



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Editorial

An approach to the correct interpretation of intestinal spirochaetosis

Una aproximación a la correcta interpretación de la espiroquetosis intestinal



Human intestinal spirochaetosis (HIS) refers to the colonization of the luminal surface of the colon and rectum by anaerobic spirochaetes from the genus *Brachyspira*.^{1,2} *Brachyspira aalborgi*, the most common species associated with HIS, was first identified in the stool of a patient from Aalborg, Denmark in 1982.³ Other species such as *Brachyspira pilosicoli* may also be involved.

First descriptions of HIS date back to 1719, when Anton Van Leeuwenhoek noticed moving spiral particles in his own stools, which he denominated “animalcules”. Thereupon, in the late 19th century, during a devastating cholera epidemic in Naples, Theodor Escherich observed spirochaetes in feces from both symptomatic and asymptomatic individuals.⁴ It was not until 1967, when Harland and Lee coined the term HIS to describe the intestinal colonization of a 64-year-old male patient who suffered from persistent diarrhea for the previous three years.^{5,6} Spirochaetes were identified in small fragments of a biopsy specimen observed under light and electron microscopy.

Since then, HIS gained recognition as a clinical entity in the late 20th century as more studies focused on the association between these bacteria and gastrointestinal symptoms. Initial reports described the presence of spirochaetes in the colonic mucosa of both symptomatic and asymptomatic individuals and numerous cases of HIS from low, middle, and high-income countries have been reported.^{7–10}

In veterinary medicine, spirochaetes represent a well-known cause of diarrhea, and they have been isolated from the feces of swine, poultry, dogs, migratory waterbirds, cats, opossum, non-human primates, and guinea pigs.¹¹ In developing countries, contaminated water and infected animals are primary sources of HIS, whereas in high-income countries homosexual intercourses constitute a common risk factor.

The improvement in microbiological techniques allowed the identification of the various species of spirochaetes that comprise the genus *Brachyspira*. Among the nine identified *Brachyspira* species, only *B. aalborgi* and *B. pilosicoli* are known to colonize humans.

HIS is found during the histological examination of a biopsy from a patient in whom a colonoscopy has been performed. Endoscopic examinations represent the mainstay procedure for the study of chronic diarrhea. Macroscopically, the appearance of the lumen of

colonoscopic studies is usually normal, though not specific findings such as mucosal ulcerations or the presence polyps may also be observed.¹⁷

The gold standard diagnosis of HIS is routine hematoxylin and eosin staining of colonic and rectal mucosa biopsies. Spirochaetes are observed on the luminal surface of enterocytes as a dense, bluish haze caused by a palisade-like arrangement of bacteria that gives the impression of a tight ‘false brush border’.¹³ Definite confirmation with Warthin-Starry silver impregnation or Dieterle stain is highly recommended, as it is immunohistochemistry. Molecular techniques, such as polymerase chain reaction (PCR), have also become valuable tools for the detection and identification of specific *Brachyspira* species. The article presented in this issue of the journal by De Gea-Grela et al. includes a series of 36 patients with a definitive diagnosis of HIS, supported by the histological finding plus a positive semi-nested PCR of *Brachyspira* spp. in feces.¹⁰ Culture methods to identify and characterize spirochaetes in biopsy specimens have also been used.¹⁴

HIS is often asymptomatic, and many individuals may not experience any noticeable symptoms. In some cases, particularly in immunocompromised individuals, HIS has been associated with non-specific gastrointestinal symptoms, such as chronic diarrhea. Its clinical spectrum is broad, ranging from asymptomatic colonization and incidental diagnosis to symptoms such as abdominal pain, meteorism, watery diarrhea, constipation, or bleeding. In the series by De Gea-Grela et al., 47% of the cases had chronic diarrhea, 28% had abdominal pain and 31% had rectal tenesmus; this last symptom might be possibly related to proctitis, which was present in 25% of cases. Concomitant STIs of the rectal mucosa, such as *Chlamydia trachomatis* or *Neisseria gonorrhoeae* infections could have been responsible of proctitis, as it has not been referred as a common symptom in HIS.

Nonetheless, the pathogenic ability of spirochaetes is still under debate, where a portion of authors consider HIS unthreatening. However, in a recent systematic review and meta-analysis HIS was significantly associated with diarrhea and abdominal pain.¹² Different authors suggest that, occasionally, the microorganism may gain pathogenicity and become invasive.^{14,15}

The link between HIS and immunosuppression, especially in patients with HIV infection, has traditionally been observed and reported, though HIS may also occur in patients with a competent

DOI of original article: <https://doi.org/10.1016/j.eimc.2023.03.001>

<https://doi.org/10.1016/j.eimc.2024.03.005>

2529-993X / © 2024 Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica. Published by Elsevier España, S.L.U. All rights reserved.

immune status. Additionally, the fact of a significantly higher prevalence of HIS amongst men who have sex with men (MSM) raises the question of whether HIS should be considered a sexually transmitted infection (STI).^{10,16–18} Unprotected sexual intercourses and participation in sexualized drug use or chemsex sessions facilitate the transmission of STIs as well as other gastrointestinal pathogens such as *Giardia duodenalis*, *Escherichia coli*, *Shigella*, *Blastocystis*, and others.¹⁹ Besides, *Entamoeba histolytica*, *Giardia duodenalis* as well as other protozoa may cause symptoms that resemble those produced by symptomatic HIS.

Ongoing research has aimed to understand the clinical significance of intestinal spirochaetosis. Some studies explored potential associations between HIS and inflammatory bowel disease and colonic polyps,¹² but no significant association has been established.

Since HIS and STIs or gastrointestinal infections may be present concomitantly, one of the main questions to be solved is whether spirochaetes are responsible for the whole spectrum of symptoms of the patient or not. Thus, when evaluating patients with eventual symptomatic HIS, screening for intestinal protozoa, bacteria and STIs is crucial for an accurate diagnosis to minimize confounding factors and avoid unnecessary invasive procedures.¹⁹

Treatment is not recommended in asymptomatic patients, and a wait-and-see attitude may be followed. However, a full course of metronidazole or tetracycline has been described as an effective treatment for anaerobic spirochaetes in symptomatic patients.

In symptomatic and immunocompromised patients, the treatment of choice is metronidazole 500 mg three times a day.²⁰ Metronidazole is a key component in the pharmaceutical arsenal for the treatment of anaerobic infections, exerting rapid bactericidal effect with a killing rate proportional to the drug concentration. An alternative treatment is doxycycline, which inhibits protein synthesis by binding with the 30S ribosomal subunit of susceptible bacteria.

Response to treatment differs from person to person; while certain patients may achieve complete remission of diarrhea and gastrointestinal symptoms, others may show no improvement even after confirmation of eradication in subsequent histologic exams.

To date, intestinal spirochaetosis remains a relatively rare and often benign condition. It is not widely recognized as a major clinical concern in the absence of specific symptoms or complications.

The history of intestinal spirochaetosis reflects the progression of scientific understanding, diagnostic capabilities, and clinical awareness of this condition over the last decades. Further research may contribute to provide additional insights into its clinical relevance and optimal management.

In conclusion, the presence of HIS in biopsies does not necessarily imply illness and the interpretation of intestinal spirochaetosis should be individualized. It is often asymptomatic, but when symptoms are present, they are generally non-specific, and it is strongly recommended to rule out other causative agents of diarrhea, especially in individuals at higher risk for STIs and other gastrointestinal pathogens transmitted through the oral-anal route. Additionally, in certain populations such as immunocompromised hosts, it may warrant attention and appropriate management.

References

- Körner M, Gebbers JO. Clinical significance of human intestinal spirochetosis – a morphologic approach. *Infection*. 2003;31:341–9.
- Tsinganou E, Gebbers JO. Human intestinal spirochetosis – a review. *Ger Med Sci*. 2010;8:Doc01.
- Hovind-Hougen K, Birch-Andersen A, Henrik-Nielsen R, Orholm M, Pedersen JO, Teglbjaerg PS, et al. Intestinal spirochetosis: morphological characterization and cultivation of the spirochete *Brachyspira aalborgi* gen. nov., sp. nov. *J Clin Microbiol*. 1982;16:1127–36.
- Escherich T. Klinisch-therapeutische Beobachtungen aus der Cholera. *Epidemie in Neapel. Ärztliche Intelligenzblatt*. 1884;31:561–4.
- Harland WA, Lee FD. Intestinal spirochaetosis. *Br Med J*. 1967;3:718–9.
- Lee FD, Kraszewski A, Gordon J, Howie JGR, Mcseveney D, Harland WA. Intestinal spirochaetosis. *Gut*. 1971;12:126–33.
- Lee JI, Hampson DJ. Intestinal spirochaetes colonizing aborigines from communities in the remote north of Western Australia. *Epidemiol Infect*. 1992;109:133–41.
- Barrett SP. Intestinal spirochaetes in a Gulf Arab population. *Epidemiol Infect*. 1990;104:261–6.
- Margawani KR, Robertson ID, Brooke CJ, Hampson DJ. Prevalence, risk factors and molecular epidemiology of *Brachyspira pilosicoli* in humans on the island of Bali, Indonesia. *J Med Microbiol*. 2004;53 Pt 4:325–32.
- De Gea-Grela A, Maldonado-Barrueco A, Cabañuz C, et al. Espiroquetosis intestinal humana como entidad asociada a infecciones de transmisión sexual. *Enferm Infecc Microbiol Clin*. 2024;42:232–6.
- Duhamel GE. Comparative pathology and pathogenesis of naturally acquired and experimentally induced colonic spirochetosis. *Anim Health Res Rev*. 2001;2:3–17.
- Fan K, Eslick GD, Nair PM, Burns GL, Walker MM, Hoedt EC, et al. Human intestinal spirochetosis, irritable bowel syndrome, and colonic polyps: a systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2022;37:1222–34.
- Van Mook W, Koek G, Van Der Ven A, et al. Human intestinal spirochaetosis: any clinical significance? *Eur J Gastroenterol Hepatol*. 2004;16:83–7.
- Brooke CJ, Margawani KR, Pearson AK, Riley TV, Robertson ID, Hampson DJ. Evaluation of blood culture systems for detection of the intestinal spirochaete *Brachyspira (Serpulina) pilosicoli* in human blood. *J Med Microbiol*. 2000;49:1031–6.
- Kanavaki S, Mantadakis E, Thomakos N, Pefanis A, Matsiota-Bernard P, Karabela S, et al. *Brachyspira (Serpulina) pilosicoli* spirochetemia in an immunocompromised patient. *Infection*. 2002;30:175–7.
- Jones MJ, Miller JN, Lance Georgel AW. Microbiological and biochemical characterization of spirochetes isolated from the feces of homosexual males. *J Clin Microbiol*. 1986;24:1071–4. <http://dx.doi.org/10.1128/jcm.24.6.1071-1074.1986>.
- Law CLH, Grierson JM, Stevens SMB, Law C. Rectal spirochaetosis in homosexual men: the association with sexual practices, HIV infection and enteric flora. *Genitourin Med*. 1994;70:26–9. <http://dx.doi.org/10.1136/sti.70.1.26>.
- Rabuszko L, Chessell C, Llewellyn C, Richardson D. Factors and presenting symptoms associated with intestinal spirochaetosis in men who have sex with men: a systematic review. *J Eur Acad Dermatol Venereol*. 2023;1–7.
- Pérez-Tanoira R, Tamarit MDP, Montaña AMV, Carmena D, Köster P, Górgolas M, et al. Increased prevalence of symptomatic human intestinal spirochetosis in MSM with high-risk sexual behavior in a cohort of 165 individuals. *Trop Med Infect Dis*. 2023;8:250.
- Tong YT, Mamoun Y. Intestinal spirochaetosis: case series and review of the literature. *Ann Clin Lab Sci*. 2020;50:386–90.

Laura Prieto Pérez^{a,b}, Miguel Górgolas Hernández-Mora^{a,b,*}

^a División de Enfermedades Infecciosas, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

^b Departamento de Medicina, Universidad Autónoma de Madrid, Spain

* Corresponding author.

E-mail address: mgorgolas@fdj.es (M. Górgolas Hernández-Mora).