Blood Parasite Identification

BP-11 Introduction

Thick and thin Giemsa-stained smears were obtained from a traveler from Indonesia with fever and edema.The specimen contained *Plasmodium falciparum*. A response of "*Plasmodium falciparum*." or "*Plasmodium* sp./*Babesia* sp. seen, referred for identification" were considered satisfactory.

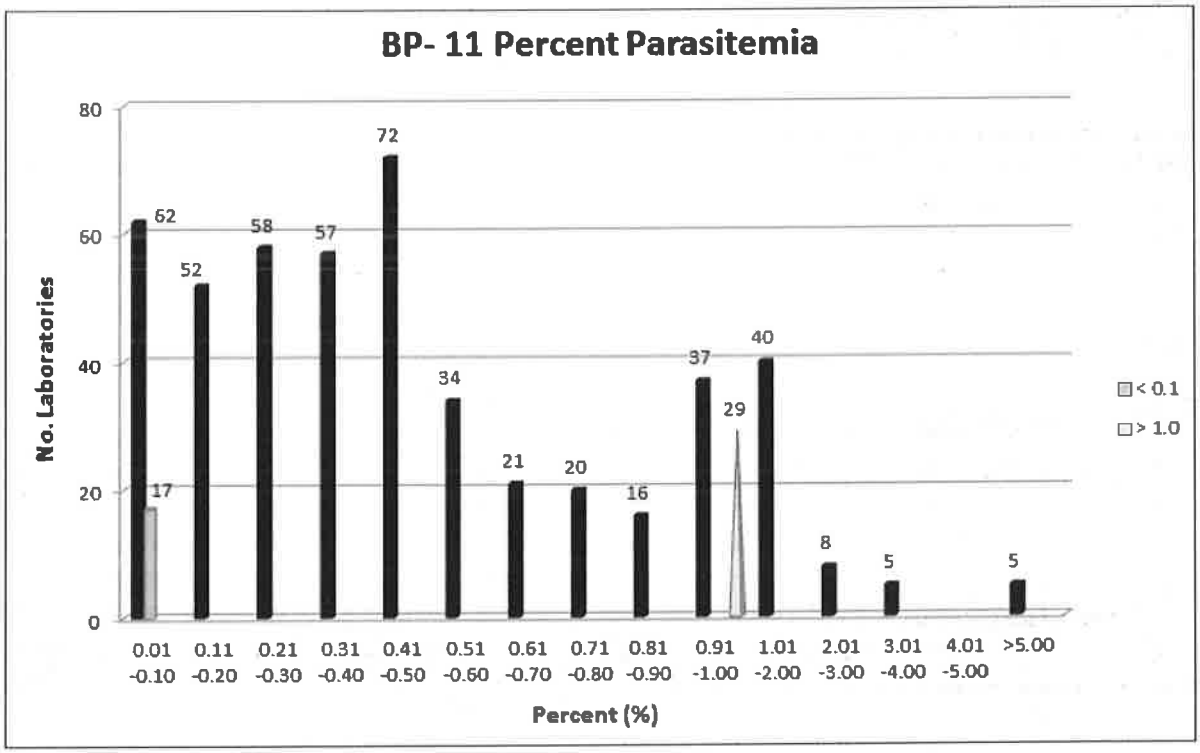
BP-11

Parasite Identification	Referees No.	Referees (33) %	Participants No.	Participants (445) %
Plasmodium falciparum	31	93.9	424	95.3
Plasmodium sp., not *P. falciparum*, referred for identification	2	6.1	8	1.8

Parasite Screen	Referees No.	Referees (15) %	Participants No.	Participants (743) %
Plasmodium sp./*Babesia* sp. seen, referred for identification	15	100.0	738	99.3

BP-11

If you have identified a *Plasmodium* sp. or *Babesia* sp.: Report percent of infected RBCs seen (number of infected RBCs per 100 red blood cells). (Ungraded)



Key morphologic features on thin blood film that suggests a diagnosis of *P. falciparum* may include:

- Normal size and shape of infected erythrocytes
- Smaller, more delicate ring stages (approximately 1/5 the diameter of the erythrocyte) frequently with two chromatin dots (so-called "head phone" forms)
- Erythrocytes infected with multiple ring forms
- Presence of ring forms at the edge of the erythrocyte (appliqué forms)
- Absence of mature trophozoites and schizonts in the peripheral blood film (may be seen if there is a delay in processing the blood specimen)
- Presence of crescent-shaped gametocytes (not always seen)
- Absence of Schüffner's stippling. Larger, comma-shaped dots (Maurer's clefts) may be seen, especially when the stain buffer is at a pH of 7.2

Distinguishing *P. falciparum* from *Babesia* spp. can be challenging, given that both have a predominance of small ring forms, infect RBCs of all ages, and can produce multiply infected RBCs. The presence of Maurer's clefts, malarial pigment, and banana-shaped gametocytes eliminate *Babesia* infection from consideration. Furthermore, *Babesia* parasites are usually more pleomorphic with spindled, elliptical and ovoid forms. Extracellular forms are also more common in babesiosis. Finally, identification of the classic "Maltese cross" or tetrad form of *Babesia* sp. is diagnostic for babesiosis. Molecular or antigen-detection methods, in addition to clinical/travel history may be useful adjuncts for distinguishing between these two similar appearing parasites.

Discussion

Causal Agents:
There are four species of *Plasmodium* that cause human malaria: *P. falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*. In addition, there are at least six species of simian *Plasmodium* that have been documented to cause zoonotic infections in humans, the most notable being *P. knowlesi*, infections of which appear to be increasing on the Malaysian peninsula.

Plasmodium falciparum occurs nearly worldwide in the tropics and subtropics, particularly in Africa and Southeast Asia. *Plasmodium malariae* also occurs nearly worldwide in the tropics and subtropics, but has a more patchy distribution than *P. falciparum*; most common in tropical Africa, Indian subcontinent, and Southeast Asia. *Plasmodium ovale* occurs primarily in tropical western Africa, but also New Guinea and Southeast Asia; *P. ovale* has not yet been documented from the New World. *Plasmodium vivax* occurs nearly worldwide in the tropics, subtropics, and some regions of northern and eastern Africa, the Middle East, the Indian subcontinent, Southeast Asia, and the Americas.

Biology and Life Cycle:
Plasmodium spp. are transmitted by mosquitoes in the genus *Anopheles*. Infected female mosquitoes inject sporozoites when taking a blood meal. Sporozoites are carried via blood to the liver where they invade hepatocytes and form schizonts. The liver schizonts rupture, releasing large numbers of merozoites that then invade erythrocytes starting the erythrocytic cycle. Early ring forms develop into mature trophozoites and take one of two pathways: 1) they develop into schizonts (which rupture and continue the erythrocytic cycle) or 2) develop into gametocytes. Gametocytes are a dead-end stage in the human host but are required for sexual reproduction in the mosquito. In the mosquito host, microgametocytes (=males) exflagellate and fertilize macrogametocytes (=females), resulting in an ookinete. Ookinetes further develop into oocysts, which when mature rupture and release the infective sporozoites. In *P. falciparum*, late trophozoites and schizonts express a protein on the surface of the erythrocytic membrane causing the infected erythrocyte to adhere to the endothelial lining of capillaries in internal organs. Thus, only ring forms and gametocytes are usually seen in well-prepared peripheral blood smears.

Diagnosis:
The ideal specimen for laboratory identification of malaria is fresh capillary blood from a finger or heel stick, with immediate preparation of thick and thin blood films. Since this is not feasible in most settings, however, venous blood collected in EDTA anticoagulant is also acceptable. It is important to transport the blood as quickly as possible to the laboratory for examination since prolonged exposure to EDTA may result in distortion of the malaria parasites and compromised morphology.

Malaria is primarily diagnosed by the identification of *Plasmodium* parasites on thin and thick blood films stained with Giemsa, Wright, or Wright-Giemsa stain. Molecular methods such as PCR may be employed when an identification cannot be made morphologically or there is morphologic evidence of a mixed infection. Rapid diagnostic tests are also commonly used to distinguish *P. falciparum* from other malaria infections. Serology is not used for routine diagnosis but may be helpful during transfusion investigations.

Typically, thick films are used for the recognition of *Plasmodium*, with a species-level identification performed on the thin film. Thin films should be read at 1000x magnification with oil for at least 100 microscopic fields. Immunologically naïve patients (eg, returning travelers born in non-endemic areas) may present with stronger clinical manifestations at a lower parasitemia. Severe malaria is currently defined as a parasitemia ≥ 2% in immunologically naïve patients and ≥ 5% in non-naïve patients.

Morphologic Identification:
Two important questions regarding morphologic identification of malaria are:

1) Is it malaria?
2) Is it *Plasmodium falciparum*?

Recognition of *Plasmodium* is based on observing stages of the parasite inside infected red blood cells. In a well-prepared specimen, the cytoplasm will stain blue and the chromatin red. Pigment (which is absent in *Babesia* infections) will present as golden-brown to black flecks. In some species, structures such as Schüffner's stippling or Maurer's clefts may be present when stained at an appropriate pH. Identification of *Plasmodium* to the species level is extremely important for patient management, as different species may be treated differently (for example, it is important to target the liver stages of *P. ovale* and *P. vivax* to prevent relapse of the disease).

The following table compares the morphologic features of the four stages of human *Plasmodium* spp.

Morphologic Criteria	*Plasmodium falciparum*	*Plasmodium malariae*	*Plasmodium ovale*	*Plasmodium vivax*
Size of infected RBC	Normal	Normal to smaller	Enlarged	Enlarged
Rings (early trophozoites)	Common; usually with thin, delicate cytoplasm and double chromatin dots; often multiple rings per infected RBC; appliqué forms common	Cytoplasm sturdy, usually with single, large chromatin dot; occasional 'birds-eye' forms	Cytoplasm sturdy, with 1-2 large chromatin dots	Large, sturdy cytoplasm, usually with large, single chromatin dot
Developing trophozoites	Rare, but may be seen if a delay in processing; form compact, pigment usually evident	Variable; may be compact to elongate (band-form) or pleomorphic and vacuolated (basket-form); pigment coarse	Compact to slightly amoeboid with dark pigment; elongation and fimbriation may be observed	Pleomorphic to grossly amoeboid; pigment diffuse and golden-brown to nearly black
Schizonts	Rare in peripheral blood; 8-24 small merozoites when mature; pigment dark, compact	6-12 merozoites when mature, often in a rosette pattern around central mass of pigment	6-14 merozoites when mature; pigment dark brown to black and discrete when mature; elongation and fimbriation may be present	12-24 merozoites when mature; may fill entire RBC; often noticeable enlarged
Gametocytes	Crescent-shaped; chromatin discrete (macrogametocyte) or diffuse (microgametocyte); Laveran's bib may be present	Small, round, compact; pigment coarse and diffuse	Round to oval, compact; if elongated and fimbriated may not fill entire infected RBC; pigment coarse, dark	Large and round to pleomorphic (may 'hug' surrounding RBCs); may fill most of infected RBC; pigment golden-brown to nearly black
Other Features	Maurer's clefts may be present; ring-form trophozoites usually predominate	Generally smaller; pigment coarse; Ziemann's stippling may be present; all stages seen	Schüffner's stippling may be present at appropriate pH; elongation and fimbriation may be observed; all stages seen	Schüffner's stippling may be present at appropriate pH; enlargement of infected RBCs usually pronounced; all stages seen

Calculating Percent Parasitemia:
The percent parasitemia is very important to calculate for prognostic purposes and also to evaluate response to antimalarial therapy.

Parasitemia can be calculated on a thin blood film as follows:

1. Count the number of infected RBCs per 100 RBCs in different oil immersion fields.
2. Apply the formula:

$$\frac{\text{\# of infected RBCs}}{\text{total \# of RBCs counted}} \times 100 = \% \text{ parasitemia}$$

Notes:

1) At least 500 RBC's should be counted, with counting 2000 or more RBCs providing the most accurate estimation of parasitemia
2) An infected RBC containing multiple parasites is calculated only once
3) Fields devoid of parasites should be included, if encountered
4) Gametocytes should not be included in the count. Justification is because: 1) many antimalarial drugs are not gametocidal and the presence of gametocytes post-treatment is not indicative of the effectiveness of the treatment and 2) gametocytes are a dead-end stage in the human host.

Clinical Significance:
In 2014, ninety seven countries and territories had ongoing malaria transmission. Over half a million people die from malaria each year. Most malaria cases and deaths occur in children in sub-Saharan Africa. In 2011, a 40-year high of 1,925 cases of malaria were reported to the CDC in the United States, almost all in recent travelers and immigrants. Although the *Anopheles* mosquito is endemic in parts of North America, malaria transmission was largely eradicated in the 1940s through public health efforts.[1]

Malaria infection can be classified as either uncomplicated or severe (complicated). In uncomplicated infections, patients present with nonspecific symptoms including fever, chills, sweats, headaches, nausea/vomiting, body aches and malaise. Symptoms classically (but infrequently observed) recur either in a two-day cycle (*P. falciparum*, *P. vivax* and *P. ovale*) or in three-day cycle (*P. malariae*). In severe infections, organ failure and/or metabolic abnormalities occur including severe anemia, acute respiratory distress syndrome, acute kidney failure, metabolic acidosis, cerebral infection, and coagulation abnormalities. Severe infection is considered a medical emergency requiring urgent treatment. *Plasmodium falciparum* can cause severe illness and death whereas *P. vivax*, *P. malariae* and *P. ovale* tend to cause less severe illness. The hypnozoite form of *P. vivax* and *P. ovale* can remain dormant in a patient's liver and cause relapsing infection.

Treatment:
Treatment of malaria should ideally wait until a laboratory diagnosis has been made. Treating "presumptively" should occur only when no other option exists. Therapy is guided by the infecting species of *Plasmodium*, the clinical status of the patient and the drug susceptibility of the infecting parasites (dependent on geographic area and previous anti-malarial treatment). Because of the rapid progression of *P. falciparum* infections and a high risk of fatality, urgent treatment is essential.

If the infection is uncomplicated, oral anti-malarial medication can provide effective treatment. However, severe infections necessitate parenteral therapy. *Plasmodium falciparum* and *P. vivax* have different drug resistance patterns in different geographic regions. Although not readily available in North America, the WHO recommends artemisinin-based combination therapy as first-line treatment in uncomplicated *P. falciparum* malaria (oral administration), severe malarial infections (intravenous administration) and *P. vivax* infections in areas of known chloroquine resistance. [2] Other, non-artemisinin based combination treatments include sulfadoxine-pyrimethamine

plus either chloroquine, amodiaquine, or atovaquone-proguanil. In recent years, resistance to artemisinins has been detected in Cambodia, Laos, Myanmar, Thailand and Vietnam.[3] For confirmed *P. vivax* and *P. ovale* infections, radical cure can be achieved with treatment using primaquine, in order to prevent relapse due to the hypnozoite form, except in high-transmission settings where re-infection is likely. Mixed-species malarial infections are not common but may be underestimated by routine microscopy.[2]

References

1. Centers for Disease Control and Prevention. Treatment of Malaria: Guideline for Clinicians. Available at: http://www.cdc.gov/malaria/diagnosis_treatment/clinicians3.html. Accessed June 23, 2015.
2. World Health Organization. Guidelines for the Treatment of Malaria. 3rd ed. Geneva, 2015.
3. World Health Organization. Malaria: Fact Sheet #94. Updated December 2014. Available at: http://www.who.int/mediacentre/factsheets/fs094/en/ Accessed online October 26, 2015.
4. Garcia LS. *Diagnostic Medical Parasitology.* 5th ed. Washington, DC. ASM Press; 2007.
5. CDC: Malaria surveillance – United States 2005. MMWR 2007;56(SS06);23-38.
6. Greenwood BM, Bojang K, Whitty CJ, Targett GA. Malaria. *Lancet*.2005;365:1487-1498.

BP-12 Introduction

The photograph challenge was obtained from a 42-year-old male from Malaysia with right lower leg swelling. The specimen contained Microfilaria-*Brugia* sp. A response of "Microfilaria-*Brugia* sp", "Microfilaria, NOS, referred for identification" and "Blood or tissue parasite, not *Plasmodium* sp. or *Babesia* sp., referred for identification was considered satisfactory.

BP-12

Parasite Identification	Referees (33) No.	%	Participants (389) No.	%
Microfilaria-*Brugia* sp	32	97.0	359	92.3
Microfilaria-*Wuchereria bancrofti*	1	3.0	22	5.7
Parasite Screen	**Referees (15) No.**	**%**	**Participants (787) No.**	**%**
Microfilaria, NOS, referred for identification	15	100.0	735	93.4
Blood or tissue parasite, not *Plasmodium* sp. or *Babesia* sp., referred for identification	-	-	51	6.5

Discussion

Causal Agent:
Lymphatic filariasis is caused by the filarid nematodes *Brugia malayi*, *B. timori*, and *Wuchereria bancrofti*. *Wuchereria bancrofti* is distributed nearly worldwide in the tropics. *Brugia malayi* is distributed in Southeast Asia and the Indian subcontinent, while *B. timori* is endemic to the Lesser Sunda Islands of the Indonesian archipelago.

Biology and Life Cycle:
All three species have a similar life cycle, and adults of all three species reside in the lymphatic vessels of the human definitive host. Gravid females release sheathed microfilariae which circulate in the blood at night, exhibiting nocturnal periodicity (except for some populations of *W. bancrofti* in Southeast Asia which do not express specific periodicity). An appropriate mosquito intermediate host becomes infected while ingesting microfilariae during the course of a blood meal. Microfilariae migrate from the midgut of the mosquito to the flight muscles where they develop into infective L3 larvae in approximately two weeks. L3 larvae migrate through the hemocoel of the mosquito to the head and mouthparts. Humans become infected when a mosquito deposits L3 larvae onto the skin while taking a blood meal. Larvae migrate to the lymphatics system where it takes several months to develop into sexually mature adults.

Diagnosis:
The diagnosis of all three species is based primarily on the identification of microfilariae in thick and thin blood films stained with Giemsa, Wright stain, or hematoxylin. Concentration procedures, such the Knott's method, may increase sensitivity. Because all three species exhibit nocturnal periodicity, the optimal time to collect blood specimens from a patient is between 10 PM and 2 AM.

All three species may possess a sheath, although the sheath may be absent in stained blood smears so the absence of a sheath should not in itself rule-out any of these species. The most important features for identifying these nematodes to the genus level are the nuclear arrangements in the head and tail. The following table summarizes the important morphologic features.

Species	Size (in stained blood films)	Sheath (color, when properly stained with Giemsa)*	Head Space (distance between anterior end of nuclear column and tip of worm)	Tail nuclei
Wuchereria bancrofti	244-296 µm	Colorless*	Short	Tail anucleate
Brugia malayi	177-230 µm	Bright pink*	Long	Terminal and subterminal nuclei present, with gaps in between
Brugia timori	310 µm avg. length	Colorless*	Long	Terminal and subterminal nuclei present, with gaps in between

*Sheath color is pH-dependent, and at times the sheath of *B. malayi* may not stain bright pink. Likewise, on rare occasions, the sheath of *W. bancrofti* has been known to stain bright pink.

There are no routine molecular or rapid tests available for lymphatic filariasis in the United States. A rapid format immunochromatographic test is available outside the U.S. however. An EIA is available for detecting circulating antibodies in blood. Unlike with microscopy, blood does not need to be collected at night to perform the EIA. This test is reliable for *W. bancrofti* and *B. malayi*, but has not been properly validated for *B. timori*. There is also some cross-reactivity with *Onchocerca volvulus* and *Loa loa*.

Clinical Significance:
Most microfilarial infections are asymptomatic with subclinical tortuosity and dilation of lymphatics. The spectrum of disease for those with symptoms includes lymphedema, hydrocele, acute attacks of febrile lymphangitis and, less frequently, pulmonary tropical eosinophilia syndrome or chyluria. The range of clinical presentations varies slightly with species and geography. For example, involvement of the genital lymphatics occurs almost exclusively with *W. bancrofti* infection. Acute symptoms are often more intense in patients from non-endemic areas. With low worm burden and a good immune response, long-term sequelae in these patients are rare. In contrast, for those who live in endemic areas and sustain repeated bites by infected mosquitos, worm burdens are higher and lymphatics are more likely to become obstructed leading to chronic lymphedema. Lymphedema occurs more commonly in the lower extremities but can also involve the upper extremities, breasts in females and scrotum in males. Subsequent skin thickening and fissuring invites recurrent bacterial infection. With time, the lymphedema and skin changes can progress to elephantiasis.

Treatment:
The treatment of choice for active lymphatic filariasis is diethylcarbamazine (DEC) because it is both microfilaricidal and active against the adult worm. Adult worms must be killed in order to prevent relapse. However, DEC is contraindicated in patients with onchocerciasis co-infection and should be used with extreme caution in those with loa loa infections. There is also some evidence that treatment targeting *Wolbachia*, the rickettsial endosymbiont bacteria that lives inside *Wuchereria* and *Brugia* spp., may stop microfilarial production. Due to low prevalence of the disease, DEC is no longer FDA-approved in the United States but can be obtained through the Centers for Disease Control and Prevention. Other therapeutic options include ivermectin (kills only microfilariae), and albendazole (has some macrofilarial activity). If lymphedema is already established, antifilarial medication has not been shown to be of benefit. Instead, management of symptoms includes exercise, elevation and local skin care.

References

1. Ash LP, Orihel TC. *Atlas of Human Parasitology*, 5th ed. Chicago, IL: ASCP Press: 2007.
2. Centers for Disease Control and Prevention, Division of Parasitic Diseases (DPD). *Laboratory Identification of Parasites of Public Concern.* http://www.cdc.gov/dpdx
3. Garcia LS. 2007. *Diagnostic Medical Parasitology*, 5th ed., Washington, DC. ASM Press.
4. Chatterjee S, Nutman TB. "Filarial Nematodes." In *Manual of Clinical Microbiology,* ed. Jorgensen JH et al., 2461-2470. Washington, DC. ASM Press, 2015.

BP-13 Introduction

Thick and thin Giemsa-stained smears were obtained from a 29-year-old medical student with repeated vomiting and fatigue after returning from Kenya. The specimen contained *Plasmodium falciparum*. A response of "*Plasmodium falciparum*" or "*Plasmodium* sp./*Babesia* sp. seen, referred for identification" were considered satisfactory. However, consensus was not reached for parasite identification.

BP-13

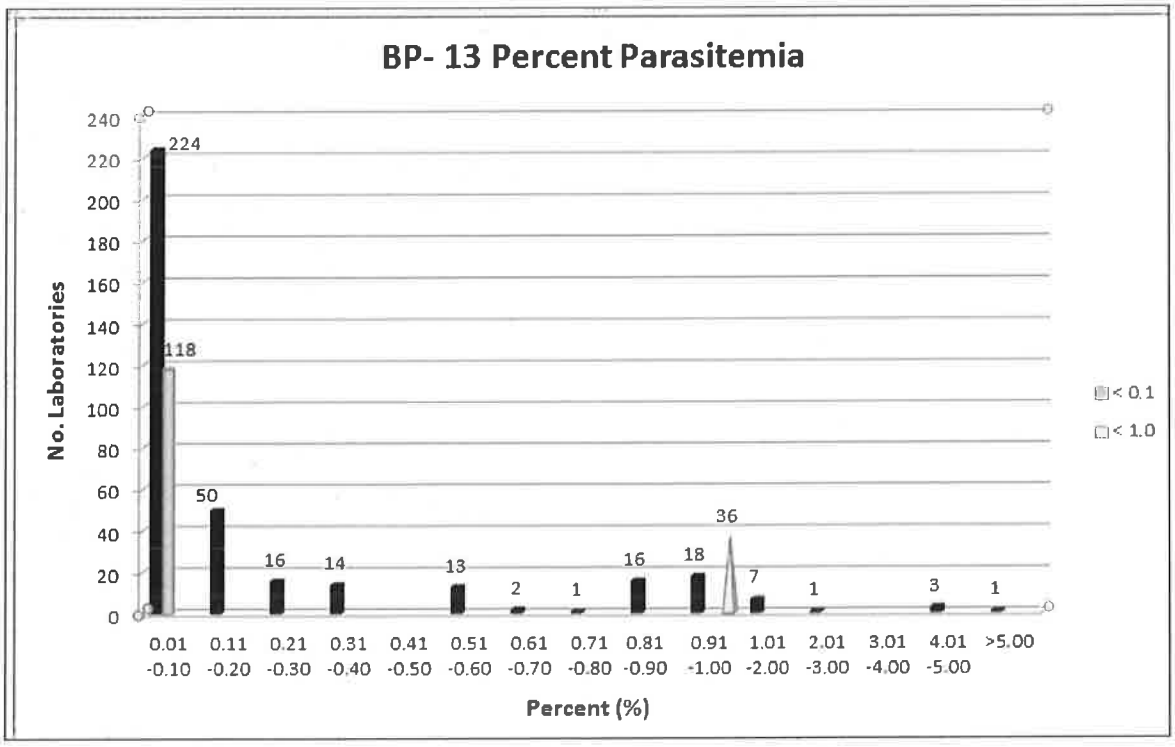
Parasite Identification*	Referees (33) No.	%	Participants (411) No.	%
Plasmodium falciparum	23	69.7	253	61.6
Plasmodium malariae	2	6.1	18	4.4
Plasmodium vivax	2	6.1	35	8.5
Plasmodium sp., not *P. falciparum*, referred for identification	4	12.1	60	14.6
Plasmodium vivax/ovale, NOS	2	6.1	31	7.5

Parasite Screen	Referees (15) No.	%	Participants (776) No.	%
Plasmodium sp./*Babesia* sp. seen, referred for identification	15	100.0	736	94.8

* Parasite identification was not graded due to lack of participant and referee consensus. BP-11 and BP-13 were unique specimens showing differences in percent parasitemia. BP-13 demonstrated a much lower percent parasitemia.

BP-13

If you have identified a *Plasmodium* sp. or *Babesia* sp.: Report percent of infected RBCs seen (number of infected RBCs per 100 red blood cells). (Ungraded)



Discussion

See discussion for BP-11 on page 3.

BP-14 Introduction

A skin lesion slide was obtained from an international traveler with fever and chills. A response of "No parasite(s) seen" or "Specimen screened for blood parasites, no organisms seen" was considered satisfactory. However, consensus was not reached for parasite screen.

BP-14

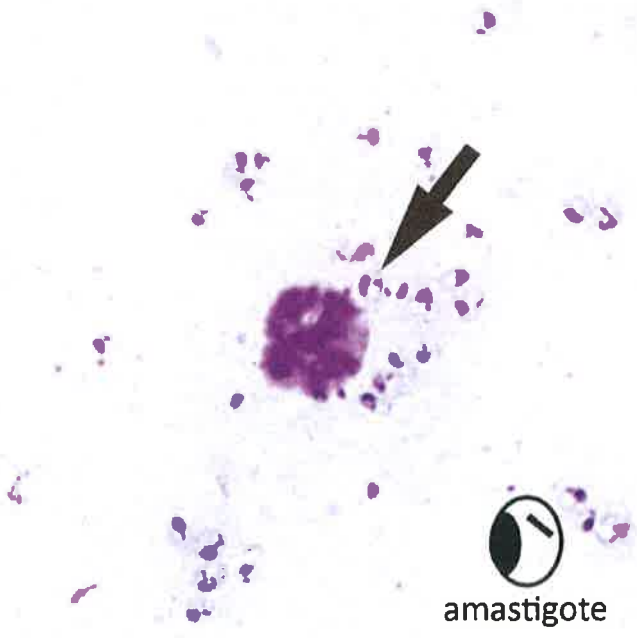
Parasite Identification	Referees (34) No.	%	Participants (401) No.	%
No parasite(s) seen	29	85.3	301	75.1
Leishmania sp.*	5	14.7	79	19.7
Parasite Screen**	**Referees (12) No.**	**%**	**Participants (651) No.**	**%**
Specimen screened for blood parasites, no organisms seen	9	75.0	452	69.4

* The cells seen in this specimen may not have appeared as cells seen in an actual clinical specimen - Scientific Committee Decision Code 30

** Parasite screen was not graded due to lack of participant and referee consensus

Discussion

This challenge was designed to simulate a negative skin squash/touch-prep. Such specimen types are typically submitted for the diagnosis of *Leishmania* amastigotes in the Parasitology laboratory. In order to report a case as being positive for amastigotes, organisms should display **both** a kinetoplast and a nucleus as seen in the image below. It should be noted that amastigotes of *Leishmania* and *Trypanosoma cruzi* are morphologically indistinguishable, although the specimen type, clinical presentation, and travel history will often favor one over the other.



BP-15 Introduction

Thick and thin Giemsa-stained smears were obtained from a 2-year-old adoptee with failure to thrive. The specimen contained *Trypanosoma brucei* (*gambiense* or *rhodesiense*). A response of "*Trypanosoma brucei*", "Blood flagellate, NOS, referred for identification" and "Blood or tissue parasite, not *Plasmodium* sp. or *Babesia* sp., referred for identification" would have been considered satisfactory.

BP-15

Parasite Identification	Referees (34) No.	%	Participants (426) No.	%
Trypanosoma brucei (*gambiense* or *rhodesiense*)	28	82.3	349	81.9
Trypanosoma cruzi	6	17.6	76	17.8
Parasite Screen	**Referees (14) No.**	**%**	**Participants (760) No.**	**%**
Blood flagellate, NOS, referred for identification	14	100.0	680	89.5
Blood or tissue parasite, not *Plasmodium* sp. or *Babesia* sp., referred for identification	-	-	72	9.5

Discussion

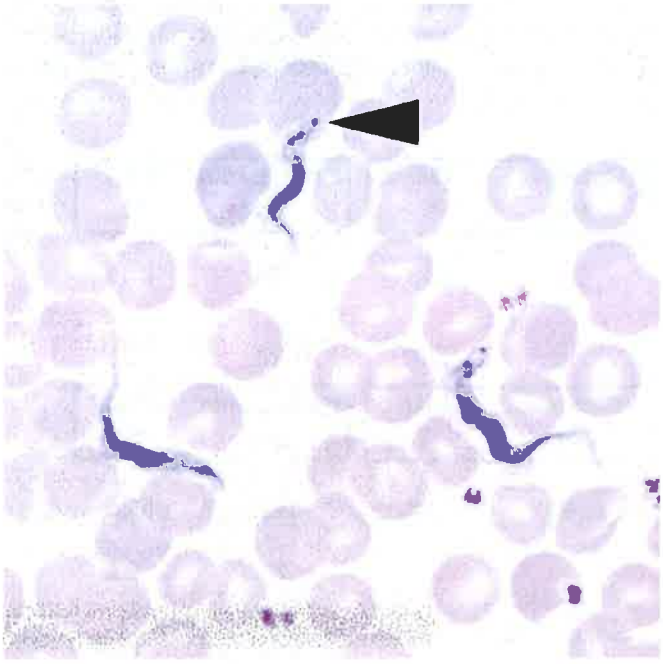
In this challenge, 17.8% of participants misdiagnosed this specimen as *T. cruzi*. Important morphologic features that favor a diagnosis of *T. brucei* over *T. cruzi* include the small kinetoplast and the presence of dividing forms.

Causal Agents:
African trypanosomiasis is caused by two subspecies of *Trypanosoma brucei*, *T. b. gambiense* (West and Central Africa) and *T. b. rhodesiense* (eastern and southeastern Africa). The type subspecies, *T. b. brucei*, does not cause human infection.

Biology and Life Cycle:
Trypanosoma brucei ssp. are transmitted by tsetse flies in the genus *Glossina*. When an infected tsetse fly takes a blood meal, metacyclic trypomastigotes are injected into the bloodstream where they transform into bloodstream trypomastigotes. There are two forms of bloodstream trypomastigotes, slender and stumpy. The slender trypomastigotes multiply by binary fission and perpetuate the blood cycle. Stumpy forms are adapted to be picked up by the tsetse fly vector. Within the midgut of the vector, stumpy forms develop into procyclic forms and multiply by binary fission. After a while, some procyclic forms leave the midgut and migrate via the hemocoel to the salivary glands, where they develop into epimastigote and eventually metacyclic forms. Metacyclic forms are non-dividing and are the infectious stage for the vertebrate host. Unlike with *T.cruzi*, there is no amastigote formation in tissue the human host, although *T. brucei* can cross the blood-brain barrier and cause central nervous system involvement.

Diagnosis:
Diagnosis of *T. brucei* is made by the finding of trypomastigotes in blood, chancre fluid, lymph node aspirates, bone marrow, and CSF. A wet preparation may be examined for motility. Concentration techniques may increase the chances for a morphologic diagnosis, including centrifugation and examination of the buffy coat. Trypomastigotes (the only stage seen in the human host) are 14-33 µm long, have a large central nucleus, a small, terminal kinetoplast at the posterior end (as seen in image below), and a free flagellum leaving the body

anteriorly. In stained blood films, it is possible to find diving forms, something not seen in cases with *T cruzi*. Currently, serologic, molecular, and rapid diagnostic (RDT) tests are not routinely available in the United States.



Clinical Significance:
Human infection with *Trypanosoma brucei* presents with two clinical manifestations. In the first, the parasite is found in the peripheral blood and symptoms include fevers, headaches, malaise, and muscle and joint aches. In the second, parasites cross the blood-brain barrier to involve the central nervous system and can be found in the cerebrospinal fluid. During second stage disease, neurologic symptoms develop and mental status declines, eventually leading to coma and death. Disease progresses at different rates depending on which subspecies is involved, with *T. b. gambiense* having a more chronic, indolent course spanning years while *T. b. rhodesiense* progresses more rapidly over a period months. If left untreated, both forms of African trypanosomiasis are fatal.

Treatment:
All people with trypanosomal infection should be treated. First-line therapy depends on stage of disease and subspecies involved. For *T. b. gambiense* infections, pentamidine isethionate is the drug of choice for first-stage disease while combination therapy with nifurtimox and eflornithine is recommended for second-stage disease. For *T. b. rhodesiense* infections, suramin is the first-line treatment for first-stage disease while melarsoprol is recommended for second-stage disease. These therapies are generally effective yet have varying toxicity profiles. Of note, adverse reactions to melarsoprol can be severe and life-threatening with 5-18% of patients developing an encephalopathic reaction which is fatal in 10-70% of these patients.

References

1. Ash LP, Orihel TC. *Atlas of Human Parasitology*, 5th ed. Chicago, IL: ASCP Press: 2007.
2. Centers for Disease Control and Prevention, Division of Parasitic Diseases (DPD). *Laboratory Identification of Parasites of Public Concern.* http://www.cdc.gov/dpdx
3. Garcia LS. 2007. *Diagnostic Medical Parasitology*, 5th ed., Washington, DC. ASM Press.