS E SINTOMAS

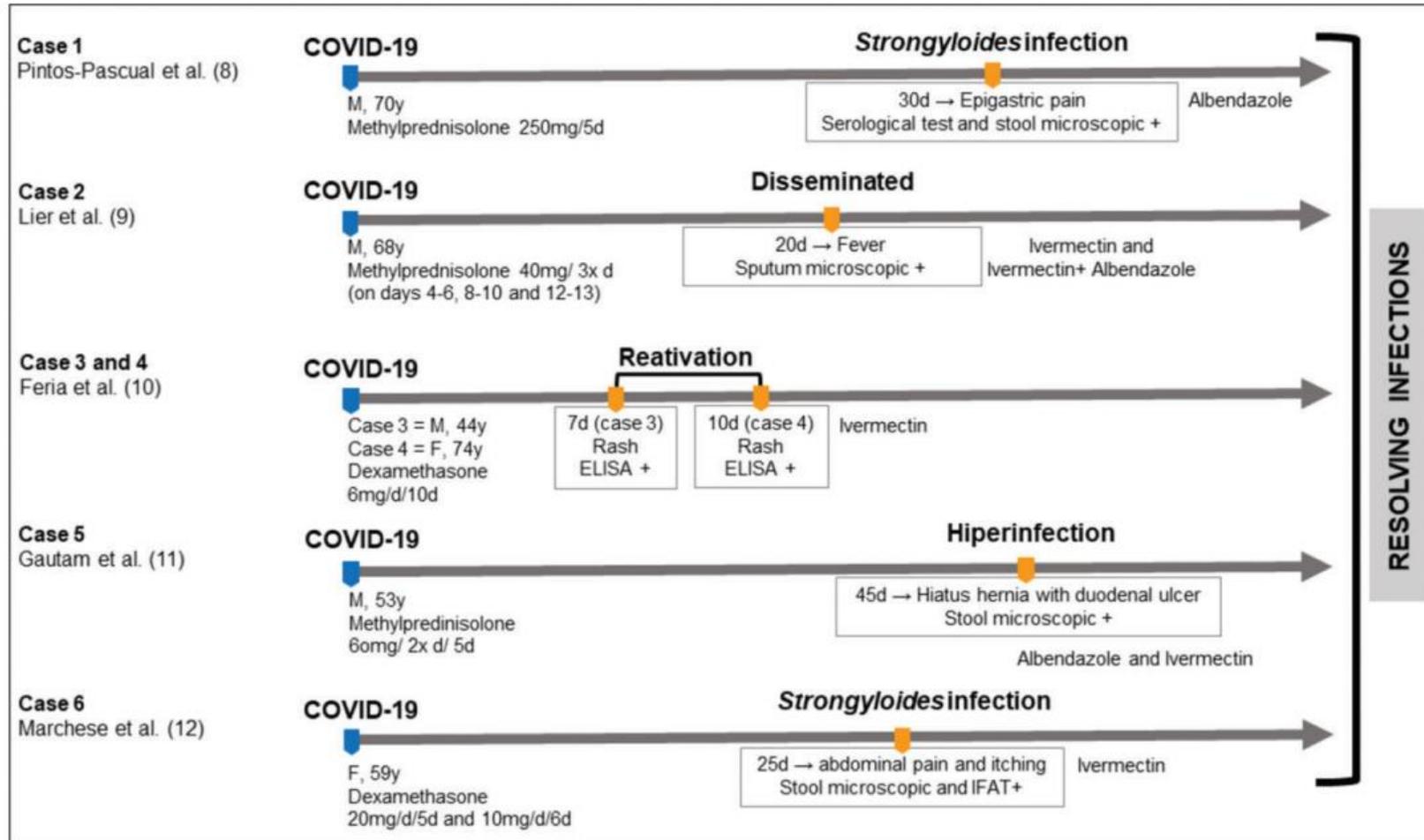
- 4) Imunodeprimidos
 - Processo de autoinfecção acelerado
 - Hiperinfecção
 - Doença disseminada: Disseminação hematogênica de Enterobactérias

- Taxa de mortalidade > 50%

ESTRONGILOIDÍASE EM TRANSPLANTE DE ÓRGÃOS

- Subestimado e pouco descrito na literatura
 - ✓ 5% dos pacientes tem infecções parasitárias
- Órgão transplantado pode ser fonte de infecção para o receptor
- Necessário diagnóstico precoce e rápido

E O COVID?



DIAGNÓSTICO

- Parasitológico
- Inmunológico
- Molecular

PARASITOLÓGICO

- Observação de Larvas em amostras biológicas
 - ✓ Fezes
 - ✓ Escarro
 - ✓ Fluidos
- Técnicas de observação direta e de cultura parasitológica

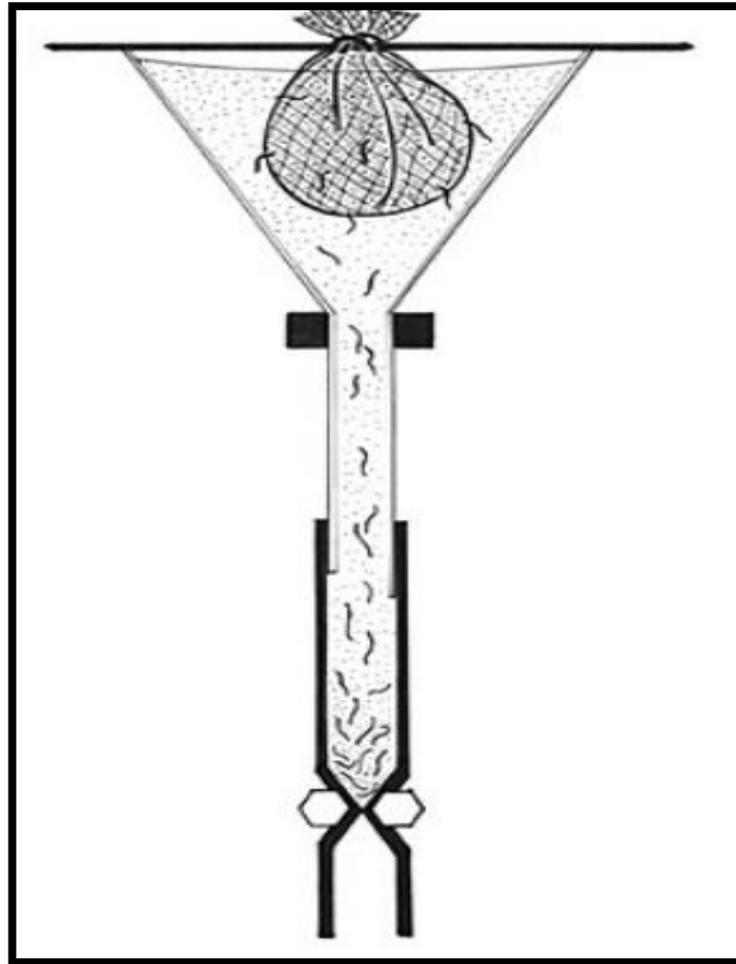
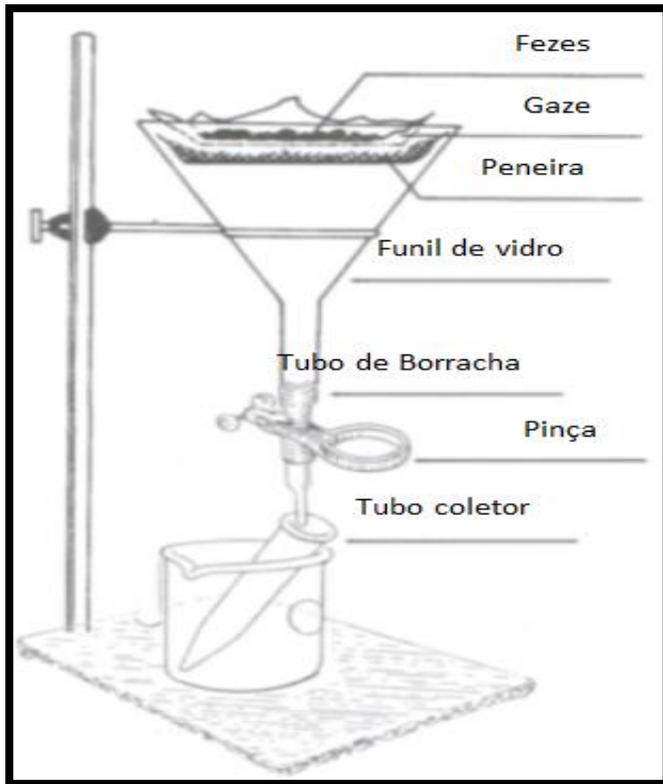
LUTZ OU HPJ



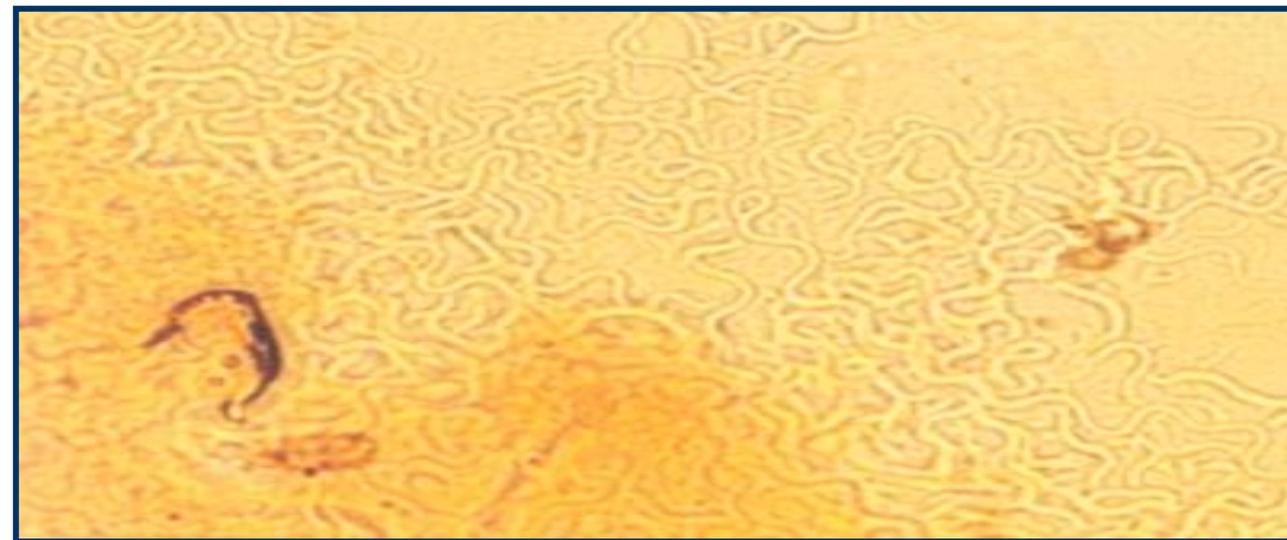
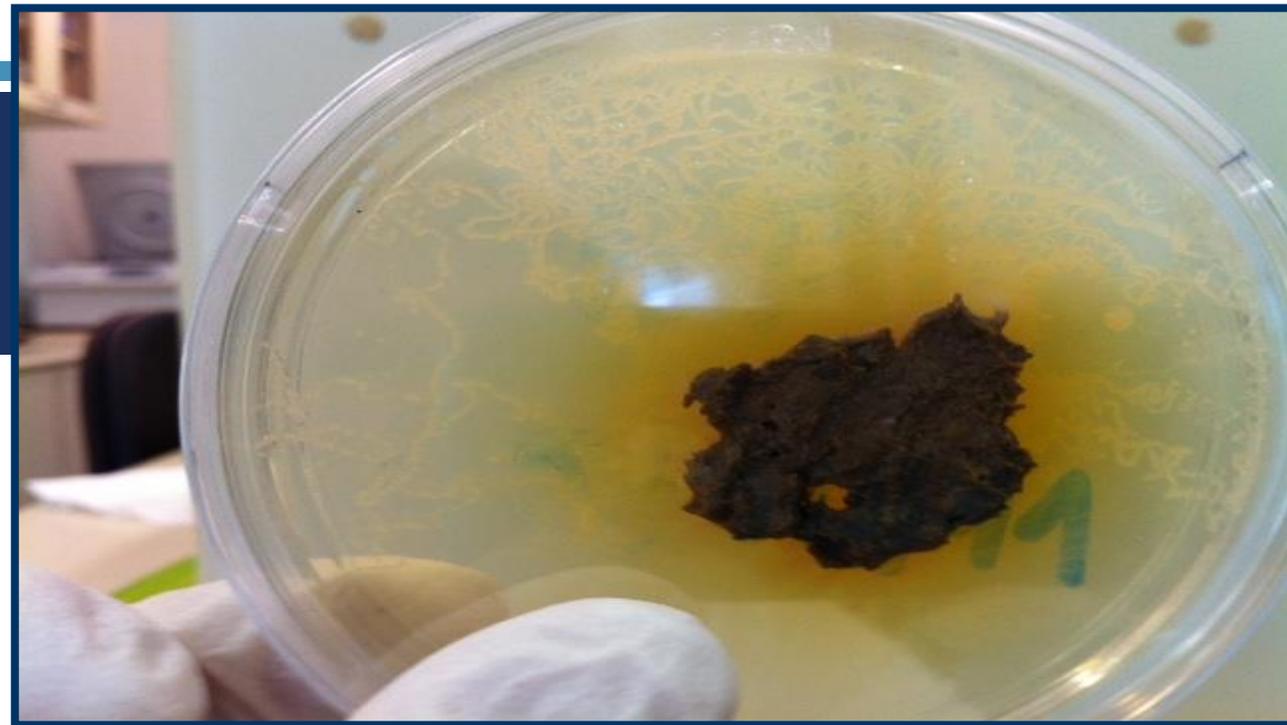
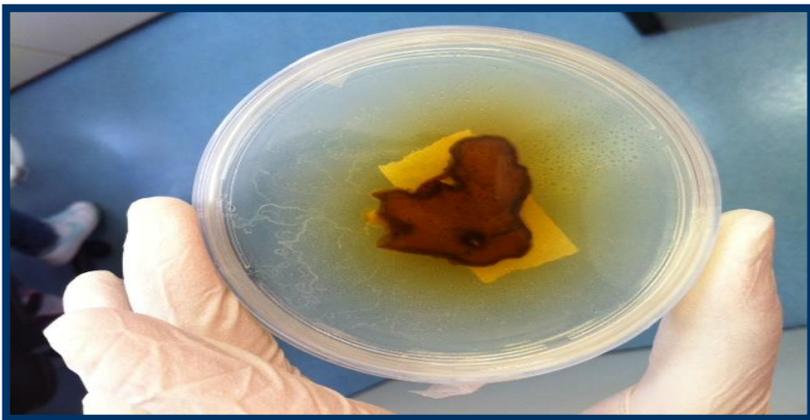
RUGAI



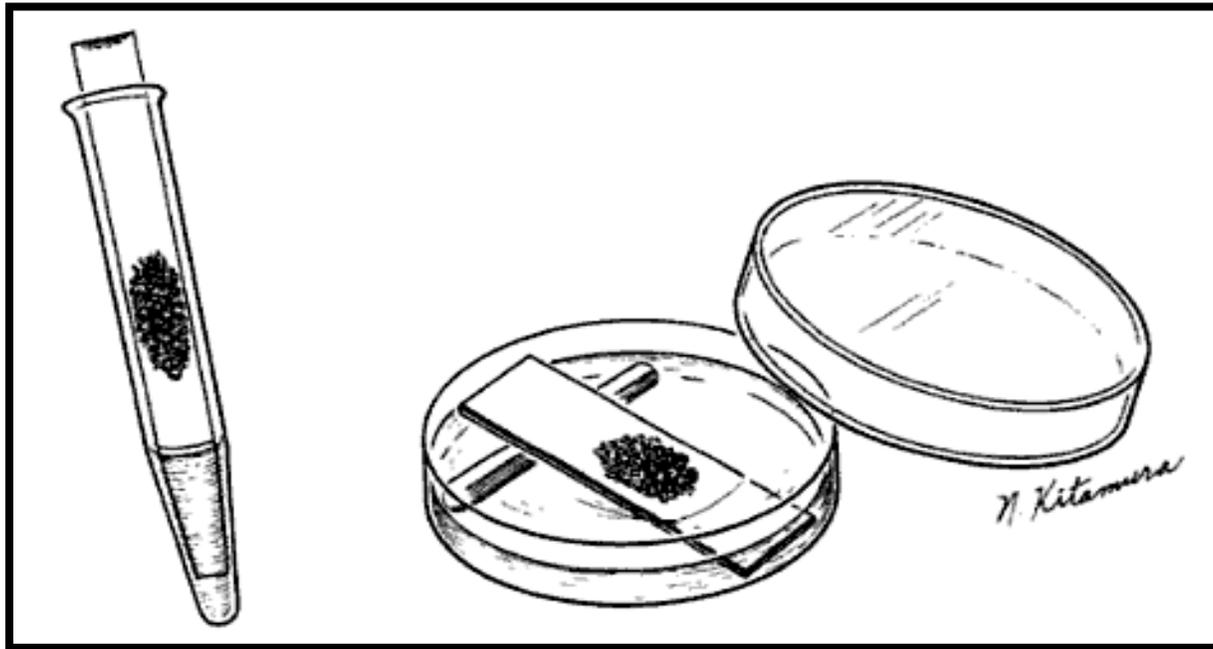
BAERMAN-MORAES



CULTURA EM PLACA DE ÁGAR



TÉCNICAS DE CULTURA



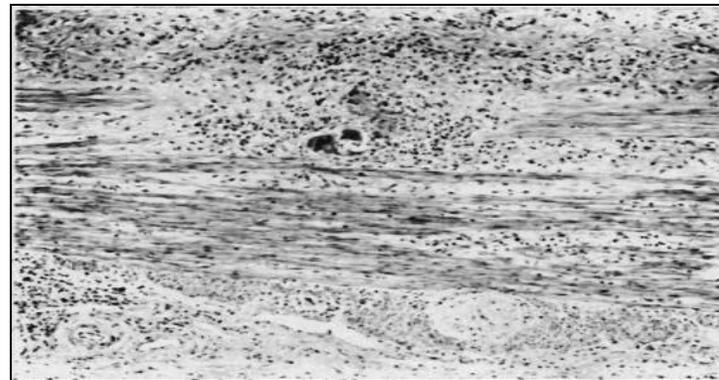
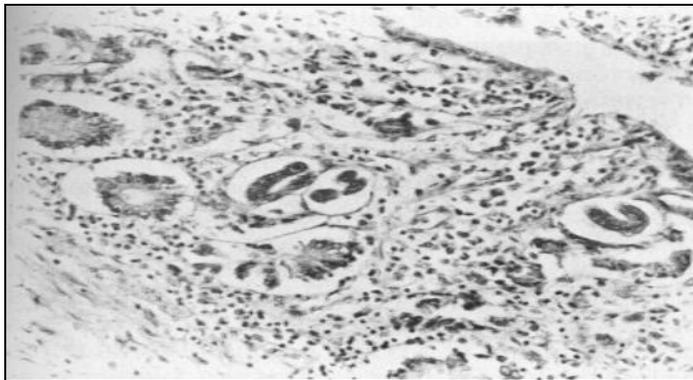
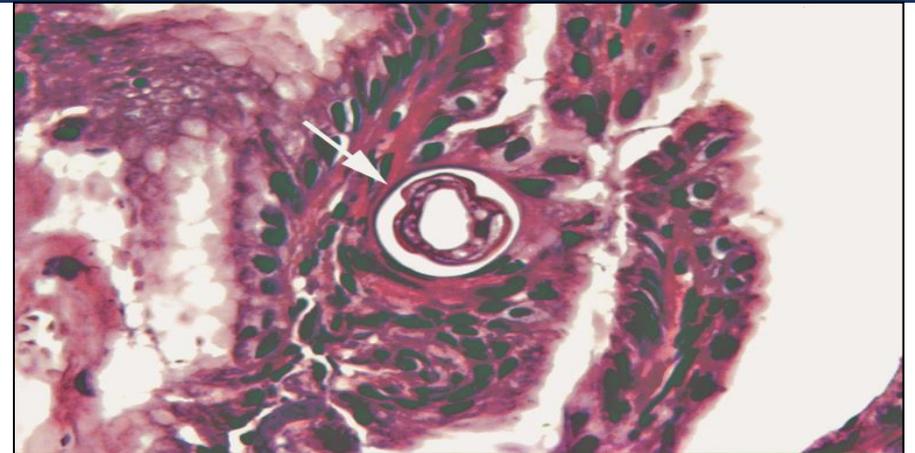
Cultura em papel de filtro

Harada e Mori, 1955

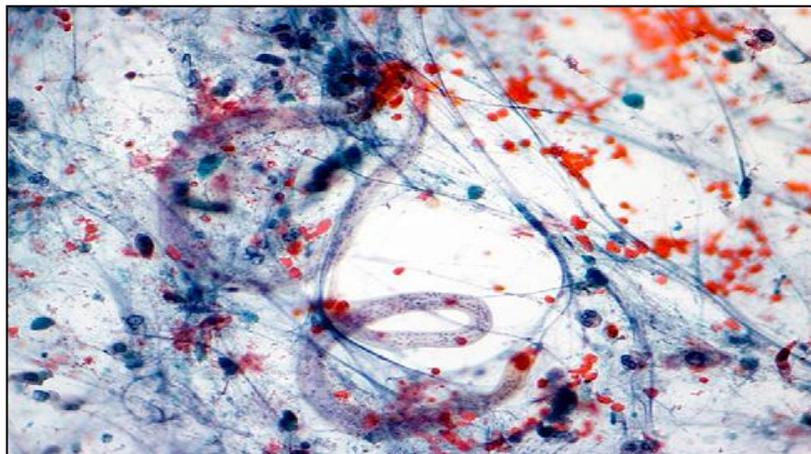


ANÁLISE DE OUTROS MATERIAIS BIOLÓGICOS

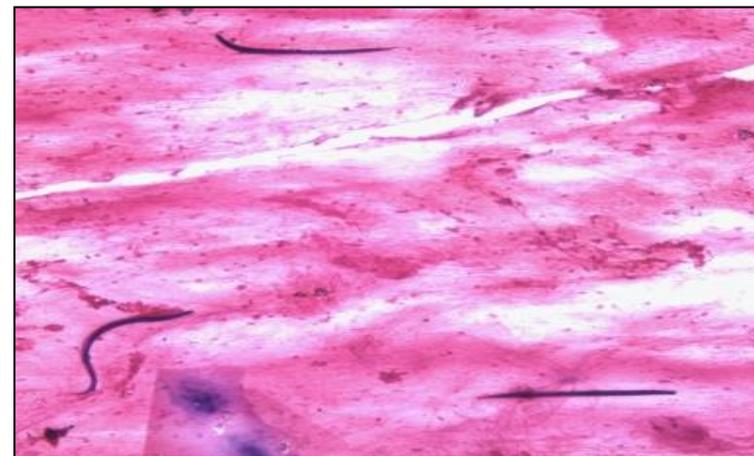
HTLV-I – biópsia – estômago (Lambertucci et al, 2005, Rev Soc Bras
Med Trop 38(4):365-366)



Necrópsia - (Godoy et al, 1998, T Rev Soc Bras Med Trop
31(5):481-485)



Corticoesteróide uso prolongado - dermatomiosite – lavado broncoalveolar (Basile et al, 2010, J Am Acad Dermatol 63(5):896-902)

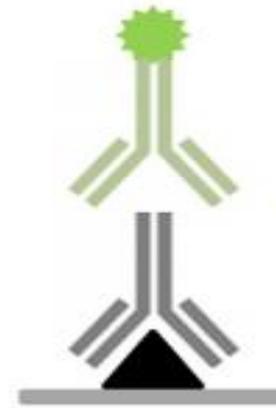
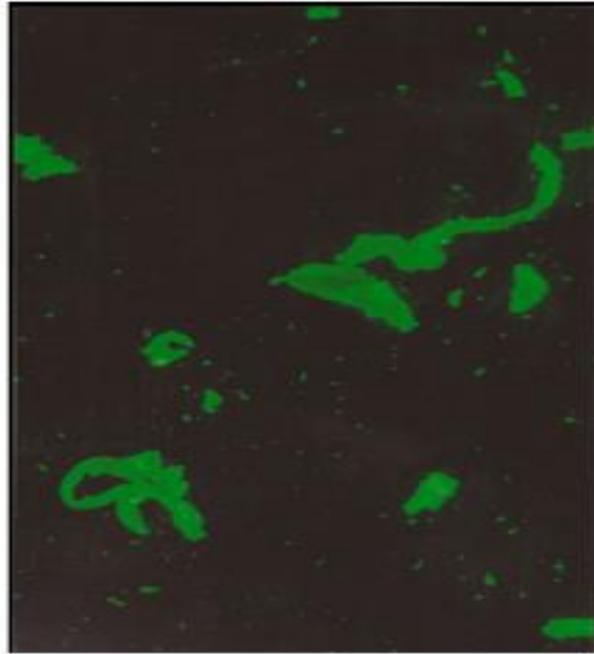


Transplante fígado – lavado broncoalveolar (Villela et al, 2009, Transpl Infect Dis 11(2):132-6)

SOROLÓGICO

- Não depende diretamente da liberação de larvas
- Detecção de anticorpos IgG anti-*Strongyloides*
- Utilização de antígenos heterólogos derivado de larvas infectantes de *Strongyloides venezuelensis*

RIFI

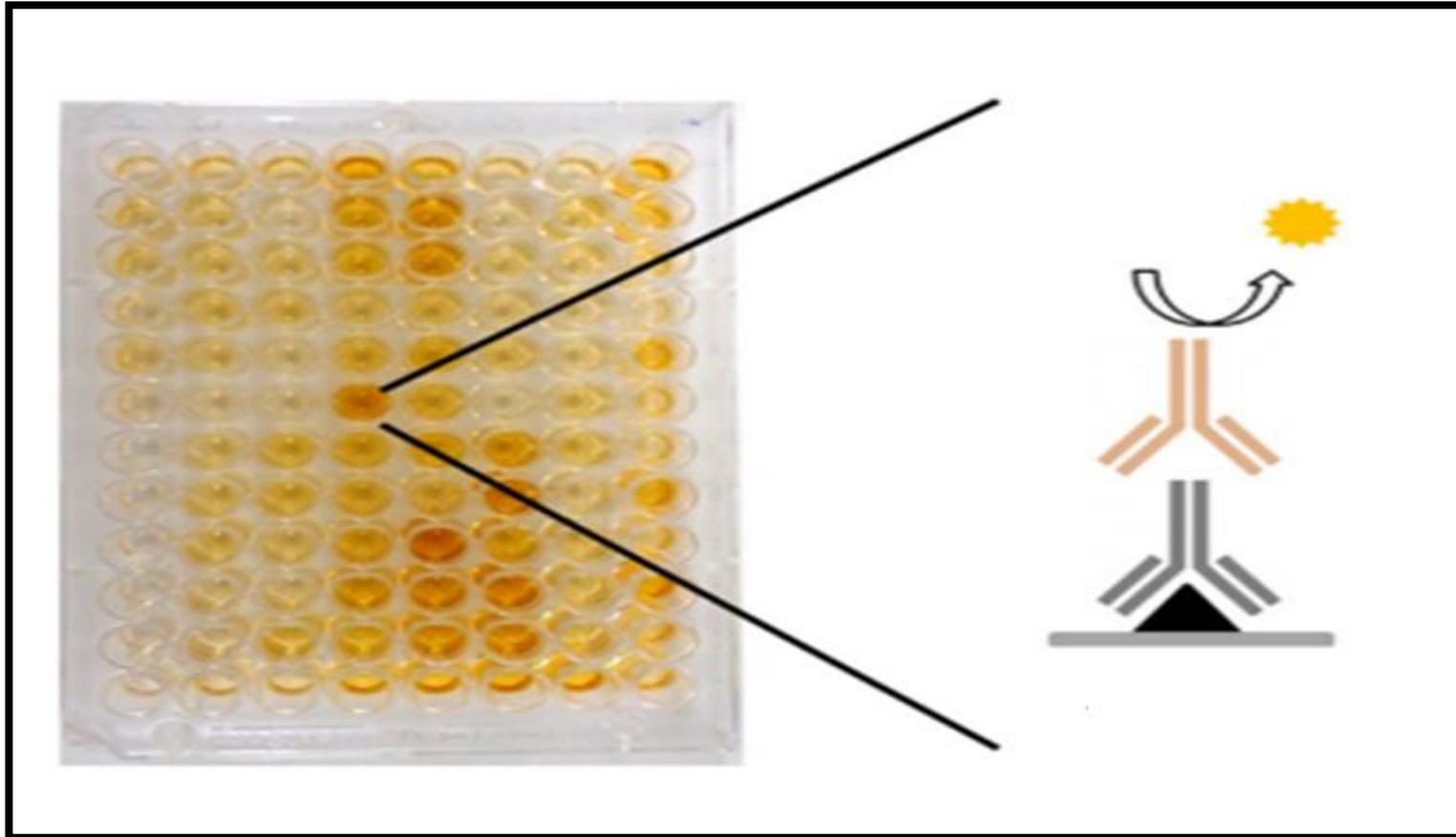


OBTENÇÃO E VARIAÇÃO NOS ANTÍGENOS

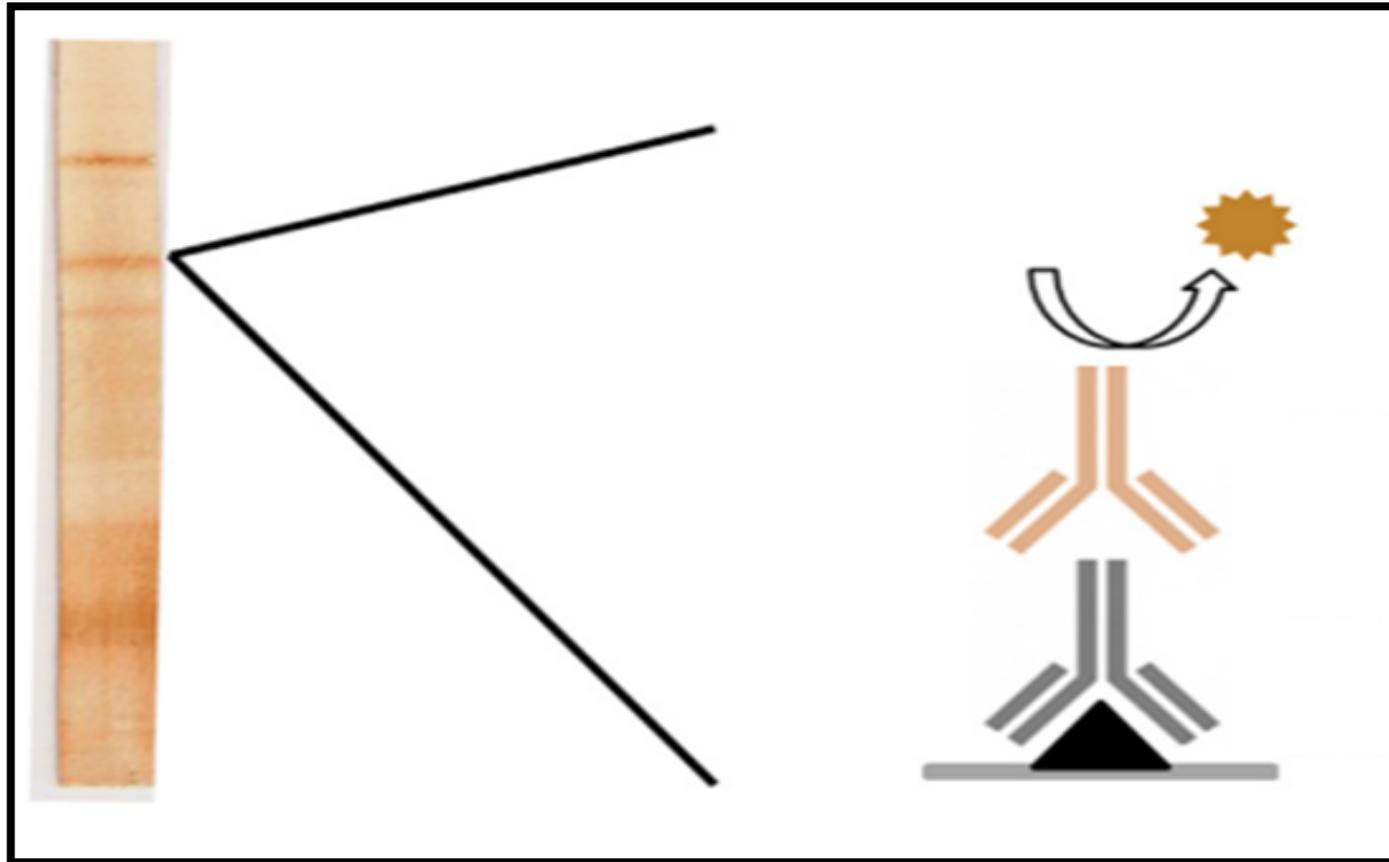
- Variação na obtenção de frações antigênicas
- Frações antigênicas tratadas com detergente ou purificadas
- Proteínas de membrana como fonte antigênica
- Uso de detergentes
 - CHAPS
 - SDS

)

ELISA



WESTERN-BLOTTING



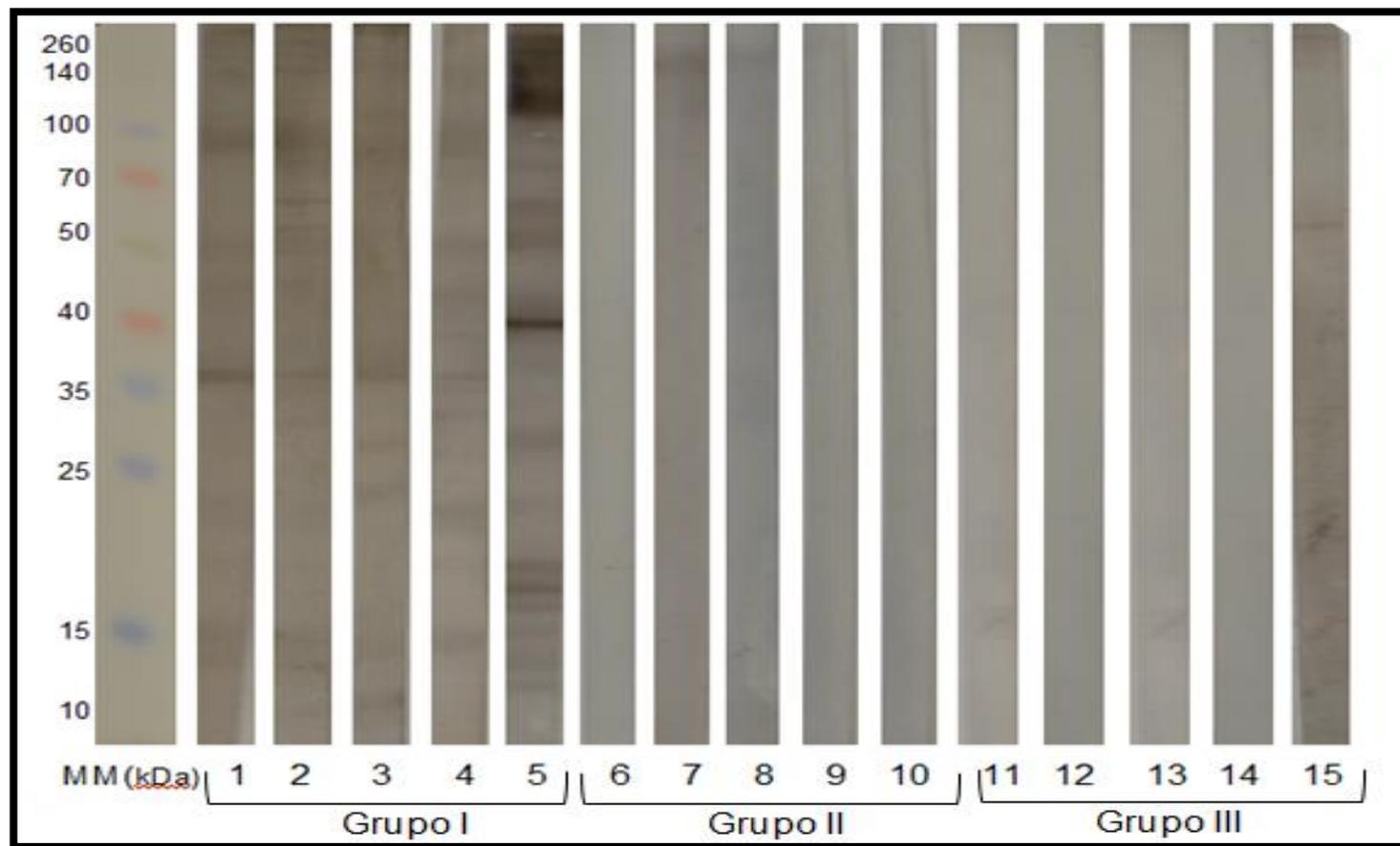


Table 2
Diagnostic values obtained by the enzyme-linked immunosorbent assay (ELISA) in human strongyloidiasis.

Number of Individuals			Antigen	Sample	Method	Sensitivity (%)	Specificity (%)	Ig Isotype	Reference
<i>S. stercoralis</i>	Healthy	Other infections							
40	30	30	Es S. ra	Serum	ELISA	80	73.4	IgG	Rodrigues et al. (2007)
40	30	30	Es S. ra	Serum	ELISA	77.5	98.4	IgG1	Rodrigues et al. (2007)
40	30	30	Es S. ra	Serum	ELISA	50	86.7	IgG4	Rodrigues et al. (2007)
40	30	30	Es S. ra	Serum	ELISA	55	96.7	IgE	Rodrigues et al. (2007)
99	20	237	S. st	Serum	AMC-ELISA	93	95	IgG	Van Doorn et al. (2007)
99	20	237	S. st	Serum	IVD-ELISA	89	97.2	IgG	Van Doorn et al. (2007)
99	20	237	S. ra	Serum	Bordier-ELISA	83	97.2	IgG	Van Doorn et al. (2007)
25	73	22	Es S. ve	Serum	ELISA	89	90	IgG	Rigo et al. (2008)
25	73	22	Es ZWIP S. ve.	Serum	ELISA	85	60	IgG	Rigo et al. (2008)
25	73	22	Es ZW S. ve.	Serum	ELISA	57	81	IgG	Rigo et al. (2008)
31	36	45	r-31 kDa S. st.	Serum	NIE-ELISA	97	95	IgG	Ramanathan et al. (2008)
31	36	45	r-31 kDa S. st.	Serum	NIE-ELISA	45	100	IgG4	Ramanathan et al. (2008)
40	40	40	Es S. ve.	Serum	ELISA	90	90	IgG	Feliciano et al. (2010)
40	40	40	Esd S. ve.	Serum	ELISA	95	95	IgG	Feliciano et al. (2010)
40	40	40	Esa S. S. ve.	Serum	ELISA	90	90	IgG	Feliciano et al. (2010)
40	40	40	Ea S. ve	Serum	ELISA	92.5	93.8	IgG	Feliciano et al. (2010)
40	40	40	Ead S. ve.	Serum	ELISA	87.5	88.8	IgG	Feliciano et al. (2010)
40	40	40	Eaa S. ve.	Serum	ELISA	77.5	78.8	IgG	Feliciano et al. (2010)
25	20	25	Esd S. ve.	Serum	ELISA	88	88.4	IgG	Ribeiro et al. (2010)
25	20	25	Esd S. ve.	Saliva	ELISA	88	88.9	IgG	Ribeiro et al. (2010)
25	20	25	Esd S. ve.	Serum	ELISA	80	86.7	IgA	Ribeiro et al. (2010)
25	20	25	Esd S. ve.	Saliva	ELISA	76	88.9	IgA	Ribeiro et al. (2010)
251	11	-	Cr-Ag S. st.	Serum	Cr-Ag ELISA	97	100	IgG	Krolewiecki et al. (2010)
251	11	-	r-31 kDa S. st.	Serum	NIE-ELISA	84	100	IgG	Krolewiecki et al. (2010)
40	40	40	Es S. ve. Con-A BF	Serum	ELISA	82.5	83.8	IgG	Gonzaga et al. (2011a)
40	40	40	Es S. ve. Con-A UF	Serum	ELISA	95	92.5	IgG	Gonzaga et al. (2011a)
40	40	40	Es S. ve. Con-A BF	Serum	ELISA	75	73.8	IgA	Gonzaga et al. (2011a)
40	40	40	Es S. ve. Con-A UF	Serum	ELISA	82.5	77.5	IgA	Gonzaga et al. (2011a)
40	40	40	Ea larvae S. ve.	Serum	ELISA	100	100	IgG	Gonçalves et al. (2012a)
40	40	40	Ea egg S. ve.	Serum	ELISA	77.5	90	IgG	Gonçalves et al. (2012a)
40	40	40	Ea female S. ve.	Serum	ELISA	75	87.5	IgG	Gonçalves et al. (2012a)
40	40	40	Ea larvae S. ve.	Serum	ELISA	92.5	88.8	IgA	Gonçalves et al. (2012a)
40	40	40	Ea egg S. ve.	Serum	ELISA	37.5	86.3	IgA	Gonçalves et al. (2012a)
40	40	40	Ea female S. ve.	Serum	ELISA	55	80	IgA	Gonçalves et al. (2012a)
50	55	50	Es S. ve. DEAE S1	Serum	ELISA	92	91.4	IgG	Gonzaga et al. (2013)
50	55	50	Es S. ve. DEAE S2	Serum	ELISA	80	82.9	IgG	Gonzaga et al. (2013)
50	50	48	Es S. st. SsAg	Serum	ELISA	76	92.9	IgG	Inês et al. (2013)
50	50	48	Es S. st. MssAg	Serum	ELISA	72	83.7	IgG	Inês et al. (2013)
50	50	48	Es S. st. SsAg	Serum	ELISA	80	90.8	IgE	Inês et al. (2013)
50	50	48	Es S. st. MssAg	Serum	ELISA	74	75.5	IgE	Inês et al. (2013)

S. ra.: *Strongyloides ratti*; S. st.: *Strongyloides stercoralis*; S. ve.: *Strongyloides venezuelensis*; Es: saline extract; Esd: saline extract detergent; Esa: saline extract aqueous; Ea: alkaline extract; Ead: alkaline extract detergent; Eaa: alkaline extract aqueous; ZWIP: extract of infective larvae treated with Zwittergent plus protease inhibitor; ZW: extract of infective larvae treated with Zwittergent without protease inhibitor; r-31 kDa (NIE): recombinant of 31 kilodaltons; Con-A BF: concanavalin-A bound fraction; Con-A UF: concanavalin-A unbound fraction; DEAE S1: unbound fraction of ion exchange resin diethylaminoethyl sepharose; DEAE S2: bound fraction of ion exchange resin diethylaminoethyl sepharose; SsAg: antigen not treated with sodium metaperiodate; MssAg: antigen treated with sodium metaperiodate; AMC-ELISA: in house method (Academic Medical Center); IVD-ELISA e Bordier-ELISA: ELISA kits; Cr-Ag: crude extract.

Table 2. Diagnostic performance of serological assays based on *Strongyloides* larvae antigens obtained from different species

ELISA based on species of parasite	Parasitological methods (95% CI)	Q	P	I ² (95% CI)
<i>S. stercoralis</i>				
Sensitivity	78.9 (59.1-90.5)	120.9	0.00	92.6 (89.2-95.9)
Specificity	83.0 (61.8-93.7)	1101.3	0.00	99.2 (99.0-99.5)
DOR	18.2(8.5-39.1)			
PLR	4.6 (2.1-10.1)			
NLR	0.3 (0.1-0.5)			
1/NLR	3.9 (2.1-7.3)			
<i>S. venezuelensis</i>				
Sensitivity	81.0 (60.0-92.0)	17.3	0.00	71.1 (46.7-96.0)
Specificity	94.0 (74.0-99.0)	128.1	0.00	96.2 (94.2-98.0)
DOR	69.2 (15.4-311.1)			
PLR	13.9 (3.0-65.4)			
NLR	0.2 (0.1-0.5)			
1/NLR	5.0 (2.0-10.0)			
<i>S. ratti</i>				
Sensitivity	49.0 (23.0-74.0)	7.96	0.16	37.2 (0.00-95.0)
Specificity	95 (89.0-98.0)	59.5	0.00	91.6 (86.5-96.8)
DOR	18 (7.0-46.0)			
PLR	9.7 (5.1-18.4)			
NLR	0.5 (0.03-0.9)			
1/NLR	4.55 (1.47-14.29)			
Serology Total				
Sensitivity	71.7 (56.0-83.4)	178.2	0.00	89.9 (86.4-93.4)
Specificity	89.9 (80.8-94.9)	1596.4	0.00	98.8 (98.7-99.1)
DOR	22.5 (10.8-46.9)			
PLR	7.1 (3.9-13.0)			
NLR	0.3 (0.2-0.5)			
1/NLR	3.2 (2.0-5.0)			

MOLECULAR

- PCRc fezes e sangue
- PCRq fezes e sangue

Table 3. Summary of findings table for the review of PCR techniques for the diagnosis of *Strongyloides stercoralis* infection.

Interpretative criteria to define: Index vs. Reference Test	Effect (95% CI)	Number of studies	Mean Prevalence (95% CI)	What do these results mean?
All PCR ^a vs. Serology or parasitological methods ^b	Sensitivity: 61.8% (42.0–78.4) Specificity: 95.3% (92.0–97.2)	17	21.1% (13.8 to 28.4)	Assuming (based on the mean prevalence) 21 out of 100 patients with SSI, eight would be missed by a single PCR test (38% of 21). Of the 79 patients without SSI, four (5%) would have a false positive result of the PCR test.
AI PCR vs. parasitological methods only	Sensitivity: 71.8% (52.2–85.5) Specificity: 93.5% (90.3–95.6)	14	18.5% (13.4 to 23.6)	Assuming 18 out of 100 patients with SSI, five would be missed by a single PCR test. Of the 82 patients without SSI, five would have a false positive result of the PCR test.
Real-time PCR vs. Serology or parasitological methods	Sensitivity: 56.5% (39.2–72.4) Specificity: 95.4% (91.7–97.5)	14	20.5% (11.6 to 29.4)	Assuming 20 out of 100 patients with SSI, nine would be missed by a single PCR test. Of the other 80, four will have a false positive result of the PCR test.
Real-time PCR vs. parasitological methods only	Sensitivity: 64.4% (46.2–77.7) Specificity: 93.9% (90.3–96.3)	12	20.3% (9.9 to 30.8)	Assuming 20 out of 100 patients with SSI, seven would be missed by a single PCR test. Of the other 80, five would have a false positive result of the PCR test.

PCR, polymerase chain reaction; SSI, *S. stercoralis* infection. Estimates for sensitivity and specificity are here reported in %.

^a Studies included conventional PCR, nested PCR, real-time PCR

^b Either Baermann method, agar plate culture, Harada-Mori culture, or a combination of fecal methods



APLICAÇÃO DAS TÉCNICAS

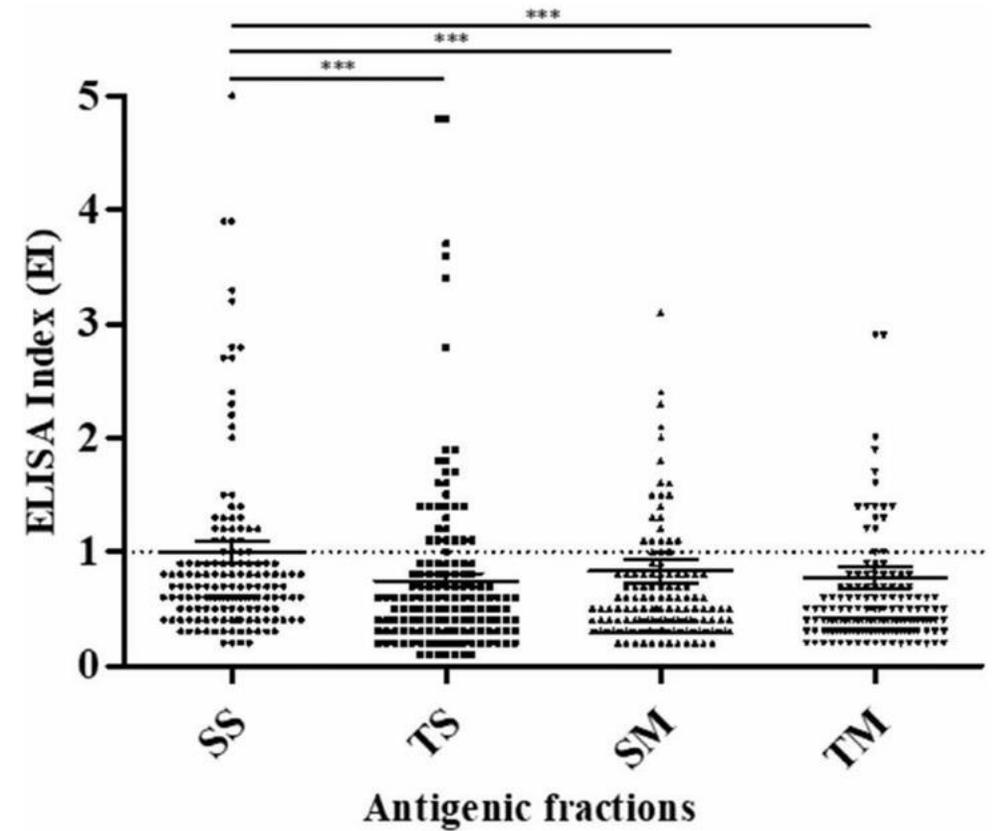


Table 1

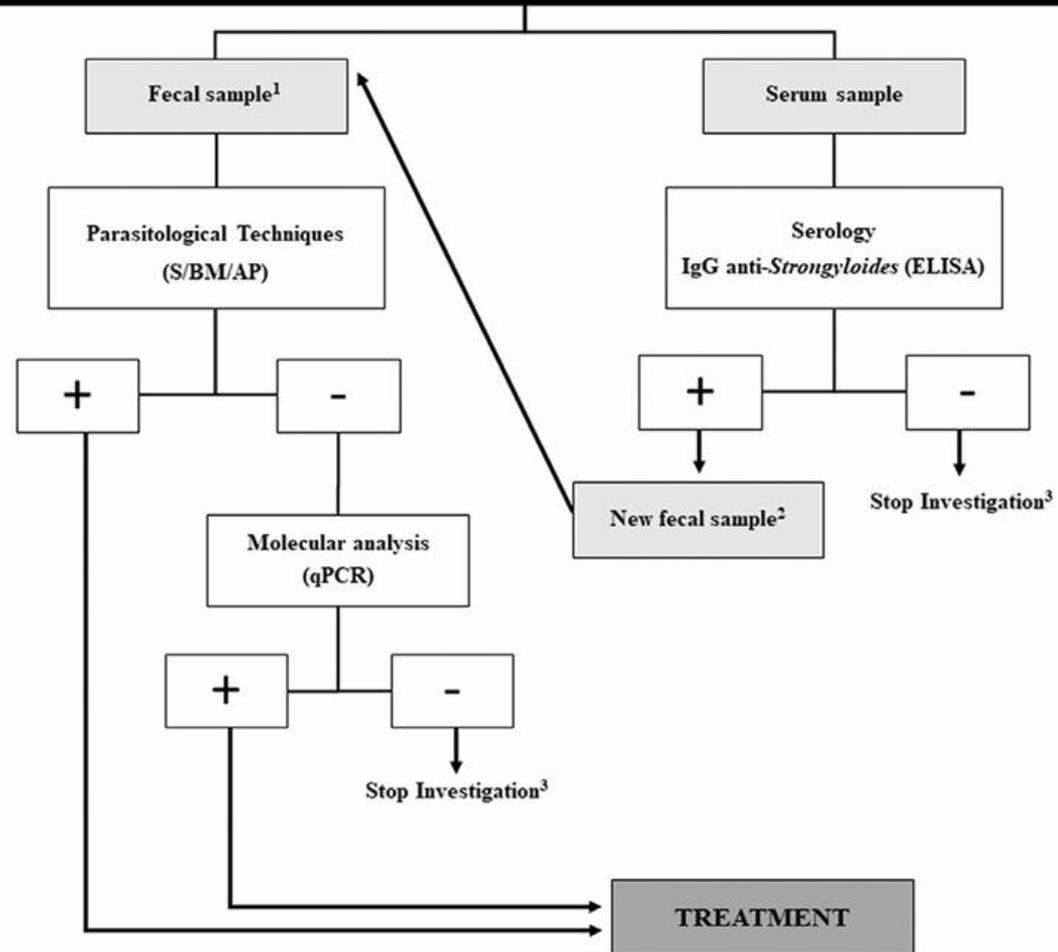
Detection of *Strongyloides stercoralis* using parasitological methods alone and in combination, in 150 stool samples from candidates for transplantation

Groups	SS	R	APC	SS+R	SS+APC	R+APC	SS+R+APC	Total
Renal transplantation	0	2	5	0	1	1	0	9
Liver transplantation	2	0	0	0	0	0	1	3
Bone Marrow Transplant	0	0	0	0	1	0	1	2
Total	2	2	5	0	2	1	2	14

SS, spontaneous sedimentation method; R, Rugai method; APC, Agar Plate culture method.



ALGORITHM FOR DETECTION OF *STRONGYLOIDES* INFECTION IN TRANSPLANT CANDIDATES



¹One fecal sample.

²Ideally request analysis of a new fecal sample or, if this is not possible, preemptive treatment with ivermectin.

³If the transplant candidate has some epidemiological data (prior exposure barefoot to the ground) and eosinophil in the peripheral blood, preemptive treatment with ivermectin may be considered.

PROFILAXIA

- Impedir o acesso de larvas filarioides existentes no solo à pele ou às mucosas de hospedeiros suscetíveis.
- Tratamento sanitário adequado para as fezes;
- Lavagem dos alimentos;
- Uso de calçados;
- Identificação, orientação e tratamento do infectado.

TRATAMENTO

- Ivermectina (200 mg/Kg)
 - ✓ Imobilização do verme por meio de uma **paralisia tônica muscular**.
 - ✓ Interação entre o fármaco e os **canais de cloro** ativados por glutamato em células nervosas e musculares causando hiperpolarização, por meio do aumento da permeabilidade a esses íons
 - Derivados benzoimidazólicos:
 - Tiobendazol (25mg/Kg 2x/ dia/ 2 dias)
 - Cambendazol (5mg/Kg)
 - Albendazol (400mg/Kg x 3 dias)
- ➔ Controle de Cura

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