Amoebiasis: current status in Australia

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Amoebiasis, a disease caused by the intestinal protozoan parasite Entamoeba histolytica, is the third leading parasitic cause of death in humans after malaria and schistosomiasis. Globally, it is responsible for 40,000–100,000 deaths a year. E. histolytica has a worldwide distribution and is endemic in Australia, with locally acquired disease occurring in Northern Australia (predominantly in Indigenous people) and, recently, in Sydney, among men who have sex with men (MSM). Other high-risk people in Australia include immigrants from countries of high endemicity (eg, India, South-East Asia) and travellers returning from such countries.

The parasite

The genus Entamoeba comprises six species that colonise the human intestinal lumen. E. histolytica (Box 1) was initially thought to be a single species, but isoenzyme and molecular studies have led to the reclassification of E. histolytica into two morphologically identical species: the pathogenic E. histolytica and the non-pathogenic E. dispar. E. moshkovskii, which is morphologically identical to E. histolytica and E. dispar but biochemically and genetically different, has been considered until recently to be primarily a free-living (non-pathogenic) amoeba. The early isolates of E. moshkovskii were free-living forms found in sewage, but human isolates have now been detected in North America, Italy, South Africa, Bangladesh, India, Iran and Australia. The pathogenic role of E. moshkovskii is yet to be adequately defined, but recent studies suggest that infection with this species can cause diarrhoea and other intestinal disorders. As E. moshkovskii is indistinguishable in its cyst and trophozoite forms from E. histolytica and E. dispar, it is not possible to differentiate the three species on the basis of traditional microscopic examination. Consequently, past studies on the prevalence of E. histolytica may be flawed if they did not consider the possible presence of E. dispar and E. moshkovskii.

Only one study has used adequate molecular techniques to determine the true prevalence of E. histolytica, E. dispar and E. moshkovskii in Australia. The study examined 9921 faecal samples submitted from patients with diarrhoea to a large metropolitan hospital in Sydney over a 4-year period. In 177 of the samples (3.0%), cysts and/or trophozoites microscopically resembling E. histolytica/dispar/moshkovskii were detected. Using molecular techniques, five patients were found to be infected with E. histolytica, 63 with E. dispar and 55 with E. moshkovskii. The study showed that, while E. dispar and E. moshkovskii are over 10 times more common, E. histolytica infections are nevertheless endemic in urban areas of Australia.

ABSTRACT

- *Entamoeba histolytica* is one of the most common parasitic infections worldwide, infecting about 50 million people and resulting in 40,000–100,000 deaths a year.
- In Australia, people at risk of infection include immigrants, travellers returning from countries of high endemicity, Indigenous people, and men who have sex with men.
- Clinical manifestations range from asymptomatic carriage to invasive disease. Amoebic colitis and amoebic liver abscesses are the most common invasive manifestations observed in Australia.
- Diagnosis depends on a high index of suspicion and laboratory investigations. Molecular methods (using the polymerase chain reaction) are the most sensitive for identifying and differentiating *Entamoeba* species.
- Treatment should always include a luminal agent to eradicate colonisation, prevent spread and/or reduce the risk of invasive disease. Medical therapy can successfully cure invasive disease, including amoebic liver abscesses.
2 Possible complications of Entamoeba histolytica infection

Intestinal disease
Pulmonary disease
Perianal disease with fistula formation
Extraintestinal disease
Liver abscess rupture:
  • Pleuropulmonary disease (the most common complication, especially with right lobe abscesses)
  • Intraperitoneal rupture
  • Pericardial rupture (uncommon, usually associated with left lobe abscesses)
Other manifestations:
  • Cerebral amoebiasis
  • Genitourinary amoebiasis (rare, more common in women than men, eg. vaginal fistulas)
  • Primary cutaneous amoebiasis
  • Amoeboma

Groups at high risk of E. histolytica infection

High-risk groups include immigrants from countries of high endemity, travellers to such countries, Indigenous Australians, and MSM.

Rates of asymptomatic carriage in immigrants to the United States are reported to be between 17% and 33%. In contrast, immigrants to Australia have a documented carriage rate of about 2%. In travellers returning to Australia, the carriage rate is unknown, and would vary greatly depending on the countries visited. International data reflect similar asymptomatic carriage rates (0.3%–10%), but differences between the countries visited and/or precautions taken need to be considered.

A number of cases of amoebiasis have been reported from northern Australia in Indigenous and non-Indigenous patients from both remote and urban regions. While most cases predate the recognition of three separate species of Entamoeba, several recent cases have definitively identified E. histolytica as the cause of locally acquired invasive amoebiasis. The true prevalence of E. histolytica in northern Australian populations is unknown, as no studies using molecular techniques have been undertaken.

The prevalence of intestinal parasites in MSM is known to be higher than in heterosexual men. The possible explanation for this correlation is the practice of oral–anal sex. As E. histolytica is transmitted via the faecal–oral route, MSM are at increased risk of being infected. In Taiwan and Japan, E. histolytica has emerged as an important parasitic infection among MSM. This has also been documented in several Australian studies. Clinicians should be aware of this association, as MSM are at risk of invasive disease.

Clinical presentation

Asymptomatic patients

In most E. histolytica infections, symptoms are absent or very mild and represent "non-invasive" disease. Generally, asymptomatic patients never become symptomatic. They may excrete cysts for a long period of time, but the majority of these patients will clear the infection within 12 months. Patients with confirmed E. histolytica infection, even if they are asymptomatic, should be treated to eliminate the organism and prevent further transmission.

Symptomatic patients

Invasive amoebiasis

Only a small proportion of people infected with E. histolytica will go on to develop clinical disease, with the most frequent manifestations being amoebic colitis and amoebic liver abscess. As amoebiasis is not a notifiable illness, the rate of invasive disease in Australia is unknown. Furthermore, as cases become more common (there were three cases at St Vincent's Hospital, Sydney, in 2006), their "newsworthiness" diminishes, with the result that further reports on such cases are less likely to be published.

Amoebic colitis

Patients with amoebic colitis present with a history of several weeks of abdominal pain and diarrhea (usually characterised by blood, mucus and faecal leukocytosis). Fever occurs in less than 40% of patients. Toxic megacolon is a complication in about 0.5% of patients, and may be a consequence of inappropriate corticosteroid treatment. Steroids play an important role in the management of inflammatory bowel disease. As amoebic colitis is

3 Diagnostic modalities

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Presentation</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Commercial kits available in Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopy*</td>
<td></td>
<td></td>
<td></td>
<td>Permanent stain kits available from Cytodent Australia Pty Ltd (Adelaide, SA) and Provence Laboratory Supplies Pty Ltd (Sydney, NSW)</td>
</tr>
<tr>
<td>Feces</td>
<td>Colitis</td>
<td>30%–50%</td>
<td>10%–50%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
<tr>
<td>Liver aspirate</td>
<td>Liver abscess</td>
<td>&lt;5% (rarely seen)</td>
<td>100%</td>
<td>Entamoeba CEUSA Path kit (Cellabs, Sydney, NSW) and E. histolytica II kit (Techlab Inc, Blacksburg, Va, USA)</td>
</tr>
<tr>
<td>Serology</td>
<td>Colitis</td>
<td>40%–60%</td>
<td>90%</td>
<td>Not commercially available</td>
</tr>
<tr>
<td></td>
<td>Liver abscess</td>
<td>95%</td>
<td>98%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
<tr>
<td>Antigen detection</td>
<td>Colitis</td>
<td>80%–99%</td>
<td>86%–98%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
<tr>
<td></td>
<td>Liver abscess</td>
<td>90%–100%</td>
<td>90%–100%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
<tr>
<td>Polymerase chain reaction</td>
<td>Colitis</td>
<td>80%–100%</td>
<td>85%–100%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
<tr>
<td></td>
<td>Liver abscess</td>
<td>80%–100%</td>
<td>90%–100%</td>
<td>Novegost Entamoeba histolytica IgG kit (IHA) (Dade Behring, Deerfield, IL, USA)</td>
</tr>
</tbody>
</table>

* Sensitivities are based on use of permanent stains. Sensitivity of microscopy increases when colonoscopy specimens are used.
**4 Diagnosis of amoebiasis**

**A: Intestinal amoebiasis**

Symptoms:
- Absent/non-specific, or
- Diarrhoea/dysentery

History/risk factors (eg, traveller, immigrant, MSM)

E. coli (E. histolytica/dispars/moshkovskii) in stool

- Positive
- Negative

Confirmation using enzyme immunoassay/molecular tests

Consider sigmoidoscopy in high-risk patient with compatible clinical picture

- Positive
- Negative

Treatment (Box 5)

Diagnosis of amoebiasis unlikely

**B: Amoebic liver abscess**

Symptoms:
- Fever
- Right upper quadrant pain/tenderness

History/risk factors (eg, traveller, immigrant, MSM)

Seiology

- Positive
- Negative

Treatment (Box 5)

If alternative diagnoses excluded, amoebic liver abscess still possible

MSM = men who have sex with men.

Amoebic liver abscess is the most common extraintestinal manifestation of amoebiasis seen in Australia and has been reported in travellers and immigrants. Patients usually present within 3 months of contracting the disease. However, prolonged latency may occur. Clinical symptoms include fever (in 87%–100% of patients), malaise, and right upper quadrant pain with no concomitant colitis (in 60%–70% of patients). Biochemical parameters are usually abnormal but non-specific. Imaging studies (ultrasound, computed tomography and magnetic resonance imaging) have excellent sensitivity for detection of liver abscesses but are unable to distinguish amoebic liver abscesses from pyogenic abscesses or necrotic tumours. E. histolytica cysts and trophozoites are rarely found in the stools of patients with liver abscess, the majority of patients having no intestinal symptoms or history of dysentery. Therefore, the diagnosis depends on a high index of suspicion (eg, consistent travel history) and appropriate laboratory investigations. Complications associated with abscess rupture are dependent on which body cavity they rupture into. Such complications are rare, with the last documented case in Australia being in 1977. Mortality rates are low (<1%) with appropriate treatment.

**Diagnostic techniques**

The diagnosis of amoebiasis is confirmed either by detecting E. histolytica parasites in the faeces or by detecting an antibody response to the parasite in the serum (Box 3, Box 4).

**Detection of E. histolytica in the faeces**

Microscopy relies on identifying E. histolytica cysts and trophozoites. It is performed on fixed faecal smears stained with a permanent stain (iron haematoxylin or trichrome). Infection with E. histolytica cannot be diagnosed on the basis of morphological criteria alone. Historically, the presence of haemophagous trophozoites (trophozoites containing ingested red blood cells) was regarded as suggestive of E. histolytica infection. However, this finding is rarely seen and has been found to occur also in non-pathogenic species.

Unfortunately, many laboratories do not routinely perform permanent stains as they are time-consuming and laborious and require specific expertise. Multiple samples are required, as the organism is shed intermittently and the sensitivity of microscopy is poor. As E. histolytica is morphologically identical to the non-pathogenic species E. dispar and E. moshkovski, microscopy can not distinguish between the three species, and further testing is required for speciation.

**Colonoscopy and flexible sigmoidoscopy are useful in patients with acute colitis when E. histolytica infection is suspected on clinical grounds but not detected in stool samples.** Examinations of scrapings and biopsies for trophozoites have a higher sensitivity than examinations of faecal specimens.

**Culture techniques** have been used to detect E. histolytica for close to 100 years. However, culture methods are time-consuming, laborious and often unrewarding, with a sensitivity of only about 50%. Further testing is required for speciation. Thus, culture methods are restricted to specialised parasitology research laboratories.

**Antigen detection methods** use monoclonal antibodies directed against various proteins of E. histolytica. Some of these assays determine the presence of the E. histolytica/dispars/moshkovskii group, while others are specific for E. histolytica only. The two stool
CLINICAL UPDATE

5 Treatment of amoebiasis

Asymptomatic carriage (treat with luminal amoebicide ONLY)
- Oral paromomycin* 500 mg three times daily for 7 days

Invasive disease (treat with tissue amoebicide and luminal amoebicide)
- Oral metronidazole 750-800 mg three times daily for 6-10 days OR
- Oral tinidazole 2 g once daily for 2-3 days (up to 10 days) and oral paromomycin* 500 mg three times daily for 7 days

Liver abscess (treat with tissue amoebicide and luminal amoebicide)
- Oral or intravenous metronidazole 750-800 mg three times daily for 14 days OR
- Oral tinidazole 2 g once daily for 5 days and oral paromomycin* 500 mg three times daily for 7 days

* Paromomycin is now the luminal agent of choice (Special Access Scheme approval is required). Alternative luminal agents are diloxanide furoate (however, production was ceased in 2003 and the drug is unavailable in Australia) and ozoquino (availability in Australia is limited).

The role of surgery is generally limited to patients with complications of invasive disease. Surgical drainage is generally unnecessary in amoebic liver abscess, as cure can be achieved with medical therapy alone.1,2,26 The role of radionucleated guided percutaneous therapeutic aspiration in uncomplicated amoebic liver abscess is controversial,26 but it has been shown to be of some clinical benefit in patients with large abscesses. Aspiration should be considered in patients with an uncertain diagnosis, lack of response to medical therapy (persistent fever > 4 days), and large abscesses at risk of rupturing (especially left lobe abscesses, as these may rupture into the pericardial space).

Conclusion

Clinicians should be aware of E. histolytica infection, as it is present in Australia as both a local and imported disease. High-risk patients include immigrants, Indigenous people and MSM. Without the appropriate clinical suspicion and laboratory investigations, the diagnosis may be missed, with possible harmful consequences.

Competing interests

None identified.

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References


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