

Synovial fluid samples were cultured to isolate *Y. enterocolitica* on *Yersinia* selective agar (Oxoid, Basingstoke, UK) and examined with a Hynzel Counter HC-333 in order to determine the count of synovial leukocytes.

Arthritis was defined as a visible joint swelling and evaluated by an increase in joint diameter and by determination of synovial exudative cell infiltration.

The results (Table 1) showed that the acute phase (1–7 days postinfection) of *Y. enterocolitica* 0:3 experimental arthritis was related to the presence of bacteria within the joints. Bacteria grown at 25°C were detected in the joints up to the seventh day postinfection, and the synovial fluid response to these bacteria during this period showed an infiltration with leukocytes ranging from 3.1×10^3 to 1.28×10^4 /mL. In the early phase (1–3 days postinfection) the polymorphonuclear leukocytes prevailed, in contrast to the later dominance of mononuclear cells. The incidence of swollen joints was greatest during the first week of the experiment.

In contrast, bacteria grown at 37°C were found only on the first day postinfection and the experimental parameters (joint swelling and number of synovial exudative cells) were slightly increased.

Of interest was the maintenance of the chronic inflammatory reaction after disappearance of viable bacteria in both experimental groups.

These data support the hypothesis of some authors [2,7] that it is not viable bacteria but some bacterial structures (e.g. lipopolysaccharide) that could persist in joints and trigger reactive arthritis. Of special interest are differences in surface cell structures expressed at 37°C and at temperatures below 30°C that affect the

pathogenicity of *Y. enterocolitica* 0:3. The acute arthritis induced by *Y. enterocolitica* 0:3 grown at 25°C developed more intensively than that induced by *Y. enterocolitica* 0:3 grown at 37°C. Therefore, the experimental rat model of arthritis caused by *Y. enterocolitica* 0:3 confirmed the importance of temperature regulation of yersinia pathogenic properties and their role in induction of reactive arthritis.

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Kidney and pancreas transplantation: postoperative infectious complications

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End-stage renal disease of the diabetic patient is an accepted indication for renal transplantation. To achieve insulin independence, a combined kidney-pancreas transplantation can be carried out [1]. However, the complication rate for this surgery is still high, particularly with regard to infections [2-5]. We conducted a retrospective study to analyze the postoperative infectious complications of the first seven combined kidney-pancreas grafts carried out at the Geneva University Hospital.

During the surgical intervention, the kidney was placed in the left iliac fossa and the pancreas contralaterally. A duodenocystectomy drained the exocrine pancreatic secretion into the urinary bladder [6,7]. Immunosuppression therapy included corticosteroids (methylprednisolone 1 mg/kg per day IV decreasing, then prednisone), rabbit polyclonal anti-lymphocyte immunoglobulins (5 mg/kg per day IV), azathioprine (5 mg/kg per day IV), and, from the fifth postoperative day, cyclosporin A (4 mg/kg per day IV). Rejection episodes were treated by supplementation of steroids, together with mono- or polyclonal antibody administration. In case of non-response or failure of the above, FK506 was utilized [8]. Ceftriaxone (2 g/day IV) and metronidazole (3 × 500 mg/day IV) were commenced intraoperatively and continued for 48 h. Selective digestive decontamination (SDD; polymyxin B (30 mg), neomycin (250 mg), vancomycin (250 mg) and 100 000 IU of mycostatin) of the oropharynx and the digestive tract was referred every 4 h, starting after orotracheal intubation, and was continued until 10 days after oral nutrition had been resumed. Prophylaxis against cytomegalovirus (CMV) with gancyclovir (2 × 5 mg/kg per day IV) for 14 days was given to a preoperative CMV-negative recipient and a positive donor. The same CMV prophylaxis was administered in cases of rejection. Routine microbiological surveillance cultures (respiratory secretions, blood, urine, abdominal drainage fluids) were performed three times a week; additional cultures were carried out when infection was clinically suspected. In cases of new, unexplained fever (>38.5°C), at least two blood cultures were drawn. Tests for viral infections, i.e. CMV early antigen in blood, urine or sputum were performed once a week.

An infectious episode was defined as the association of compatible clinical signs, symptoms, laboratory tests and a microbiological pathogen recovered from a normally sterile body site and the introduction of an antimicrobial regimen directed against the incriminated microorganism. Bloodstream infection required the presence of clinical signs of sepsis and the isolation of microorganisms such as *Staphylococcus aureus*, Gram-negative bacteria or *Candida* species in at least one

blood culture. For other pathogens, at least two positive blood cultures, or one positive blood culture associated with a documented primary infection site, were required. Pneumonia was diagnosed according to clinical signs and symptoms (fever, cough, dyspnea), the appearance of a new infiltrate on chest radiography and heavy growth of organisms in purulent tracheal secretions or bronchoalveolar lavage fluid. These samples were examined after Gram-staining for the detection and quantification of leukocytes and organisms. The recovery of *Pneumocystis carinii* in bronchoalveolar lavage together with new infiltrates on chest X-ray defined *Pneumocystis carinii* pneumonia. Diagnosis of peritonitis required clinical signs, the presence of leukocytes (>100 white blood cells per high-power field) and positive cultures in peritoneal fluid obtained by percutaneous puncture or during surgery. An abscess was defined as a localized collection of purulent fluid, with typical clinical findings and positive microbiological cultures, confirmed by computerized tomography or laparotomy. The diagnosis of urinary tract infection required the isolation of at least 10⁵ microorganisms/mL once, or 10⁵ yeast/mL on two occasions, associated with at least two of the following: dysuria; pollakiuria; and/or pyuria (10 white blood cells per high-power field). A wound infection was defined as an infection occurring at an incision site within 30 days after surgery involving the skin, subcutaneous tissue, or muscle located above fascial layer. The diagnosis of fungal infection was based on either: (1) positive blood culture, or (2) isolation of fungi from an abdominal sample with evidence of peritonitis or an abdominal abscess. CMV infection was confirmed by seroconversion of CMV-specific IgG and IgM in a previously sero-negative patient (primary infection), or by detection of a significant rise (more than four dilutions) in CMV IgG antibodies with or without detectable CMV IgM antibodies (secondary infection or reactivation). Leuko-cytes from peripheral blood cocultured with human embryogenic lung fibroblasts for 6 weeks and showing a cytopathogenic effect confirmed CMV infection in some cases. CMV disease was diagnosed when CMV infection was temporally associated with: (1) gastro-enteritis—upper or lower gastrointestinal symptoms with CMV detected in biopsy material from the gastrointestinal tract; (2) hepatitis—abnormal liver function tests in the absence of bacterial or fungal infection and/or transplant rejection, with CMV detected on liver biopsy by virologic and/or histologic techniques; (3) pneumonitis—pulmonary chest symptoms and/or a typical chest radiographic pattern, lack of clinical response to antibiotics and evidence of CMV in bronchoalveolar lavage fluids.

Table 1 Postoperative infectious episodes per patient and infection site

Patient no.	Days after TX	Site	Bacteria/Fungus/Virus
1	10	Urine	<i>Klebsiella pneumoniae</i>
	46	Urine	<i>K. pneumoniae</i>
	176	Urine and abdomen	<i>Torulopsis glabrata</i>
2	6	Urine	<i>Candida albicans</i>
	21	Urine	<i>C. albicans</i>
	28	Urine	<i>K. pneumoniae</i>
	49	Urine	<i>C. albicans</i>
3	9	Abdomen	<i>Staphylococcus epidermidis</i>
	34	Abdomen	<i>S. epidermidis</i> + <i>C. albicans</i>
	59	Urine	<i>C. albicans</i>
4	20	Urine	<i>Enterococcus</i>
	38	Urine	<i>Enterococcus</i> + <i>S. epidermidis</i>
5	11	Blood	CMV
	97	Urine	<i>Pseudomonas aeruginosa</i> + <i>S. epidermidis</i> + CMV
6			No infection
7 ^a	8	Abdomen	<i>S. epidermidis</i> + <i>C. albicans</i>
	8	Blood	<i>C. albicans</i>
	35	Blood	<i>C. albicans</i>

^adied; Tx, transplantation.

The seven patients spent a total of 559 days in hospital, i.e. 170 days in the surgical intensive care unit and 389 in the visceral surgery clinic. One patient died of infection on the 69th post-transplant day. The bacteriologic sampling consisted of 887 bacteriologic specimens, including 346 blood cultures. There were 17 infectious episodes, 13 caused by one micro-organism and four polymicrobial (Table 1). Only one patient had no infectious episodes. Only three infection sites were involved. The urinary tract was the most often infected site, followed by the peritoneal cavity and the blood.

Fungal infections were responsible for 41% of all infectious episodes, and *Candida* spp. were responsible for 89% of these. Two episodes of arterial mycotic aneurysm at the site of the arterial anastomosis used to rearterialize the homograft were diagnosed. Thirty-five per cent of all infectious episodes were caused by bacteria, and coagulase-negative staphylococci were the most frequent bacteria isolated. Both bacteria and fungi or bacteria and CMV grew in 12% and 6% of the cultures, respectively. CMV (6% of all infections) was isolated twice in the blood and once in the urine, at different periods in the same patient. One case of protozoal infection (toxoplasmosis) was diagnosed post mortem.

Using predefined infection definitions, our retrospective analysis of kidney-pancreatic transplantation

shows that six of seven patients developed one or more severe infections, all of them originating from either the urinary tract or the peritoneal cavity. Studies on similar patient populations showed an infection rate between 56% and 90% of the patients with predominant urinary tract infection (mean 76%) [3,9-15]. An interesting element is that fungal infections developed in more than 25% of the transplanted patients, and this infection rate is not altered by either SDD with antifungal prophylaxis or systemic administration of antifungal therapy [2,5,16-19]. This tendency is confirmed by Sollinger, who described a large series of kidney-pancreas transplants and concluded that 'fungal infection occurs with significant frequency despite aggressive antifungal therapy and prophylaxis' [20]. The prevalence of urinary tract infections is not surprising and many factors may contribute. For example, surgically induced mucosal trauma and sutures, pancreatic exocrine secretions in the bladder, which raise the urine pH and may induce an inflammatory reaction, and the prolonged use of bladder catheter, are factors contributing to bacterial growth [21]. Such a high infection rate when exocrine pancreatic bladder drainage is used has stimulated renewed interest in enteric drainage [22,23] and has encouraged the development of alternative techniques such as the transplantation of Langerhans islets [24].

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In vitro activity of linezolid and eperezolid against anaerobic bacteria

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