

PATHOPHYSIOLOGY
PARASITIC DISEASES

Laboratory Manual
and Case Histories

2006

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Parasitic Diseases, 2006
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Parasitic Diseases Slide Collection

Slide Number

1. Hookworm - eggs in stool
2. *Necator americanus* - adult male
3. *Necator americanus* - adult female
4. *Ancylostoma duodenale* - adult male
5. *Ancylostoma duodenale* - adult female
6. Hookworm attached to intestine
7. Hookworm larvae in skin
8. Hookworm larvae - rhabditiform
9. Hookworm larvae - filariform
10. *Strongyloides stercoralis* larvae - rhabditiform
11. *Strongyloides stercoralis* - all stages
12. *Ascaris lumbricoides* - eggs in stool
13. *Ascaris* larvae in lung
14. *Enterobius vermicularis* - clear sticky tape swab with eggs
15. *Enterobius vermicularis* - adult male
16. *Enterobius vermicularis* - adult female
17. *Enterobius vermicularis* in appendix
18. *Trichuris trichiura* - eggs in stool
19. *Trichuris trichiura* - male
20. *Trichuris trichiura* - female
21. *Schistosoma mansoni* - lung, eggs in pseudotubercles
22. Schistosome - adults
23. Schistosome cercariae
24. *Schistosoma mansoni* - eggs in stool
25. *Schistosoma mansoni* - rectal biopsy
26. *Schistosoma mansoni* - eggs (mostly calcified) in colon
27. *Schistosoma haematobium* - eggs in urine
28. *Schistosoma haematobium* - eggs in bladder
29. *Schistosoma haematobium* - bladder, calcified eggs
30. *Taenia saginata* - eggs from perianum
31. *Taenia saginata* - gravid segment
32. *Taenia solium* - gravid segments
33. *Cysticercus cellulosae* - muscle section (also Sarcocystis)
34. *Echinococcus granulosus* - "hydatid sand"
35. *Echinococcus granulosus* - hydatid cyst in liver
36. *Echinococcus granulosus* - hydatid cyst in lung
37. *Strongyloides stercoralis* - parasitic female
38. *Strongyloides stercoralis* - adult, eggs, larvae in intestine
39. *Ascaris lumbricoides* - adult worm in appendix

40. *Entamoeba histolytica* - trophozoites in stool
41. *Entamoeba histolytica* - trophozoites in stool
42. *Entamoeba histolytica* - cysts (*E. nana* - cysts) in stool
43. *Entamoeba histolytica* - colon
44. *Entamoeba histolytica* - colon
45. *Entamoeba histolytica* - in lung
46. *Entamoeba histolytica* - in liver
47. *Giardia lamblia* - troph., cysts
48. Dysentery (*Shigella sp.*) - cellular exudate in stool
49. *Toxoplasma gondii* - peritoneal exudate - mouse
50. *Plasmodium vivax* - blood smear, Giemsa stain
51. *Plasmodium vivax* - blood smear, Giemsa stain
52. *Plasmodium vivax* - blood smear, Giemsa Stain
53. *Plasmodium vivax* - blood smear, Giemsa stain
54. *Plasmodium malariae* - blood smear, Giemsa stain
55. *Plasmodium malariae* - blood smear, Giemsa stain
56. *Plasmodium falciparum* - blood smear, Giemsa stain
57. *Plasmodium falciparum* - gametocytes
58. *Plasmodium falciparum* - liver
59. *Plasmodium falciparum* - spleen
60. *Plasmodium falciparum* - brain
61. *Plasmodium falciparum* - placenta
62. *Plasmodium falciparum* - blood smear, Giemsa stain
63. *Cryptosporidium parvum* oocysts in stool

INTRODUCTION TO LABORATORY STUDY

Your laboratory manual has been designed to provide directions for study of laboratory material and to correlate this material with the case histories, the textbook, and formal presentations.

CASE HISTORIES: All of the patients presented in your manual were real cases involving various aspects of parasitic diseases. Place yourself in the position of the physician-in-charge and then proceed. Before doing so, however, it is essential that you work through the didactic portion of each laboratory session in order to acquire skills at microscopic diagnosis.

LABORATORY STUDIES: It is important to keep lenses of the microscopes clean and to adjust lighting properly. It is important to have a working oil lens. If you are having problems, please ask us for help.

DRAWINGS: Optional. If drawings help you to learn to identify the diagnostic stages of the various parasites, use pages provided in the manual.

DEMONSTRATIONS: Living, preserved, whole and sectioned material, reprints, chemotherapeutic agents and study aids are placed on display in a designated side room. The materials are intended to enrich the laboratory experience. Please **DO NOT** bring notebooks to the demonstrations. Simply enjoy the displays and return as soon as possible to your laboratory section after viewing them.

Note:

Figures referred to in this manual correspond to those in:

Parasitic Diseases, 5th ed.
Despommier, Gwadz, Hotez, and Knirsch.
Apple Trees Productions, LLC, 2006

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Nematodes (The roundworms)

***Enterobius vermicularis* (Pinworm)**

INFECTION:

Infection occurs with the ingestion of embryonated eggs (slide #14; Figs. 16.3, C.37).

ADULT PARASITES:

Study adult female (slide #16; Fig. 16.1). The male is smaller, with a curved tail. Males, (slide #15) unlike females, do not actively migrate out of the intestine and are rarely seen in the stool (see demonstration).

PATHOLOGY:

Pinworms have not been shown to cause disease in the G.I. tract. However, they are often associated with pathological changes in the appendix, even though they do not induce such changes. Therefore, it is important to recognize them in surgical specimens (slide #17; Fig. 16.2). Note characteristic alae (wing-like projections). Is there evidence of pathology in the appendix? What could have caused this condition?

DIAGNOSIS:

Eggs are usually not found in feces, but are located on the perianal region of the skin. Therefore, a sticky tape swab is used to collect the eggs for microscopic examination (see demonstration).

DEMONSTRATIONS:

Transparent plastic tape swab from heavily infected wife of a second year medical student who had a period of intense perianal pruritus every 4-6 weeks. What was the etiology of the pruritus?

Whole adult male and female worms.

CASE HISTORY 1

S.M., a 2-year-old white male, was brought to the clinic, because of a complaint of restlessness at night and itching in the perianal area. The mother claims to have seen a moving, white thread-like object near the child's anus. When S.M. was examined in the clinic, no abnormalities were found, except for erythema of the perianal skin. The intern in charge ordered a stool examination for ova and parasites.

1. Case History Slide # 1 represents this specimen. List your findings.
2. An alert P&S-educated resident reviewed the chart and concluded that the intern ordered an improper test. What test should have been ordered?
3. What time of day should this test be done to increase the chances of positive diagnosis? Why?

Slide #14 represents that test. List your findings.

4. What therapy and management would you prescribe for this child?
5. What additional steps would you take?

Trichuris trichiura (Whipworm)

INFECTION:

This parasite is acquired by man through the ingestion of embryonated eggs of *Trichuris*, which are found in fecally contaminated soil (slide #18).

ADULT PARASITE:

See demonstration.

PATHOLOGY:

The cycle is direct, and in severe infection many adult male, (slide #19; Fig. 17.2), and female worms, (slide #20; Fig. 17.1) are embedded in the caecum and colon. Note the long narrow esophagus.

DIAGNOSIS:

The eggs of *Trichuris trichiura* (slide #18; Figs. 17.3, C.38) are readily identified in the stool.

DEMONSTRATIONS:

Section of *Trichuris* in the intestine.

Gross specimen of infected mouse intestine with adult *Trichuris*

muris, a related species of whipworm.

CASE HISTORY 2

M.C., a 3-and-9/12-yrs-old female from Santo Domingo was seen in the clinic because of diarrhea of two months' duration. She suffered from Pica and drank three bottles of cow's milk per day. Examination revealed a vigorous, but pale child, who had a protuberant abdomen. The remainder of the examination, including a digital rectal exam, was normal. Laboratory tests revealed Hgb. of 5.2, WBC - 11,700, and a normal differential count. Reticulocyte count was 7%.

Because of severity of the diarrhea, she was admitted to the hospital. There, her stool was sent for a bacterial culture and for examination for ova and parasites. Bacterial cultures revealed *Shigella flexneri*. The stool examination is represented by Case History slide # 2.

1. What are your findings?

2. What would you recommend for this child?

CASE HISTORY 3

C.C., a 2-year-old sister of M.C., also had diarrhea and anemia. She was admitted to the hospital several days later because of the severity of her disease. Her stool culture revealed no enteric pathogens. Stool for ova and parasites was obtained and is represented by Case History slide # 3.

1. What are your findings?

2. What treatment would you recommend for this child?

Ascaris lumbricoides

INFECTION: This infection is acquired by the ingestion of embryonated eggs that usually enter our environment through fecally contaminated food.

HELMINTH EGGS and LARVAE are best located with low power (10X ocular, 10X objective) and reduced light. Use the high power for details of structure and if necessary to make the definitive diagnosis. A scanning lens is very useful for the study of large specimens such as whole mounts of most worms, tapeworm proglottids and many arthropods. The 10X ocular on your microscope will also be useful for low power viewing by inverting and holding it directly up against the slide.

Slide M (from soil), embryonated egg containing fully developed second stage larva. This is an infective egg that took four weeks to develop.

ADULT PARASITES:

The adult worms are large (25-30cm long; Fig. 18.1), and the females and males live free in the lumen of the small intestine.

PATHOLOGY:

The larvae hatch from the eggs, penetrate the small intestine and migrate by way of the blood stream to the lungs causing a transitory pneumonia-like syndrome (slide # 13; Fig. 18.5).

The adult worms may also migrate (e.g. during bouts of high fever not related to *Ascaris* infection, or irritating drugs), ending up in such abnormal sites as the liver, gall bladder, pancreas, peritoneal cavity, appendix (slide # 39; Fig. 18.2), and pharynx. Severe damage is the usual result of this migration. Also in heavy infections, a bolus of worms may cause intestinal blockage and thus becomes a pediatric emergency.

DIAGNOSIS:

Unfertilized (Fig. C.41) as well as fertilized eggs (slide #12; Fig.18.3, C.39, C.40) may be present in the stool. Light infections in which only females are present are characterized by unfertilized eggs only.

In unfertilized eggs, note variations in size and shape, thin shell, interior completely filled with refractile granules. Compare with fertilized eggs.

DEMONSTRATIONS:

1. Female and male adults. Note smaller male with hooked tail.
2. 3rd stage larva in lung. Note presence of sections of larvae and tissue infiltration, hemorrhagic pneumonia.

CASE HISTORY 4

J.R., a 7-year-old Puerto Rican male, was brought to Vanderbilt Clinic because of a cold. He came to New York two years before and had always been in good health. The examination revealed a well developed, well nourished boy who had no abnormal findings except for rhinorrhea. His Hgb. was 13.2 and his WBC was 8400, with a normal differential. He was treated symptomatically. In addition, he was given a tuberculin test and his stool was sent to the Parasitology Laboratory for examination.

Case History Slide # 4 represents the specimen of this patient.

1. List your findings.
2. What would you recommend for this child?
3. What would you recommend to the parents in order to prevent re-infection to their children?

M.R. was brought back to the hospital 36 hours later, because of abdominal pain. At this time, he appeared quite ill, had a diffusely tender abdomen, with some rebound tenderness. X-ray of the abdomen revealed free air under the diaphragm. Surgical consultant made the diagnosis of appendicitis with perforation and the patient was admitted for emergency surgery. He was given intravenous ampicillin and the penicillin therapy was discontinued. At the time of surgery, the appendix appeared not inflamed and showed no evidence of perforation. Further exploration disclosed a small oval perforation of the ileum, with no evidence of necrosis. There was purulent exudate throughout the peritoneal cavity. The surgeon closed the perforation primarily and irrigated the peritoneal cavity with saline solution. Bacteriological culture of the peritoneal exudate revealed, in a subsequent report, *Escherichia coli* and *Enterobacter* each sensitive to ampicillin. The original throat culture revealed group A beta hemolytic *Streptococcus*. The patient made an uneventful recovery and was discharged after 10 days of IV antibiotics.

4. In his operative note, the surgeon stated that he could not explain the cause of the ileal perforation. Can you?

CASE HISTORY 6

A 16-month-old boy who had not been out of New York State was seen at an upstate New York hospital June 27, with a temperature of 101.9°F rectally, and a persistent cough. The clinical diagnosis was pneumonia, and penicillin VK was begun orally.

Past history Normal birth and developmental growth.

Present illness: Health good except for repeated chest colds with cough and fever. Five months previously he had a cold, non-productive cough, slight dyspnea (worse at night), slight fever, lack of appetite and diarrhea. Symptoms disappeared gradually except for the cough that grew worse at night time, accompanied by dyspnea.

The mother related that the baby was allergic to wool blankets. She also stated that he had been seen eating dirt in the garden on one occasion (PICA). The child ate some uncooked pork sausage two weeks previously; this was following by a slight diarrhea.

Physical Examination: Temperature 101.9 F rectally. Lungs showed diminished breath sounds and occasional crepitant rales, especially over the right base. There was no cyanosis. The throat was moderately red. Otherwise, physical examination was negative. A chest X-ray was reported with scattered areas of "congestion."

Hemoglobin 10.0 grams.
120,000 W.B.C.: 28% Polymorphonuclear
neutrophils,
18% lymphocytes, 0.5% monocytes, 50%
eosinophils,
0.5% basophils, 2% neutrophilic
myelocytes, 0.5%
basophilic myelocytes.

Diagnosis: At this point the diagnosis was acute eosinophilic leukemia. The child was transferred to Babies Hospital for further study and therapy. Further questioning of the parents revealed that the family cat had been tested for worms.

Physical examination now revealed the liver to be enlarged 4 cm. below the costal margin and the spleen enlarged 1 cm. below the costal margin. W.B.C. 86,000 with 57% eosinophiles. Platelets normal in number and morphology. Stool negative for eggs and parasites. Total blood protein 7.6 gms. per cent, albumin 4.9 gms. globulin 2.7 gms. per cent.

HOOKWORMS & *Strongyloides stercoralis*

Necator americanus* and *Ancylostoma duodenale

(Hookworm)

INFECTION:

Infection is acquired through the active penetration of filariform larvae into the skin (slide #7; Fig. 19.1) from the fecally contaminated soil (slide #9; Fig. 20.5). Note the long slender appearance, short esophagus. (see demonstration).

ADULT PARASITE:

The adult *Necator americanus* (Slides # 2, # 3) suck blood, but actually feed primarily on villus tissue (slide # 6).

Note size of male and female worms and their shape. The female's tail is pointed, whereas the male worm has a hand-like posterior bursa. Slides # 4 and # 5 are of *Ancylostoma duodenale* males and females (Figs. 19.2, 19.3), respectively.

PATHOLOGY:

Iron-deficiency anemia is the major consequence of infection, and arises from the adult worms' penchant for sucking blood.

DIAGNOSIS:

Hookworm eggs are present in slide # 1 (Figs. 19.4, C.42). There are several nematode eggs that can be confused with those of hookworm. Their presence may lead not only to false diagnosis, but also to what appears to be failure of treatment (see demonstration).

DEMONSTRATIONS:

Meloidogyne (Heterodera) egg - a harmless plant root nematode which we ingest and digest, freeing the eggs in our stool.

Trichostrongylus egg. In the U.S., occasionally found in patients from the Near East, Far East and Asia. Responds to the usual treatment for hookworm (e.g., Pyrantel pamoate).

Ascaris eggs that have lost their mammalated coating (Fig. C.40).

CASE HISTORY 7

J.D., a nine-year-old child, came to New York from Utuado, Puerto Rico, "two years ago" with his parents and four brothers and sisters. His school teacher noted that he was thin, pale and listless. After consultation with the school nurse, the boy was sent to the New York City Tropical Disease Diagnostic Clinic at 600 W. 168th Street. Here it was found that his hemoglobin was 9.2 grams, and W.B.C. 7,200 -- eosinophils 2%. Stool examination (Slide # 1) revealed a few *Ascaris* eggs and numerous hookworm eggs.

1. Where were these parasites probably acquired?
 - a. *Ascaris*

 - b. Hookworm

2. Are the child's infections dangerous to his family and schoolmates?

3. Therapy:
 - a. *Ascaris*

 - b. Hookworm

3. What public health measures are indicated?

Vermis

Wavering white prayer on a grass blade,
Screwing, searching heat, like the blindman's cane.
Pincushion flesh my soul, mouth suckers my spade,
I find you, root into you, plant and dig.
Burrow in, blood wake, membranous clot clog,
burrow in, disappear, save one rose stain.

Threaded into blue plasma slip stream, I suck blood
broth,
slithe veins, and swim the mangrove branching path
from orange glow to dark, into pushing half
high tide flow, the raining corpuscle blows
soft upon my needle face. Pressed, pushed to go
into the rhythmmed writhing heart long last.

In loamy gut waters, I stretch supine.
Mouth hooked to entrails, ride the tide of wine,
Olive oil, wasabi sauce and rich mince meat pie.
The restless chorus of baby worms stretches
my middle wide. I moan a song and retch
them out, they will claim the green world mine.

A worm's retirement home, in the sweet meats
of the brain. Wrapt by electricity,
coiled up, intoxicated, I'm breathing
memories, shopping lists, Euclidean forms.
Erased by the ravenous diet of worms,
lost to a chaos of epileptic storms.

Dr. Andrew Moran
P&S Class of 2001

Strongyloides stercoralis

INFECTION:

Infection is acquired by penetration of the skin by the filariform larva (slide # 9; Fig. 20.5) found in fecally contaminated soil.

ADULT PARASITE:

Only the female adult is parasitic for man (slide # 37; Fig. 20.2a), whereas both male and female free living adults can be found in the fecally contaminated soil (slide # 11; Fig. 20.1).

PATHOLOGY:

Diarrhea of three to six-weeks duration. Bacterial sepsis is a frequent sequela in hyper-infective strongyloidiasis. An intense inflammatory process in the lamina propria may also be seen (slide # 38; Fig.20.2b).

DIAGNOSIS:

The rhabditiform larva (slide # 10; Figs. 20.3, C.43) is the stage of this parasite which is commonly seen in freshly passed feces. This larval form must be distinguished from the larva of hookworm (Fig. 20.5). Why? (Compare slide # 10 with slide # 8).

DEMONSTRATIONS:

1. Rhabditiform larva
2. Filariform larva
3. Free-living male
4. Free-living female
5. Parasitic female, in situ.

CASE HISTORY 8

H.M., a 47 y/o white male anthropologist, was admitted into CPMC with diarrhea of two weeks duration. A history of travel over the last several months included Tasmania, Papua New Guinea, Bora Bora, and numerous small Micronesian archipelagoes. At most times, H.M. ate and drank locally in the homes of the peoples he was studying. Physical exam revealed an emaciated, listless individual with reduced skin rebound. No other unusual features were noted at the time of admission. Laboratory work up included a stool examination (stained smear and concentration), CBC and a complete chemistry profile. All tests were consistent with diarrhea as the chief clinical complaint. A peripheral eosinophilia of 12% alerted the physician to the possibility of a parasitic infection as the cause of H.M.'s disease. The first stool examination and culture was negative. A stool sample taken the next day was also negative for both tests. A third stool, however, taken on the third day post-admission was positive. Please examine slide # 10

1. List your findings:
2. Where do you think H.M. acquired his infection?
3. What drug(s) would you recommend?
4. If left untreated, what do you think H. M.'s disease progression would be? Explain.

5. If H.M. became immunosuppressed without being treated, what would be the likely outcome of the infection? Why?

6. Are there reservoir hosts for this agent? If so, do they present a danger to any special group(s) of people?

7. List two medical conditions that favor the maintenance of this infection over long periods of time.

Cestodes (The segmented flatworms)

***Taenia saginata* (beef tapeworm)**

and

***Taenia solium* (pork tapeworm)**

INFECTION:

Man acquires *T. saginata* by eating undercooked or raw beef containing the cysticercus stage (Fig. 29.2, similar to *T. saginata*), while infection with *T. solium* is contracted through the ingestion of raw or undercooked pork (see demonstration of gross specimen cysticercus stage). Slide #33 and Fig. 29.1 are examples of meat infected with the cysticercus stage of *Taenia sp.*

ADULT WORM:

The adults of *T. saginata* (Fig. 28.3) and *T. solium* (Fig. 29.3) live in the small intestine (see demonstration of whole mount of an entire adult worm). The proglottids containing eggs (gravid segments) are passed in the feces (slides # 31 and # 32; Figs 28.4, 29.7).

The eggs (slide # 30; Figs. 28.5, 29.5, C.57) are released as the segment disintegrates in the soil and either cow or pig ingests them, thereby acquiring the intermediate stage of the infection (cysticercus).

PATHOLOGY:

The adult worms cause no clinical symptoms.

DIAGNOSIS:

Eggs can be found in feces or on the perianal region, as with the commonly occurring *Enterobius vermicularis* (pinworm). Often, a whole proglottid or series of connected proglottids is brought to the diagnostic laboratory by the patient.

The two species of *Taenia* can be distinguished by injecting the gravid proglottids with an opaque dye or India ink and counting the central uterine branches (Figs. 28.4, 29.7).

T. saginata has 15-30 branches, whereas *T. solium* has only 7-12 branches. The eggs of all *Taenia* spp. look alike.

DEMONSTRATIONS:

1. Whole adult worms
2. Scolex of each species
3. Egg
4. Mature proglottid of each species
5. Gravid proglottid of each species

CASE HISTORY 9

P.T.S., a first year medical student originally from Indonesia, had been in good health, and had no medical problems. However, on November 3, he saw white, flat objects about 4 mm x 7 mm in his stool that he diagnosed as tapeworm segments. A "segment" was brought in to the parasitology laboratory by P.T.S. but it was in such poor condition that a diagnosis could not be made on gross examination. Therefore, the material was macerated, revealing typical *Taenia* eggs. On November 5, the patient experienced mild abdominal pain. Stool examination at this time revealed *Ascaris lumbricoides* eggs, but no *Taenia* eggs.

LABORATORY DATA: H.B. 12.5 grams %, W.B.C. 8,500; eosinophils 12%.

1. It was decided to treat the patient's *Ascaris* infection first;
 - a. What is the drug of choice against *Ascaris*?
 - b. Is it a toxic drug?
 - c. How does *Ascaris* harm man?
2. A subsequent stool specimen did contain segments of tapeworm. What is your opinion about the species (see slide # 32)?

Beef is seldom eaten in Bali, but pork is a very common source of protein. The pig is prepared by "gulling" which cooks the outside of the pig, but the interior meat may not be thoroughly cooked. While in his native Surabaya, P.T.S. had occasionally eaten beef, usually well done. During the past summer he spent part of August and September in Bali and ate considerable pork at this time. At the time his tapeworm was discovered he had returned from Bali and had been in Surabaya for approximately three months.

3. If the patient became infected in Bali during the summer, July and August, could the tapeworm (*T. saginata* or *T. solium*) mature in 3 months?
4. What stage of the parasite did P.T.S. ingest to become infected with an adult tapeworm?
5. What is the drug of choice for this adult tapeworm?
6. Why must special precautions be taken to prevent vomiting by patients under treatment for *Taenia solium* ?
7. What is the only criterion for successful therapy?

8. How can *T. solium* infections be prevented?

a. By the individual

b. By the community

DEMONSTRATIONS: Whole mount of *Cysticercus cellulosae*, the cyst stage of *T. solium*. Note the bladder and the invaginated neck and scolex. Note size, the hooks and suckers on the scolex.

Sections of cyst removed from the brain of patients. Is it *Cysticercus cellulosae*?

Cysticercus cellulosae in a child's eye, removed because of suspected retinoblastoma.

CASE HISTORY 10

Patient B.C., who arrived in the United States August 13, 1980 was admitted to Neurological Institute, P&S, August 25.

PRESENT ILLNESS: The patient is a 34-year-old non-English-speaking right-handed, Colombian grocery clerk, who was admitted because of seizures. At the age of 12 he noted convulsions that began with numbness of the left upper extremity producing clonus, unconsciousness and left-sided headache. No further episodes occurred until 2 years prior to the present admission, at which time episodes preceded by momentary double vision began to occur approximately every 30 days. The left foot became cold on motion and on 5 occasions the patient became unconscious for approximately 5 minutes. During 2 episodes the patient could not talk. His most recent seizures were on: 5/2 - 6/5 - 7/31 - 8/1 and 8/2. In addition to the seizures, the patient had noted progressive weakness and sharp pain in left extremity for 2 years.

NEUROLOGICAL EXAM: Positive findings included a left hemiparesis without a sensory defect and left facial weakness.

X-RAY EXAMINATION: 8/26 Skull Films - revealed calcification, in the neighborhood of the inferior temporal horn. Right common carotid arteriogram, 8/31 - revealed a vessel-free area in anterior right parietal lobe, suggesting a mass in that area. No soft tissue calcification of the arms and legs was demonstrated by X-ray. Chest appeared normal on X-ray. Pneumoencephalogram 8/31 - revealed right parasagittal tumor depressing the right third ventricle.

LABORATORY DATA: A lumbar puncture was done on 8/29, spinal fluid revealed 24 W.B.C. all lymphs, total protein 22 mg%. Blood count: Hematocrit 40%, ESR 12 mm/1hr., W.B.C. 7,000, Neut. 60, Eos. 5, Lymph. 30, Mono. 5. Urinalysis: normal. Electrocardiogram: normal. Echinococcus test (IHA) weakly positive, ESR 12 mm/hr.

SURGICAL EXPLORATION: On 9/12, Right fronto-parietal craniotomy was done and at that time 3 cysts were found on the motor strip. The first cyst was noted to be approximately 1 X 2 cm. in size and was aspirated through the burr hole opening. The second cyst was in the sulci of the motor strip and was approximately 3 X 4 cm. in diameter. The patient had several seizures post-operatively on 9/12 and 9/15.

1. In view of the X-ray findings, what kinds of cysts are possible and how would you approach the differential diagnosis of his disease ?

2. What characteristics serve to identify them?

3. What test is diagnostic for this patient?

3. Since the diagnosis is cysticercosis, how would you interpret the Echinococcus test in this patient?

4. What was the purpose of the X-ray survey of the arms, legs and chest?

5. How could a stool - or transparent plastic tape - examination aid in the diagnosis of this infection?

Echinococcus granulosus

INFECTION:

Humans acquire *E. granulosus* by ingesting the eggs found in dog feces (slide # 30; Figs. 28.5, 29.5, C.57). In this instance, we resemble the intermediate host, the sheep, and can support the development of the hydatid cyst (slide # 35; Figs. 32.9, 32.13).

ADULT WORM:

People cannot harbor the adult worm (Fig. 32.8), but all canidae are able to do so (dogs, wolves, etc.). The dog acquires the adult worm by ingestion of the hydatid cyst containing the protoscolices (see demonstration of adult worm). This adult tapeworm is one of the smallest, consisting of only three segments.

PATHOLOGY:

The hydatid cyst can be thought of as a space-filling lesion and can be found anywhere throughout the body, but is usually found in the liver (Slide # 35) or lungs (Slide # 36).

The hydatid membrane (Fig. 32.10) is delicate and is easily ruptured, thereby allowing the hematogenous spread of protoscolices to other organs of the body. Each protoscolex is capable of forming an entire new adult tapeworm in the dog, or an hydatid cyst in the intermediate host (sheep, humans).

Anaphylaxis is a serious complication following rupture of the cyst.

DIAGNOSIS:

X-rays, ELISA, finding "hydatid sand" in sputum after cyst ruptures (slide # 34; Fig. 32.14).

DEMONSTRATIONS:

1. Whole worm of *E. granulosus*
2. Hydatid cyst
3. "Hydatid sand"

CASE HISTORY 11

A 62-year-old American housewife of Greek origin consulted her physician on March 4, 1977 for recurrent pain of two weeks' duration in the right upper quadrant. The patient was born and spent her youth in a small town in Greece where dogs and sheep were numerous, and her family owned a dog from time to time. Since her arrival in New York in 1934, the patient has made three visits to Greece, the first in 1938, for six months, and the other two in 1950 and 1975, for two months each. She denied having had any contact with dogs in New York, except for a puppy that the family had acquired during their last visit to Greece in 1975.

A presumptive diagnosis of hydatid cyst of the liver was made on the basis of (1) a history of residence in an *Echinococcus* endemic area, (2) a history of *Echinococcus* disease in a brother, (3) the finding of a palpable, somewhat tender mass in the right upper quadrant, and (4) roentgenographic evidence of a localized area of increased, non-calcified density in the right upper quadrant. The complement-fixation test result was negative on one occasion and doubtful on another. The hemagglutination test gave a positive result in a serum dilution of 1:10,240.

The patient was operated on March 15, 1977; a cyst, 9 cm. in diameter, was removed intact from the liver without seepage or spillage. Its inner wall was translucent, extremely friable, and 0.5 cm. in thickness. On section, the cyst contained cloudy fluid with a whitish, sandy sediment, which on microscopic examination revealed many scolices and hooklets of *E. granulosus*.

Several months later, the patient again noted recurrent pains in her right upper quadrant which radiated to her right shoulder and back. There was no nausea or vomiting. Her abdomen was slightly spastic in the right upper quadrant. The liver edge was not palpable. The white blood cell count was 6,800/cm, with 2% eosinophils. The complement-fixation test was positive (3+), and the hemagglutination test was positive in a serum dilution of 1:160. X-ray examination revealed a cyst in the liver that was not demonstrable in

previous films. Thirteen and one-half months after the removal of her first Echinococcus cyst a second cyst, 15 cm. in diameter, was removed from the substance of the liver. Her recovery from the operation was uneventful.

Epidemiologic studies undertaken at the request of the surgeon disclosed that the patient owned a 2-year-old German Shepherd dog which was acquired in Salonica, Greece, in July, 1975, when it was 4 weeks old. Inquiry of the owner of the dog as to its dietary regimen prior to its importation revealed that the dog ate "everything, including scraps of meat". The animal remained with the family except for a period of 45 days, during which time it was confined in a veterinary kennel for partial paralysis of its posterior limbs. The dog received the usual vaccinations for rabies and distemper, had been de-wormed twice presumably for roundworms, and allegedly has been in good health. Two stool specimens of the dog were examined by the diagnostic laboratory, and both specimens contained Taenia eggs.

1. What is the treatment of hydatid cyst of man?

2. How can infection with hydatid cyst be prevented?
 - A. In an individual?

 - B. In his domestic animals?

 - C. In the community in general?

TREMATODES (The unsegmented flatworms)

Schistosoma mansoni

INFECTION:

Humans acquire *S. mansoni* by coming in contact with the cercaria (Slide # 23; Fig. 33.13), which has been released from the snail vector (Fig. 33.11, 33.12) into fresh water. The cercaria enters the host by penetrating the unbroken skin where it transforms into the schistosomula before moving to the liver where it matures into an adult (Figs. 33.1, 33.2, 33.3a, 33.3b).

ADULT WORM:

Adult worms are harbored in the venous system surrounding the small intestine (Slide # 22; Figs. 33.3a, 33.3b). Note size, sexual differences, suckers and tuberculations (small, raised "bumps" on the tegument).

PATHOLOGY:

The pathologic effects of the schistosomes are due to the damage done by their eggs to the various organs and tissues in which they lodge. Note eggs in lung (slide # 21). Dead eggs in lung capillaries elicit pseudo-tubercles. Obstruction of pulmonary blood flow may result in a condition known as *cor pulmonale*.

DIAGNOSIS:

Some patients have striking signs and symptoms, but light infections often produce no clinical evidence for many years, hence diagnosis is made by stool examination for eggs (slide # 24; Figs. 33.4, C.62, C.63). If no eggs are found and schistosomiasis is still suspected, a rectal snip often reveals the eggs in positive cases (Slides # 25, 46; Fig. 33.22).

DEMONSTRATIONS:

1. Live eggs
2. Live adults
3. Live cercariae
4. Spleen and liver of infected mouse

Schistosoma japonicum

DEMONSTRATIONS:

1. Eggs of *S. japonicum* (feces) - an attenuated lateral spine may be seen.
2. Eggs of *S. japonicum* in which the lateral spine is not visible.

Schistosoma haematobium

PATHOLOGY AND DIAGNOSIS:

The adult *S. haematobium* worms usually live in the venous system of the urinary bladder and pudendal plexus. The terminal-spined eggs (Figs. 33.6, C.65) of this parasite migrate through the urinary bladder and are passed in urine. Slides # 28 and # 29; (Figs. 33.8, 33.17) shows chronic inflammation due to *S. haematobium* eggs. Are terminal spines visible? Many eggs are calcified.

DEMONSTRATIONS:

Snip of urinary bladder with eggs of *S. haematobium*

Section of urinary bladder with eggs of *S. haematobium* and squamous cell metaplasia. The chronic irritation due to the eggs may lead to carcinoma of the bladder.

Schistosome dermatitis

Schistosome dermatitis (Fig. 33.19) is due to skin penetration by mammalian and avian schistosome cercariae, which become "strangers in a strange land".

DEMONSTRATIONS:

Schistosome dermatitis and snail hosts.

CASE HISTORY 12

H.R., a forty-year-old white male, who was born in Puerto Rico and lived there for twenty years before emigrating to New York, was admitted to Presbyterian Hospital for an evaluation of a mass in his abdomen. He had been in his usual state of good health, but on a recent physical examination related to a new employment, he was noted to have a mass in the left upper quadrant of his abdomen. He was seen in the Vanderbilt Clinic, where the examining physician described the mass as extending to 12 cm below the left costal margin, in the mid-clavicular line. It was firm, non-tender, and had a notch, characteristic of that in the spleen. The physician concluded that the mass was an enlarged spleen and recommended an evaluation of the causes of this enlargement. In the course of the out-patient investigation, the only abnormal tests indicated a white count of 1,800, with a normal differential, a platelet count of 90,000 and a stool examination, which revealed objects seen on slide # 24. Thus a diagnosis of schistosomiasis was made.

1. What is the pathological basis for this patient's illness?

After the patient was admitted to the Medical Service of the Presbyterian Hospital, the abnormally low white count was confirmed as well as a low platelet count of 68,000/cc.

2. How are the findings of the depressed white cell and platelet counts related to schistosomiasis?

Liver function tests were normal. A barium swallow examination and esophagogastrosopy were normal.

3. Why were they done?
4. What is the drug of choice? What are its side effects?

The patient withstood the therapy well and three months following its completion there was no evidence of any *Schistosoma mansoni* ova in several stool examinations. The patient was able to begin his new employment.

5. If the barium swallow or esophagogastrosocopy revealed the abnormality associated with schistosomiasis, what additional therapy might have been considered?
6. What are the causes of death from infections with *Schistosoma mansoni* and *S. japonicum*?
7. What are the causes of death from *S. haematobium*?

CASE HISTORY 13

A 29-year-old male New Yorker, toured the world for 7 months beginning in February, 1978. He visited Hawaii, Japan, Hong Kong, Macao, Thailand, Singapore, Malaya, Cambodia, Burma, India, Pakistan, Syria, Egypt, Lebanon, Cyprus, Jordan, Turkey, Greece, and all European countries except Italy, Portugal, Ireland, Scotland, and the Iron Curtain countries. He traveled as economically as possible, staying in Salvation Army or YMCA hotels or their equivalent. While in Egypt, from June 1 to 6, 1978, he bathed in large pans or tubs using water stored in ceramic crocks that were periodically filled from nearby canals or rivers. On one occasion, he bathed in the Nile for about ten minutes.

The trip was characterized by frequent severe episodes of diarrhea, recurrent angioneurotic edema of the eyelids attributed to an allergic reaction to antibiotics used in the treatment of gonorrhea contracted in Hong Kong, fatigue, weight loss, occasional periods of fever, and nervousness. He consulted with various physicians in a number of countries and, except for gonorrhea, no specific diagnosis was made.

Following his return to the U.S., he consulted several physicians and was advised he probably had trichinellosis because of the history of swollen eyelids and eosinophilia of 47% to 55%. Numerous stool and urine examinations were negative as were X-rays of the gastrointestinal tract. In mid-1979, he passed an *Ascaris*. Beginning in the late fall of the same year, he developed terminal smarting on urination, which was attributed to prostatitis and for which he received periodic course of prostatic massage during the next two years. Finally, in the fall of 1981, he developed urgency, frequency, nocturia, and dark grossly bloody urine. He was cystoscoped by a urologist in the upstate community in which he lived and then referred to another physician because of an apparent bladder tumor. The following is an abstract from the hospital record.

PHYSICAL EXAMINATION: A well-developed, well-nourished male had the following positive findings; pterygium of left eye; small, soft node at angle of right jaw; left varicocele, right testis

smaller and softer than left; prostate minimally enlarged and non-tender.

Urine microscopically showed a few red blood cells (RBC) and few WBC. Hemoglobin was 15 gm and hematocrit was 42%. The WBC count was 5,900 with 4% eosinophils on one differential and 20% eosinophils on a second. Blood sugar and BUN were within normal limits. Urinary cytologies were negative for malignant cells. Submitted retrograde pyelogram of July 21, 1981, showed normal upper urinary tracts. Chest X-ray was negative.

Cystoscopy and biopsy were carried out in December 1981. Bladder was of normal capacity and contour. Scattered throughout the bladder were numerous, small, punctate elevations of the bladder mucosa without any visible change in the normal lemon-yellow color of the bladder lining. These lesions appeared submucosal in location. High on the posterior wall of the bladder were irregular, partially confluent, reddened, raised areas with a surface midway in appearance between that of papillary neoplasm and bullous edema, but not characteristic of either. The latter areas totaled several square centimeters but were resected completely transurethrally. The post-operative course was uneventful.

DIAGNOSIS: *Schistosoma haematobium* was readily established by the presence of characteristic eggs of *S. haematobium* in granulomatous lesions in various stages of evolution in the bladder tissue removed at operation. However, in view of the geographic areas covered by the patient, and his life style, additional studies were carried out to exclude the existence of the other species of schistosomes endemic in the areas involved. Only *S. haematobium* was found, and numerous eggs were present in all urine specimens examined prior to treatment.

TREATMENT: Metrifonate 7.5 mg/KG PO was given every 2 weeks for 6 weeks without ill effects.

The patient has remained asymptomatic relative to the genitourinary tract. Cystoscopy was performed on August 22, 1982, six months after treatment and again on March 13, 1983, more than a year after chemotherapy had been completed. The findings are described as follows:

August 22, 1982 - The bladder is of normal capacity and contour without evidence of acute inflammatory change. Scattered throughout the bladder except over the trigone are numerous punctate, pale, slightly elevated areas apparently sub-mucosal in location that represent scars surrounding areas of schistosoma infection. The overlying mucosa appears slightly paler than normal.

March 13, 1983 - Cystoscopy reveals no residua. Bladder is very mildly trabeculated and the mucosa is very slightly dull and hyperemic. Bladder capacity and contour are grossly within normal limits. Both ureteral orifices appear normal. Scattered over the bladder wall in patches and most evident on the posterior wall are areas 1 to 3 cm. in greatest diameter in which one sees small, whitish, granular deposits apparently in the submucosa with overlying normal-appearing bladder mucosa.

1. In which of the countries the patient visited is *Schistosoma haematobium* endemic?

2. Underline the following signs and symptoms present in this patient that may be related to schistosomiasis:

a. diarrhea b. angioneurotic edema
of eyelids

c. fever d. weight losse.
eosinophilia

f. urinary frequency and pain

3. Approximately 18 months after the beginning of the patient's world-wide trip, he spontaneously passed as *Ascaris lumbricoides*. Do you think this worm was responsible for any of items a - f in question #2?

4. What relation does *Undie Venis* (quote from Shakespeare's *Julius Caesar*) have to this patient's diagnosis?

5. What are the late consequences of this patient's infection?

6. Should the patient be isolated?

PROTOZOANS

Malaria

(*Plasmodium. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*)

INFECTION:

There are two distinct phases of the life cycle of the malaria parasite, one in the mosquito (sexual), and one in the human (asexual). Since the asexual phase is more important to the clinician, the laboratory exercise will concentrate on this aspect of the infection.

The female anopheline mosquito (see demonstration) transmits the infection from person to person through the injection of the sporozoite stage of the parasite (see demonstration).

Asexual Infection in Human:

I. Exoerythrocytic Stages:

These stages of the infection occur intracellularly in the parenchymal cells of the liver (see demonstration) and give rise to the erythrocytic stages.

II. Erythrocytic Stages (see Figs. 9.16-9.19 for a summary of their morphology):

The table in this section gives the differential morphology of all blood stages of the three main human species of malaria.

A. Signet ring stage (Immature Trophozoite)

Named for its resemblance to a signet ring, this early trophozoite of *Plasmodium spp.* is found within the red cell and usually occurs as a single parasite.

Slides # 50, 51, 52, 53 show RBCs with rings of *P. vivax*. Slides # 54 and 55 show RBCs with rings of *P. malariae*. Slides # 56 and 62 show RBCs with rings of *P.*

falciparum. (see Figs. 9.3, 9.16-9.19, C.6, C.9, C.11).

B. Mature trophozoite stage

This stage of development is characterized by an enlargement of the malaria parasite's cytoplasm within the red cell.

Slide # 50 contains excellent trophozoites of *P. vivax* (Figs. 9.4, 9.17). Note infected RBC's enlarged appearance compared to non-infected red cells, and the presence of Schuffner's dots). Slide # 54 has typical *P. malariae* trophozoites (Figs. 9.7, 9.18). Note the similarity in size of infected and non-infected red cells). Mature trophozoites of *P. falciparum* are rarely seen in peripheral blood due to their adherence to endothelial cells of capillaries (see demonstration and slide # 60 of brain tissue).

C. Schizont stage

The schizont stage of the red cell infection is the final step in the division cycle and results in the formation of merozoites, which are released when the infected red cell ruptures. Schizonts of *P. vivax* (Fig. 9.17) and *P. malariae* (Figs. 9.6, 9.18) can be found, with some difficulty, on slides # 50 and 54. *P. falciparum* schizonts are extremely rare in peripheral blood. All three species in the schizont stage are shown on demonstration.

D. Gametocytes

The precursors of sex cells of *Plasmodium spp.* are the microgametocyte (male) and the macrogametocyte (female). Again, this stage of the infection is difficult to find, especially for *P. vivax* and *P. malariae*. However, gametocytes of *P. falciparum* (Figs. 9.2, 9.16, C.8) are so characteristic in their shape (slide # 57)

that a definitive diagnosis can be made if only one is seen. Gametocytes are best seen on the "thick smear" portion of each slide, but their recognition in this type of preparation requires the skill of a trained technician; therefore you should concentrate your efforts on the "thin smear" portion of each slide.

Sexual infection in Anopheles mosquito:

All stages of the sexual phase of the life cycle of malaria are on demonstration.

MALARIA - DIFFERENTIAL DIAGNOSIS IN BLOOD

	<u>P. vivax</u>	<u>P. malariae</u>	<u>P. falciparum</u>
Size of infected cell	Many are enlarged	Normal or small	normal
Color of infected cell	May be pale	Dark	Normal
R.B.C.	May have Schüffner's dots	Ziemann's dots (rare)	Maurer's dots (rare)
Stages in peripheral blood	All	All	Rings and crescents
Small trophozoite (early rings)	Heavy chromatin dot, and cytoplasmic ring; pseudopodia	Thick, heavy cytoplasm and chromatin dot	Delicate cytoplasm; small chromatin dot; double dots and infection; "applique" forms
Large trophozoite	Large single mass chromatin, irregular cytoplasm. Brown pigment. Parasite fills cells	Elongate chromatin. Cytoplasm dense. "Band forms." Pigment dark and coarse	Seen in peripheral blood in heavy infections, only
Schizont	12-24 merozoites	6-12 merozoites "Rosette"	8-24 merozoites. In peripheral blood in heavy infections, only
Gametocytes	Large; circular or oval	Large; oval or circular. Dark pigment	Crescent

PATHOLOGY:

Malaria is characterized by three clinical features: periodic chills and fevers, splenomegaly, and anemia.

1. Anemia arises from the destruction of erythrocytes when the merozoites burst out of the infected RBC, but is greater than can be accounted for by this mechanism. The rise in temperature is also correlated with the synchronous release of merozoites.
2. The liver and spleen (Fig. 9.15) also harbor numerous parasitized red blood cells (slides # 58 and 59). Note the abundant malarial pigment. The parasites are difficult to see in tissues that are sectioned and stained with Hematoxylin and Eosin rather than Giemsa stain.
3. The central nervous system complications of falciparum malaria infection are due to anoxia caused by plugging of the capillaries by parasitized red blood cells. Study slide # 60.
4. The placenta infected with malaria may have many parasites (slide # 61). Is there evidence they are passing the placental barrier into the fetus?

DIAGNOSIS:

Thick and thin blood smears stained with either Wrights or Giemsa. The laboratory technician is required by Center for Disease Control and Prevention regulations to scan a thin blood smear under oil immersion for malaria for at least 20 min. before declaring "no parasites seen".

A PCR test can also be useful, especially in transfusion malaria cases where a portion of the transfused blood is still available.

DEMONSTRATIONS:

1. Complete erythrocytic cycle for *P. vivax*, *P. malariae*, and *P. falciparum*.
2. Exoerythrocytic stages of *Plasmodium falciparum* in liver cells.
3. Sexual cycle in mosquito:
 - a. exflagellation of microgametocyte in mosquito mid-gut.
 - b. ookinete (zygote) in mid-gut.
 - c. oocyst in stomach wall.
 - d. sporozoites
4. Vectors of human malaria.

CASE HISTORY 14

Mrs. A.G., a 47-year-old housewife born in Colombia, was admitted to the Presbyterian Hospital complaining of intermittent chills and fever of five days' duration. She has lived in New York for the past 30 years, but visited Colombia on a recent occasion.

PRESENT ILLNESS: The present illness began five days prior to admission when the patient returned from a two months' visit to Colombia to see her sister and nephew. The latter's home was in the country. On the return trip she developed fever and shaking chills five days prior to admission. Four days prior to admission she had normal temperature in the morning, but developed temperature of 102°F and shaking chills in the afternoon -- this subsided in the evening. Three days prior to admission and again two days prior to admission similar events occurred with a febrile peak to 103-104°F respectively preceded by shaking chills, with a nearly normal temperature between.

DIAGNOSIS: Influenza.

She was treated with antipyretics. On the day prior to admission her temperature remained normal all day. On the day of admission the patient began to note a left pleuritic type chest pain associated with a slight cough. Shaking chills occurred in association with temperature rise to 105°F. She then came to the hospital.

PHYSICAL EXAMINATION: B.P. 120/80; P. 120; Temp. 105°F. A well-developed obese woman acutely ill. Heart normal, chest normal except for scattered rales beneath left breast. Abdomen obese, no palpable masses. There was tenderness in the left upper quadrant.

LABORATORY EXAMINATION: Erythrocyte sedimentation rate: 14 mm/hr, Hgb. 14; W.B.C. 6,650; P.M.N. 80%. Urine analysis: sp. gr. 1.018, acid; 5-10 wbc/hpf, 2-5 rbc/hpf; elevated alkaline phosphatase; slightly elevated bilirubin 1.1 mg %; normal SGOT and SGPT.

The patient was afebrile within the fourth hour of admission. On the morning after admission the spleen tip became palpable and tender. A blood smear was obtained at the time of admission (Case History slide # 14).

1. What is your diagnosis?

2. What is the treatment recommended?

CASE HISTORY 15

A.C., a 30-year-old male airline pilot, spent six days in West Africa, visiting Accra, Ghana and Kinshasa, Zaire. He became ill nine days later complaining of fever and diarrhea. Because he was a Christian Scientist, he did not consult a physician. A friend who spoke with him on the telephone six days after his illness began, realized that the patient sounded confused. Seven days after onset of illness, the patient was found in shock and was hospitalized immediately. Physical examination revealed disorientation, low blood pressure, and rapid pulse and stiffness of the neck. There were no abnormalities of the lungs, and liver and spleen were not enlarged. There was no jaundice and no skin rash. Blood count revealed severe anemia with Hgb. of 7.5 gm. W.B.C. was 13,500 with a normal differential.

Case History Slide # 15 is a blood smear obtained from this patient.

1. What is your diagnosis?
2. What is the pathogenesis of this patient's cerebral disease?
3. What was the probable incubation period of this disease?
4. How would you treat this patient?
5. How soon after diagnosis should treatment begin? Why?

CASE HISTORY 16

L.C., a six-month-old North American boy, was admitted to Babies Hospital because of recurrent fever of two and one-half month's duration. The patient was the product of a full term pregnancy. The mother was Rh negative. Because of the low Hgb of the infant, exchange blood transfusion was performed on the patient immediately after birth. He required no further therapy and was sent home on the seventh day of life. He was well thereafter until one month of age when his Hgb was noted to be 10.1 and a booster transfusion was recommended and given. At the age of two months the patient had developed multiple skin infections and had low grade fever. He was treated with antibiotics, but the skin lesions did not disappear. At the age of three months, again because of anemia, he received a third blood transfusion. At the age of four months he became febrile; his temperature rose to 104°F. No specific diagnosis was made at that time, and he was unsuccessfully treated with a variety of antibiotics. He was then admitted to another hospital and received his fourth blood transfusion, at the age of five months. Physical examination and laboratory studies at that hospital were reported to be within normal limits, except for Hgb of 9.6 gm. Shortly after the discharge from the hospital, he became febrile again and this time fever persisted for two weeks. Therefore, he was readmitted. Physical examination then revealed a febrile child who was well developed, and well nourished. The only abnormal findings were splenomegaly, with the spleen edge 8 cm. below the left costal margin. Laboratory examination revealed a Hgb of 9.4, W.B.C. of 3,000, with a normal differential. Urinalysis was normal; stool was negative for blood; barium enema revealed no abnormalities; bone marrow was normal, except for some hyperplasia of the erythropoietic elements. An intravenous pyelogram was reported as normal. The patient remained febrile throughout his first week of hospitalization, the highest reported temperature being 103°F. A diagnosis of hypersplenism was made.

One week after admission, the patient underwent a laparotomy, during the course of which the enlarged spleen was removed. Sections of the spleen revealed considerable amounts of iron pigment. The patient showed improvement of his anemia, his Hgb having risen to 14.3 gm. On the fifth day following the operation,

the patient again became febrile and thereafter continued to run daily intermittent fever. These episodes differed from those recorded prior to the operation in that they were preceded by chills. He was then transferred to Babies Hospital where a routine blood smear was obtained and it is represented on Case History slide #16.

1. What was the probable etiologic basis for this disease?

2. Could this disease have been responsible for "hypersplenism"?

3. What therapy would you prescribe? Why?

4. When should a blood smear be taken on a patient with suspected malaria? Why?

5. How soon should the patient's symptoms abate following the initiation of therapy?

Toxoplasma gondii

INFECTION:

Toxoplasma gondii (an obligate intracellular protozoan) is usually acquired by humans through the ingestion of raw or under-cooked meat in which is found a pseudocyst containing trophozoites (slide # 49; Fig. 11.2).

TROPHOZOITE:

The trophozoite stage (also referred to as the tachyzoite stage) can be maintained *in vitro* in a variety of animal cells (see Fig. 11.3, and demonstration).

PATHOLOGY:

T. gondii invades numerous organs, infecting a broad spectrum of cell types (see demonstration).

DIAGNOSIS:

Inoculation of suspension of biopsied material into mice, IgM-ELISA, PCR, Immunofluorescent antibody (IFA), Complement Fixation (CF).

DEMONSTRATIONS:

1. Infected fibroblasts with "rosettes" of *T. gondii* trophozoites (tachyzoites).
2. Rabbit liver infected with *T. gondii* trophozoites (tachyzoites).

CASE HISTORY 18

A twelve-week-old girl was admitted to Babies Hospital, because of failure to thrive. No abnormalities had been noted at birth and she was discharged from the nursery on her fifth day of life as a presumably well infant. On admission she was noted to be lethargic; her head circumference was 44 cm (105th percentile for age and sex); her anterior fontanel was wide open and tense; fundoscopic examination revealed bilateral chorioretinitis.

Ventricular tap revealed fluid with a high content of protein (1580 mg%) and normal sugar. There were no cells. Ventriculogram showed obstruction at the foramen of Monro and dilated ventricles. A diagnosis of hydrocephalus was made and a suspicion of toxoplasmosis was raised.

Toxoplasma serologic tests were as follows:

TEST	TITER	
	MOTHER	CHILD
Indirect fluorescent antibody	1:2048	
	1:4096	
ELISA Test (IgG)	1:64	1:128

Mouse inoculation of the ventricular fluid was negative for *T. gondii*.

1. Can you make a definitive diagnosis of congenital infection based upon the results of these tests? Explain.

GIARDIA, ENTAMOEBIA & CRYPTOSPORIDIUM

Giardia lamblia

INFECTION:

This flagellated protozoan is acquired through the ingestion of the cyst stage (slide # 47; Figs. 1.2, 1.6.b, C.2).

TROPHOZOITE:

The trophozoite (i.e., the non-infectious stage) lives in the small intestine, closely apposed to the columnar epithelium. Slide # 47 contains trophozoites (Figs. 1.1, 1.3, 1.4, 1.6a) and cysts (Figs. 1.2, 1.6b).

CYST:

The cyst is resistant to drying, temperature changes, and a wide range of other environmental changes.

PATHOLOGY:

"Malabsorption syndrome" related to fats is the major complication of this infection.

DIAGNOSIS:

Microscopical examination of the patient's stool for trophs and cysts. The string test ("Enterotest") is a valuable diagnostic adjunct. In addition, duodenal aspiration has proven useful.

DEMONSTRATION:

1. Cyst
2. Trophozoite

CASE HISTORY 19

A.R. is a 40-year-old anthropologist, who returned from a field trip to Upper Volta and The Cameroons. Approximately two weeks prior to his return he developed cramping abdominal pain and diarrhea. These symptoms continued until his visit to this hospital, by which time he had eight to twelve loose stools a day. Physical examination revealed no abnormalities. Laboratory studies revealed Hgb. of 14.5, white count of 5600 with a normal differential. Stool examination was requested.

Case History Slide # 19 represents the findings.

1. What is your diagnosis?
2. What therapy would you recommend for this patient?
3. What sub-set of patients are thought to be unusually susceptible to this infection?
4. What is one serious consequence of this infection?
5. If stool examination is negative, but this disease is still suspected, what diagnostic procedures may be helpful?

Entamoeba histolytica (parasitic) and ***Entamoeba coli***
(commensal)

E. histolytica

E. coli

- | | | |
|----|--|--|
| 1. | Active progressive movement | Sluggish indeterminate movement |
| 2. | Clear pseudopodia put out almost explosively | |
| 3. | Endoplasm finely granular | Endoplasm more coarsely granular |
| 4. | No bacteria in food vacuoles | Many food vacuoles; contain bacteria, fecal debris, etc. |
| 5. | Often contains red blood cells | No red blood cells |
| 6. | Nucleus not usually visible | Nucleus usually visible |

Nucleus

- | | | |
|----|----------------------------|-----------------------------|
| 1. | Peripheral chromatin even. | Peripheral chromatin uneven |
| 2. | Central nucleolus | Eccentric nucleolus |

Cysts

- | | | |
|----|---|--|
| 1. | 5-20 um; usually 7-15 um | 15-20 um |
| | Nuclei not visible unstained | Nuclei visible unstained |
| 2. | 4 - nucleate | 8 - nucleate |
| 3. | Chromatoid bodies heavy with blunt, rounded ends; visible unstained | Chromatoid bodies thin, splinter-like; not visible unstained, uncommon |

Entamoeba histolytica

INFECTION:

The cyst of *E. histolytica* (slide # 42; Figs. 12.2, C.16a-C16c) is infective for man and is usually acquired through contaminated water or food.

TROPHOZOITE:

The motile stage is the trophozoite (slides # 40 and 41; Figs. 12.1, 12.3, 12.7, C.15). Motility can best be judged when a freshly passed, slightly diarrheic stool is presented to the laboratory. (It is an old, but true, axiom that the closer the patient's anus is to the microscope, the better the technician's chances are of finding moving trophozoites of *E. histolytica*).

The morphology of the *E. histolytica* trophozoite varies somewhat from patient to patient, and from strain to strain of amoeba.

Some general characteristics are given in the table in this section of the manual, but it would be impossible to become expert at their recognition in the short time allotted to you for this laboratory exercise. In attempting a diagnosis, however, you will become acutely aware of the great value to any hospital of a competent parasitology technician.

Slide # 48 is a preparation made from a patient suffering from Shigella dysentery. Note the numerous white cells. Compare this slide with slides # 40 and 41.

CYST:

The cyst contains four nuclei in its mature state (slide # 42, also see demonstration). Once again, please consult the table for a comprehensive review of the morphological characteristics which enables you to differentiate *E. histolytica* from other amoebae of humans, except for *E. dispar*.

PATHOLOGY:

- A. Sections of human intestine showing lesions and amoebae, stained with routine Hematoxylin and Eosin which does not bring out characteristic amebic morphology.
 - 1. Early stage of amoebic ulcer, slide # 43. Note amoebae at bases of crypts and in submucosa and muscle layers.
 - 2. Later stage showing undermining ulcer, slide # 44; Fig.12.4). Note large areas of necrosis in submucosa and muscle layers. Look for amoebae at junction of necrotic and normal tissues.
- B. Amoebic abscess of liver (Slide # 46) and lung (Slide # 45).
- C. Demonstration of hepatic amoebiasis stained to show details of amoebae.
- D. Pulmonary amoebiasis (see demonstration).
- E. COMMENSAL INTESTINAL PROTOZOA, in fresh stools. Two mounts are usually made, in saline and iodine, and studied with low and high dry objectives. Stained preparations of intestinal protozoa may be examined first with low and high dry objectives, but details must be studied under the oil immersion lens with best possible illumination (see demonstration).

DIAGNOSIS:

Identify live trophs in fresh stool. PCR to distinguish *E. histolytica* from *E. dispar*. Serology (IHA, counter-electrophoresis, CF test). Serology is mostly useful regarding extra-intestinal amoebiasis.

DEMONSTRATIONS:

1. Cyst, early
2. Cyst, mature
3. Trophozoite
4. Histopathology of hepatic abscess
5. Non-pathological amoebae associated with man (see Diagnostic Atlas, p. 323):
 - a. *Endolimax nana* (Trophs and cysts of each)
 - b. *Entamoeba coli* (Trophs and cysts of each)
 - c. *Iodamoeba butschlii* (Trophs and cysts of each)
6. *Blastocystis hominis*

CASE HISTORY 20

C.S., 31 years old, developed a bloody diarrhea with tenesmus while traveling from Hong Kong to Singapore on a trip as company representative to the Far East. He was examined by a physician in Singapore, found to have "amoebiasis" on stool examination, and treated with metronidazole, 750 mg three times daily and tetracycline 250 mg four times daily, both for seven days. His symptoms cleared promptly.

He returned to the United States, and on his way home stopped to visit friends in Arizona. His symptoms returned. His friends gave him some tetracycline, and the acute diarrhea improved, but he continued to have abdominal cramps and several loose to watery stools daily.

In New York he consulted a clinical parasitologist. He reported that he had heard metronidazole was no longer effective, and the recurrence of his diarrhea confirmed his opinion; he wished stronger medicine. When asked about his sexual orientation, he stated that he was a homosexual, and upon further questioning, did acknowledge anal sexual contacts in Hong Kong, Singapore and Arizona.

The physician found the patient's abdomen to be mildly tender throughout, and some increase in tenderness in the right lower quadrant. Sigmoidoscopic examination revealed a diffusely inflamed rectosigmoid mucosa without ulceration. Trophozoites of *E. histolytica* were present in warm, liquid stool specimen. Symptoms responded rapidly to a course of metronidazole 750 mg. three times daily for 10 days (diiodohydroxyquin 650 mg. PO tid for 20 days). Stool examination two weeks afterward were negative; the patient did not return subsequently.

1. What stage of the parasite infected C.S.?

2. What measures should C.S. be advised of to prevent recurrence of his amoebiasis?
3. Should efforts be made to have C.S.'s sexual partners examined for amoebiasis and then treated if necessary?
4. Should a patient with amoebiasis be isolated from others? Explain.
5. What is the significance of finding Charcot-Leyden crystals in the stool?
6. What is an amoeboma and how is it differentiated from other lesions?

Cryptosporidium parvum

INFECTION:

These intracellular protozoan parasites of the gastrointestinal tract infect a wide variety of mammals. *Cryptosporidium parvum* is the species principally responsible for clinical disease in man and domestic animals, which can serve as reservoirs of human infection. The parasites are worldwide in distribution and are considered pathogenic for all ages and both sexes. Most cases are subclinical, although an acute, self-limiting gastroenteritis can occur in immunocompetent hosts. However, in infants, and immunocompromised adults, particularly in AIDS patients, severe diarrhea and fatalities can occur.

OOCYSTS:

The infective stage is the oocyst (Slide # 63; Figs. 10.1, C.13), which is passed in the feces, and contains four sporozoites. When the oocyst is swallowed, the sporozoites are released and initiate the infection in columnar epithelial cells of the small intestine.

PATHOLOGY:

Hypersecretion of intestinal fluid occurs with infection. This leads to loss of water and electrolytes and a diarrhea resembling that of cholera, but no toxin has been demonstrated. Prolonged infection can also lead to villous atrophy.

DIAGNOSIS:

Oocysts are identified in stool specimens, that are either immersed in a sucrose solution to allow the oocysts to float to the surface (i.e. with watery diarrhea), or in the case of loose stool, smeared directly on a glass slide, then fixed and stained with Kinjoun acid fast stain and examined microscopically. Various stages of the parasite can also be identified in histological sections of the gut.

DEMONSTRATION:

1. Oocysts in fecal smear stained with Kinjoun acid fast stain.

CASE HISTORY 21

C.C. is an HIV+, 46-year-old black man who is homeless, with a history of intravenous drug and alcohol abuse. He was admitted with a chief complaint of two weeks of anorexia, rigors, productive cough, watery diarrhea and a 23-pound weight loss over the past four weeks. C.C. was referred to CPMC by the shelter where he had been staying.

Physical findings:

In Area A his oral temperature was 100.9 F, respiratory rate was 28, blood pressure 120/72 and pulse 96 and regular. Notable on examination was oral thrush, cervical adenopathy, right basilar rales with dullness to percussion at the right base. The patient had profuse, watery, light brown diarrhea, which was guaiac negative. Abdominal, rectal and neurological examinations were unremarkable.

Laboratory findings:

WBCs were 7,200 (71p, 7b, 91, 2m), Hgb/Hct=9.4/29.3, MCV=83. Na⁺ 129, Cl⁻ 97, CO₂ 25, Mg⁺⁺ 1.6. CXR revealed a RLL infiltrate. Stool sent for parasite examination (Slide # 63; Fig. 10.1, D.13).

The patient was started on Cefuroxime, 750 mg IV q8^o + Mycostatin. Sputum grew out *Maraxella catarrhalis*.

1. What infectious agents must be included in the differential diagnosis of an immunocompromised patient with diarrhea?
2. What concurrent problems need to be addressed in patients with cryptosporidial diarrhea?
3. How would you treat this patient?

MEDICALLY IMPORTANT ARTHROPODS

The importance to human health of arthropods, the pathology they cause directly, and the diseases they transmit, is well known. It can be said that tropical medicine would be far less complex but for the arthropod borne diseases. Malaria, yellow fever, West Nile, dengue, and filariasis are all transmitted by mosquitoes. Sandflies transmit the various forms of leishmaniasis, while tsetse flies carry African trypanosomes, the cause of sleeping sickness. In the Old and New Worlds, river blindness or onchocerciasis is carried by blackflies, and in Central and South America kissing bugs are the insidious vectors of Chagas' disease. It is important to note that most of these diseases are best controlled by controlling the insect vector. Curative medicine is seldom effective for mass treatment of human populations in endemic areas.

Each vector species has its own ecological requirements, and to review the life cycles and population dynamics of even the more important species would require a full semester's work, not an unreasonable requirement for a well-trained physician and certainly a necessity for an individual contemplating a career in tropical medicine.

General medical practitioners in the U.S. should expect to encounter a variety of arthropod-associated maladies. Many of the more serious will have been contracted in the tropics. The traveler may return with any of a long list of arthropod-transmitted viral, bacterial, protozoal or helminth infections. Certainly, many will return suffering discomfort from insect bites or stings. Not infrequently, he or she may return harboring the arthropod itself.

A. The Insects

- 1) Myiasis - By definition, myiasis is an infestation with a maggot, the larval stage of a fly. Certain species of flies develop as obligate parasites, requiring living tissue in which to mature.

Dermatobia hominis - the human bot fly of Central and South America

Cordylobia anthropophaga - the tumbu fly of Africa

Various species of facultatively parasitic flies may lay their eggs on or near sores or necrotic tissue. The maggots hatch out and burrow into the wound, usually feeding on dead tissue. However, some species may cause serious damage and death if left untreated. Both U.S. and tropical species can cause myiasis.

TREATMENT - Maggots must be removed from the wound individually.

- 2) The Biting Flies - In addition to their capacity to transmit pathogens, the bites of certain diptera can be annoying, painful or dangerous. Individuals can become sensitized to the salivary secretions of some species and suffer severe reactions.

Mosquitoes in the U.S. still transmit various, occasionally epidemic, viral diseases, and are capable of transmitting usually tropical pathogens if given the opportunity.

TREATMENT - Avoid areas where biting flies are common. Repellents containing DEET may be effective. When bitten, avoid scratching, treat with local anesthetics.

- 3) Lice - Head lice continue to plague school children, and regular outbreaks are reported, often in affluent suburbs.

Body lice are often found on derelicts and "street people."

The crab louse, the "butterfly of love", is enjoying a renaissance along with a number of venereal diseases.

TREATMENT - Various shampoos, creams and lotions are available which will kill the lice but not prevent re-infestation.

- 4) Fleas - Dog and cat lovers are regularly plagued with fleas after their pets leave home and the fleas are forced to find a new host. Others may share the flea with its natural host. Sensitization to the bite can occur and reactions can be painful.

TREATMENT - Local anesthetics can ease discomfort of bites. Pets and pet bed areas can be treated with insecticide dusts; flea collars are useful.

B. The Arachnids

- 1) Scabies - The human itch mite is a small, particularly irritating pest, transmitted by contact, which burrows into the skin. Infection may be prolonged and painful. Children are particularly susceptible.

TREATMENT - Compounds useful against lice are also effective against scabies.

- 2) Ticks - The list of tick-borne diseases transmitted in the U.S. is long and growing. Rocky Mountain Spotted Fever, Colorado Tick Fever, babesiosis and Lyme disease are some of the more common.

Tick paralysis can result from the prolonged attachment of ticks, usually in children. Removal of the ticks produces remarkable recovery.

TREATMENT - Removal of tick. A few drops of chloroform or ether on the tick's head will relax it; then grasp the anterior portion of the tick near the head and pull straight back with steady traction.

PREVENTION: Avoid areas where ticks are common, check children regularly for ticks, use repellents containing DEET.

C. Entomophobia

Inordinate fear of insects and arachnids is not uncommon. The general disgust with flies, maggots, and cockroaches is natural, resulting from awareness of their association with filth and low levels of sanitation.

Some individuals insist that they are constantly under attack by various insect species. If the culprits are found and identified, treatment or preventive measures can be suggested. In many cases, the pests are imaginary and the individual difficult to convince.

CASE HISTORY 22

The etiology of a chronic, atopic, eczematoid, dermatitis with psoriasis with lichenification of the skin and crusting under the fingernails in a noninstitutionalized male mongoloid had gone undiagnosed for 13 years. His condition never responded completely to "appropriate" therapy, including steroids, until 3 distinct epidemics of classical scabies, totaling 54 cases, originated among patients and staff of a Dermatological Hospital Service. An epidemiological study pointed to this one patient as the source of the epidemics. Proper diagnostic techniques revealed the cause of his condition, and treatment resulted in a complete cure of his pruritus and lichenification.

1. How does Norwegian scabies differ from classical scabies?
2. In what group of individuals is Norwegian scabies most common?
3. What affect would steroids have on the infestation?

4. Where and for what does one look to diagnose classical scabies?
5. What morphological characteristics of the causative organism aid in the diagnosis?
6. What is the relationship of the typical scabies rash to the numbers and location of mites?
7. What is the treatment for scabies?
8. In addition to treatment, what other procedure should you follow in keeping with good medical practice?

CASE HISTORY 23

This 10-year-old boy was playing in the yard of his home in New Jersey and was found unconscious and exhibiting right-sided major seizures. During the ambulance ride to the hospital, his father, a physician, noted four little puncture marks on the boy's right hand between the thumb and index finger. Concomitantly, the right arm began to swell, and a violaceous hue was noted on the volar forearm and medial elbow. The thumb and index fingers were cyanotic.

The convulsions responded to phenobarbital, Dilantin and Valium.

LABORATORY DATA: The initial laboratory findings included: Urinalysis: Albumin 4 +; few to many red blood cells; white blood count 28,000; platelet count 535,000; erythrocyte sedimentation rate 45.

COURSE IN THE HOSPITAL: By the third day the albuminuria and hematuria cleared. The right arm was swollen, and a dusky violaceous hue. There was poor capillary filling in the thumb and index finger. Lesions were noted on the thenar eminence, volar forearm and medial aspect of the elbow. These lesions were edematous and tender with central purpura surrounded by ischemic white zones bordered by erythema. Bullae were on the Dorsum of the right hand. A bee allergy test was negative.

SURGICAL REPAIR AT PRESBYTERIAN HOSPITAL: Over the ensuing six weeks at home these lesions developed eschars with subsequent sloughing. The tip of index finger had sloughed and there was necrosis of the tip of the thumb to the distal interphalangeal joint.

Skin grafts were applied to the sloughed lesions.

A search was made to find the brown fiddler spider in the environs of the boy's home. Seventeen spiders were collected but none were Loxosceles. However, the brown fiddler spider Loxosceles reclusa has been reported from New Jersey.

CASE HISTORY 24

A seven-year-old girl from South Carolina was in excellent health until June, when within a period of 48 hours a progressive ascending paralysis involving all four extremities developed. She experienced difficulty in swallowing and her speech became indistinct. Her reflexes were completely absent. On hospitalization an engorged tick was removed from the back of her neck, beneath her hair. In the next two days she improved dramatically and was discharged from the hospital.

LABORATORY DATA: The following tests were done in the hospital and were all within normal limits: complete blood count; urine analysis; serum electrolytes, Na, K, Cl, Ca, Mg; blood urea nitrogen; serum, cholesterol, protein electrophoretic pattern, glutamic oxaloacetic transaminase plasma and red cell cholinesterase; electrocardiogram; electroencephalogram; cerebrospinal-fluid cell count and protein.

Studies indicate that the female tick injects a toxin which is supposed to act in the vicinity of the neuromuscular synapse and interfere with the release of acetylcholine. More recent studies indicate that this may not be the mode of action, for there is a slowing of motor conduction but no alteration in sensory conduction of the peripheral nerves.

1. If the tick were not found and removed what might have happened?

2. How would you remove this tick?

