

A new ELISA to detect cystic echinococcosis

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Erasmus MC

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Disclosure

- Institut Virion\Serion GmbH
 - Supplied test kits
 - Provided financial compensation for labor

- No role in:
 - Analysis and interpretation of data
 - Writing of the report
 - Decision to submit article

Background

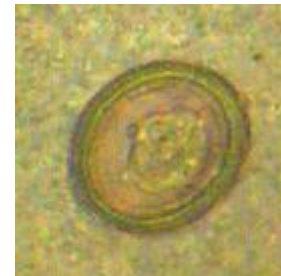
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 - Parasitic disease
 - Caused by tapeworm

Background

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 - Parasitic disease
 - Caused by tapeworm
- *E. granulosus*
- *E. multilocularis*
- *E. oligarthrus*
- *E. vogeli*

Background

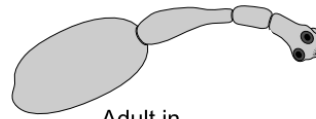
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 - Caused by tapeworm
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Life cycle

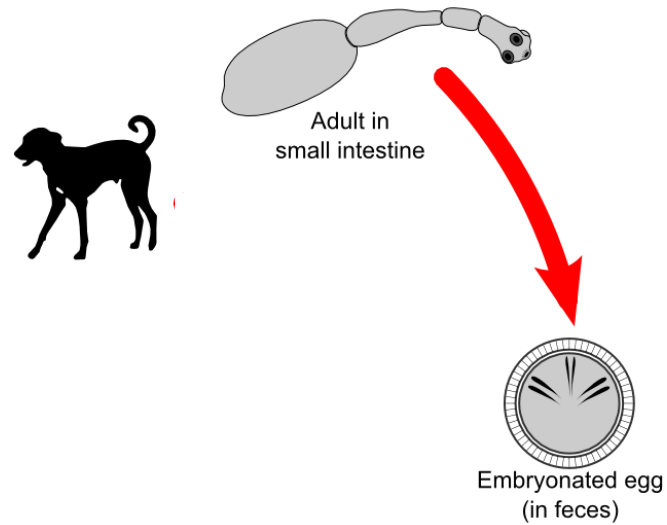


Life cycle

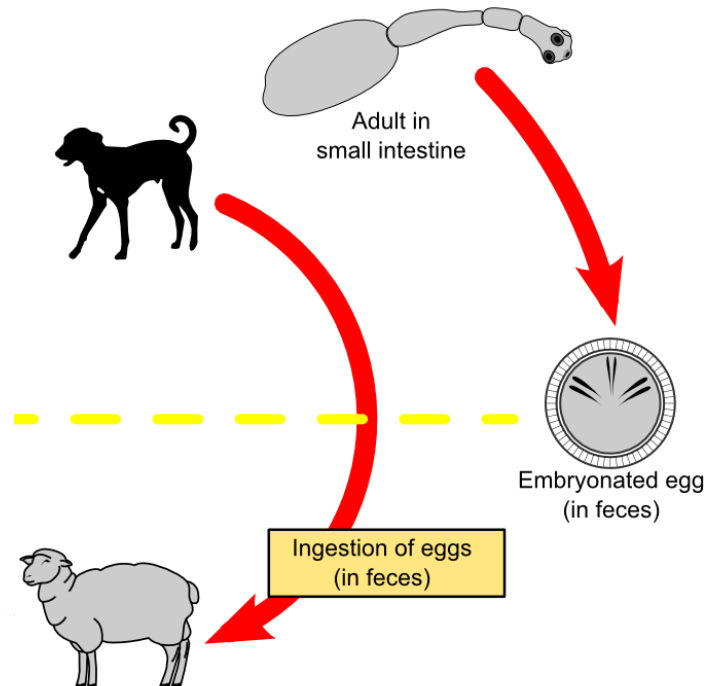


Adult in
small intestine

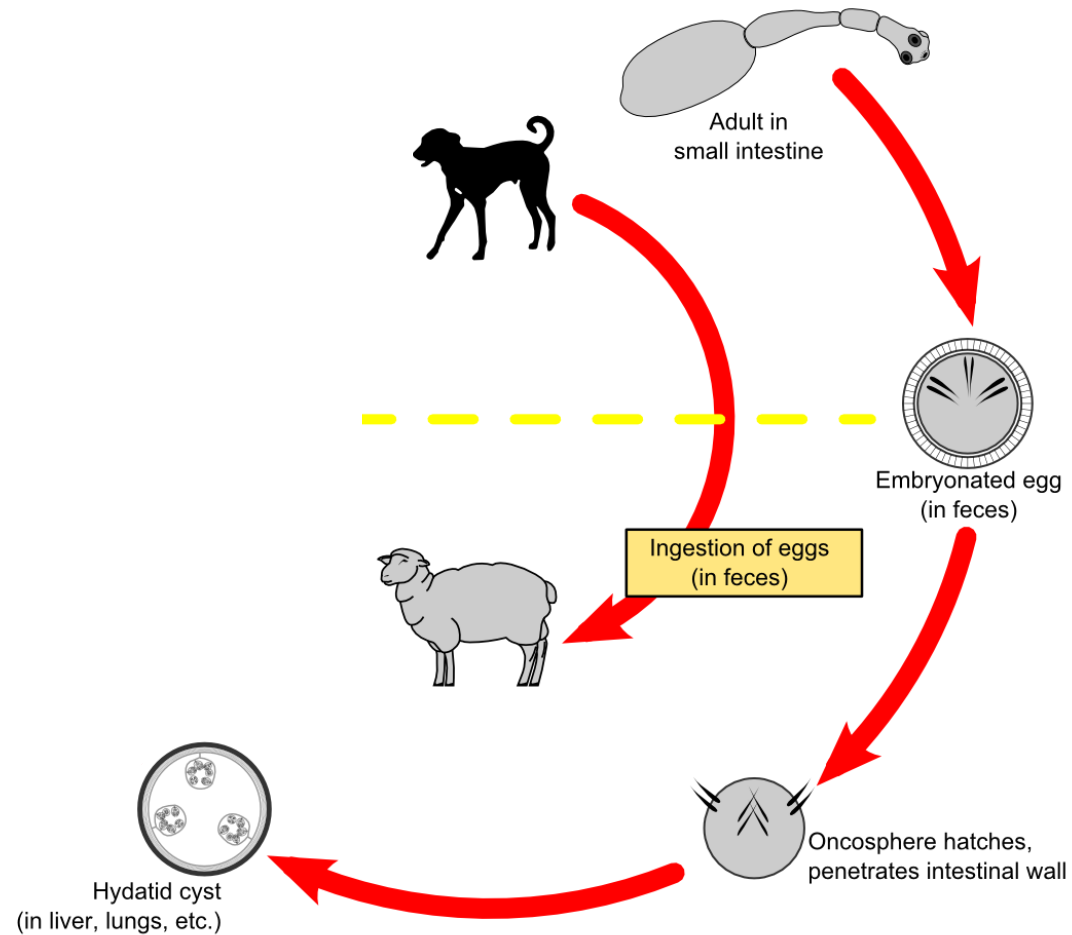
Life cycle



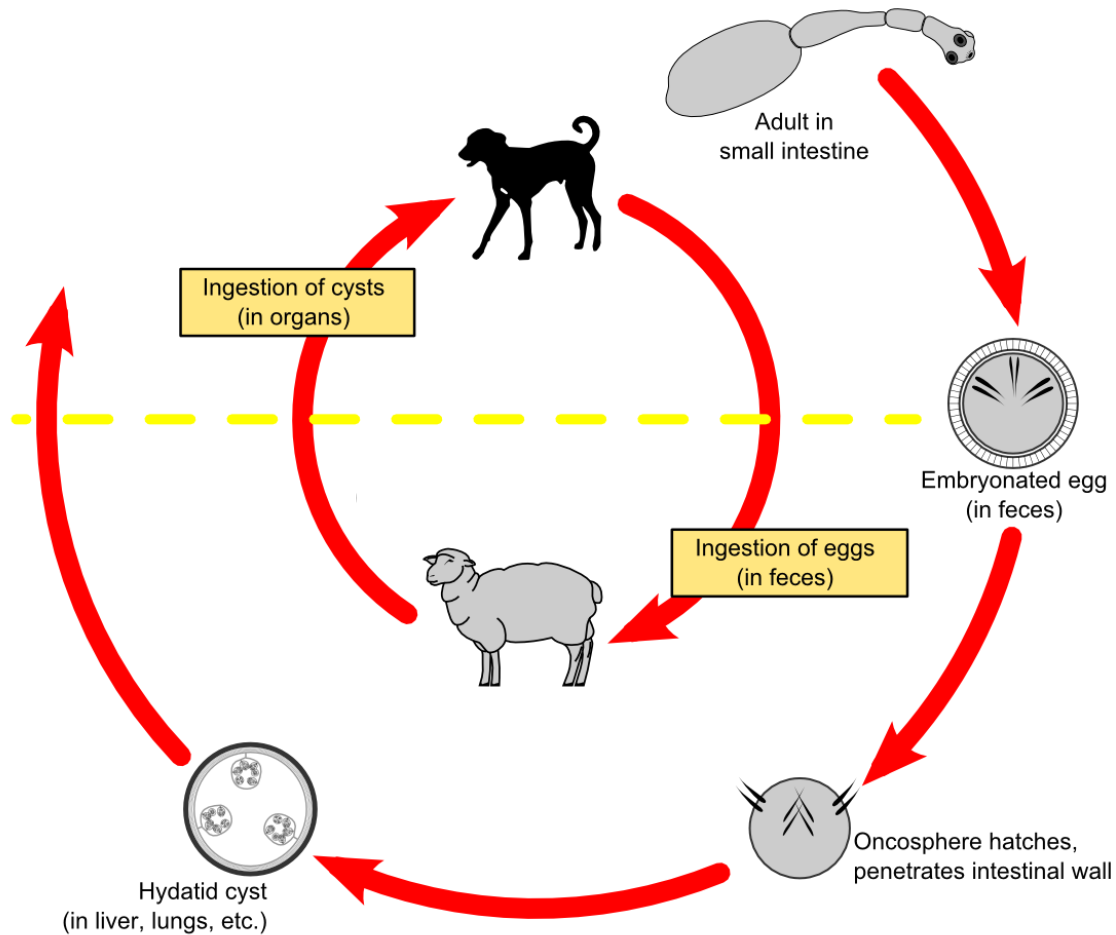
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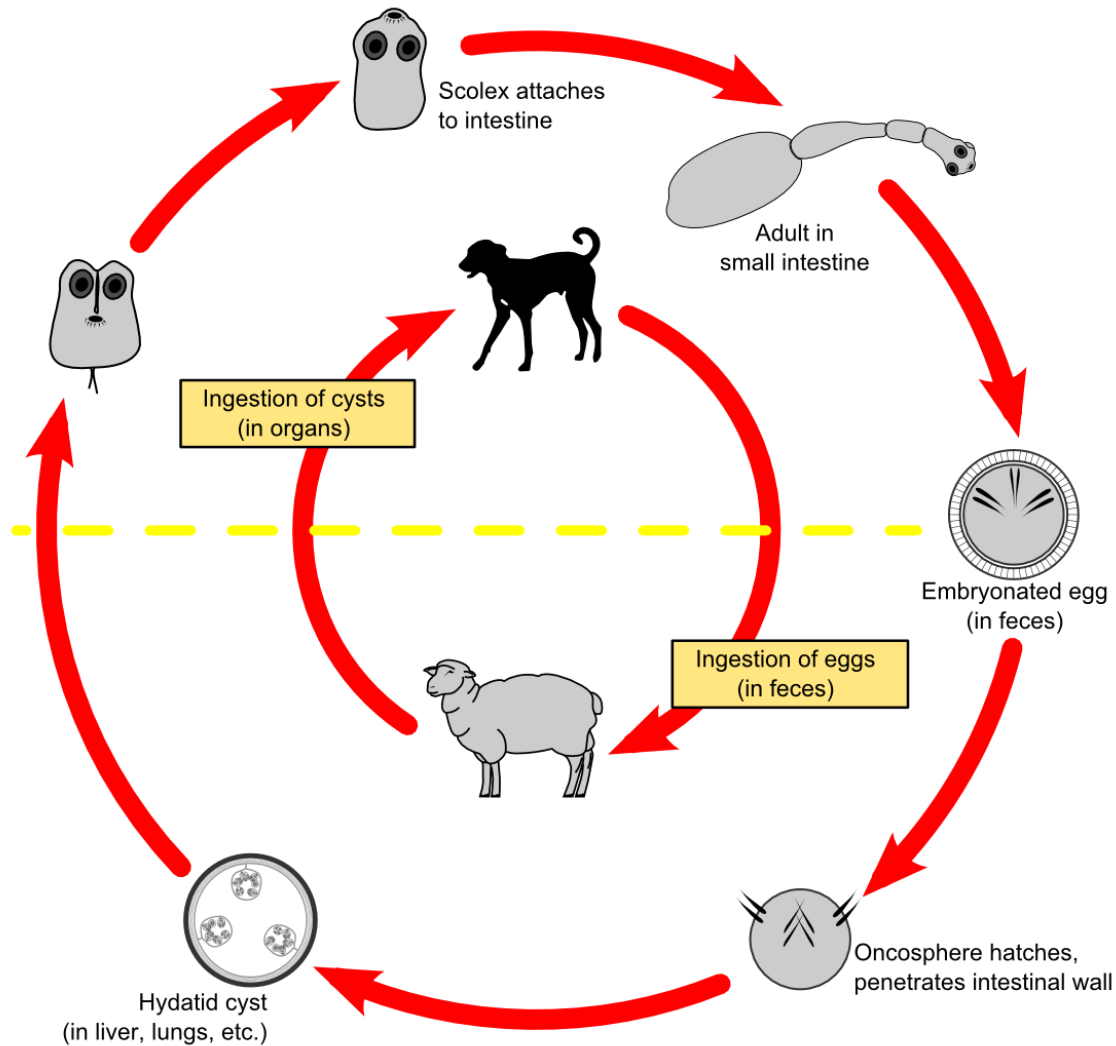
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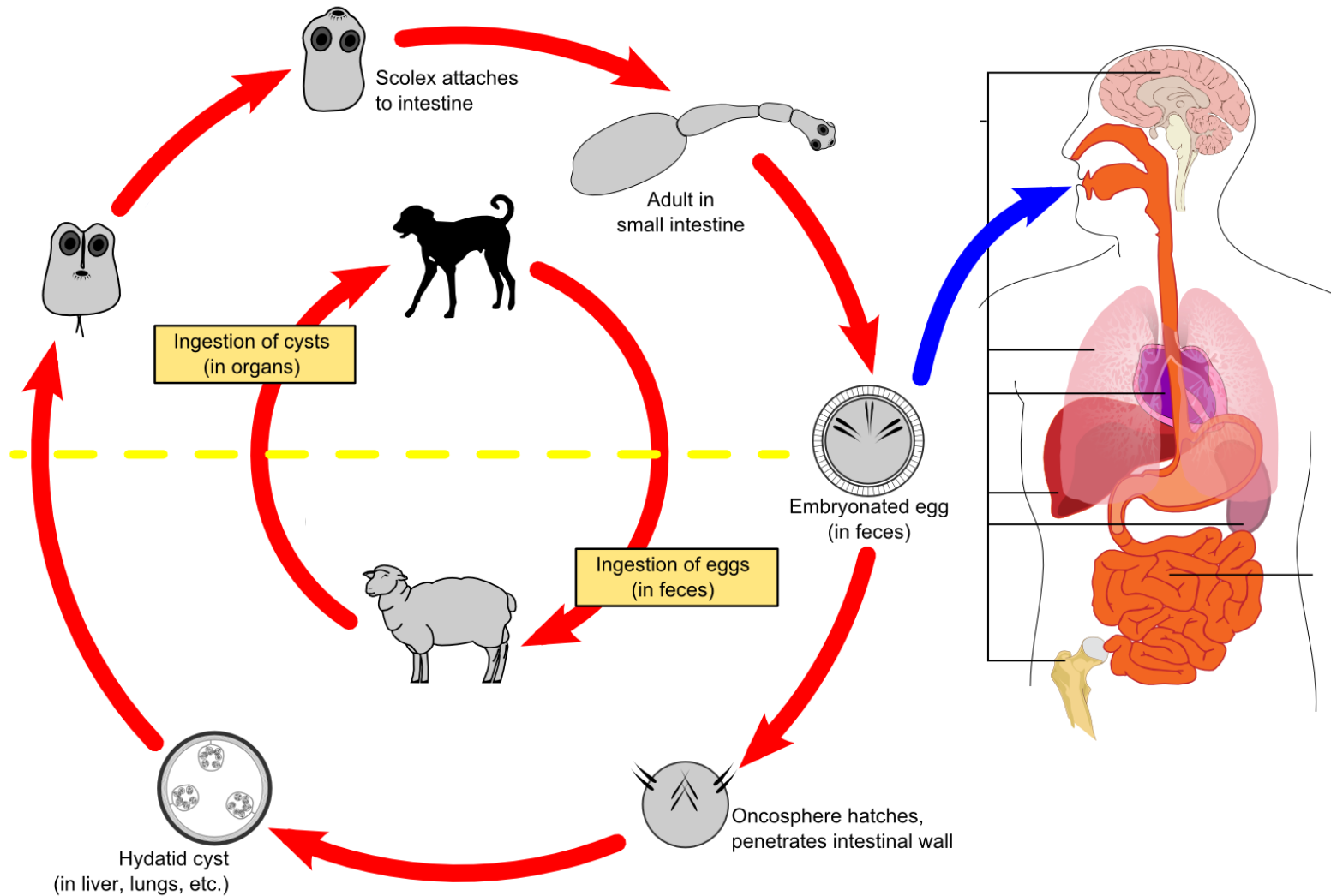
Life cycle



Life cycle



Life cycle



Disease in humans

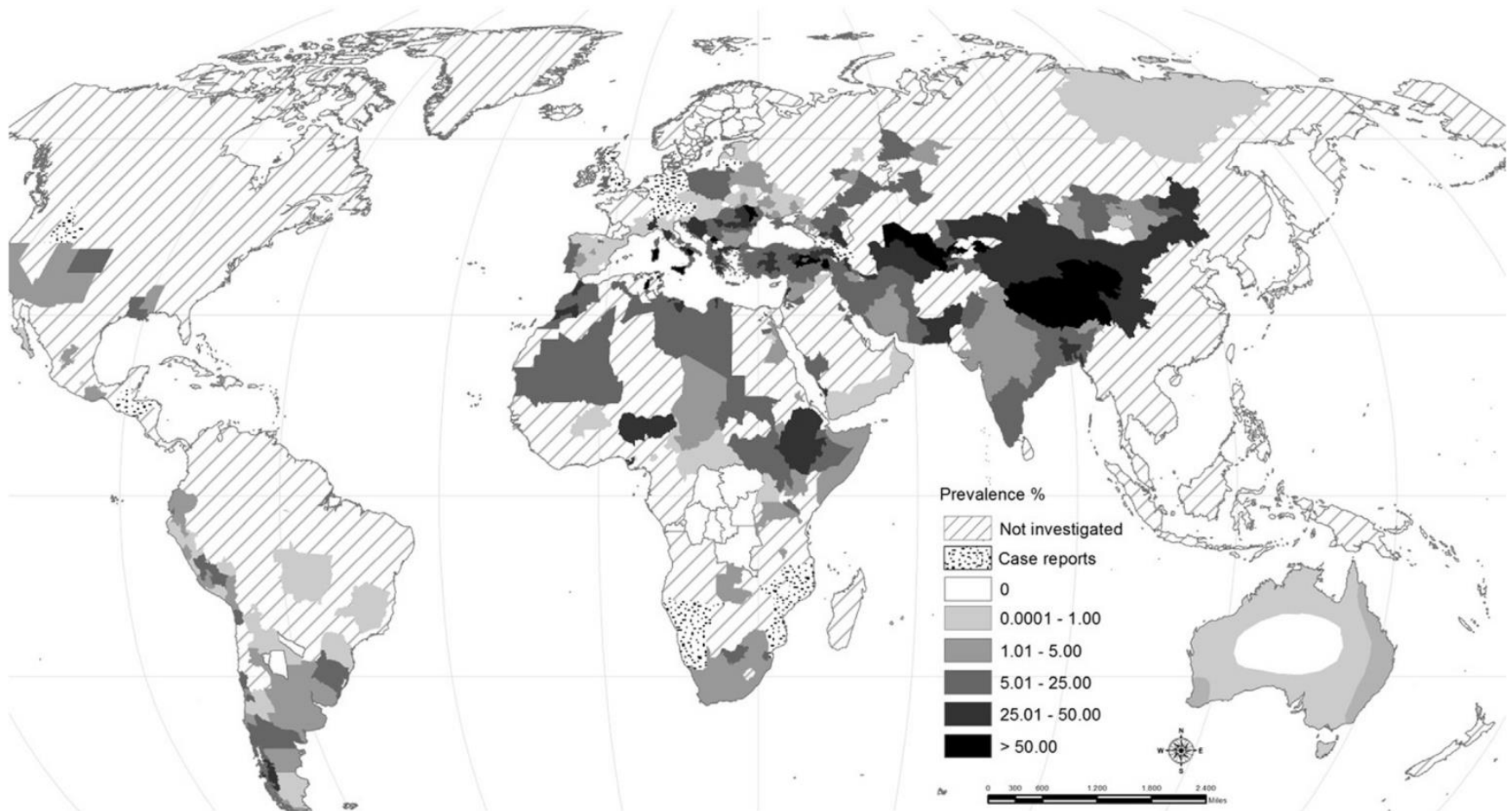
- Cystic echinococcosis
- Alveolar echinococcosis

Disease in humans

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Disease in humans

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- Cysts form in liver (75%), spleen, lung, brain, heart and kidneys
- Mainly large cysts induce clinical symptoms
 - Symptoms related to cyst location
- Liver cyst:
 - Abdominal pain
 - Jaundice
 - Fever

Diagnosis

- Imaging techniques
 - Ultrasonography
 - CT
 - MRI

Diagnosis

- Imaging techniques
 - Ultrasonography
 - CT
 - MRI
- Classification
- Staging
- Treatment response

Diagnosis

- Serology
 - ELISA
 - Western blot
 - IHA

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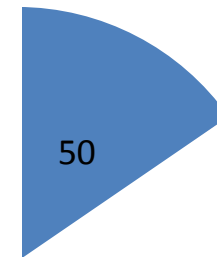
- Serology
 - ELISA
 - Western blot
 - IHA
- Complimentary role
- If imaging is inconclusive
- Lack of standardization
- Commercially available ELISAs infrequently studied
- Examine the clinical performance of SERION ELISA

Methods

- Analysed serum samples:

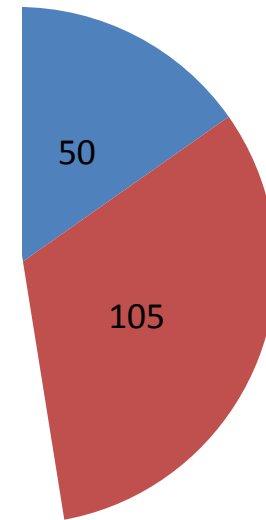
Methods

- Analysed serum samples:
- Cystic Echinococcosis (50)
 - Microscopic analysis of cyst fluid (8)
 - Imaging + IHA / western blot / IE / CBR (42)
 - Diagnosis was made by multidisciplinary team



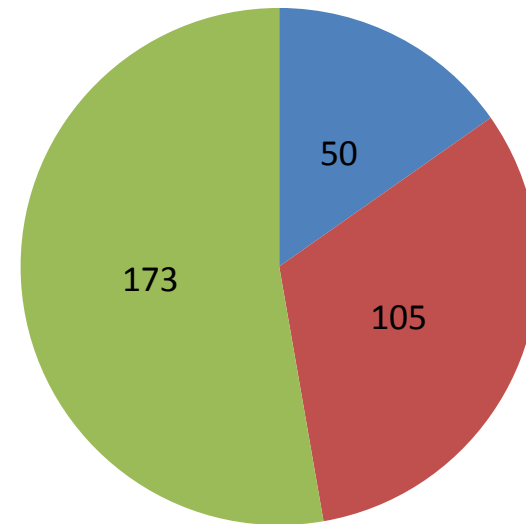
Methods

- Analysed serum samples:
- Cystic Echinococcosis (50)
- Healthy controls (105)
 - Blood donors



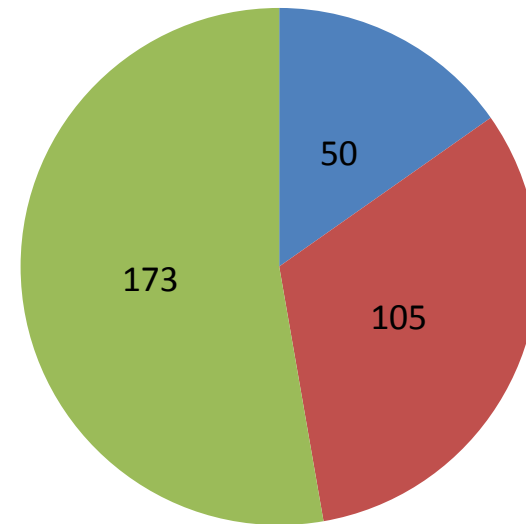
Methods

- Analysed serum samples:
- Cystic Echinococcosis (50)
- Healthy controls (105)
- Infectious disease controls (173)
 - Helminthiases
 - Bacterial infections
 - Other



Methods

- Analysed serum samples:
 - Cystic Echinococcosis (50)
 - Healthy controls (105)
 - Infectious disease controls (173)
-
- According to instructions of manufacturer
 - All serum samples analysed in duplicate



Results

Patients with CE

	No. samples	Sensitivity (%)
Pos (Co ≥ 10.0)	49	98.0
Neg (Co < 10.0)	1	

Results

	Patients with CE		Healthy controls	
	No. samples	Sensitivity (%)	No. samples	Specificity (%)
Pos (Co ≥ 10.0)	49	98.0	4	
Neg (Co < 10.0)	1		101	96.2

Results

	Patients with CE		Healthy controls		Infectious disease controls	
	No. samples	Sensitivity (%)	No. samples	Specificity (%)	No. samples	Specificity (%)
Pos (Co ≥ 10.0)	49	98.0	4		40	
Neg (Co < 10.0)	1		101	96.2	133	76.9

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Pos (Co ≥ 15.0)	46	92.0				
Indec (Co ≥ 10.0 Co < 15.0)	3					
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Pos (Co ≥ 15.0)	46	92.0	3		14	
Indec (Co ≥ 10.0 Co < 15.0)	3		1		26	
Neg (Co < 10.0)	1		101	97.1	133	91.9

Conclusion (I)

- Additional group of indecisive results
 - Minor decrease in sensitivity
 - Increase in specificity
 - Especially in infectious diseases control group

Conclusion (I)

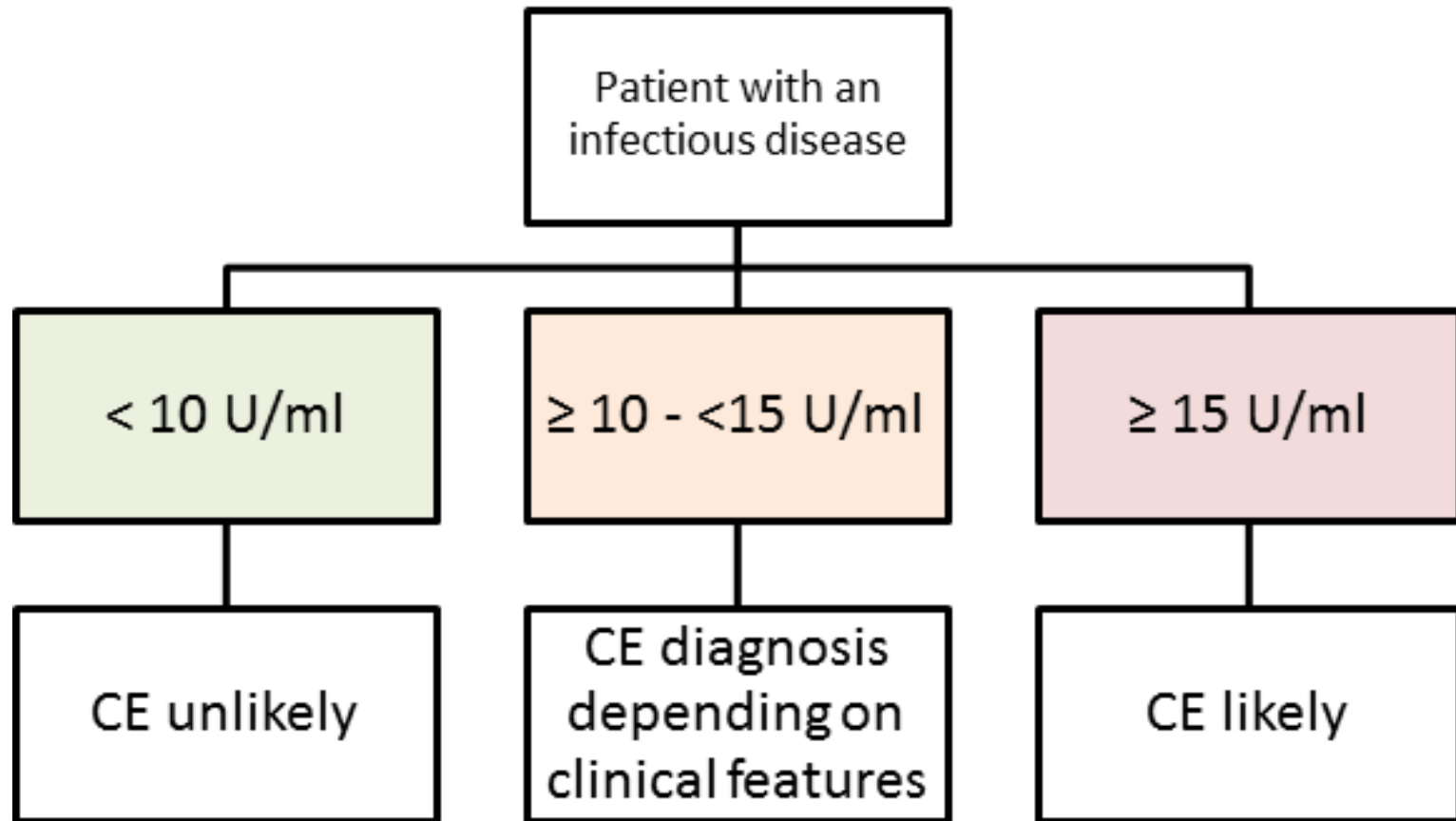
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 - Very low in western countries
 - Impact on positive predictive value
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- Additional group of indecisive results
 - Minor decrease in sensitivity
 - Increase in specificity
 - Especially in infectious diseases control group
- Prevalence of cystic echinococcosis varies geographically
 - Very low in western countries
 - Impact on positive predictive value
 - With high specificity, this problem is constrained
- Useful test in clinical practice
 - Even in western countries

Conclusion (I)

- Interpretation of results in clinical practice



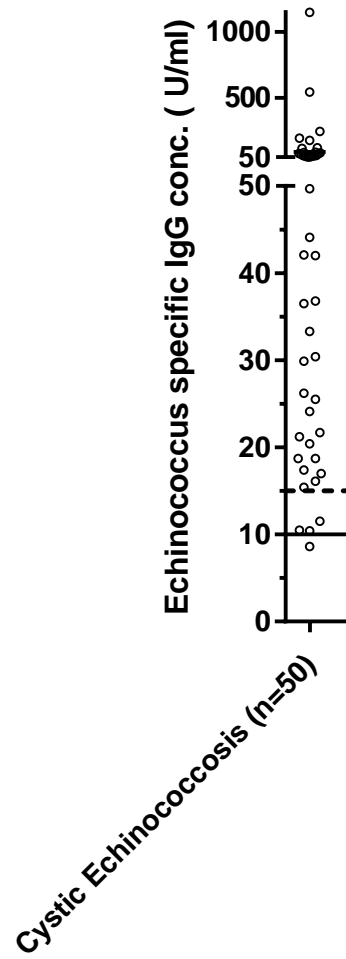
Results

- Cross-reactivity

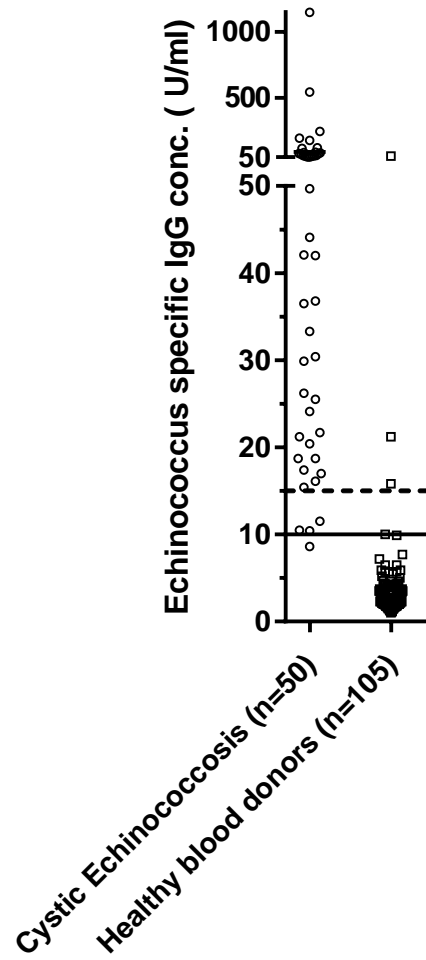
Results

- Cross-reactivity
 - Difference between
 - Helminthiases
 - Bacterial infections

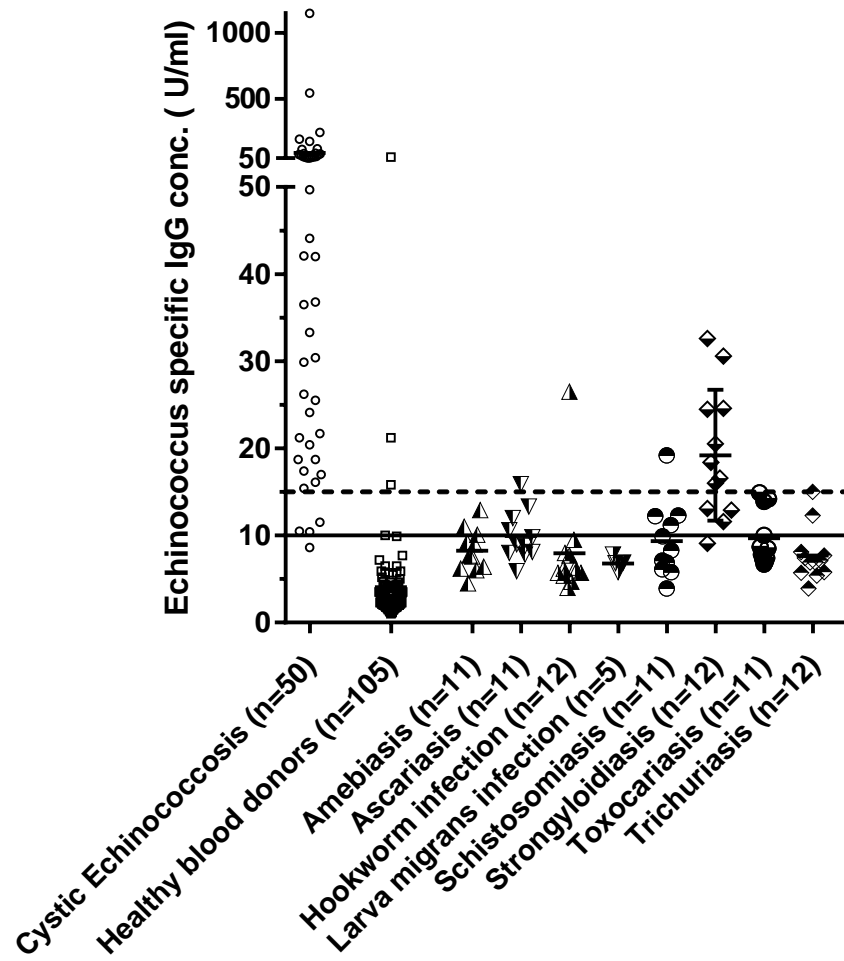
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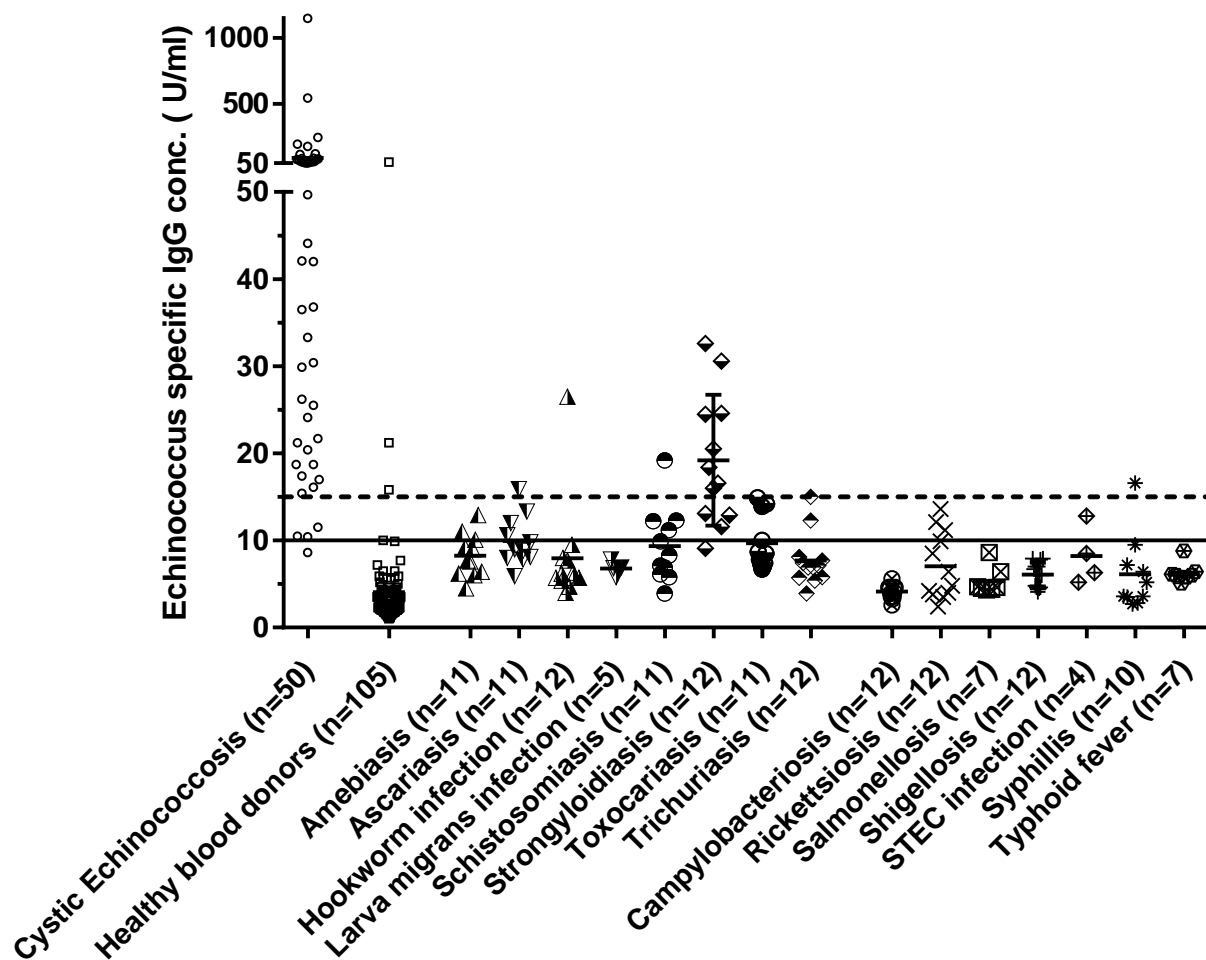
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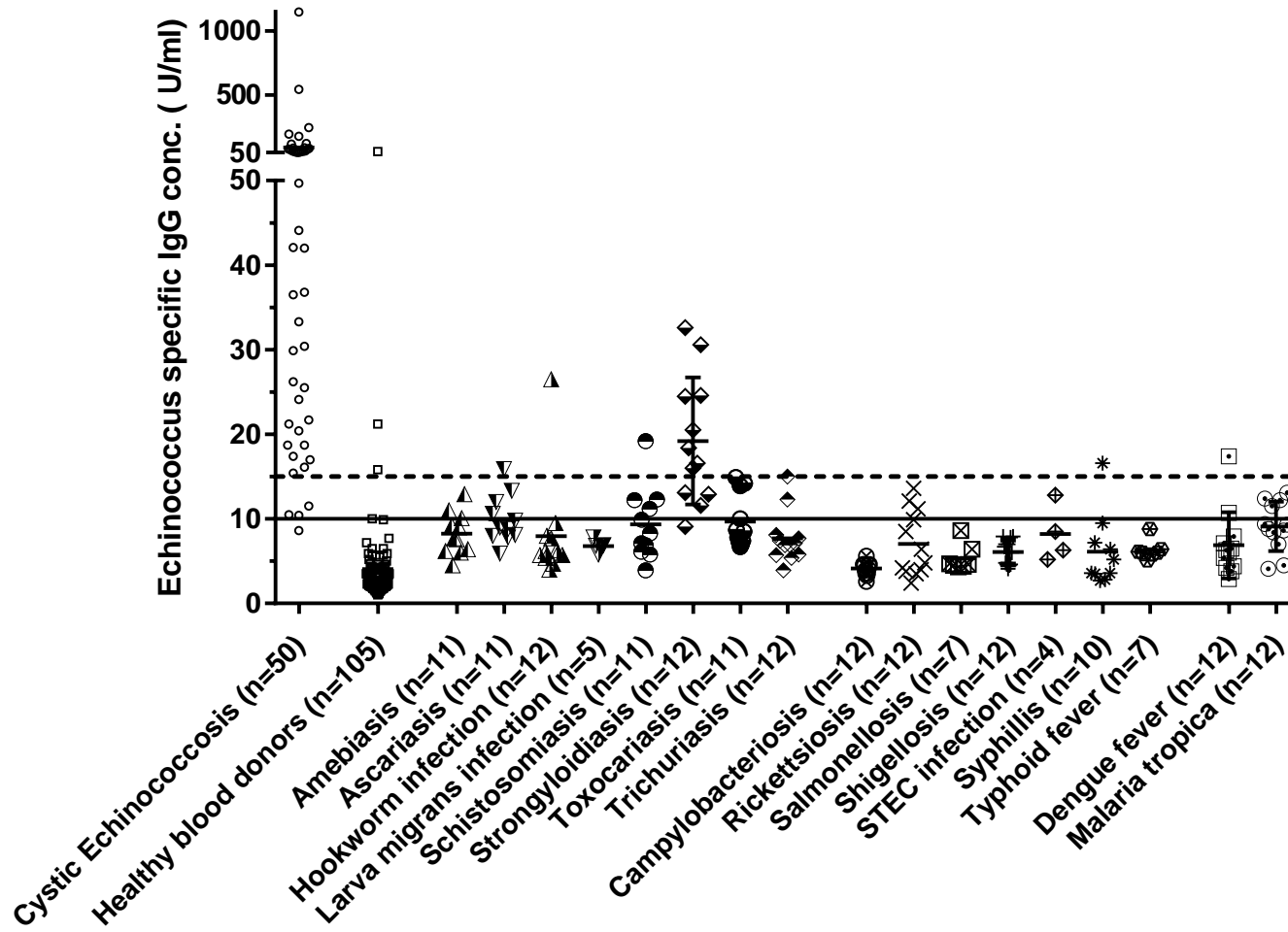
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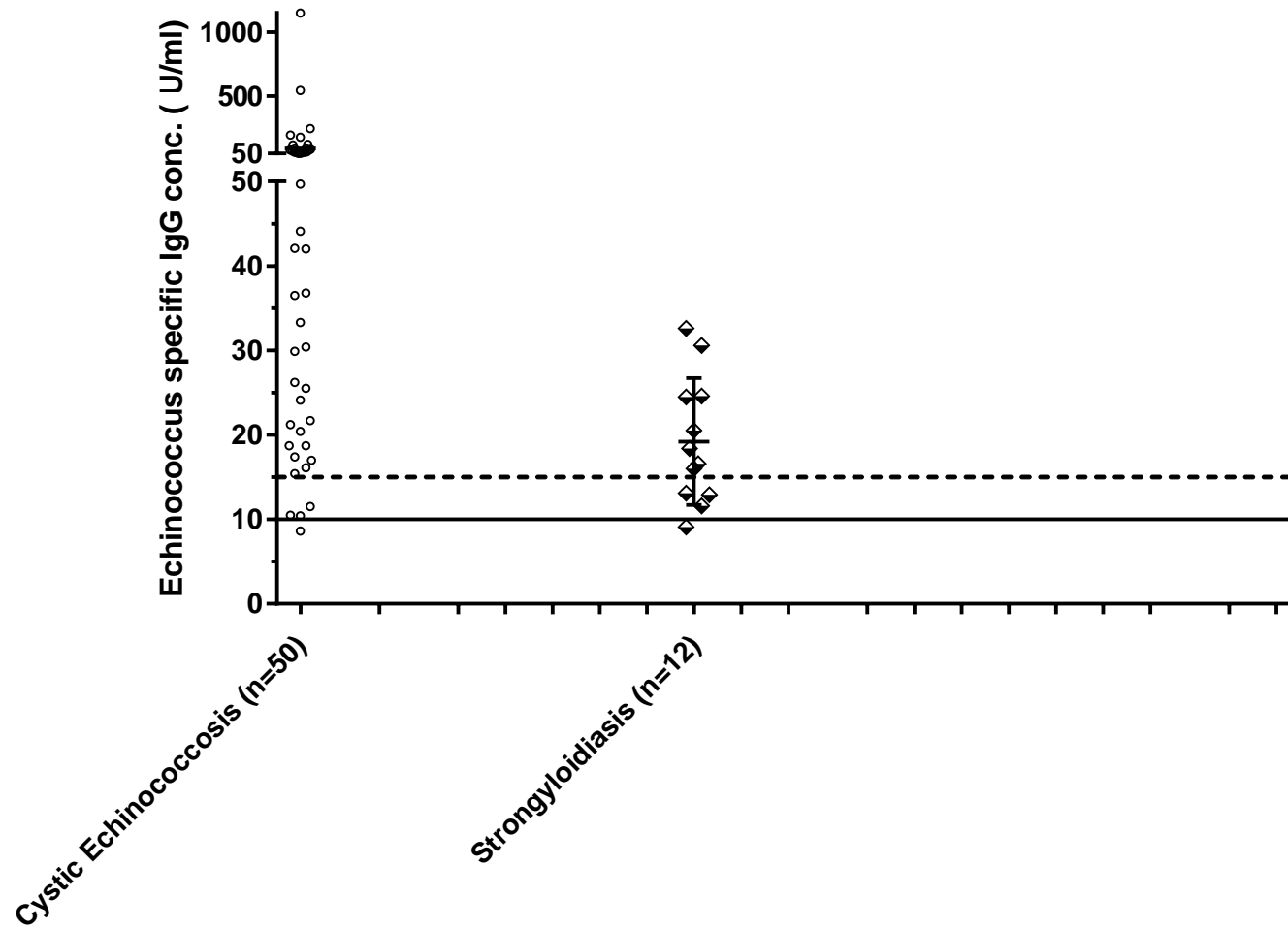
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- High cross-reactivity in helminthiases
 - Especially strongyloidiasis (91.7%)
- Strongyloides is able to auto-infect
 - Continuous triggering of immune system
 - Steady production of antibodies
- Cause of high cross-reactivity?
 - Reported for several other ELISAs

Case – Reliability of serology upon cyst rupture

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- 41-year-old female from Afghanistan
- No relevant past medical history
- Referred to the emergency department
- Acute stomach ache
- Collapse

Case – Reliability of serology upon cyst rupture

- Physical examination:
 - Weak peripheral pulsations
 - BP 100/60
 - HR 128/min
 - Additional physical examination: No abnormalities

Case – Reliability of serology upon cyst rupture

■ Blood analysis

Hb	9.3
CRP	4
Creatinin	77
Leukocytes	39×10^9
Leuko diff	
Bands	18%
Eosinophils	0%
Basophils	0%
Neutrophils	49.7%
Lymphocytes	27.1%
Monocytes	1.5%
ASAT	115
ALAT	93

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- 50 x 50 mm cystic lesion in liver
 - Possible signs of rupture

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- DD
 - Liver abscess
 - Ruptured *Echinococcus granulosus* cyst
- Echinococcus serology

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Case – Reliability of serology upon cyst rupture

- DD
 - Liver abscess
 - Ruptured *Echinococcus granulosus* cyst
- Echinococcus serology
 - Negative IHA
- Despite lack of convincing evidence:
 - Albendazole 5 mg/kg twice daily
 - Broad spectrum antibiotics

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- From ICU to ward after 5 days
- White blood cell count, CRP, liver enzymes decreased
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- After 3 weeks; serology titer of 1:10240

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- Why was serology negative at presentation?

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Case – Reliability of serology upon cyst rupture

- Why was serology negative at presentation?
- Very early infection without antibody production?
- Large cyst (5 cm)
 - Infection duration of 5 years

Case – Reliability of serology upon cyst rupture

- Why was serology negative at presentation?
- Very old cyst with calcification and low host-pathogen interaction?

Case – Reliability of serology upon cyst rupture

- Why was serology negative at presentation?
- Very old cyst with calcification and low host-pathogen interaction?
- Multivesicular cysts visualized
- Spontaneous rupture

Case – Reliability of serology upon cyst rupture

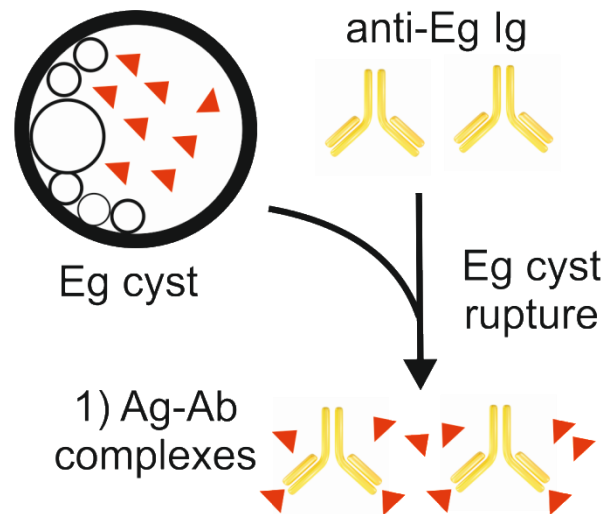
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Case – Reliability of serology upon cyst rupture

- Why was serology negative at presentation?
- Excess of antigen release from ruptured cyst
- All available antibodies are bound to antigen
- No reaction in IHA or ELISA

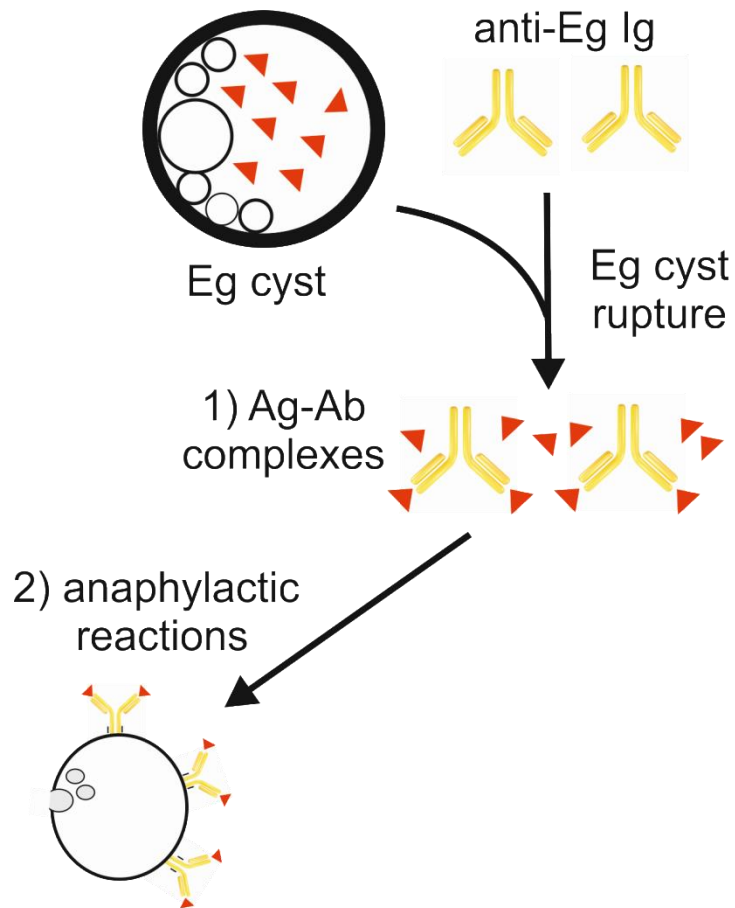
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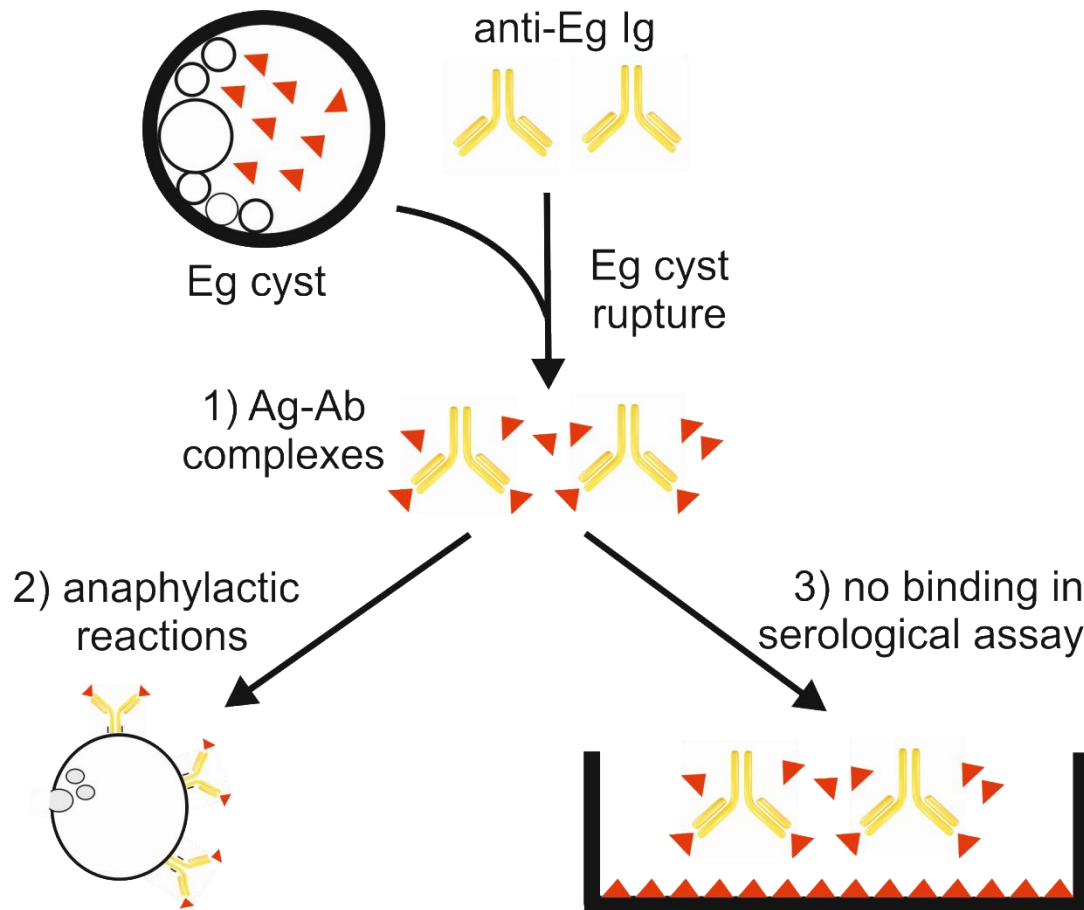
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Case – Reliability of serology upon cyst rupture

- Why was serology negative at presentation?

- Watch out for false negative echinococcus serology after cyst rupture
 - 2 similar cases in EMC

Acknowledgements

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