

Leukemia and risk of recurrent *Escherichia coli* bacteremia: genotyping implicates *E. coli* translocation from the colon to the bloodstream

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Received: 15 April 2013 / Accepted: 22 April 2013 / Published online: 7 May 2013
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Abstract In patients with leukemia, the portal(s) and reasons for the persistence of an *Escherichia coli* recurrent bacteremia remain unclear. Adult Hematology Clinic (AHC) databases at the State Clinical Hospital in Gdańsk were reviewed to evaluate the frequency of *E. coli* bacteremia between 2002 and 2005. Blood and bowel *E. coli* strains were obtained and the genetic relatedness of the strains was analyzed. The rate of *E. coli* bacteremia per 1,000 admissions at the AHC was higher (85.0) than in the other clinics of the hospital (2.9), $p < 0.001$. A higher mortality was observed in patients with a history of *E. coli* versus non-*E. coli* bacteremia [30/95 (31 %) vs. 53/430 (12 %), $p < 0.001$]; 72.8 % of patients with leukemia had an unknown source of bacteremia. In 2005, 6 out of 25 (24 %) patients with leukemia had ≥ 2 episodes of *E. coli*-positive blood cultures. These gastrointestinal *E. coli* isolates were replaced within 3–8 weeks with a new *E. coli* H genotype. A recurrent episode of bacteremia was usually caused by an infection with a transient *E. coli* H genotype

identical to that found in the subject's bowel. Consistent with the definition of bowel/blood translocation, the bowel appeared to be a portal for *E. coli* in these subjects and, hence, a clear source for their recurring bacteremia.

Introduction

While the presence of a hematologic malignancy has been considered a risk for recurrent vancomycin-resistant *Enterococcus* (VRE) bacteremia, the recurrence of *Escherichia coli* bacteremia in patients with leukemia has not been well studied [1–3]. Although *E. coli* is recognized as an important pathogen in recurrent bacteremia, patients who have a bacteremia caused by a Gram-negative organism reportedly have a relatively low risk (6 %) of recurrent episodes [2–9]. In patients with a hematologic malignancy and recurrent bacteremia, VRE colonize the gastrointestinal tract and often persist in the colon for several months [1]. Despite clinical and laboratory examination, in leukemia, the source or portal of infection in those patients with recurrent bacteremia often remains unknown. Further, we lack data on the short- versus long-term *E. coli* colonization of the bowel and the associated risk of recurrent bacteremia. Several factors may contribute to the risk of recurrent bacteremia. First, *E. coli* may remain viable in the hospital environment for several months [10–18]. Susceptible patients such as those who have leukemia may be at risk for recurrent infection with a *E. coli* strain(s) that persists in such a hospital environment. Based on current trends, the risk of recurrent *E. coli* bacteremia, although low, may also increase due to the increasing prevalence of an “alarm” antibiotic-resistant *E. coli* [10]. Other factors that may increase the risk of *E. coli* bacteremia are frequent hospitalizations and the longer survival of patients with leukemia. Because the frequency of

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E. coli recurrent bacteremia is reportedly low, the risk of mortality in patients with recurrent *E. coli* versus non-*E. coli* bacteremia is under-investigated and remains unclear. In this study on *E. coli* bacteremia, we determined the source/portal of recurrent infection, the mortality incidence in those with a history of *E. coli* versus non-*E. coli* bacteremia, and the similarity of *E. coli* genotypes in blood and bowel over time. This aimed to define whether a recurrence of bacteremia was caused by the same genotype persisting in the bowel as a pathogen or if the recurrence was caused by a transient new colonizer. Here, we report that recurrent *E. coli* bacteremia was a frequent event in leukemic malignancy and was accompanied by an increased risk of mortality. Recurrent bacteremia was not caused by persistent colonizers: blood re-infections mostly occurred with a new *E. coli* genotype that was also temporarily present in the bowel, suggesting that the bowel was the source of the translocating pathogen.

Materials and methods

Patients and collection of samples

The analysis was focused on the Independent State Clinical Hospital at Gdańsk University of Medicine (State Hospital), with a total number of 1,265 hospital beds and 34 subspecialty clinics and/or wards, including an Adult Hematology Clinic (AHC). The databases in the State Hospital and the microbiology laboratory were reviewed to identify those patients who had Gram-negative bacteremia between January 1, 2002 and December 31, 2005. All patients with recurrent episodes [at least two episodes that occurred 30 days apart or also occasionally shorter intervals (see results for patient P1) with blood culture results negative in the interim] were identified. In addition, all *E. coli* cultures obtained from blood and stool samples from 25 patients with leukemia (collected during the period 2004–2005 at the AHC) were saved and stored at -80°C . A single bacteremic episode was defined by positive blood cultures performed on a single patient within a 7-day period. Polymicrobial bacteremia was considered to be Gram-negative if at least one Gram-negative organism was isolated in the blood culture. Bacteremic episodes with onset >48 h after admission were considered to be nosocomial. A recurrence of bacteremia was defined as a second episode of bacteremia during the study period that was caused by the same Gram-negative species. A relapse was defined as a recurrence of bacteremia caused by the same strain that caused the initial infection. A re-infection was defined as a recurrence of bacteremia caused by a different strain than the one that caused the initial infection [>3 bands difference in pulsed-field gel electrophoresis (PFGE) or coefficient of similarity $<90\%$] [19]. Bacteremia was considered to be due to a

gastrointestinal tract translocation when: (a) an isolate with the same DNA fingerprint as the blood isolate was obtained from a stool specimen ($>10^8$ CFU/g of feces); (b) no alternative primary site of infection was detected; (c) urine culture results were negative [$<1,000$ colony-forming units (CFU)/mL]; and (d) no acquired digestive tract abnormalities were present [20].

Genotyping by PCR MP and REA-PFGE

Frozen isolates were thawed and cultured on trypticase soy agar with 5 % sheep blood agar (Becton Dickinson) and incubated at 37°C for 24 h. Species identification was done with a Vitek identification card (bioMérieux Vitek). The polymerase chain reaction melting profiles (PCR MP) procedure was carried out according to the method described for *E. coli* isolates [21]. This method allows specific gradual amplification of genomic DNA in terms of thermal stability starting from less stable DNA fragments amplified at lower Td values to more stable ones amplified at higher Td values. This feature may be used to obtain sets of electrophoretic patterns of DNA fragments amplified during ligation-mediated (LM) PCR performed at various denaturation temperatures. A low Td during LM PCR leads to limited and specific amplification of a small number of DNA fragments characteristic for the bacterial strain. Restriction endonuclease analysis (REA)-PFGE was performed with restriction digestion of the chromosomal DNA with 20 U of *Xba*I (Sigma) and with the FIGE Mapper Electrophoresis System (Bio-Rad), according to a method described previously [21].

Statistical analysis

Data were statistically analyzed using the Microsoft Excel 2007 program. Categorical variables were compared using Chi-square analysis. *p*-values less than 0.05 were considered to be significant.

Results

Bacteremia at the Independent State Clinical Hospital, years 2002–2005

The hospital's and microbiology laboratory's databases between 2002 and 2005 included records for 152,388 patients admitted, including 2,741 patients admitted to the AHC. While the frequency of bacteremia among all the admitted patients to the State Hospital was 1.6 %, the patient population in the AHC had a significantly higher bacteremia rate of 19.1 % ($p<0.001$) (Table 1). The observed difference in the frequency of bacteremia in those subjects in the general population of the State Hospital versus those in the AHC

Table 1 State Hospital admissions, number of blood cultures, and *Escherichia coli* bacteremias in the years 2002–2005

	AHC	Other clinics	Total	<i>p</i> * AHC vs. other
Number of patients hospitalized	2,741	149,647	152,388	–
Number (%) of patients with positive blood cultures	525 (19.1 %)	1,974 (1.3 %)	2,499 (1.6 %)	<0.001
Number of positive blood cultures/rate per 1,000 admissions	3,387/1,235.7	5,359/35.8	8,746/57.4	<0.001
Number of Enterobacteriaceae isolates/rate per 1,000 admissions	531/193.7	1,053/7.0	1,584/10.4	<0.001
Number of <i>E. coli</i> strains/rate per 1,000 admissions	233/85.0	431/2.9	664/4.4	<0.001
Number of unique patients/cases of bacteremia with presence of <i>E. coli</i>	95/223	235/429	330/652	–
Number (%) of ESBL <i>E. coli</i>	20 (0.53 %)	20 (0.33 %)	40 (0.41 %)	0.008

**p* < 0.05 was considered to be significant

was also calculated as the rates in blood cultures per 1,000 admissions. While, overall, the State Hospital rate was 57.4 per 1,000, it was dramatically higher for the AHC (1,235/1,000) and significantly lower for the remaining State Hospital clinics (35.8/1,000).

In order to understand the increased frequency of bacteremia in the AHC, the analysis was focused on Gram-negative microorganisms. We revealed that Enterobacteriaceae were more frequently isolated in the AHC ward. While the State Hospital rate of Gram-negative bacteremia was low (10.4 per 1,000), the rate was significantly higher for AHC subjects (193.7 per 1,000). Among the Enterobacteriaceae, the most frequently isolated was *E. coli*; rates of 85.0 and 2.9 per 1,000 for the AHC and the remaining State Hospital clinics, respectively, were noted. The State Hospital records identified a total of 652 episodes of *E. coli* bacteremia, of which 223 occurred in 95 AHC patients. This suggested the occurrence of multiple bacteremic episodes and/or recurrent *E. coli* bacteremia in some patients (Table 1).

Recurrence or persistence of bacteremia may be a result of a therapeutic failure due to the presence of so called “alarm” microorganisms that are resistant to multiple antibiotics. Between 2002 and 2005, there were only 40 bacteremias of extended-spectrum beta-lactamase (ESBL) *E. coli* in the entire

State Hospital, and half of these cases were from the AHC. These data suggest that antibiotic resistance was less likely to be a primary factor in the recurrence of *E. coli* bacteremia.

To understand the underlying cause(s) of the increased frequency of bacteremia at the AHC, we performed an analysis of the identified sources/portals of infection (Table 2). While an extra-intestinal source of bacteremia was found in the majority of clinics, in the AHC, only 27.4 % of cases had this as an identified source. The most frequent portal of *E. coli* bacteremia was the urogenital tract. However, while a urogenital source of *E. coli* accounted for 16.8 % of bacteremia for AHC patients, this number was 83.8 % in Internal Medicine and 39.3 % in Surgery. These data are consistent with our hypothesis that, in roughly 72.6 % of AHC patients (Table 2) with an unknown *E. coli* portal, the bowel was the likely source of their infection.

As the frequency of *E. coli* bacteremia was higher in the AHC ward (which serves a patient population with leukemia/lymphoma), we focused our further analyses on these patients (Table 3). The highest rate of *E. coli* bacteremia was observed in patients with myeloid leukemia, lymphoblastic leukemia, and Hodgkin’s lymphoma (22.2 %, 20.4 %, and 27.3 %, respectively), while lower rates were observed in patients with multiple myeloma and immunocytoma (11.7 %

Table 2 Frequency (%) of *E. coli* isolated from the blood of patients, with sources/portals of infection known/unknown

	AHC Patients, n/%	Internal Medicine Patients, n/%	Surgery Patients, n/%	Intensive Care Unit Patients, n/%	Pediatric Hematology Patients, n/%	Other pediatric clinics Patients, n/%
Total	95	149	39	30	12	23
Known	26/27.4 %	148/99.3 %	37/94.9 %	30/100.0 %	9/75.0 %	23/100.0 %
Urogenital tract	16/16.8 %	125/83.8 %	13/39.3 %	7/38.8 %	3/25.0 %	4/17.3 %
Vascular catheters	1/1.0 %	3/2.0 %	3/9.0 %	0/0.0 %	5/41.6 %	4/17.3 %
Respiratory tract	5/5.2 %	10/6.7 %	5/15.1 %	13/72.2 %	0/0.0 %	15/65.2 %
Wound	4/4.2 %	10/6.7 %	16/48.4 %	10/55.5 %	1/8.3 %	0/0.0 %
Unknown	69/72.6 %	1/0.7 %	2/5.1 %	0/0.0 %	3/25.0 %	0/0.0 %

Table 3 Frequency of *E. coli* bacteremia and number of episodes in AHC patients with myeloid leukemia, lymphoblastic leukemia, multiple myeloma, immunocytoma, and Hodgkin's lymphoma in the years 2002–2005

	Myeloid leukemia			Lymphoblastic leukemia			Multiple myeloma			Immunocytoma			Hodgkin's lymphoma			Other		
	P, n	PB, n/%	E, n	P, n	PB, n/%	E, n	P, n	PB, n/%	E, n	P, n	PB, n/%	E, n	P, n	PB, n/%	E, n	P, n	PB, n/%	E, n
Total	212	47/22.2	117	93	19/20.4	41	77	9/11.7	17	83	12/14.5	23	22	6/27.3	17	38	2/5.2	8
Recurrent bacteremia	132 ^a	10/7.6	10	56 ^a	4/7.1	4	28 ^a	1/3.6	1	37 ^a	2/5.4	2	16 ^a	3/18.7	3	12 ^a	2/16.6	2

P number of patients, PB patients with *E. coli* bacteremia, E episodes with *E. coli* bacteremia

^a All bacteremia, including bacteremia with *E. coli*

and 14.5 %, respectively). *E. coli* monobacteremia represented 20.7 to 22.7 % of all *E. coli*-infected blood cultures in patients with leukemia and lymphoma, and 9.3 % to 12.3 % in multiple myeloma and immunocytoma.

Because the frequency of *E. coli* recurrent bacteremia is reportedly low, the risk of mortality in patients with recurrent *E. coli* versus non-*E. coli* bacteremia is under-investigated and remains unclear. Table 4 summarizes data on the number of AHC patients who died, relative to their history of *E. coli* bacteremia. Out of 525 patients with a history of bacteremia, 83 (15.8 %) patients died due to the bacteremia itself. Out of 95 patients with a history of *E. coli* bacteremia, 30 (31 %) patients died. In contrast, out of 430 patients with a history of bacteremia caused by pathogens other than *E. coli*, 53 (12 %) patients died. The number of deaths connected to their basic diseases was similar for those with or without a history of *E. coli* bacteremia ($p=0.134$). These results suggest that a history of *E. coli* bacteremia, per se, was associated with increased risk of mortality ($p<0.001$).

Genetic typing for the characterization of *E. coli* isolates from patients with leukemia/lymphoma and recurrent bacteremia

Since we postulated that the source/portal of recurrent infection would be the bowel, we focused on the similarity of *E. coli* genotypes in blood and bowel isolates over time. To define whether a recurrence of bacteremia was caused by the same genotype persisting in the bowel as a pathogen (or if the re-infection was caused by a transient new colonizer), we first characterized *E. coli* DNA fingerprint patterns produced by PCR MP and REA-PFGE. DNA fingerprinting of 65 *E. coli* isolates from blood and/or bowel identified 32 genotype patterns, which were named H1 to H32 (Fig. 1, representative results by using the PCR MP method). Among the most frequent genotypes, the H2 pattern was represented in nine *E. coli* isolates, H17 and H22 were represented in six isolates each, and the remaining H types were restricted to one or two *E. coli* isolates (Table 5). *E. coli* genotype H2, which represented a nosocomial strain, was identified in the blood cultures of four patients with leukemia. The other frequent genotype (*E. coli* H22) was isolated from the blood of two patients (P10 and P18). Among the genotypes that were less frequent, *E. coli* H9, H11, H13, H15, H16, H20m and H30 were isolated from both the blood and the bowel samples (one patient for each genotype), which is consistent with an *E. coli* isolate H fingerprint specificity.

Recurrent *E. coli* bacteremia was associated with re-infection by different *E. coli* H genotypes

Among the 25 patients with leukemia/lymphoma hospitalized between 2004 and 2005, six patients (P1, P9, P11, P15, P23,

Table 4 Mortality of patients hospitalized in the AHC in the years 2002–2005

	Patients with history of <i>E. coli</i> bacteremia	Patients without history of <i>E. coli</i> bacteremia	Total	<i>p</i> -Value
Number of patients with positive blood cultures	95	430	525	–
Number of patients who did not die during hospitalization	38	289	327	0.002
Number of patients who died due to basic disease	27	88	115	0.134
Number of patients who died due to bacteremia	30	53	83	<0.001

and P25) had two or more episodes of positive *E. coli* blood cultures. In patient P9, we identified two episodes of bacteremia, each caused by a different *E. coli* H genotype (H20 and H23, respectively). Patient P11 developed two episodes of *E. coli* bacteremia including genotypes H28 or H29.

Correlation between the presence *E. coli* H genotypes in the bowel and blood cultures

Figure 2 presents examples of *E. coli* H fingerprints showing identical DNA patterns of isolates from the bowel and the blood. For example, patient P5 had a blood and bowel culture positive for *E. coli* H11. Patient P1 showed several episodes of bacteremia and identical blood and bowel *E. coli*, suggesting that a different *E. coli* inhabitant of the bowel translocated to the bloodstream. Patient P1 was hospitalized six times between September 9th 2004 and September 30, 2005, and spent a total of 236 days in the hospital due to a recurrent *E. coli* bacteremia with multiple *E. coli* isolates/H fingerprints, with identical *E. coli*

isolates/H fingerprints identified in the bowel and with no evidence of another obvious source of infection (Table 5). Five blood cultures obtained within the above-mentioned period were positive for *E. coli*. *E. coli* isolated from blood and stool (cultures done on same day, May 10th) showed an identical H16 genotype. Following episodes of bacteremia (May 22nd, 25th, and 27th, and August 7th) were caused by an ESBL *E. coli* H17 genotype. This *E. coli* H17 was isolated from the patient's urine on June 20th and from his stool on August 7th. Following bone marrow transplant, the patient received ciprofloxacin, and beginning May 9th, he was treated with piperacillin, tazobactam, and amikacin. Once a positive result of ESBL *E. coli* isolated from blood was obtained, an additional antibiotic (meropenem) was added to the therapeutic strategy and continued until July 6th, 2005. Thus, in our select patient, the *E. coli* H genotype that caused bacteremia was eliminated from the vascular bed following antibiotic treatment. After an asymptomatic period, the infection was replaced with another rare *E. coli* H genotype identical to that identified in the bowel at the time. In agreement with the established bacteriologic and DNA fingerprinting criteria for translocation, in the absence of an alternative source of infection in these patients, recurrent *E. coli* bacteremia resulted from *E. coli* translocation from the bowel to the bloodstream.

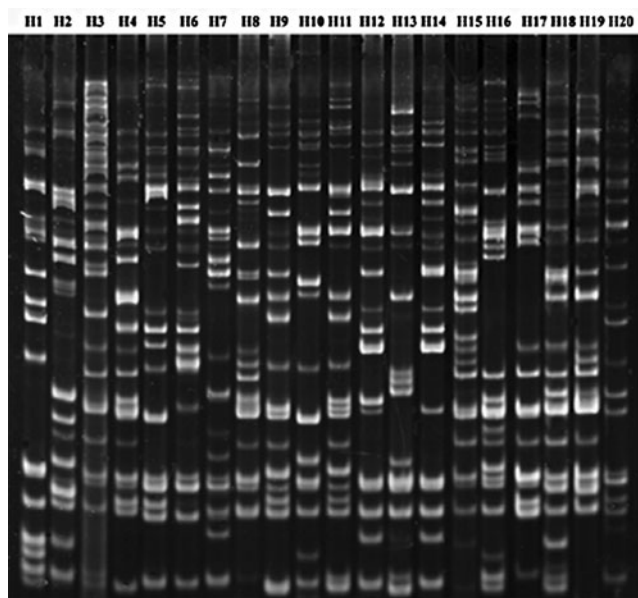


Fig. 1 Polymerase chain reaction melting profiles (PCR MP) fingerprints for representative *Escherichia coli* isolates from patients of the Adult Hematology Clinic (AHC) ward showing H genotypes from H1 to H20. PCR MP fingerprinting H types are given above each lane. The DNA amplicons were electrophoresed on 6 % polyacrylamide gels

Discussion

Septicemia and/or bacteremia is the 13th leading cause of death in the United States, and the age-adjusted mortality rate associated with sepsis has increased over the last five decades [2, 3]. In the United States, about 500,000 cases of sepsis occur each year, one-fourth of which are associated with Gram-negative bacteremia [4]. Gram-negative bacteremia is a serious infection, for which the estimated crude mortality rate is 20–50 % [5]. It is estimated that 6–10 % of patients who have an episode of Gram-negative bacteremia will have one recurrent episode [6–9]. *E. coli* was reported as only the fourth most common cause of nosocomial bacteremias [10–16, 22].

In present study, we report that, unexpectedly, recurrent *E. coli* bacteremia was a frequent event in leukemic malignancy, and that blood re-infection usually occurred with a new *E. coli* DNA H genotype present in the bowel. We observed that the recurrent *E. coli* bacteremia in these leukemic patients was

Table 5 Patients' clinical histories and results of the genotyping of *E. coli* isolates

Clinical recognition	Patient	Isolate	Date of isolation (day.-mo.-yr)	Specimen source	Genotype	
Myeloid leukemia	P1	1	23-09-2004	Blood	H1	
		2	05-02-2005	Blood	H7	
		3	05-02-2005	Blood	H8	
		4	05-02-2005	Blood	H9	
		5	07-02-2005	Stool	H9	
		6	07-02-2005	Stool	H10	
		7	10-05-2005	Blood	H16	
		8	10-05-2005	Stool	H16	
		9	19-05-2005	Blood	H16	
		10	19-05-2005	Blood	H16	
		11	22-05-2005	Blood	H17	
		12	22-05-2005	Blood	H17	
		13	25-05-2005	Blood	H17	
		14	25-05-2005	Blood	H17	
		15	27-05-2005	Blood	H17	
		16	08-07-2005	Blood	H17	
	P2	17	22-10-2004	Blood	H4	
	P3	18	22-10-2004	Blood	H2	
	P4	19	24-11-2004	Blood	H2	
	P5	20	15-02-2005	Blood	H11	
		21	15-02-2005	Blood	H11	
		22	18-02-2005	Stool	H11	
		23	18-02-2005	Stool	H12	
		24	18-02-2005	Stool	H11	
		25	18-02-2005	Stool	H12	
		P6	26	22-02-2005	Blood	H13
			27	25-02-2005	Stool	H13
	P7	28	05-03-2005	Blood	H14	
	P8	29	28-04-2005	Blood	H15	
		30	28-04-2005	Stool	H15	
		P9	31	28-07-2005	Blood	H20
	32		01-08-2005	Stool	H20	
	33		30-09-2005	Blood	H23	
	34		30-09-2005	Blood	H23	
	P10		35	16-08-2005	Blood	H22
		36	16-08-2005	Blood	H22	
		37	16-08-2005	Stool	H22	
	P11	38	31-09-2005	Blood	H25	
		39	04-11-2005	Blood	H28	
		40	04-11-2005	Blood	H29	
	P12	41	29-11-2005	Blood	H31	
	P13	42	05-12-2005	Blood	H32	
	Lymphoblastic leukemia	P14	43	16-11-2004	Blood	H5
			44	13-09-2004	Blood	H2
			45	12-10-2004	Blood	H2
		P16	46	17-06-2005	Blood	H19
		P17	47	29-07-2005	Blood	H21
			48	29-07-2005	Blood	H21
		P18	49	30-08-2005	Blood	H22

Table 5 (continued)

Clinical recognition	Patient	Isolate	Date of isolation (day.-mo.-yr)	Specimen source	Genotype	
Hodgkin's lymphoma		50	30-08-2005	Stool	H22	
		51	05-09-2005	Stool	H22	
		P19	52	02-11-2005	Blood	H26
		P20	53	04-11-2005	Blood	H27
		P21	54	06-11-2005	Blood	H30
			55	06-11-2005	Stool	H30
		P22	56	06-10-2004	Blood	H3
		P23	57	26-11-2004	Blood	H2
			58	28-11-2004	Stool	H2
			59	29-11-2004	Stool	H2
			60	15-03-2005	Stool	H2
			61	18-03-2005	Blood	H2
		P24	62	27-01-2005	Blood	H6
		P25	63	06-07-2005	Blood	H18
			64	23-10-2005	Blood	H24
		65	23-10-2005	Blood	H24	

caused either by hospital strains (e.g., *E. coli* genotype H2) or by multiple, rare H genotypes, each representing a different *E. coli* strain of unknown origin. On multiple occasions, we found different *E. coli* H genotypes in blood samples isolated during consecutive episodes of bacteremia, despite an effective therapy following the initial infection. The lack of an

identified focus of infection suggested that, after the elimination of *E. coli* from the bloodstream, another transient bowel inhabitant disseminated to the vascular bed. To our knowledge, the current clinical literature describes only one study including evidence of direct translocations of *E. coli* from the bowel to the circulation and which involves newborns with urinary tract infections [20].

A study of VRE bacteremia concluded that recurrent VRE bacteremia was uncommon, and that recurrent episodes were separated by 3 months and were caused by identical or related VRE strains [1]. Our study showed that *E. coli* which were resident in the bowel of a patient with leukemia were much less stable and the dominant genotype changed over a period of a few weeks. Thus, in contrast to an expected persistent several months colonization with the same strain, we observed that episodes of recurrent bacteremia represented independent re-infection events originating from the re-established new bowel *E. coli* isolates. Re-infection with *E. coli* is consistent with a study by Johnson et al. [23], who examined *E. coli* isolates from 35 children with recurrent urinary tract infection (UTI). Five of the nine patients were re-infected with new strains. We hypothesize that antibiotic therapy destabilized the normal intestinal flora and increased the risk for re-colonization with potentially pathogenic transient *E. coli* colonizers.

The exact mechanism of translocation of indigenous bacteria from the gut is not known but may involve the overgrowth of intestinal bacteria, a deficiency in the host's immune defenses, and/or damage to the intestinal mucosal barrier [24]. The possibility exists that immunosuppressive therapy resulting in the dysfunction of white cells or the invasive capacity of some *E. coli* allow the translocation of *E. coli* to the mesenteric circulation [24–29].

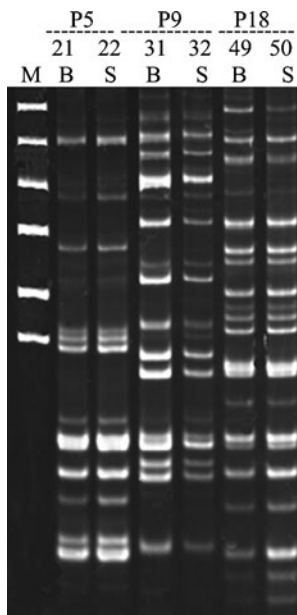


Fig. 2 Representative results of monitoring the spread of bacteria within patients by using the PCR MP technique. The isolates shown represent three patients: genotype H11 from patient P5, genotype H20 from patient P9, and genotype H22 from patient P18. Lanes marked by numbers indicate the number of the isolate shown in Table 5. Lanes marked by B and S contain strains isolated from blood and stool, respectively. The DNA amplicons were electrophoresed on 6 % polyacrylamide gels

The detection of frequent recurrent *E. coli* bacteremia suggests the need for a careful patient evaluation, as the risk of mortality is potentially higher compared to those with a history of non-*E. coli* bacteremia. Our data suggest that standards for the prevention of recurrent bacteremia should be re-evaluated. Clinical trials might include novel regimens for selective decontamination to eradicate the transient *E. coli* H genotypes from the gut and, therefore, reduce the risk for recurrent bacteremia [30].

Acknowledgments This work was supported by the Polish Ministry of Science and Higher Education grant no. N401331239 to A.Ś. and, in part, by U54 RR026140 (NCRR)/U54 MD007593 (NIMHD). The authors express their gratitude to Diana Marver PhD for her editorial comments and suggestions.

Conflict of interest The authors certify that they have no potential conflicts of interest.

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