Table 1 Prevalence of colorectal neoplasia in liver-transplant recipients, compared with selected studies from the literature in average-risk populations

	LTR	de Jong <i>et al</i> ^f	Strul <i>et al</i> ^f	Imperiale <i>et al</i> ^g	Soon <i>et al</i> ^f	Lieberman <i>et al</i> ^f	Schoenfeld <i>et al</i> ^o
Number of patients	92	342	1177	906	4859	3121	1463
All neoplasia (%)	21.7	6.1	20.9	11.0	18.9	37.5	20.4
Advanced neoplasia (%)	8.7	2.0	6.3	3.5	4.6	10.5	4.9
Ratio advanced/all neoplasia	0.40	0.33	0.30	0.32	0.24	0.28	0.24
Advanced neoplasia (%)							
<50 years	8.6	1.0	1.0	3.5	3.0	—	—
50–59 years	12.9	8.3	2.9	—	3.8	5.7	3.3

LTR, liver transplant recipients.

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Visceral leishmaniasis causes fever and decompensation in patients with cirrhosis

Infections and fever due to bacterial infections are well-known complications of liver cirrhosis, and often trigger decompensation and death.¹ Visceral leishmaniasis (VL), a protozoan infection endemic in the Mediterranean area, causes a febrile disease, the clinical and laboratory features (splenomegaly, pancytopenia, reduced serum albumin and increased γ -globulin concentrations) of which largely overlap with those of cirrhosis.^{2–3} Although the areas where VL is endemic coincide with areas where the prevalence of cirrhosis is high, no study has described VL in patients with cirrhosis.

During a 12-year period, all patients with cirrhosis admitted for decompensation and fever lasting more than 1 week, unresponsive to broad-spectrum antibiotics, underwent diagnostic procedures for VL. For each case diagnosed as VL, three consecutive cases of bacterial infection observed in the same period were enrolled. Cirrhosis was defined by liver histology or clinical, laboratory, ultrasonographic and endoscopic findings. VL was diagnosed by the immunofluorescent-specific antibody test (IFAT) and confirmed by the identification of *Leishmania* from Giemsa-stained smears of bone marrow or spleen

aspirates.⁴ Bacterial infections were diagnosed by standard clinical procedures. All patients were followed up for 6 months after diagnosis.

In total, 11 patients with VL and 33 with bacterial infections were enrolled. Table 1 summarises the main clinical and laboratory data at presentation.

Patients with VL received standard-dose liposomal-amphotericin B (l-AmB; nine cases)⁵ or meglumine antimoniate (two cases). Fever resolved within 72 h in patients receiving l-AmB and after 7 days in those receiving antimonials. No severe drug-related adverse reaction was recorded. Improvement in haematological parameters and reduction in liver enzymes, spleen diameter and anti-*Leishmania* antibody titre were recorded during the follow-up period in all patients with VL. The Child–Pugh class rapidly and stably improved in patients with VL (fig 1). The mortality was 17% for patients with bacterial infections and 0% for patients with VL.

VL was a troublesome diagnosis in patients with cirrhosis, as shown by the time from the onset of symptoms and diagnosis. This delay resulted from failure to consider this unusual diagnosis and was responsible for a progressive worsening in liver function. Indeed, once VL was cured, cirrhosis reverted to Child class A in all but one patient.

Apart from a long-lasting fever, there were no clear-cut clues to suspect VL. Some significant differences in the presentation data between VL and bacterial infections were found (table 1), but their clinical use is hampered by a substantial overlap of the laboratory values between VL and bacterial infection cases. Only white blood cell and γ -globulin data are of potential value.

IFAT serology is a sensitive and specific test for the diagnosis of VL in patients with cirrhosis; notably, IFAT was negative in all patients with bacterial infections and in 51 additional patients with cirrhosis without fever (table 1). In a series including 16 patients with

cirrhosis, a strip test using *Leishmania* K39 antigen was sensitive and specific.⁶ The diagnostic flow-chart for patients with cirrhosis with unexplained fever should include the anti-VL antibody test, thus avoiding the routine use of invasive diagnostic techniques. Once the diagnosis is established, l-AmB is a safe and effective treatment.

The study was not designed to assess whether the patients with cirrhosis are at a higher risk of acquiring VL than those without cirrhosis. Assuming that there are 10 000–20 000 patients with cirrhosis per year in our area, the annual incidence of VL among patients with cirrhosis was 0.5–1/10 000—that is, 8–17-fold higher than the incidence (0.06/10 000) among the adult population in the same area ($p < 0.001$).^{7–9}

Overall, the study underlines the need to consider this unusual cause of fever and decompensation in patients with cirrhosis when they are living in or have travelled through an area endemic with VL.

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Figure 1 Child–Pugh class before and after treatment for visceral leishmaniasis.

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Table 1 Main demographic, clinical and laboratory features at admission in patients with cirrhosis with visceral leishmaniasis or bacterial infections

Parameter	VL cases (n = 11)	Bacterial infections (n = 33)	p Value
Age (years)	60 (51 to 62)	67 (64 to 71)	0.002
Time from onset of symptoms (days)	60 (47 to 120)	4 (2.5 to 5)	<0.001
Fever (°C)	38.5 (38 to 39)	37.2 (36.5 to 37.8)	0.004
Spleen size* (cm)	17 (15 to 19)	15 (13.8 to 16.6)	0.04
Child to Pugh C (%)	2 (18)	6 (18)	NS
Child to Pugh B (%)	5 (45)	14 (42)	NS
Creatinine (mg/dl)	0.9 (0.85 to 1.05)	0.89 (0.70 to 1.2)	NS
AST (U/l)	100 (35.5 to 183.5)	65 (39 to 120)	NS
Bilirubin (mg/dl)	1.2 (0.84 to 2.01)	2.49 (1.57 to 3.58)	0.004
Haemoglobin (g/dl)	10.3 (9.2 to 10.9)	12.4 (10.8 to 13.6)	0.003
White blood cells ($\times 10^3$)	2.9 (2.10 to 3.45)	5.8 (4.2 to 8.0)	0.001
Platelets ($\times 10^3$)	88 (80 to 96.5)	78 (56 to 105)	NS
γ -Globulin concentration (g/dl)	3.5 (3.2 to 4.4)	1.93 (1.61 to 2.52)	<0.001
Erythrocyte sedimentation rate (mm/h)	105 (94 to 110)	28 (20 to 49)	0.005
Number positive for anti-Leishmania antibodies†	11	0.00	<0.001

Quantitative data are expressed as median (interquartile range) and compared using the Mann to Whitney U test. Fisher's exact test was used to compare qualitative variables.

*As measured by ultrasonographic examination.

†Anti-Leishmania antibodies were negative in 51 additional consecutive patients with cirrhosis without infections and γ -globulins above 2.5 g/dl.

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Magnifying videoendoscopic findings of Peyer's patches in the terminal ileum of Crohn's disease

It has been reported that Crohn's disease initially occurs as tiny aphthoid lesions at the sites of lymphoid follicles in the gastrointestinal tract.^{1–3} The follicle-associated epithelium (FAE) of the gut-associated lymphoid tissues such as Peyer's patches (PPs)^{3–4} is a single layer of epithelial cells covering each follicle and forms a dome between the surrounding villi.^{3–4} Endoscopic observation of PPs in patients with Crohn's disease has rarely been performed in clinical settings.^{1–3, 5–6}

A total of seven patients with active Crohn's disease and 19 age- and sex-matched healthy controls were enrolled. Chromoendoscopy was carried out with crystal violet and/or indigo carmine to identify PPs. The FAE on the domes of PPs was examined by magnifying endoscopy. The macroscopic appearance of PPs was classified into two categories, a nodular or convolute elevation pattern (E type, fig 1A) and a flat pattern (F type, fig 1B), corresponding to lymphoid follicle and lymphocyte aggregation types, respectively, as described by Fujikura *et al.*⁷ E-type PPs are associated with definite lymphoid follicles and abundant lymphoid hyperplasia, whereas F-type PPs consist of aggregated lymphocytes and reticulum cells, which were loosely mixed together.⁷ Two endoscopic biopsy specimens taken from the domes of PPs were subjected to histopathological analysis and scanning electron microscopy.³ All patients gave their written informed consent after approval by the university ethics committee.

The seven patients with Crohn's disease (four men and three women) had a mean age of 26 years (range 16–42 years). Six patients had minimal lesions including small ulcers and erosions within the PPs. There were 11 E-type and 8 F-type PPs in the control group, whereas all the PPs in patients with Crohn's disease

were classified as F type. On magnifying chromoscopy, most of the domes within PPs in controls rose into a little mound and were surrounded by dense villi (fig 2A). However, flat, distorted domes, surrounded by scattered villi (fig 2B), were identified in six patients with Crohn's disease. Repeat endoscopy in remission stage after total parental nutrition or enteral feeding with an elemental diet showed that the irregularity of domes improved in four of the six patients with Crohn's disease, accompanied by densely surrounding villi, albeit the appearance of the PPs remained of E type. A non-caseous epithelioid granuloma was histopathologically seen in six of seven patients. On electron microscopy, M cells were seen on the domes in all cases.

PPs of Crohn's disease were exclusively categorised as F type, whereas E type was predominant in the age- and sex-matched controls. On observation by magnifying endoscopy, most patients with Crohn's disease had irregularly even domes surrounded by sparse villi. Initial lesions of Crohn's disease are postulated to be aphthous erosions of the domes in PPs,⁶ and we identified some erosions on the domes' FAE. Taken together, the F-type PPs in Crohn's disease can reflect the irregularly affected domes with few covering villi. Thus, the FAE of patients with active Crohn's

Figure 1 Chromoendoscopic view with a magnifying videocolonoscope (Olympus CF-240ZI, indigo carmine and crystal violet for (A) and (B), respectively). Nodular elevation of Peyer's patches (E type) and flat Peyer's patches (F type) for (A) and (B), respectively.