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humans, Whipple’s disease is rare. The higher prevalence of T. whipplei in certain populations is not associated with a higher prevalence of Whipple’s disease, sug gesting that only people with as yet unknown predisposing factors will develop this condition. Epidemiology There is asymptomatic carriage of T. whipplei, mainly in faeces, the prevalence of which depends on age, exposure, and geograph ical area. The prevalence of T. whipplei in faeces of European healthy adults has been estimated to be 3%, but faecal carriage is higher among populations with poor personal hygiene, such as homeless people, those in contact with faeces (e.g. sewer workers), and among the relatives of patients or chronic carriers in Europe (Table 15.10.6.1). The prevalence of asymptomatic carriage is higher in Africa and Asia than in Europe. The typical patient with classic Whipple’s disease is a Caucasian male of approximately 50 years of age. A national population-based study in the USA indicated a prevalence of 9.8 cases of Whipple’s disease per million people. Clinical features T. whipplei is involved in chronic infections and has also been re cently associated with acute infections such as gastroenteritis, pneu monia, and bacteraemia. Chronic infections include disseminated Whipple’s disease and localized infections. Classic Whipple’s disease is a systemic disease as T. whipplei is not only systematically detected in the intestinal tract, but the bac terium can be also observed in most of the organs: it can be detected in the blood, saliva, faeces, cerebrospinal fluid (even in the lack of neurological manifestations), brain, heart, eyes, and skin (even if no cutaneous abnormality is observed). No systemic involvement is ob served in chronic localized infections (saliva and faeces are mostly negative for T. whipplei), and the potential for relapse is not the same as in classic Whipple’s disease. These several differences suggest a Table 15.10.6.1 Prevalence of T. whipplei in faeces of healthy people depending on age, exposure, and geographical area Population Young children in France French general adult population Underground sewer workers in Europe Homeless people in France Adults in rural Gabon Adults in rural Senegal Relatives of T. whipplei patients or carriers (France) Children in rural Gabon Children in rural Senegal and Laos Prevalence <1% 3% ~12% 17.4% 38% ~48%

 different susceptibility to T. whipplei between patients with classic Whipple’s disease and those with chronic localized infections, al though it has been recently shown that classic Whipple’s disease can appear among people who have been diagnosed and treated, years before, for localized T. whipplei endocarditis. Classic Whipple’s disease The typical patient, a Caucasian male (in approximately 80% of cases) of middle age (about 50 years old), initially complains of intermittent arthralgias (75%). Patients suffer also from chronic digestive troubles with diarrhoea (75%) and/or weight loss (85%). The diagnosis is often made after the appearance of clinical manifestations such as weight loss or digestive troubles in patients treated with immuno suppressive therapy (about 4 months) for rheumatological disease, including corticosteroids and tumour necrosis factor antagonists. T. whipplei can nearly affect all organs and lead to many manifest ations. Patients can complain of nonspecific symptoms such as fever, fatigue, abdominal pain, cough, and myalgia. Lymphadenopathy, mainly mediastinal and mesenteric, can be detected. Various neuro logical manifestations can mimic almost all neurological diseases, the most frequently observed presentations include cognitive changes, ranging from memory impairment to dementia, as well as psychiatric disorder (e.g. personality changes, depression). Endocarditis, peri carditis, and myocarditis also occur in patients with classic Whipple’s disease. Eye and lung involvements are observed. Skin pigmentation was reported for many years, but now seems to be observed less fre quently, which may be attributable to earlier diagnosis. Chronic localized Whipple’s disease Many chronic localized T. whipplei infections without systemic and histological intestinal involvement have been observed. Endocarditis Endocarditis is the most frequent localized manifestation, the typical patient being an afebrile Caucasian male of

approximately 60 years old, exhibiting mainly cardiac insufficiency or (less frequently) em bolic events. Localized T. whipplei endocarditis can transform sec ondarily into classic Whipple’s disease. Neurological The most common neurological symptoms in localized T. whipplei encephalitis are cognitive impairment, ataxia, and supranuclear ophthalmoplegia. An association of dementia, cerebellar ataxia, and weight gain has also been described. Ocular Chronic uveitis can be unilateral or bilateral, and posterior, inter mediate, and/or anterior conditions that are resistant to or even worsened by corticosteroids. A correlation between the diagnosis of T. whipplei uveitis and a history of ocular surgery has been observed, suggesting potential nosocomial transmission of the bacterium or that use of corticosteroids during ocular surgery could activate la tent ocular infection. Differential diagnosis Whipple’s disease is in the differential diagnosis for a wide spectrum of diseases including inflammatory rheumatic diseases, diseases causing malabsorption, sarcoidosis, lymphoma, Addison’s disease, as well as a variety of neurological diseases. Clinical investigation The best molecular tool currently available to detect T. whipplei is a specific quantitative real-time PCR test targeting repeated sequences of the bacterium. Rigorous criteria must be applied to interpret mo lecular assays, including the systematic use of positive and negative controls, and verification of the quality of DNA extracts. (a) (b) Fig. 15.10.6.1 Detection of Whipple’s disease by PAS staining and immunohistochemical analysis. PAS staining of a duodenal-biopsy specimen shows reduced villous architecture and macrophages (magenta) in the lamina propria (a). Immunohistochemical staining with polyclonal rabbit anti-T. whipplei antibody (at a dilution of 1:2000) and Mayer’s haemalum counterstaining show T. whipplei in a duodenal-biopsy specimen (brown) (b). Images courtesy of Hubert Lepidi.

Revision #1
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