Sarcocystis in animal and human infections
Ronald Fayer
USDA, ARS

Sarcocystis: ~ 130 species
Species in muscle or nervous tissue of domestic animals

<table>
<thead>
<tr>
<th>Cattle</th>
<th>Sheep</th>
<th>Ovis</th>
<th>Reindeer</th>
<th>Cameroon</th>
<th>Horse</th>
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<tbody>
<tr>
<td>S. cruzi</td>
<td>S. arieticanis</td>
<td>S. gigantea</td>
<td>S. meigleri</td>
<td>S. cameli</td>
<td>S. bertramii</td>
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<tr>
<td>syn. S. bovicans</td>
<td>syn. S. ovifelis</td>
<td>syn. S. ovicana</td>
<td>S. rangi</td>
<td>S. fayeri</td>
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<td>S. hirsuta</td>
<td>S. tenella</td>
<td>S. rangeli</td>
<td>S. rangiferi</td>
<td>S. suicanis</td>
<td>S. bovifelis</td>
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<tr>
<td>syn. S. bovominis</td>
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<tr>
<td>Goat</td>
<td>Llama</td>
<td>Camel</td>
<td>Sus scrofa</td>
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<td>Capra hircus</td>
<td>Lama glama</td>
<td>Camelus dromedarius</td>
<td>S. meicheriana</td>
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<td>S. capracanis</td>
<td>S. aucheniae</td>
<td>S. melancia</td>
<td>syn. S. suicanis</td>
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<td>S. tenella</td>
<td>S. bovicanis</td>
<td>S. sullwagonis</td>
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<td>S. cameli</td>
<td>S. suicanis</td>
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</table>

Miescher: White threadlike cysts in mouse muscles
Sarcocystis melicheriana named for cysts in pigs
Electron microscopy shows apicomplexan organelles
Sexual stages & oocysts demonstrated in vitro
Carnivore final hosts identified
Identification by molecular methods


Sarcocystis life cycle
Definitive host (predator)
Exogenous
Ingestion of infective stages
Sporocyst
Sporoogy
Merozoites
Cyst wall
Cytokinesis
Egg
Zygote
Sporozoites
Definitive host (prey)
Sporozoites
Sporocyst
Intermediate host (prey)
Exogenous
Ingestion of infective stages
Sporocyst
Sporoogy
Merozoites
Cyst wall
Cytokinesis
Egg
Zygote
Sporozoites
Definitive host (prey)
Sporozoites
Sporocyst

Life cycle of Sarcocystis

EXCYSTATION
Sporocyst
Float
After CO₂ exposure
After exposure to trypsin-bile

EXCYSTATION
Intravascular in arterioles
1st asexual stage
2 weeks after exposure

Lung

Intravascular 2nd asexual generation in capillaries ~ 4 weeks after ingesting sporocysts

Brain

Kidney

Schizont

Muscle

Bloodborne
3rd asexual generation ~ 30 days after exposure

Intracellular merozoites

Extracellular merozoite

Mature intramuscular cysts

Heart

Intraneural or intramuscular
4th asexual generation
40+ days after exposure

Immature cysts with metrocytes

Brain

Muscle

10/06/2010
Dog eating cattle muscle

Canine Small intestine

Fertilized macrogamont

Oocyst with sporozoites

Canine Small intestine

Micro

Macro

Fertilized Macro

Sporocysts in fecal float

**Sources of pathogenic species for livestock**

<table>
<thead>
<tr>
<th>Intermediate Host</th>
<th>Species</th>
<th>Pathogenicity</th>
<th>Final Host</th>
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<tbody>
<tr>
<td>Cattle</td>
<td>S. cruzi</td>
<td>Highly pathogenic</td>
<td>Canids, Raccoon</td>
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<td>S. hirsuta</td>
<td>Low</td>
<td>Felids</td>
</tr>
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<td>S. hominis</td>
<td>Low</td>
<td>Primates</td>
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<td>Sheep</td>
<td>S. tenella</td>
<td>Highly pathogenic</td>
<td>Canids, Dog</td>
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<td>S. arcticanae</td>
<td>Intermediate</td>
<td>Cat</td>
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<tr>
<td></td>
<td>S. gigantea</td>
<td>Non-pathogenic</td>
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<tr>
<td>Goats</td>
<td>S. capracanis</td>
<td>Highly pathogenic</td>
<td>Canids, Dog</td>
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<td>Cat</td>
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<tr>
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<td>S. moulei</td>
<td>Non-pathogenic</td>
<td></td>
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<td>Pigs</td>
<td>S. meischeriana</td>
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<td>Canids, raccoon</td>
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<td></td>
<td>S. suinominis</td>
<td>Highly pathogenic</td>
<td>Primates</td>
</tr>
<tr>
<td></td>
<td>S. porcifelis</td>
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</tbody>
</table>
Gross signs of infection

Rhinitis

Glossitis

Hemorrhage

Weight Loss

Retarded Growth

Uninfected

Pair fed

Infected

Uninfected

DIET

Most Significant IGF-I effectors

WHOLE BODY IGF-I PRODUCTION

THYROID

INSULIN

IGF-I

FAT

Hepatic IGF-1 receptors

Muscle

Bone

Fat

Immune system

Brain

Pituitary

Pancreas

Liver

Stomach

Adipose tissue

Kidney
Depresses

- Autocrine growth factors
- Synthesis of RNA for Anabolic Enzymes
- Hematopoiesis
- Cartilage Formation
- Bone Formation
- Lipid Accumulation
- Myogenesis
- Pituitary Hormone Secretion
- Appetite
- Energy Metabolism
- Protein Synthesis in vivo

Promotes

- Cartilage Resorption
- Bone Resorption
- Inflammatory Response
- Hematopoiesis
- Neutrophilic Leukocytes
- ACTH-Glucocorticoid Production
- Catecholamine Release
- Biphasic Effects on
  - Blood Glucose
  - Plasma Insulin
  - Plasma Glucagon

Kills

Selected neoplastic cells

Depresses

- Microvessel or "Tie" Production
- Vasculature

ACTIVITIES OF TNFα RELATED TO GROWTH

Protozoa: Sarcocystis, Toxoplasma, Plasmodium, Babesia, Leishmania, Trypanosoma

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Gross signs of infection

- Paralysis
- Opisthotonus
- Torticollis

Hair loss / Wool breaking

- Rat tail

Laminitis / Foot Lesions

Hemorrhage

- Adrenals
- Fascia
- Heart
Serous Atrophy of Fat

Histopathology
Mononuclear cell infiltration

Muscle
Kidney

Histopathology
Pericardial Fat

Von Kossa
Alizaron Red

Histopathology
Cardiac muscle
Reproductive Problems

Retention Placentas

Fetal Death

**ACUTE MATERNAL SARCOCYSTOSIS LEADING TO FETAL DEATH**

- Transmission of organisms to fetus
- Loss of erythrocytes
- Clotting disorder
- Fever
- Inflammation
- Macrophages
- TNF
- Vascular damage
- Arachidonic acid metabolites
- Hypoxia
- Hyperthermia
- Fetal Hypothalmic-Pituitary-Adrenal Axis
- Direct lesions
- Death
- Fetal cortisol
- Direct lesions
- Fetal death
- Placenta
- Placenta
- Progesterone, Estrogen
- Decidua, fetal membranes
- Prostaglandin synthesis
- Myometrial contraction
- Expulsion of Fetus

**SOURCES OF OUTBREAKS**

New York

Pennsylvania

**WILD CARNIVORE FINAL HOSTS**

Coyote

Raccoon

Fox

Wild Carnivore Final Hosts
Prevalence in retail beef

In northeast US 60 of 110 samples were PCR positive for Sarcocystis and 41 sequenced representatives were identified as *S. cruzi* (Pritt et al., 2008).

In Belgium 97.4% of samples collected from minced beef were sequence analysis positive for *S. hominis* (van Geel et al. 2007).

Molecular methods have been used to differentiate species of *Sarcocystis* based on 18s ribosomal DNA.

* S. hirsuta, *S. hominis* and *S. cruzi* identified in cattle and bison (Fischer and Odening, 1998).

* Sarcocystis from a water buffalo nearly identical to *S. hominis* (Yang et al., 2001).

* Indicating that meat from multiple ruminant species can be potential sources for human infection with *S. hominis*.

MULTIPLE CLOSELY RELATED INTERMEDIATE HOSTS FOR THE SAME SPECIES OF SARCOCYSTIS

Intestinal sarcocystosis in humans

Based on limited, somewhat focal surveys, more prevalent in Europe than any other continent (Dubey Speer, Fayer 1989).

- 10.4% of fecal specimens was found in children in Poland.
- 7.3% of samples from Germany.
- 1.1% of 1229 apprentices from Viet Nam who worked in Central Slovakia in 1987-1989.
- In Brazil, Sarcocysts found in all 50 beef samples. Based on cyst wall structure, *S. hominis* (94%), *S. hirsuta* (70%), and *S. cruzi* (92%). Kibble positive for *S. hominis* was fed to 7 human volunteers; 6 excreted sporocysts, 2 developed diarrhea (Kibbe et al., 2003).
- In Spain, after eating raw beef, a patient with abdominal discomfort, loose stools, and *S. hominis* oocysts in the feces (Clavel et al., 2001).
- In Tibet, Sarcocystis was detected in 42.9% of beef specimens in the marketplace, *S. hominis* and *S. suihominis* were found in stools from 21.8% and 0 to 7% of 926 persons, respectively (Yu, 1991).
- In NE Thailand, 4.6-8.0% of >1600 persons (>Tungtrongchitr et al. 2007).

**Muscular sarcocystosis in humans is rare**

- Approximately 46 cases reported by 1990, most from Asia and Southeast Asia. (Dubey Speer, Fayer 1989).
- In India, sarcocysts were found in biopsies from 4 cases with lumps or pain in limbs (Menon et al., 1996).
- Additional cases, supported by histologic evidence, include 13 from Southeast Asia, 11 from India, 5 from Central and South America, 4 each from Africa, Europe, and the United States, one from China, and 2 of undetermined origin.
- Outbreak: 7 persons of a 15 member military team in Malaysia is the largest group occurrence on record (Almeida et al., 1995).
- Total 103 (Fayer 2004).

**Clinical signs of intestinal sarcocystosis in humans**

Volunteers who ate raw pork containing *S. suihominis* shed oocysts. Dramatic signs appeared 6 to 48 hr after eating the pork. These signs included blood, nausea, loss of appetite, stomachache, vomiting, diarrhea, difficulty breathing, and rapid pulse. Volunteers who ate well-cooked meat from the same pigs had no clinical signs (Rommel and Heydorn, 1972; Heydorn, 1977).

Volunteers who ate raw beef containing *S. hominis* shed oocysts in their feces. One person became ill 6 to 6 hr after eating the beef. Signs included nausea, stomach ache and diarrhea (Rommel and Heydorn, 1977).

Six persons in Thailand who reportedly ate beef from zebu cattle uncooked in hot-chili dishes (but who may have eaten a variety of other animal products; authors note) developed segmental necrotizing enteritis with internal stages attributed to *Sarcocystis* and Gram-positive bacilli (Bunyaratvej et al., 1982).

A volunteer had abdominal distension 5 hr after eating cysts in minced pork, watery diarrhea 13 times from 8-36 hr, vomiting 4 times, chills and fever of 39.5C, dizziness, headache, joint and muscle ache, anorexia, and anorexia. Oocysts found in feces 10 DAI and sporocysts 12 DAI. (Li et al., 2007).

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Clinical signs of muscular sarcocystosis in humans

- Only 8 human cases of *Sarcocystis* were reported with evident vasculitis and/or myositis (McLeod et al., 1980).
- 7 U.S. military personnel in Malaysia developed acute fever, myalgias, bronchospasm, pruritic rashes, lymphadenopathy, and subcutaneous nodules associated with eosinophilia, elevated erythrocyte sedimentation rate, and elevated creatinine kinase levels (Amess et al., 1999). Sarcocysts were found in biopsies.

Muscular sarcocystosis in humans: what we don’t know

- Acute fulminant infection in a captive-born rhesus monkey with immature and mature schizonts in endothelial cells throughout the body and mature sarcocysts in muscle.
- 18s rRNA gene sequences had 95-96% homology with several species of *Sarcocystis* but complete identity was lacking (Lane et al., 1998).
- That report indicates the susceptibility of a primate to life-threatening infection with unknown species of *Sarcocystis* even in the apparent absence of a typical definitive host.
- Likewise, where does human muscular infection come from? Species we are not aware of?

Human muscular infection

- *S. cruzi* from dogs can infect cattle (*Bos taurus*), water buffalo (*Bubalus bubalis*), and bison (*Bison bison*).

Humans most likely become infected by ingesting food or water contaminated with feces from a carnivore or omnivore that participates in a primate-carnivore cycle.

Are there other possible sources?

Sarcocystis neurona

**final host**

- Horse
- Grant’s Zebra
- Domestic cat
- Canadian lynx
- Dog
- Raccoon
- Pacific harbor seal
- American Elk
- Sea otter
- Skunk
- Fisher
- 9-Banded armadillo
- Beavers
- Black and white ruffed lemur
- Blue-eyed black lemur
- Ring-tailed lemur
- Ring-tailed lemur
- Caracal
- Brown bear
- Brown-headed cowbird
- Bald Eagle

**Intermediate hosts**

- Opossum
- Badger
- Squirrel
- Porcupine
- Skunk
- Opossum
- Blue-winged teal
- Band-tailed pigeon
- Gravelly neotame
- Perdido duck
- Pacific loon
- Bufflehead duck
- American coot
- Glossy ibis
- Waterhen
- Yellow billed duck
- Red-tailed hawk
- Great black-backed gull
- American white pelican
- Snowy owl
- Great blue heron
- Red-tailed hawk
- Snowy owl
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- Red-tailed hawk
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- Great blue heron
- Red-tailed hawk
- Snowy owl

Treatment

There is no known treatment for intestinal or muscular sarcocystosis in humans.

Prophylaxis in livestock utilized anti-coccidial drugs.

Prevention

Cook meat to 60, 70, and 100 C for 20, 15, and 5 minutes.
Freeze meat at -4 or -20 C for 48 and 24 hours.
Do not drink water from rivers, streams, ponds, lakes, etc.

Educate consumers, farmers, and shepherds.
Improve farming conditions.
Detect these parasites in slaughtered animals and in foodstuff.
Control sewage sludge on pastures and drinking water resources.
Reduce contacts between livestock and wild animals that represent an important reservoir. (Pozio, 2008)
Sarcocystis singaporensis

Product Trade/Brand Name: PRORODENT
1.3 Registration Code Numbers
For Indonesia, by CV Hetts BioLestari: Registration in process
For Thailand, by Uniseeds Co. Ltd.: 1558/2545; 18 June 2002, Department of Agriculture, Ministry of Agriculture and Cooperatives
For Vietnam, by Vietnam Agricultural Science Institute (VASI), Hanoi: 311/05 ECR; 23 May 2006, Ministry of Agriculture and Rural Development
For Laos, by General Services Lao Co. Ltd. (GSL): 00096 P; 13 October 2006, Department of Agriculture

One gram bait pellet plus parasites for application in Europe contains $2.5 \times 10^4$ sporocysts.

Rats in rice field

Maize damage

Rat tails collected on farms in NE India

SUMMARY

SPECIES OF SARCOCYSTIS
LIFE CYCLE
STAGES: LIGHT MICROSCOPY; E/M
GROSS SIGNS OF INFECTION
HISTOPATHOLOGY
CLINICAL SUMMARY CHART
REPRODUCTIVE FAILURE
DOMESTIC AND WILD CARNIVORES
HUMAN INFECTION
TREATMENT AND PREVENTION
SARCOCYSTIS AS A RODENTICIDE