

Transfusion-Transmitted *Yersinia enterocolitica* Sepsis

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Bacterial sepsis has become the most frequent infectious complication of transfusion. Although *Yersinia enterocolitica* is a common enteropathogen usually causing relatively mild disease, it is nevertheless a prominent cause of life-threatening post-transfusion infection. To gain a better understanding of the clinical presentation and prognosis of this rare occurrence, we performed a systematic and detailed review of 55 published cases, which we present here after a description of the mechanisms underlying the contamination of red blood cell preparations by *Y. enterocolitica*. The symptoms are rapid-onset septic shock sometimes heralded by atypical symptoms, such as explosive diarrhea, with an overall fatality rate of 54.5%. Although the pathophysiology involves transfusion of preformed bacterial endotoxin, timely administration of effective antibiotics seems to improve the prognosis. Increased vigilance of the blood supply could help mitigate this transfusion hazard, although cost-effective strategies are difficult to define for this highly serious but infrequent event.

Systematic screening of blood donations for the presence of blood-borne viruses in recent years has resulted in a dramatic decrease of viral infections after blood transfusion [1, 2], and bacterial sepsis has become the most frequent infectious complication of transfusion in developed countries [2–4].

Red blood cell (RBC) preparations are the most frequently transfused blood component [5–7]. Although contamination of platelet concentrates are predominantly attributable to Gram-positive bacteria from the skin flora, contaminations of RBC products involve primarily Gram-negative organisms (mostly members of the *Enterobacteriaceae*) of endogenous origin [2, 7, 8]. *Yersinia enterocolitica*, associated with ~46% of documented cases of clinical sepsis from contaminated RBCs [9], is paradigmatic of such Gram-negative agents transmitted by blood infusion and triggering severe sepsis and septic shock. Nevertheless, this is an infrequent event, with estimates of 1 *Y. enterocolitica* post-transfusion sepsis (PTS)/10⁵–10⁷ transfused RBC units [5, 10].

In our study, we analyzed all available literature descriptions of *Y. enterocolitica* PTS to (1) delineate the salient clinical

features, (2) determine the fatality rate and its evolution over time, (3) identify predictive factors of fatal outcome, and (4) gain insights about appropriate therapeutic and preventive measures. We first present a review of *Y. enterocolitica* epidemiology and physiology and the mechanisms of blood product contamination by this bacterial species.

The published cases were identified through searches of the IsiWeb of Science, Isi Current contents, PubMed and Science Direct databases, and the bibliographic databank maintained by the French Yersinia Reference Center, where older case reports that are no longer accessible through standard bibliographic searches could be found. Articles in English, French, and German were included. All cases with culture-proven transmission of *Y. enterocolitica* through transfusion of contaminated blood product (49 cases) were included, as were probable cases defined by the association of signs of sepsis appearing during or shortly after transfusion and either positive results of culture of patient blood shortly after transfusion (5 cases), and/or evidence that the donor was experiencing *Y. enterocolitica* bacteremia at the time of blood obtainment, such as digestive symptoms or positive serum antibody titers to *Y. enterocolitica* (4 cases). Statistical analyses were performed using the Prism, version 5, for Mac software (GraphPad Software), using Student's *t* test or Mann–Whitney *U* test, depending on the distribution of the data, to compare continuous variables and the χ^2 or Fisher's exact test, depending on the population size, to compare categorical variables.

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YERSINIA ENTEROCOLITICA: A COMMON ENTEROPATHOGEN

Y. enterocolitica is an enteropathogen, member of the *Enterobacteriaceae*, transmitted through the feco-oral route, and generally responsible for self-subsiding febrile diarrhea and abdominal pain [11–13]. Sometimes, the infection involves mesenteric lymph nodes and presents as a pseudoappendicular syndrome, which can lead to the removal of a healthy appendix [12, 13]. The disease strikes predominantly children and young adults, and, in this age group, it represents the second or third most frequent bacterial diarrhea [12–14]. The incubation period after ingestion of the organism is 1–11 days, with diarrhea lasting from a few days to a few weeks (average of 2 weeks), and pathogenic yersiniae are recovered from the stool during, on average, at a mean of 6 weeks [15–17]. Septicemic and systemic infections due to *Y. enterocolitica* are frequently associated with an underlying condition, such as diabetes, alcoholism, malnutrition, or iron overload or with desferrioxamine or immunosuppressive therapy [11–13].

Y. enterocolitica is widespread worldwide, with a predominance for cold and temperate regions. Six *Y. enterocolitica* biotypes have been recognized: 1A, 1B, and 2–5. All but the 1A biotype are pathogenic. The *Y. enterocolitica* strains are also characterized by O-Ag serotypes. The most common pathogenic bioserotypes worldwide are 4/O:3 and 2/O:9 [18]. *Y. enterocolitica* is psychrotrophic and can multiply, albeit slowly, at temperatures as low as -2°C [19, 20].

MECHANISMS OF BLOOD PRODUCT CONTAMINATION BY YERSINIA ENTEROCOLITICA

Contamination of Blood Products Occurs Before Blood Collection and Processing

Blood unit contamination by *Y. enterocolitica*, which is not part of the skin flora, is thought to result from an asymptomatic bacteremia in the donor at the time of blood sample obtainment [21, 22]. A normal bowel movement seems to produce a 10% incidence of transient bacteremia from the gut flora, particularly in the postprandial period, and intestinal infections may increase this percentage [23, 24]. The bacteremic episodes are asymptomatic because the bacterial densities transferred to the bloodstream are low (ie, generally <10 colonies per mL of blood) [21, 25]. It has been suggested that *Yersinia* bacteremia might be more frequent and/or longer-lasting in hypersideremic patients; therefore, special care should be given to donor screening in the Mediterranean countries because of the high incidence of chronically transfused thalassemic patients in those areas [26]. Several studies have revealed an ability of prestorage leukodepletion procedures, such as buffy coat

removal or use of leukocyte-reduction filters, to reduce the growth of *Y. enterocolitica* in experimentally inoculated RBC suspensions [27, 28]. This indicates that *Y. enterocolitica* associates with white blood cells in the artificially infected blood and, perhaps, in naturally contaminated donated blood.

***Yersinia enterocolitica* Can Readily Multiply in Blood Units**

Because it is psychrotrophic, *Y. enterocolitica* is not inhibited at whole blood and RBC concentrate storage temperatures ($2\text{--}6^{\circ}\text{C}$). Bacterial multiplication is supported by glucose and adenine (energy and carbon sources for *Yersinia*), which are part of the anticoagulant-preservative and additive solutions; RBC concentrates are prepared at a pH of 7.3, which is within the optimal range (7–8) for *Y. enterocolitica* growth [13].

Although growth of virulent *Y. enterocolitica* strains is inhibited in calcium-free media, this effect only appears at temperatures $>30^{\circ}\text{C}$ [29], and *Y. enterocolitica* strains therefore survive in stored blood anticoagulated by citrate chelation.

Experimental inoculations of whole blood or RBC bags with low *Y. enterocolitica* inocula ($0.1\text{--}10$ cfu/mL) regularly yielded bacterial concentrations of $\geq 10^8\text{--}10^{10}$ cfu/mL after 3–5 weeks of incubation at 4°C [24, 25, 30–32]. In these experiments, a characteristic lag phase of 1–3 weeks was noted, suggesting that *Y. enterocolitica* active growth starts when enough iron has been released in the bag by RBC hemolysis. The release of free hemin results solely from spontaneous hemolysis, because *Y. enterocolitica* has no known hemolytic activity.

Severe Sepsis and Septic Shock Results From Massive Delivery of Bacterial Toxins in the Bloodstream

Severe sepsis and septic shock are the consequences of a generalized (systemic) and uncontrolled inflammatory response to the infection, rather than the direct effect of microorganisms [33–38]. In Gram-negative bacteria, the lipid A moiety of the cell wall component lipopolysaccharide is a powerful activator of macrophages and is believed to be the principal initiator of septic shock, although other bacterial components are also likely to be involved [33–35, 38]. When transfused blood products are heavily contaminated by Gram-negative bacteria, large amounts of microorganisms and endotoxin are introduced into the patient circulatory system, leading to a rapidly developing severe sepsis or septic shock.

PRESENTATION OF THE PUBLISHED CASES OF YERSINIA ENTEROCOLITICA POST-TRANSFUSION SEPSIS

Fifty-five descriptions of *Y. enterocolitica* PTS published during 1975–2007 were analyzed. The details of the individual case reports are presented in Table 1 (online only).

Characteristics of the patient population are summarized in Table 1. The overall fatality rate was 54.5%. Symptoms, usually

of sudden onset, started during or at the end of transfusion of the contaminated unit in 41 cases (79%). The reported time from transfusion to first symptoms was always ≤ 3 hours. The most frequently reported symptoms were fever, rigors (together, they were noted in 90% of the cases), and hypotension. Although fever and hypotension were sometimes delayed, rigors, digestive symptoms, chest and/or back pain, and cutaneous symptoms were described as alerting symptoms, initially isolated, or among the first manifestations of the *Y. enterocolitica* PTS. In 3 cases (Table 1; online only), the patients were anaesthetized during transfusion, and in 2 cases (Table 1; online only), they were already septic before the transfusion was started. These circumstances seem to have obscured the clinical onset of *Y. enterocolitica* PTS and delayed the diagnosis. Four of these 5 patients died.

Older age was significantly associated with fatal outcome (Table 1). A short time from transfusion to symptoms was most often reported in cases resulting in fatalities. However, the fact that the symptoms started during transfusion, with prompt discontinuation of the procedure, or after it was completed did not significantly influence the outcome, nor did the amount of transfused blood for those patients who did not receive the entire contaminated unit. Fever was, surprisingly, significantly higher in recipients who subsequently recovered from *Y. enterocolitica* PTS (Table 1). However, hypotension (associated or not with other signs of shock) and digestive symptoms were more frequently described in fatal cases. The main indications for transfusion were cancer related, specified as such in 21 cases. Patients in this subgroup had a higher fatality rate (61.9%) than did patients transfused for other reasons (50%), but the difference was not statistically significant ($P = .39$).

Fifty-four of the implicated blood products were RBC components (Table 2 and Supplementary Table 2) that were a mean of 25.6 days old, with no difference between the groups of fatal and nonfatal cases. With the exception of units for 2 recipients who recovered, all RBC units were ≥ 14 days old, and 4–5-week-old RBC units transmitted as many *Y. enterocolitica* infections as 2–3- and 3–4-week-old units together (Figure 1). Units > 5 weeks old were possibly less frequently transfused during the study period, because storage periods of 6 weeks were not in use before suitable additive solutions in RBC preparations became available [39, 40]. Six of the patients with *Y. enterocolitica* PTS had received autologous RBC donated before a planned surgical procedure (Table 2 and Table 1; online only).

Y. enterocolitica was isolated from all blood bags subjected to culture but only once from the attached tubing (Table 3 and Table 1; online only). The biotype frequencies reflected the overall biotype distribution of pathogenic *Y. enterocolitica* strains [18].

The antibiotic regimens given to the patients are shown in Table 1 (online only), and the first-line and pre-PTS antibiotic treatments are summarized in Table 4. *Y. enterocolitica* strains belonging to the most common bioserotypes 4/O:3 and 2/O:9 produce β -lactamases, which render them resistant to penicillins, aminopenicillins, and first-generation cephalosporins in vitro [41]. These strains exhibit variable sensitivity to second-generation cephalosporins in vitro, but third-generation cephalosporins are usually active, as are trimethoprim-sulfamethoxazole and fluoroquinolones [42–44]. In vivo, in spite of some reports of *Y. enterocolitica* infection that failed to respond to a third-generation cephalosporin [44–46], a retrospective study of 43 *Y. enterocolitica* septicemia cases found that including a third-generation cephalosporin in the antibiotic treatment was associated with a 85% recovery rate, whereas benzylpenicillins, aminopenicillins, first-generation cephalosporins, and amoxicillin-clavulanate were not effective [47]. Trimethoprim-sulfamethoxazole, tetracycline, and fluoroquinolones also show consistent in vivo activity and are antibiotics of choice for severe *Y. enterocolitica* infection [18, 44, 47]. Although the latter antimicrobial agents were rarely prescribed in *Y. enterocolitica* PTS cases, 13 patients were given a third-generation cephalosporin shortly before the contaminating transfusion or as a first-line response to the ensuing sepsis. In this subgroup, the recovery rate was 69%, whereas it was 41% among the patients who had received only other antibiotics (Table 4). The 3 patients who were already receiving a third-generation cephalosporin at the time of the contaminating transfusion survived (Table 4). Thus, although the pathophysiology of post-transfusion septic shock involves preformed toxic bacterial products, the data suggest that promptly administered anti-*Y. enterocolitica* antibiotics can combat the effects of the transfusion of massive numbers of the bacterium. This could explain in part why the overall fatality rate among the *Y. enterocolitica* PTS case reports decreased from 62% for cases published before 1991 to 46% among cases published later (Tables 1 and 2; online only).

Characteristics of the implicated donors are listed and summarized in Table 2 (online only) and Table 5. Twenty-three donors (51%) had experienced gastrointestinal symptoms, in most cases, at donation or during the preceding month. Of 14 donor stool cultures performed at various times after the transfusion accident, only 4 yielded a *Y. enterocolitica* strain of the same (bio)serotype as the strain isolated from the corresponding transfused blood. A majority (89.5%) of the donors had serum antibodies reacting to the contaminating strain or to reference strains of the same serotype. The serologic test results were sometimes positive for extended periods up to 18 months after donation. In 9 cases, donors already had, at donation, circulating *Y. enterocolitica*-specific antibodies that were detected retrospectively in blood products derived from that donation.

Table 1. Characteristics of the Recipient Population

Characteristics	Fatal cases (N = 30)	Nonfatal cases (N = 25)	P
Sex			
Male	15 (50%)	12 (48%)	.90
Female	14 (47%)	12 (48%)	
Unknown	1 (3%)	1 (2%)	
Age			
Mean; range (years)	59.2; 13–85	42.1; 11–87	< .01
≤60 years	10	18	< .005
>60 years	18	6	
Unknown	2	1	
Indication for transfusion			
Cancer related	13 (43%)	8 (32%)	.92
Orthopedic surgery	5 (17%)	5 (20%)	
Vascular surgery	3 (10%)	4 (16%)	
OB-GYN indications	2 (7%)	2 (8%)	
Other	6 (20%)	5 (20%)	
Unknown	1 (3%)	1 (4%)	
Start of symptoms			
After transfusion ^a	7 (23%)	6 (24%)	> .99
During transfusion	21 (70%)	18 (72%)	
Mean vol. transfused (ml)	120 (N = 11)	120 (N = 7)	.96
Unknown/NA	2 (7%)	1 (4%)	
Symptoms			
Fever	23 (77%)	20 (80%)	.95
Mean temperature (°C)	38.9	39.6	< .01
Hypotension or shock	26 (87%)	16 (64%)	.02
Rigors, chills	16 (53%)	17 (68%)	.33
Digestive symptoms ^b	15 (50%)	5 (20%)	.02
Organ failure			
Renal failure	9 (30%)	4 (16%)	.20
DIVC	8 (27%)	6 (24%)	.76
Lethargy or confusion	8 (27%)	5 (20%)	.52
Respiratory distress	4 (13%)	5 (20%)	.72
Hepatic failure	3 (10%)	0	.24
MOF (≥2 organ failures)	14 (47%)	8 (32%)	.27
Others			
Chest and back pain	2	3	
Normal or slightly elevated blood pressure		3	
Hemoptysis		1	
Rhabdomyolysis		1	
Slight urticaria		1	
Wheezing		1	
Shock w/o tachycardia	1		
Exanthemic rash	1		
Sweating	1		
Unknown	1	0	

NOTE. OB-GYN, obstetrics and gynecology; NA, not applicable; MOF, multiple organ failure.

^a Median time from transfusion end to symptoms among fatal cases = 10 minutes (range = 0–180 minutes). In 3 cases of the non-fatal group, the interval between end of transfusion and symptoms was specified: ~ 0, 60 minutes, and 180 minutes.

^b Digestive symptoms were as follows: nausea, vomiting, diarrhea (sometimes explosive), and abdominal pain.

Table 2. Implicated Blood Product

	Fatal cases (N = 30)	Nonfatal cases (N = 25)
Red blood cells	30	24
Autologous	1	5
Mean age of RBC units in days	25.42* (N = 26)	25.89* (N = 19)
Pooled platelets	0	1
Age		Unknown

NOTE. *P = .87

DISCUSSION

The present work is a systematic review of 55 published cases of *Y. enterocolitica* PTS. The results represent a comprehensive summary of the currently accessible information regarding the clinical description and circumstances surrounding this rare accident. Cumulative data show that the signs of *Y. enterocolitica* PTS are generally of sudden onset appearing during or shortly after (≤ 3 hours) the transfusion, sometimes heralded by digestive symptoms, chest and/or back pain, or even cutaneous rashes. Particular attentiveness is required for blood recipients who are anesthetized or already septic when transfusion is initiated, because these circumstances can blur the clinical onset of *Y. enterocolitica* PTS. Bacterial cultures must be performed on the main bag and not on the test-tubing. This literature review also provides evidence that antimicrobials effective against *Y. enterocolitica* should be promptly administered to the patient as soon as a transmission-associated sepsis is suspected.

Y. enterocolitica contamination of donated blood samples is believed to be primarily intrinsically occurring in the donor from an intestinal source before blood harvesting and processing.

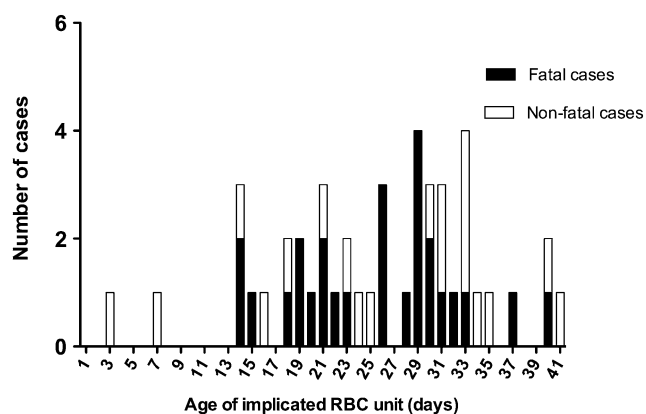


Figure 1. Frequency distribution of *Yersinia enterocolitica* post-transfusion sepsis (PTS) cases according to the age of the implicated red blood cell (RBC) unit. The height of the bars indicates the total number (fatal plus nonfatal) of *Y. enterocolitica* PTS cases caused by RBC units of the corresponding age.

Table 3. Characteristics of the Implicated *Yersinia* Strains

	Fatal cases (N = 29)	Nonfatal cases (N = 25)
Isolated from the following:		
Transfused and patient's blood ^a	22	12
Transfused blood only ^a	6	9
Patient's blood only	1	4
Serotype		
O : 3	16	17
O : 9	6	5
O : 5,27	4	0
O : 20	1	0
O : 1,2,3	0	1
Unknown	2	2

^a The strains were always isolated from the main bag. In one instance the strain was also isolated from the accompanying test-tubing. However, 11 other test-tubings attached to *Y. enterocolitica*-positive RBC bags were negative upon culture.

In support of this view, a majority of the implicated donors had clinical, bacteriological, or serological signs compatible with recent or ongoing *Y. enterocolitica* gastroenteritis at donation. Some blood banking systems defer donors with a recent (from a few weeks to a few months) history of diarrhea or febrile gastroenteritis [3, 48], and this review indicates that deferral of all donors with digestive symptoms on the day of donation or in the preceding month would have avoided at least 18 *Y. enterocolitica* PTS cases (Table 5 and Supplementary Table 2). Several donors indicated no ongoing or recent illness in response to predonation questioning but recalled the symptoms retrospectively during the post-*Y. enterocolitica* PTS investigation, which emphasizes the importance of careful predonation interviewing. At least 4 of 6 autologous donors in the present series (Supplementary Tables 1 and 2) had experienced gastroenteritis within a few days before or after donation, and 2 had seen a physician for the problem. Nevertheless, this fact was overlooked possibly because autologous blood is not perceived as dangerous, although it is as prone as allogeneic blood to bacterial contamination by intrinsic or extrinsic (during blood collection or processing) ways [40]. Two of the autologous donors (Supplementary Table 1) were below the age limit for donating to the general blood supply and, thus, belonged to the age class with the highest prevalence of *Y. enterocolitica* infection. *Yersinia* serologic testing in the donor at donation would have avoided at least 9 PTS occurrences. However, circulating *Yersinia*-specific antibodies can be present for extended periods after recovery from the gastrointestinal infection; thus, such screening would unnecessarily exclude healthy donors. In countries with high *Y. enterocolitica* seroprevalence, this could restrict the blood supply to levels incompatible with the population needs [24]. The data suggest that *Y. enterocolitica* is more frequently transmitted by RBC

Table 4. Antibiotic Treatment

	Fatal cases N = 30	Nonfatal cases N = 25
Ongoing antibiotic treatment ^a		
PEBL ^b	5	1
PEBL + aminoside	1	1
Fluoroquinolone	1	0
Trimethoprim-sulfamethoxazole	0	1
Third-generation cephalosporin	0	1
Third-generation cephalosporin + PEBL	0	1
Third-generation cephalosporin + fluoroquinolone	0	1
Unknown	23	19
Ongoing and/or first-line antibiotic treatment		
None	4	4
PEBL	2	4
PEBL + aminoside	7	3
Fluoroquinolone + aminoside	1	0
Third-generation cephalosporin	1	3
Third-generation cephalosporin + aminoside	2	3
Third-generation cephalosporin + aminoside + PEBL + co-trimoxazole	0	1
Third-generation cephalosporin + fluoroquinolone	1	1
Third-generation cephalosporin + fluoroquinolone + PEBL	0	1
Unknown	12	5

NOTE. ^a Ongoing antibiotic treatments: antibiotic treatments that the patients were already receiving at the time of the contaminating transfusion.

^b PEBL: beta-lactams poorly effective against *Y. enterocolitica* = benzylpenicillin, ampicillin, amoxicillin, amoxicillin/clavulanate, ureidopenicillin, imipenem, first- and second-generation cephalosporins.

units >4 weeks old. However, one-third and more than one-half of *Y. enterocolitica* PTS cases were associated with RBCs <3 and <4 weeks old, respectively, so that reducing the storage time to 4 or even 3 weeks would leave a substantial proportion of *Y. enterocolitica* PTS occurrences.

Because not all cases of *Y. enterocolitica* PTS are recognized or published and the proportion of cases that are reported is likely to vary from country to country [49], this literature review does not provide accurate data for the incidence and geographic distribution of *Y. enterocolitica* PTS at a global level. Nonetheless, estimates were made during the 1990s of 1 *Y. enterocolitica* PTS in 500 000 (United States) and 65 000 (New Zealand) transfused RBC units [10, 50]. These figures, based on published cases and on reports to the US Food and Drug Administration that were required only for fatal complications of transfusion, were probably underestimates. However, subsequent prospective studies and hemovigilance system data yielded incidences that were actually even lower. A nationwide American study identified a single case of *Y. enterocolitica* PTS from 1998 through 2000, when ~24 million RBC units were transfused [5]. The New Zealander hemovigilance system detected only 1 *Y. enterocolitica* PTS among a total of ~470 000 RBC units transfused during 2005–2008 [51]. The French hemovigilance system recorded 11 *Y. enterocolitica* PTS cases per 72×10^6 RBC units delivered during 1994–2003 [52] and none in 15×10^6 RBC units delivered during 2004–2009 [3, 53]. These data

suggest that the transfusion-associated *Yersinia* risk has diminished in some countries since the mid-1990s. This evolution probably results, at least in part, from improved prevention measures, such as universal leukoreduction of blood products [3]. Another nonexclusive possibility is that it represents the receding of a peak in incidence linked to variations in *Y. enterocolitica* epidemiology [50].

Y. enterocolitica PTS is a rare event for which exact incidence can only be estimated by prospective and systematic recording of all occurrences at a multinational scale. This may be possible in the future, thanks to the development of national hemovigilance systems in an increasing number of countries and their coordination into networks [54–56]. Optimized use of these systems could help to identify factors influencing the incidence and/or the outcome of the accident. It is difficult for a severe but rare occurrence, such as *Y. enterocolitica* PTS, to strike the right balance between the cost and expected benefit of screening and preventive measures. The best compromise can vary from country to country depending on the local epidemiology of *Y. enterocolitica* and constraints on the blood supply. It is encouraging that the progressive implementation of an array of fairly simple measures aimed at improving transfusion safety was accompanied by a possible reduction in *Y. enterocolitica* PTS incidence in some countries [3, 5, 51]. However, these measures have not eliminated the risk of *Y. enterocolitica* PTS [49, 51, 52, 57–59] (and Dorothy Dinesh, New-Zealand Blood Service,

Table 5. Characteristics of the Donors

Characteristics	Donors for fatal cases	Donors for nonfatal cases	All donors
Sex			
Male	11	13	24
Female	2	2	4
NS	17	10	27
Age in years: mean, range (N)	46.8 ^a , 19–77 (6)	33.2 ^a , 12–74 (12)	37.8, 12–77 (18)
Gastro-intestinal symptoms			
None	12 ^b	10	22
At donation	2	2	4
≤1 month before donation	8	6	14
1–2 months before donation	0	0	0
2–6 months before donation	2	1	3
>6 months before donation	0	1	1
After donation (interval)	0	1 (11 days)	1
NS	6	4	10
Stool culture			
Positive	2 ^c	2 ^d	4
Negative	10	5	15
NS	18	18	36
Yersinia serology			
Positive ^e	20	14	34 ^e
Negative	2	2	4
NS	8	7	15
NA	0	2 ^f	2 ^f

NOTE. NS, not specified; NA, not applicable.

^a $P = .20$.

^b In one case, there were gastrointestinal symptoms in the family on the day of donation.

^c The co-procultures were done 2 and 6 months after donation. In both cases, the *Yersinia* strain was of the same bioserotype as the strain isolated from the patient's and the transfused blood.

^d In both cases, the co-proculture was done 25 d after donation, and the bioserotype of the strain matched that of the strain isolated from the transfused blood.

^e Thirteen donors were tested at donation: 9 were positive and 4 were negative. Most serology tests (35/51 = 68.6%) were performed between 2 and 8 weeks after donation. In 3 cases, the serology was still positive 12–18 months after donation.

^f In both cases, the donor was also the recipient (autologous blood) and the serology test was done after the contaminating transfusion, which may have been the trigger of the antibody response.

personal communication), and medical personnel must always be alert to relevant symptoms appearing during or shortly after a RBC transfusion.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://www.oxfordjournals.org/our_journals/cid/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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Potential conflicts of interest. All authors: no reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed in the Acknowledgments section.

References

- Klein HG. How safe is blood, really? *Biologicals* **2010**; 38:100–4.
- Stramer SL. Current risks of transfusion-transmitted agents: a review. *Arch Pathol Lab Med* **2007**; 131:702–7.
- Andreu G, Caldani C, Morel C. Reduction of septic transfusion reactions related to bacteria contamination without implementing bacteria detection. *ISBT Science Series* **2008**; 3:124–32.
- Stainsby D, Jones H, Asher D, et al. Serious haards of transfusion: a decade of hemovigilance in the UK. *Transfus Med Rev* **2006**; 20:273–82.
- Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. *Transfusion* **2001**; 41:1493–9.
- Perez P, Salmi LR, Follea G, et al. Determinants of transfusion-associated bacterial contamination: results of the French BACTHEM Case-Control Study. *Transfusion* **2001**; 41:862–72.
- AABB. 2007 National Blood Collection and Utilization Survey report. Available at: <http://www.aabb.org/programs/biovigilance/nbcus/Pages/default.aspx>. Accessed 25 July 2011.

8. Brecher ME, Hay SN. Bacterial contamination of blood components. *Clin Microbiol Rev* **2005**; 18:195–204.
9. Wagner SJ. Transfusion-transmitted bacterial infection: risks, sources and interventions. *Vox Sang* **2004**; 86:157–63.
10. Centers for Disease Control and Prevention. Red blood cell transfusions contaminated with *Yersinia enterocolitica*—United States, 1991–1996, and initiation of a national study to detect bacteria-associated transfusion reactions. *JAMA* **1997**; 278:196–7.
11. Smego RA, Frea J, Koornhof HJ. Yersiniosis I: Microbiological and clinicoepidemiological aspects of plague and non-plague *Yersinia* infections [Review]. *Eur J Clin Microbiol Infect Dis* **1999**; 18:1–15.
12. Carniel E, Autenrieth I, Cornelis G, et al. *Y. enterocolitica* and *Y. pseudotuberculosis*. In: Dworkin MM, Falkow S, Rosenberg E, Schleifer K-H, Stackebrandt E, eds: *The Prokaryotes, a handbook on the biology of bacteria*, Third ed. Vol 6. Singapore: Springer, 2006.
13. Cover TL, Aber RC. *Yersinia enterocolitica*. *New Engl J Med* **1989**; 321:17–24.
14. Petersen AM, Nielsen SV, Meyer D, Ganer P, Ladefoged K. Bacterial gastroenteritis among hospitalized patients in a Danish county, 1991–93. *Scand J Gastroenterol* **1996**; 31:906–11.
15. Marks MI, Pai CH, Lafleur L, Lackman L, Hammerberg O. *Yersinia enterocolitica* gastroenteritis: a prospective study of clinical, bacteriological, and epidemiologic features. *J Pediatr* **1980**; 96:26–31.
16. Grenier B. [*Yersinia enterocolitica* gastroenteritis in children]. *Medicine Et Maladies Infectieuses* **1982**; 12:685–9.
17. Bitzan M, Knapp W, Mauff G, Pulverer G. Significance of *Yersinia enterocolitica* isolates and antibody titers—a prospective study in patients with enteritis and healthy controls under bacteriological, serological, epidemiological and clinical aspects. *Zentralbl Bakteriol Mikrobiol Hyg A* **1983**; 254:78–88.
18. Bottone EJ. *Yersinia enterocolitica*: the charisma continues. *Clin Microbiol Rev* **1997**; 10:257–76.
19. Adams MR, Little CL, Easter MC. Modelling the effect of pH, acidulant and temperature on the growth rate of *Yersinia enterocolitica*. *J Appl Bacteriol* **1991**; 71:65–71.
20. Mollaret HH, Thal E. *Yersinia*. In: Buchanan RE, Gibbons NE, eds. *Bergey's manual of determinative bacteriology*. 8th ed. Baltimore, MD: Williams & Wilkins Co, **1974**; 330–2.
21. Burger R, Gerlich W, Gurtler L, et al. *Yersinia enterocolitica*. *Transfus Med Hemother* **2005**; 32:138–46.
22. Prentice M. Transfusing *Yersinia enterocolitica*. *Br Med J* **1992**; 305:663–4.
23. Brown SE, White SE. *Yersinia enterocolitica* and transfusion-induced septicemia. *Anesth Analg* **1988**; 67:415–7.
24. Stenhouse MA, Milner LV. *Yersinia enterocolitica*. A hazard in blood transfusion. *Transfusion* **1982**; 22:396–8.
25. Bradley RM, Gander RM, Patel SK, Kaplan HS. Inhibitory effect of 0 degree C storage on the proliferation of *Yersinia enterocolitica* in donated blood. *Transfusion* **1997**; 37:691–5.
26. Roussos A, Stambori M, Aggelis P, et al. Transfusion-mediated *Yersinia enterocolitica* septicemia in an adult patient with beta-thalassemia. *Scand J Infect Dis* **2001**; 33:859–60.
27. Hogman CF, Engstrand L. Factors affecting growth of *Yersinia enterocolitica* in cellular blood products. *Transfus Med Rev* **1996**; 10:259–75.
28. Cervia JS, Wenz B, Ortolano GA. Leukocyte reduction's role in the attenuation of infection risks among transfusion recipients. *Clin Infect Dis* **2007**; 45:1008–13.
29. Portnoy DA, Falkow S. Virulence-associated plasmids from *Yersinia enterocolitica* and *Yersinia pestis*. *J Bacteriol* **1981**; 148:877–83.
30. Arduino MJ, Bland LA, Tipple MA, et al. Growth and endotoxin production of *Yersinia enterocolitica* and *Enterobacter agglomerans* in packed erythrocytes. *J Clin Microbiol* **1989**; 27:1483–5.
31. Gibb AP, Martin KM, Davidson GA, Walker B, Murphy WG. Modeling the growth of *Yersinia enterocolitica* in donated blood. *Transfusion* **1994**; 34:304–10.
32. Malbrunot C, Guiyoule A. Growth of *Yersinia enterocolitica* in red blood cells units. *Méd Mal Infect* **1990**; 20:273–8.
33. Riedemann NC, Guo RF, Ward PA. The enigma of sepsis. *J Clin Invest* **2003**; 112:460–7.
34. Annane D, Bellissant E, Cavaillon JM. Septic shock. *Lancet* **2005**; 365:63–78.
35. Nguyen HB, Rivers EP, Abrahamian FM, et al. Severe sepsis and septic shock: review of the literature and emergency department management guidelines. *Ann Emerg Med* **2006**; 48:28–54.
36. Vincent JL. Sepsis definitions. *Lancet* **2002**; 2:135.
37. Nguyen HB, Smith D. Sepsis in the 21st century: recent definitions and therapeutic advances. *Am J Emerg Med* **2007**; 25:564–71.
38. Aird WC. The role of the endothelium in severe sepsis and multiple organ dysfunction syndrome. *Blood* **2003**; 101:3765–77.
39. AABB. Technical manual. Brecher ME, ed., 15th ed. Available at: <http://www.aabb.org>. Accessed 19 April 2011.
40. Klein HG, Spahn DR, Carson JL. Red blood cell transfusion in clinical practice. *Lancet* **2007**; 370:415–26.
41. Pham JN, Bell SM, Martin L, Carniel E. The beta-lactamases and beta-lactam antibiotic susceptibility of *Yersinia enterocolitica*. *J Antimicrob Chemother* **2000**; 46:951–7.
42. Stock I, Wiedemann B. An in-vitro study of the antimicrobial susceptibilities of *Yersinia enterocolitica* and the definition of a database. *J Antimicrob Chemother* **1999**; 43:37–45.
43. Stolk-Engelaar VM, Meis JF, Mulder JA, Loeffen FL, Hoogkamp-Korstanje JA. In-vitro antimicrobial susceptibility of *Yersinia enterocolitica* isolates from stools of patients in The Netherlands from 1982–1991. *J Antimicrob Chemother* **1995**; 36:839–43.
44. Hoogkamp-Korstanje JA. Antibiotics in *Yersinia enterocolitica* infections. *J Antimicrob Chemother* **1987**; 20:123–31.
45. Noble RC. Failure of cefotaxime in the treatment of *Yersinia enterocolitica* sepsis despite in vitro susceptibility. *Curr Ther Res* **1989**; 46:692–4.
46. Wilkinson TJ, Colls BM, Chambers T, Ikram RB. Blood transfusion acquired *Yersinia enterocolitica* sepsis: two cases. *N Z Med J* **1991**; 104:120.
47. Gayraud M, Scavizzi MR, Mollaret HH, Guillemin L, Hornstein MJ. Antibiotic treatment of *Yersinia enterocolitica* septicemia: a retrospective review of 43 cases. *Clin Infect Dis* **1993**; 17:405–10.
48. Walthers-Wenke G. Incidence of bacterial transmission and transfusion reactions by blood components. *Clin Chem Lab Med* **2008**; 46:919–25.
49. Adjei AA, Kuma GK, Tettey Y, et al. Bacterial contamination of blood and blood components in three major blood transfusion centers, Accra, Ghana. *Jpn J Infect Dis* **2009**; 62:265–9.
50. Theakston EP, Morris AJ, Street SJ, Baker BW, Woodfield DG. Transfusion transmitted *Yersinia enterocolitica* infection in New Zealand. *Aust N Z J Med* **1997**; 27:62–7.
51. NZBlood. Haemovigilance program. Available at: <http://www.nzblood.co.nz/Clinical-information/Haemovigilance-programme/Annual-haemovigilance-report>. Accessed 25 July 2011.
52. Leclercq A, Martin L, Vergnes ML, et al. Fatal *Yersinia enterocolitica* biotype 4 serovar O: 3 sepsis after red blood cell transfusion. *Transfusion* **2005**; 45:814–8.
53. Afssaps. French hemovigilance site. Available at: <http://www.afssaps.fr/Activites/Hemovigilance/Hemovigilance/>. Accessed 25 July 2011.
54. Reesink HW, Panzer S, Gonzalez CA, et al. Haemovigilance for the optimal use of blood products in the hospital. *Vox Sang* **2010**; 99:1–16.
55. “National menus” section of the International Haemovigilance Network Web-site. Available at: <http://www.ihn-org.net>. Accessed 25 July 2011.
56. Prinoth O. Systems for monitoring transfusion risk. *Blood Transfus* **2008**; 6:86–92.
57. Funk MB, Gunay S, Lohmann A, Henseler O, Keller-Stanislawski B. Evaluation of measures aimed to reduce serious adverse

- transfusion reactions (hemovigilance data from 1997 to 2008). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* **2010**; 53:347–56.
58. Funk MB, Günay S, Lohmann A, Witzhausen C, Henseler O. Haemovigilance report 1997-2008: assessment of reports of serious adverse transfusion reactions. Available at: http://www.pei.de/cln_092/Share-dDocs/Downloads/fachkreise/haemovigilanz/publikationen/haemovigilance-report-1997-2008.html. Accessed 25 July 2011.
59. Momose S, Taira R, Muraoka M, et al. Haemovigilance data for five years by Japanese red cross blood service: transfusion-related adverse reactions and infections from 2004 to 2008 (Meeting abstract). *Vox Sang* **2009**; 97:165.