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Transfusion-Associated Bacterial Sepsis

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INTRODUCTION

Although sepsis from bacterial contamination of blood is a very infrequent event in transfusion medicine, episodes of transfusion-associated sepsis may lead to fatal outcomes or other serious sequelae and therefore are an issue of concern. This review examines the frequency of occurrence, the organisms implicated, potential sources of contamination, blood component storage ramifications, and possible interventions for transfusion-associated sepsis. Additional reviews relating to this subject have been written (3, 14, 49, 51, 88).

Erythrocytes, platelets, and plasma are prepared from whole blood by centrifugation and stored under well-established conditions. Although a small fraction of these components may initially contain some bacteria from a variety of potential sources, the levels at the time of collection are usually thought to be too low (<10 CFU/ml) to result in sepsis upon immediate transfusion. With storage of erythrocytes (up to 42 days at 1 to 6°C) and platelets (up to 5 days at 20 to 24°C), however, organisms may proliferate to levels of around 10^7 to 10^9 CFU/ml or more. Transfusion of blood components containing high levels of bacteria will result in sepsis and occasionally death, especially if the immune system of recipients, who are often on chemotherapy, is compromised.

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MEASURES OF FREQUENCY OF BACTERIAL CONTAMINATION IN BLOOD PRODUCTS

There are three "measures" of the frequency of bacterial contamination in blood components. One appraisal is the incidence of fatalities caused by transfusion-associated sepsis, when the organism recovered from the septic patient is the same as the one isolated from the component. Approximately 4% (2 of 70 incidents) of the transfusion-related fatalities reported to the Food and Drug Administration (FDA) during 1976 through 1978 were associated with bacteria in blood components (64). This measure increased to approximately 11% (10 of 89 incidents) for the period spanning 1986 to 1988 (64, 118). In the same period, on the order of 60 million units of blood components were transfused (132). Therefore, on average, there was roughly 1 death per 6 million transfused units which was attributed to sepsis.

The frequency of nonfatal outcomes of transfusion-related sepsis is not well characterized. However, these events are likely to greatly outnumber fatal outcomes. Transient fever during or following transfusion, or febrile transfusion reactions, is not uncommon and may occasionally be caused by blood components that contain bacteria. However, the majority of cases are attributed to the patient's immune response to transfused leukocytes. Morrow and coworkers found that bacterial contamination that was associated with febrile transfusion reactions occurred once in approximately 1,700 "pools" of random donor platelets transfused, representing 10,219 individual units (a therapeutic dose of platelets is generally a pool consisting of six to ten individual platelet concentrates) or once in 19,519 single-donor platelets transfused (90). Single-donor platelets are obtained by a process called apheresis in which donor whole blood is collected, anticoagulated, and separated by a sophisticated centrifuge into cellular blood components and plasma. The unwanted cells (in this case, erythrocytes and many leukocytes) and plasma are reinfused to the donor. One unit of apheresis platelets is therapeutically equivalent to a pool of random donor platelets but is prepared from one collection from a single donor. To be regarded as transfusion associated in the Morrow study, the organism found in a blood culture from the febrile patient had to be the same species and have the same antibiotic susceptibility as the organism isolated from the implicated pool of platelets. Similar frequencies of bacterial contamination in platelet concentrates that were associated with febrile transfusion reactions were reported by Barrett and coworkers (10).

Numerous other studies have used culture methods to measure the frequency of bacteria present in blood components. Of the three measures, this one varies the most widely; it is susceptible to errors in aseptic technique, and the observation cannot be confirmed by comparing bacterial strains isolated from the blood component and that of the patient. Most often, these studies have focused on bacterial contamination of random donor platelet concentrates, with positive cultures ranging from 0 to 10% (6, 7, 22, 23, 31, 48, 72, 125, 154) and apheresis platelets ranging from 0 to 5% (2, 29, 83, 133). In over 75% of "contaminated" platelet concentrates, fewer than 10 organisms per ml were detected (6, 22, 31). For frozen, thawed, and deglycerolized erythrocytes, positive cultures ranged from 0 to 0.2% (105, 110). Differences reported in these studies may be due to breaches in aseptic technique, the number of components sampled and their age and storage conditions, and the sample volume and culturing conditions.

ERYTHROCYTES AND WHOLE BLOOD

Reported Episodes of Transfusion-Associated Sepsis and the Implicated Organisms

Although a number of organisms have poor viability in whole blood or exhibit a growth lag, some strains do not. Interpolated data from values presented by Högman and coworkers suggest that *Staphylococcus aureus* and *Pseudomonas aeruginosa* can undergo 1 to 2 doublings in whole blood held for 8 h at room temperature (62). Currently, erythrocytes can be prepared from whole blood that is held at room temperature for up to 8 h after collection or from chilled (1 to 6°C) whole blood units stored for up to 3 days. After preparation, these erythrocytes are stored at 1 to 6°C for up to 42 days. Not surprisingly, these conditions select for the growth of psychrophilic bacteria. The implicated organisms in recent episodes of sepsis resulting from erythrocyte transfusions are given in Table 1, and their frequency of occurrence is shown in Fig. 1. Based on all of the data compiled from reports presented in Table 1, roughly three-fourths of all occurrences involved *Yersinia enterocolitica* and *Pseudomonas fluorescens*. About one-half of all events resulting from transfused erythrocytes involved *Y. enterocolitica* alone. However, other psychrophilic organisms, such as *Pseudomonas putida* and *Campylobacter jejuni*, have also been implicated (128). All incidents of sepsis, with the exception of *Treponema pallidum* and one case of *Y. enterocolitica*, occurred from transfusion of erythrocytes stored for more than 14 days; most cases occurred after 25 days.

Y. enterocolitica

Individuals infected with *Y. enterocolitica* are typically asymptomatic at the time of blood donation (1, 142). In one study, approximately two-thirds of donors implicated in *Yersinia* transmission later recalled gastrointestinal illness prior to donation (32, 152); most of these individuals reported mild or moderate rather than severe diarrhea (73) that occurred 8 to 30 days prior to donation (142). Tipple and coworkers demonstrated that one infected donor, who was seronegative at the time of donation, had detectable *Y. enterocolitica*-specific antibody 52 days postdonation (142). This information and the timing of diarrhea symptoms relative to the date of donation suggest that infected donors develop *Y. enterocolitica*-specific antibody several weeks after donating the contaminated unit.

Several serotypes of *Y. enterocolitica* have been observed in septic recipients. In the United States, most recent episodes of transfusion-acquired *Y. enterocolitica* sepsis have been caused by the O:3 serotype (142). However, sepsis has also been documented with the O:1,2,3 (142), O:5,27 (152), O:8 (142), O:9 (1), and O:20 (142) serotypes.

Initially, the majority of the reported incidents led to death. The frequency of fatalities caused by *Y. enterocolitica* in erythrocyte transfusions has declined recently (73), perhaps because of increased awareness of the potential for sepsis from contaminated erythrocyte units.

In vitro growth in erythrocytes. Several workers have described the growth of *Y. enterocolitica* in stored units of erythrocytes deliberately inoculated with the organism shortly after component preparation (5, 127). After a lag time of 7 to 14 days, the organism grew in refrigerated erythrocytes with an 18- to 20-h doubling time and reached a level of 10^9 at stationary phase within 38 days (5). There was a rapid increase in endotoxin production between 21 and 34 days,

TABLE 1. Reported episodes of clinical sepsis from bacterial contamination of erythrocyte products[a]

Organism	Positive culture from patient (no.)	Positive culture from donation (no.)	No. of deaths	Time from blood collection to transfusion (days)	Source of contamination	Reference
Yersinia enterocolitica	1	2	1	21–30	NS	Stenhouse and Milner (127)
	1	1	1	NS	NS	Schmitt et al. (120)
	1	0	1	29	Donor[b]	Bjune et al. (13)
	1	1	1	21	Donor[b]	Wright et al. (155)
	1	1	1	21	NS	Galloway and Jones (45)
	1	1	0	31	NS	Bufill and Ritch (24)
	1	1	0	NS	NS	Janot et al. (66)
	0	1	0	7	Donor[b]	Jacobs et al. (65)
	1	1	1	26	Donor[b]	Mollaret (87)
	5[c]	7	5	26–40	Donor[d]	Tipple et al. (142)
	1	1	0	16	Donor	Bruining and deWilde-Beekhuizen (19)
	1	1	1	28	Donor[b]	Collins et al. (28)
	NS	1	1	NS	Donor[b]	Elrick (39)
	1	1	0	NS	Donor	Munro and Lye (92)
	1	Autologous	0	41	Donor	Richards et al. (113)
	0	1	1	26	Donor	Stubbs et al. (131)
	2	2	1	NS	Donor	Wilkinson et al. (151)
Pseudomonas fluorescens	2	3	2	16–19	NS	Khabbaz et al. (75)
	0	2	0	NS	NS	Tabor and Gerety (134)
	0	1	1	23	NS	Phillips et al. (106)
		1	0	18	NS	Gibaud et al. (47)
	2	2	1	NS	NS	Murray et al. (94)
	1	1	1	32	NS	Scott et al. (121)
	0	1	0	28	NS	Foreman et al. (44)
	1	1	1	NS	NS	Morduchowicz et al. (88)
Psychrophilic pseudomonads	0	1	1	NS	NS	Honig and Bove (64)
Treponema pallidum	1	0	0	<1	Donor[e]	Soendjojo et al. (126)
	1[f]	0	0	<1	Donor[d]	Risseeuw-Appel and Kothe (114)
Pseudomonas putida	0	1	1	NS	NS	Tabor and Gerety (134)
Pseudomonas putida, nonhemolytic streptococci	1	1	NS	NS	?Anesthesia	Taylor et al. (138)
Flavobacterium sp.	0	2	NS	NS	NS	Thuillier and Gandrille (141)
Campylobacter jejuni	1	0	1	NS	Donor[b]	Pepersack et al. (104)
Enterobacter cloacae	1	1	1	NS	NS	Bettigole et al. (12)
Diphtheroids	NS	1	1	NS	NS	Morduchowicz et al. (88)
Escherichia coli and other strains	1	1	0	NS	NS	Morduchowicz et al. (88)
Serratia liquifaciens	1	1	1	20	NS	Wolf et al. (153)
	1	1[g]	0	26	NS	Jeppsson et al. (68)

[a] This table was updated from reference 49 with permission of the publisher. NS, not stated or undetermined.
[b] High-specific antibody titer postdonation.
[c] One case previously reported (12).
[d] Positive test result: Venereal Disease Research Laboratory (VDRL) and fluorescent treponemal antibody, postdonation.
[e] Positive test result: VDRL postdonation.
[f] Positive VDRL and fluorescent treponemal antibody.
[g] Whole blood.

and maximum levels (≈315 ng/ml) were reached between 28 and 34 days. The lag time for growth (3 to 9 days) and endotoxin production (6 to 9 days) in another study by Kim and coworkers was shorter and may reflect how different conditions (initial inoculum levels, anticoagulant, and erythrocyte additive solutions) impact *Y. enterocolitica* growth in vitro (77). These data collectively suggest the important role of erythrocyte storage in *Y. enterocolitica* septicemia. The significance of erythrocyte storage on *Y. enterocolitica* sepsis was also exemplified when a patient showed signs of severe transfusion reaction (confusion, cyanosis, respiratory distress, and severe shaking chills) after receiving 100 ml of his own blood (41-day autologous erythrocytes) (113). Blood culture of patient and erythrocyte samples showed that both harbored the same

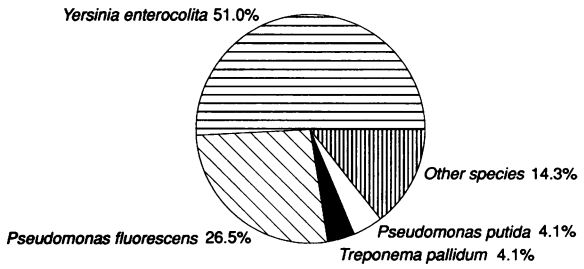

FIG. 1. Bacterial species associated with sepsis from erythrocyte transfusions. Data are derived from cases described in the references listed in Table 1. The case of *Serratia liquefaciens* septicemia from transfusion of a whole blood unit (68) was not included.

strain of *Y. enterocolitica* (bacterial count in erythrocyte unit, 10^8 CFU/ml).

Virulence. Under appropriate environmental conditions, *Yersinia* spp. may display a virulence phenotype, and virulence may play a role in the establishment and nature of an infection. The factors that regulate the expression of virulence are not well understood, although virulence is known to be expressed at 37°C (but not at 22°C) and is inhibited by high calcium concentrations (71, 84, 103, 108). It is important to note that the citrate-based anticoagulants present in most primary collection containers reduce the effective calcium concentration by chelation. After infection, the organism invades host intestinal mucosal cells (108) and can evade host defenses in blood by expressing several plasmid-encoded virulence genes that result in resistance to serum inactivation and phagocytosis (8, 81, 82, 103, 139). In studies involving intradermal inoculation of *Y. enterocolitica* into the backs of rabbits, plasmidless strains, which can be easily isolated from virulent strains during routine culture (58, 108), were found in neutrophils and mononuclear cells 12 h after inoculation, while plasmid-bearing strains were localized extracellularly (81).

Leukodepletion filters. Several research groups have recently reported that the proliferation of *Y. enterocolitica* in deliberately inoculated blood may be prevented or inhibited by prestorage leukofiltration (21, 63, 77, 149) and, to a much lesser extent, buffy coat depletion (50, 107) of erythrocytes. The mechanism by which filters remove leukocytes is not well understood. However, evidence suggests that leukocyte removal occurs mainly by nonspecific affinity to nonwoven fiber substrates (100). Some nonfibrous but porous materials (not in clinical use) have the ability to remove leukocytes by sieving effects (80). Theoretically, bacteria may be filtered from blood components by two mechanisms. Organisms may be directly removed by attachment to the filter substrate, or they may be indirectly removed by interacting with leukocytes, which, in turn, are removed by the filter. For example, Wagner and coworkers have demonstrated direct removal of approximately 1 $\log_{10}$ of *Y. enterocolitica* (serotype O:8) from saline or leukodepleted erythrocyte suspensions by leukocyte reduction filters (147). Similar results have been reported by AuBuchon and Pickard (7). Alternatively, bacteria can be indirectly removed by phagocytic cells. Although some bacteria can bind to these cells without additional modification, other organisms, such as encapsulated strains of *Escherichia coli*, *S. aureus*, pneumococci, and *Haemophilus influenzae*, require opsonization by antibody and complement prior to binding and phagocytosis (129). Other conditions that influence the extent of phagocytosis include the type of phagocytic cells present in the blood component, the component storage temperature (binding, opsonization, and phagocytosis are reduced at 4°C), and the duration of room temperature storage prior to filtration (55).

It is not known whether virulence plays a role in the localization of *Y. enterocolitica* in blood of asymptomatic donors. However, if it does, then some in vitro spiking experiments involving leukodepletion may not reflect outcomes that would be obtained with naturally infected blood (24, 115, 147). The absence of measurable yersiniae in these studies may have been influenced by the localization of the organism. If the organism were avirulent, extracellular organisms would be extensively killed by bacteriocidal factors in plasma, and any intracellular organisms that remained would be directly removed by leukocyte depletion. On the other hand, virulent organisms, which should be resistant to the bacteriocidal effects of plasma and localized extracellularly, may not be adequately removed by the leukodepletion filter.

PLATELET CONCENTRATES

Reported Episodes of Transfusion-Associated Sepsis and the Implicated Organisms

In the United States, platelet concentrates and apheresis platelets are stored in oxygen-permeable containers with agitation at 20 to 24°C for up to 5 days. These conditions tend to favor the growth of aerobic bacteria capable of rapid growth rates at room temperature. Table 2 lists organisms recovered from platelet products that have been associated with septic episodes. Figure 2 shows their frequency of occurrence. The highest percentage of episodes involves coagulase-negative staphylococci or *Staphylococcus epidermidis*. It is also interesting to note that sepsis from diphtheroids rarely occurs, even though this group represents the second most frequently observed type of organism isolated from platelets after *S. epidermidis* (49). Other implicated organisms include *S. aureus*, *Enterobacter cloacae*, *E. coli*, and *Pseudomonas* and *Bacillus* species. There appears to be a much greater diversity of organisms associated with sepsis from platelets than with sepsis from erythrocytes (Tables 1 and 2).

Similar to the experience with sepsis from contaminated erythrocyte units, most episodes of sepsis arising from contaminated platelets occur with units late in the storage period (4 or 5 days; Table 2), when high titers of organisms are potentially present. In fact, concerns over elevated frequencies of bacterial sepsis after transfusion of older units and in vitro demonstrations of the potential for rapid microbial growth in platelet concentrates led the FDA in 1985 to reverse their 1983 decision to extend the storage time of platelet concentrates from 5 to 7 days (36).

Random Platelet Pools Versus Single-Donor Platelets

In the United States, both apheresis and pooled random donor platelets are transfused to recipients. Six to ten random donor platelet concentrates, constituting a therapeutic dose, are pooled up to 4 h prior to transfusion. Sepsis can occur if any one of the individual units is contaminated with high levels of bacteria. In contrast to random donor platelets, apheresis products are not pooled and can provide one or even two therapeutic doses.

Morrow and coworkers observed that the rate of sepsis caused by pooled random donor units was approximately 12 times that for apheresis products (90). Similar results were

TABLE 2. Reported episodes of clinical sepsis from bacterial contamination of platelet products[a]

Organism	Positive culture from patient (no.)	Positive culture from donation (no.)	No. of deaths	Time from blood collection to transfusion (days)	Source of contamination	Reference
Staphylococcus epidermidis	1	0	0	5–7	NS	Braine et al. (16)
	1	1	1	3	NS	Barrett et al. (10)
	NS	1	NS	NS	NS	Halpin et al. (54)
	1	1	0	5	NS	Muder et al. (91)
	2	2	1	1	NS	Buchholz et al. (22)
Coagulase-negative staphylococci	4	3	0	3–4	Skin	Anderson et al. (4)
	1	3	0	5	NS	Morrow et al. (90)
Gram-positive cocci	0	1	1	NS	NS	Honig and Bove (64)
Staphylococcus aureus	1	1	1	3	Donor[b]	Goldman and Blajchman (49)
	1	1	1	5	NS	Morrow et al. (90)
	1	1	0	6	NS	Heal et al. (56)
Serratia marcescens	1	1	1	NS	NS	Buchholz et al. (22)
	3	2	1	1–3	Tube	Blajchman et al. (15)
	1	1	0	NS	NS	Van Lierde et al. (144)
Streptococci, viridans group	NS	0	0	5–6	NS	Braine et al. (16)
	0	1	0	1	NS	Morrow et al. (90)
Bacillus cereus	NS	2	NS	NS	NS	Halpin et al. (54)
	0	1	1	NS	NS	Morduchowicz et al. (88)
Flavobacterium sp.	1	1	0	2	NS	Buchholz et al. (22)
	NS	0	0	5–6	NS	Braine et al. (16)
Treponema pallidum	1	0	0	NS	Donor	Chambers et al. (26)
Enterobacter cloacae	2	2	0	2	NS	Buchholz et al. (23)
Salmonella cholerae-suis	7	3	2	<1	Donor	Rhame et al. (112)
Escherichia coli	1	1	0	3	NS	Arnow et al. (6)
Salmonella heidelberg	1	1	1	5	Donor	Heal et al. (56)
Group A beta-hemolytic streptococci	0	1	0	NS	Donor[b]	Douglas et al. (38)
	0	1	0	2	NS	Morrow et al. (90)
Pseudomonas aeruginosa	NS	1	NS	NS	NS	Halpin et al. (54)
Streptococcus pneumoniae	0	1	0	5	NS	Morrow et al. (90)

[a] This table was updated from reference 49 with permission of the publisher.
[b] Source of contamination not established definitely.

reported by Barrett and coworkers (10). On the surface, these data might suggest that the 10- to 12-fold difference in sepsis rates between the two platelet products was due to a recipient's 6- to 10-fold-greater donor exposure from pooled products. However, there is another confounding factor that probably contributes to this difference: the average storage time of apheresis platelets is often less than that for random donor platelets. On the basis of the data of Morrow et al., longer platelet storage times are correlated with higher rates of sepsis (also see Table 2). In the Morrow study, the mean storage time for apheresis platelets was 1.48 days compared with 3.76 days for random donor platelets. Although the storage times of culture-positive apheresis and random donor platelets are similar in the Barrett study, the authors unfortunately do not

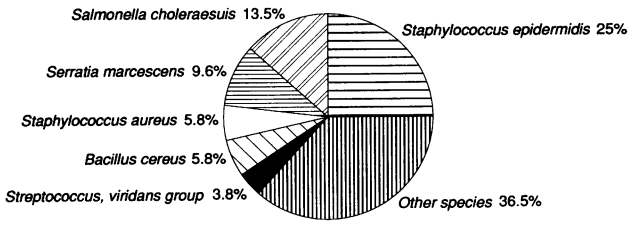

FIG. 2. Bacterial species associated with sepsis from platelet transfusions. Data are derived from all cases described in the references listed in Table 2. Coagulase-negative staphylococci were included with *S. epidermidis*.

report their overall mean storage time of apheresis compared with random donor platelets (10).

Bacterial Growth in Deliberately Inoculated Platelet Concentrates

Several studies have demonstrated the ability of organisms to proliferate in inoculated platelet concentrates during routine storage at 20 to 24°C (16, 57, 69, 70, 96, 109). Bacterial strains differ in their lag phase and growth characteristics. For example, in one study by Punsalang and coworkers, *S. aureus* and *Klebsiella pneumoniae* exhibited a 2-day lag before exponential growth. Other organisms, such as *Enterococcus faecalis*, showed no growth lag. Growth rates can be rapid, with doubling times of 3 h or less; stationary-phase levels of 10^8 to 10^9 CFU/ml can be reached in 3 to 5 days (109). Care needs to be exercised, however, in interpreting these growth curves, because the conditions used to culture microorganisms before inoculation can profoundly affect the lag-phase duration. Nevertheless, data from these studies have clearly established the potential for rapid growth of numerous bacterial species during storage of platelet concentrates.

Leukocyte Filtration

Unfortunately, the efficacy of leukocyte filtration for removal of bacteria is unclear. Buchholz and coworkers reported that leukodepletion (using a PL10-A filter [Asahi, Tokyo, Japan]) reduced the levels of some organisms but not others (platelet concentrates were prepared from inoculated whole blood) (20). Sherburne and colleagues failed to observe differences between the titers of *S. aureus* in control and leukodepleted (using a Pall PL-50 filter [Pall Biomedical, Glen Cove, N.Y.]) platelet concentrates (prepared from inoculated platelet-rich plasma that was subsequently leukodepleted) (124). Brecher and colleagues and Wenz and coworkers also failed to observe reduction in bacterial levels following leukodepletion of contaminated platelet concentrates (18, 150).

One experiment involving filtration and bacterial growth has been carried out with buffy coats (the interface layer between erythrocytes and plasma following centrifugation of whole blood) (62). Buffy coats are currently being used in some European blood centers as an alternative way to prepare platelet concentrates. Högman and coworkers reported that buffy coats that were leukodepleted before inoculation with *S. epidermidis*, *S. aureus*, *E. coli*, *P. aeruginosa*, and *Propionibacterium* sp. had higher titers during storage than unfiltered buffy coats (62).

These studies, with their differing outcomes and methodologies, point to the complexities in evaluating the use of leukocyte depletion filters for bacterial removal. For example, experimental results of bacterial levels in leukodepleted platelets may be strongly influenced by whether filtration was performed before or after inoculation.

PLASMA

Plasma can be prepared from whole blood or collected by apheresis and is usually frozen as soon as possible thereafter; subsequent storage is at 18°C or below. If plasma is used for transfusion, it is thawed in a water bath (using a plastic overwrap) or microwave instrument and transfused immediately or stored between 1 and 6°C for up to 24 h before transfusion. These conditions do not tend to favor bacterial survival or growth. There are, however, two reported cases of septicemia arising from transfusion of plasma. One was attributed to contamination of the water bath used for thawing (25); the other was reported to involve *Serratia marcescens* (40).

SOURCES OF CONTAMINATION

In most cases of sepsis from transfusion, the source of the contamination is not easy to identify. However, insight can be gained about the probable routes of transmission by considering the species of organism isolated as well as by reviewing the few cases in which the source may be inferred. Potential sources include intrinsic contamination or contamination of the phlebotomy site, donor bacteremia, contamination of blood containers or needles, and contamination of processing equipment.

Donation

Health questions. As part of the donation process, prospective donors are required to answer health questions which include how well they are feeling, whether they have had cold, flu, or sore throat symptoms, and whether they have recently taken medications. Other questions are designed to evaluate individuals whose travel or behavior increases their risk of parasitic or viral disease. Another question inquires whether the prospective donor has had dental work recently in order to temporarily defer donors who may have transient bacteremia from this source.

Preparation of phlebotomy site. Prior to blood collection or apheresis, the donor's arms are inspected for evidence of intravenous drug use or the presence of skin diseases. Several cleaning agents are acceptable to prepare an arm for venipuncture, including iodine tincture, iodine polyvinylpyrrolidone (PVP-I), or green soap followed by acetone-alcohol. The cleansing agent is used to scrub the phlebotomy site. Depending on the procedure used, the scrub is removed and/or a second cleansing agent is used (148). Care is taken not to touch the cleansed phlebotomy site prior to needle insertion.

Contamination of the phlebotomy site has been implicated by many investigators as the source of transfusion-associated sepsis involving common skin bacteria, such as *Staphylococcus* species. In one study by Anderson and coworkers, four positive blood cultures of a coagulase-negative *Staphylococcus* species out of 17 plateletpheresis donations by one donor were obtained when blood was drawn from a heavily used, "dimpled" site of the antecubital fossa, despite careful iodophor cleansing (4). Transfusion of these units resulted in two cases of sepsis. Phlebotomy from the nondimpled left antecubital fossa repeatedly yielded negative cultures. Similar results were obtained in four additional veteran apheresis donors with dimpled phlebotomy sites on one arm. Results from this study, with the use of an autocontrol from the undimpled arm, suggest that scarring at the phlebotomy site may provide an environment where skin bacteria can grow and are protected from disinfectants. In addition to skin bacteria, soil bacteria (most notably, *P. fluorescens*) have been isolated from skin prior to disinfection (128) and have also been implicated in a significant fraction of sepsis occurrences linked to contaminated erythrocytes. Other environmental soil organisms, such as *P. putida*, have also been implicated in transfusion-transmitted sepsis.

A number of alternative cleansing or disinfection solutions or procedures are used in other countries. A survey of these methods along with their respective bacterial contamination rates of platelet components is given in Table 3. No one procedure appears to be consistently better than another.

More information about how disinfection procedures impact

TABLE 3. Comparison of effectiveness of skin preparation methods

Method	No. of platelet components tested	Platelet contamination rate (% culture positive of tested component)
Ethanol + chlorhexidine	650	0
Ethanol + ethanol	1,040	0
Ethanol[a]	500	0–0.2
PVP-I + PVP-I	9,000	0.05
Quaternary ammonium salts[b]	10,000	0.05–0.13
PVP-I	2,000	0.17–0.89
PVP-I[c]	1,500	0.95
Ethanol or PVP-I[d]	560	1.2

[a] Administered one or more times.
[b] Administered three times.
[c] Open system.
[d] One blood center in this country uses PVP-I; the remaining use ethanol.

blood contamination rates has been obtained from microbiological analysis of blood specimens collected for clinical testing (for example, at hospital emergency rooms) rather than for blood collected for transfusion. Some investigators take the position that blood cultures are rarely contaminated by bacteria that originate from the skin (122). Others believe that bacteria from the skin are responsible for many contamination events and that some disinfectants are superior to others (11). For example, in a double-blind study by Strand and coworkers, tincture of iodine was reported to be superior to PVP-I for disinfecting the phlebotomy site (130). These authors attributed the decreased blood contamination rate to faster disinfection with tincture of iodine (3.7% for iodine tincture versus 6.3% for PVP-I). Schifman and Pindur found that PVP-I followed by a 70% isopropyl alcohol–10% acetone scrub led to fewer contaminated blood cultures (2.2% versus 4.6%) than PVP-I followed by a 70% isopropyl alcohol scrub (119). Since there is little overlap in these studies of disinfectants used or microbiologic measurement techniques, a comprehensive evaluation of numerous skin disinfectants by a standard methodology could provide important information on whether there is an optimal technique for phlebotomy site preparation. Finally, the process of arm preparation would be better understood if quantitative distinctions could be made about the rate, extent, and duration of disinfection.

Donor Bacteremia

Several organisms have been linked to bacteremia in asymptomatic donors, e.g., *Y. enterocolitica* (1, 142) and *Salmonella* species (56), which can invade the intestinal mucosa and become blood borne (30, 56). Asymptomatic individuals can either exhibit no prior symptoms or harbor low-level blood infections for several weeks after symptoms of gastroenteritis have subsided (1, 142). In a somewhat unusual case, an outbreak of transfusion-acquired *Salmonella cholerae-suis* septicemia was traced to a plasmapheresis donor who, unknowingly, had *Salmonella* osteomyelitis of the tibia with low-grade bacteremia (112).

Other infections may infrequently cause transfusion-transmitted sepsis. Syphilis has been reported to occur after transfusion of fresh blood components even though the donor's serological tests were nonreactive (26, 114, 126). Fortunately, the spirochete reportedly does not survive refrigerated storage (49). Components that are contaminated with *Serratia liquefaciens* (68, 153) or viridans group streptococci (16) may represent extremely rare instances of blood-borne bacterial transmission caused by dental procedures (49). However, bacteremias from dental work are not of long duration (typically 30 min) (51), and individuals who have undergone recent dental procedures are excluded from donating. Despite the observation that *Borrelia burgdorferi*, the agent of Lyme disease, can survive in components during refrigerated and room temperature storage (9) and that the incidence of Lyme disease in some areas has increased by 163% since 1977 (9), there has been no documented case of transmission of the organism by transfusion.

Blood Containers

Although rarely observed since the change to closed, sterile, plastic blood collection container systems, contamination from inadequately sterilized blood container sets or set overwraps does occur. Two related outbreaks of sepsis have been documented: both involved *Serratia marcescens*. One case occurred in Denmark, where investigators demonstrated that clinical isolates from three septic patients, from the implicated blood units (all units were collected using blood containers from a single manufactured lot), and from samples obtained from the blood container manufacturing plant were a single ribotype (59). In a survey of 1,515 blood components in Denmark, *Serratia marcescens* was isolated from 11 (0.73%) of the units. The same lot of containers was implicated in transfusion-acquired *Serratia marcescens* septicemia in Sweden (61). Investigators suspect that the source of contamination may have been external to the container sets (59).

Another episode of *Serratia marcescens* contamination occurred in Canada and involved blood sample vacuum tubes (15). This incident, presumably caused by backflow of blood from the contaminated vacuum tubes to the primary collection bag (from where the samples were being taken), resulted in three cases of sepsis. Subsequent investigation revealed that 82% of the same lot of tubes from a single manufacturer was contaminated, while no organisms were found in six other lots.

Processing Equipment

Several reports caution readers about bacterial contamination in water baths (17, 25, 89, 112). In one, *Pseudomonas cepacia* was isolated from two units of thawed, cryoprecipitate (a plasma by-product) and one unit of frozen, thawed, and deglycerolized erythrocytes (112). Subsequent investigation revealed the use of the same water bath for thawing. Even though it was disinfected with povidone-iodine and refilled with fresh deionized water daily, quantitative cultures of the bath yielded a *P. cepacia* titer of 1.8×10^6 CFU/ml. In the other occurrence, a patient became septic after receiving a thawed unit of plasma (25). Culture of the patient's blood and the water in the bath revealed contamination with *P. aeruginosa* pyocin type 1C. These episodes emphasize the need to keep blood containers dry by using plastic overwraps or to use dry procedures for thawing.

CURRENT RECOMMENDATIONS FOR INVESTIGATING SUSPECTED CASES OF TRANSFUSION-ASSOCIATED SEPSIS

When a patient develops clinical signs compatible with receipt of a contaminated component, the *Technical Manual* of the American Association of Blood Banks (148) recommends that the transfusion be immediately stopped and the component be inspected for visible signs of clots, hemolysis, or abnormal color. A Gram stain of material from the suspected

unit should be performed as well. Finally, the patient's blood, the suspected component, and all intravenous solutions administered should be cultured under aerobic and anaerobic conditions at refrigerator, room, and body temperatures (148).

Many investigators confirm that sepsis is associated with transfusion by typing the organisms isolated from the patient and from the residue in the containers that were transfused (Tables 1 and 2). Testing has also included antibiotic susceptibility tests (90). Identity of strains has also been demonstrated by DNA restriction analysis (91) and other molecular techniques (123).

INTERVENTIONS

Additional Donor Questions

Following the reports of *Y. enterocolitica* outbreaks in 1988 and 1990 (32, 152), several investigators considered whether donor screening questions relating to recent gastrointestinal illness might be effective. Grossman and colleagues reported that 0.6% of donors gave an affirmative answer to the question, "Have you had two or more unusual episodes of diarrhea with fever or unusually severe abdominal pain within the last 4 weeks"? Four percent of all donors responded positively to the question, "Have you had any diarrhea in the last month?" (53). Since the majority of asymptomatic *Yersinia* donors reported mild or moderate symptoms of diarrhea, the second question would appear to screen out more potentially infectious individuals. In an unpublished study by the Centers for Disease Control, 9.7% of 6,000 donors reported general symptoms of gastrointestinal illness 30 days prior to donation (73). These results suggest that questions of this nature may screen out an unacceptable number of healthy donors. Furthermore, one-third of donors who transmitted *Y. enterocolitica* did not observe gastrointestinal symptoms (73, 142).

Altered Erythrocyte Properties of Contaminated Units

Several erythrocyte properties appear to be altered in bacterially contaminated components. Hemolysis in erythrocyte units with high levels of *Y. enterocolitica* was found by Kim and colleagues to be five times that of uncontaminated, paired controls (78). In addition, Kim and coworkers noted that heavily contaminated erythrocyte units often appear much darker than normal (76). This darker color can be discerned by comparing the color of the container to that of attached tubing, which is sealed at the time of component preparation. The color change during growth of psychrophilic bacteria first appears in units with titers exceeding 4×10^8 CFU/ml (147). Heavily contaminated erythrocytes that display this darkened appearance also have low oxygen tension (<5 torr [1 torr $\simeq$ 133 Pa]) compared with uncontaminated components (>50 torr) (76). Similar observations have been made by Wenz and colleagues (149). Presumably, this phenomenon is caused by competition of bacteria and erythrocytes for oxygen and is responsible for the darkening. The higher levels of methemoglobin measured in contaminated units (two- to fourfold over uncontaminated controls) may partially contribute to this color change as well (149). Color alterations have also been observed in heavily contaminated units containing *Enterobacter agglomerans* and an unidentified gram-negative bacillus (76). Other, more subtle changes may also appear. For example, extracellular erythrocyte pH declines by 0.13 to 0.18 unit when *Y. enterocolitica* reaches titers exceeding 4×10^8 (145).

Altered Platelet Properties of Contaminated Units

Myhre and coworkers reported that bacterial contamination of platelet concentrates can result in significant declines in extracellular pH beyond the values that are typically observed (95). As expected, *S. epidermidis*, *S. aureus*, *Bacillus cereus*, *E. coli*, and other organisms that produce acid as a by-product of glycolysis significantly lowered extracellular pH by day 3 of storage. Similar results with *S. epidermidis* have been recently obtained by Brecher and colleagues, who also demonstrated that differences between the control and contaminated platelets were evident when titers reached a level of 3×10^6 CFU/ml (18).

A number of organisms did not alter extracellular pH beyond the normal 6.0 to 7.4 range in the Myhre study. *Acinetobacter lwoffii*, which does not readily form acids, cannot directly alter platelet pH. Other organisms, such as *Klebsiella* spp., *Bacillus subtilis*, and *Proteus mirabilis*, did not cause significant declines in platelet extracellular pH because the organisms can metabolize the citrate (present as anticoagulant) and lessen the impact of acidification. Therefore, acidification of the medium by bacterial proliferation is not universal, and dangerously high titers may be reached before pH declines beyond normal levels.

Another indicator of bacterial contamination of platelet concentrates is the cessation of platelet "streaming" or "swirling." Platelet swirling is the consequence of changes in macroscopic light refraction that are observed when platelets are oriented by their normal discoid shape during liquid flow. Myhre and coworkers found that cessation of swirling was closely correlated with declines in pH observed in contaminated components (95). Like pH, dangerously high levels of bacteria can be present in platelet products without noticeable changes (95).

Reduction of Erythrocyte and Platelet Storage Times

Because bacterial strains often proliferate in blood components during storage, some consideration has been given to shortening storage times in the hope of reducing transfusion-associated sepsis. In 1986, concern about several sepsis-related fatalities and a study (16) that documented the rapid proliferation of bacteria following intentional inoculation of platelet concentrates prompted the FDA to reduce the storage time of platelets from 7 to 5 days (36). Similar concerns about several cases of *Y. enterocolitica* septicemia and fatalities resulting from the transfusion of erythrocyte components led the FDA to consider but not approve a reduction of erythrocyte storage time in 1991 (98, 117). Reasons for this decision included the infrequent incidence of transfusion-related *Y. enterocolitica* septicemia, the observation that some contaminated units whose transfusion resulted in sepsis were stored for less than 2 weeks at 1 to 6°C, and concerns that a reduction of erythrocyte storage time would exacerbate shortages in the blood supply that often occur during January and the summer months. Thus, the benefits of a potential reduction in the incidence of sepsis (resulting from a reduction in blood component storage time) must always be weighed against the problems associated with blood shortages.

Antibiotics

The inclusion of antibiotics in additive solutions or primary containers has been considered an intervention to prevent bacterial proliferation in stored blood (146). However, the effectiveness of any antibiotic would be limited to the susceptible strains; resistant strains would presumably continue to be

a problem. Furthermore, the adverse consequences of any particular antibiotic must be carefully considered. Individuals can experience hypersensitivity reactions and other side effects that occasionally lead to death from antibiotics. Even fairly safe antibiotics like the aminoglycosides still produce an occasional incident of rash, urticaria, febrile reaction, hypotension, and anaphylactic shock (116). Therefore, before routine addition of antibiotics to blood components could be considered a feasible intervention, the risk of serious adverse side effects would have to be less than the risk of transfusion-related sepsis.

Testing

Microscopy. The microscopic evaluation of Gram- or acridine orange-stained blood smears has been considered a bacterial screening test to be performed just before transfusion. The limits of reproducibly detecting bacteria in blood smears are approximately 10^5 to 10^6 CFU/ml with the Gram stain (111) and 10^4 to 10^5 CFU/ml with acridine orange (85). Barrett and coworkers followed the incidence of bacterial contamination associated with transfusion reactions from blood components over a 5-year period (10). There were 2,208 transfusion reactions from 51,278 transfusions of apheresis platelets, platelet concentrates, erythrocytes, and plasma. Of 1,898 reactions evaluated, seven components gave positive bacterial cultures. Gram staining was performed on residual components from six of the seven components that gave positive cultures; three of the six positive cultures were positive by Gram stain. Only one of the seven patients who received these contaminated products had any clinical sequelae. In this recipient, the contaminated unit may have been a contributing cause of death (10).

In additional studies, Gram staining was performed before transfusion of 3,829 apheresis platelets. Although eight platelets gave a positive Gram stain smear, only two were culture positive. Barrett and coworkers concluded that culture and Gram staining are poor screening techniques and suggested that more sensitive and specific bacterial detection methods are needed (10).

Culture methods. Instrumented blood culturing systems that result in more rapid detection of bacteria than do traditional manual broth or agar plate culturing techniques have been introduced (2, 99, 140). Many of these systems rely on detecting the increasing levels of CO_2 released with bacterial proliferation. However, these methods generally require 1 to 5 days of incubation to ensure minimum false-negative rates. Therefore, reliance on a negative result from these culturing systems would effectively reduce the length of time available to transfuse platelets from 5 to 3 days or less. Furthermore, since only a small fraction of the blood component is cultured (less than 10 ml) and the samples must be taken at the time of blood collection or component preparation, these methods may not be effective in detecting bacteria in freshly drawn units in which contamination levels may be less than one organism per sample volume.

Nucleic acid hybridization. Several investigators have described a novel application of a chemiluminescence-linked rRNA gene probe system to detect bacterial contamination in platelet concentrates (18, 27, 60, 74). Using a "universal" hybridization probe that recognizes a sequence of rRNA conserved among bacteria, the researchers can routinely detect a number of relevant bacterial species in platelet concentrates with levels greater than 10^4 CFU/ml. Similar results have been obtained in erythrocytes (60, 74). Since results can be observed on a luminometer within hours rather than days, this test could potentially be performed just before transfusion. Therefore, screened platelet products could be transfused anytime during the storage period. Another advantage includes the potential objectivity of the test, which is based on the quantitative measurement of light. One area for improvement would be automation and reduction of the time required to complete the procedure for RNA extraction, hybridization, and hydrolysis. Current manipulations require approximately 1 h from sample procurement to test results.

PCR. A PCR-based assay for the detection of *Y. enterocolitica* has been developed by several investigators (41, 42). Using primers to detect sequences in the *virF* gene of the PYV plasmid and the chromosomal *ail* gene, Feng and coworkers were able to detect *Y. enterocolitica* at a level of 5×10^3 CFU/ml from a 100-μl whole-blood sample. The authors speculated that cell debris and protein, as well as prokaryotic and eukaryotic nucleic acids, interfered with the specific hybridization of primers and were responsible for reducing the assay's sensitivity. The preparation of nucleic acid samples from whole blood was also quite involved and employed multiple centrifugation steps, protease treatment, and boiling of samples. Also, the PCR thermocycling procedure took approximately 3 h to complete 35 cycles. Improvement to greatly simplify the procedure may be required before PCR-based protocols could be routinely performed in already busy hospital transfusion services. Other difficulties with PCR-based procedures, such as extraneous contamination with the resultant detection of false-positive signals, would have to be addressed and overcome. Finally, detection would be limited to one species of bacteria unless conserved sequences, like those of rRNA, could be identified.

Properties of an "ideal" bacterial test for blood banking application. The ideal test for bacteria in blood components should be simple to perform, rapid enough to be carried out in hospital transfusion services concurrently with compatibility testing, and not prohibitively expensive. Preferably, the same test could be used with erythrocytes, platelets, and plasma products and would have an easy-to-interpret endpoint that requires no (or very simple) instrumentation. The false-positive rate should be low and the false-negative rate should be as close to zero as feasible (certainly less than the incidence of sepsis). Tests should be capable of detecting all organisms at levels that are below those that have been associated with sepsis from transfusion.

OTHER ASPECTS: IMMUNOSUPPRESSIVE EFFECTS OF TRANSFUSION

Transfusion of allogenic blood can have generalized immunological effects on patients. An important early example of the immunosuppressive effect of blood was reported by Opelz et al., who found that (allogeneic) transfusion prior to kidney transplant significantly reduced transplant rejection (101). Later, investigators described the effects of transfusion of allogeneic blood on cancer recurrence and bacterial infections in recipients. Only a general outline of transfusion-related immunosuppression and infection is given here. For comprehensive treatment, the reader is directed to several review articles (46, 136, 143).

Numerous clinical studies have linked perioperative transfusion and an increased incidence of postsurgical bacterial infection (33, 34, 35, 43, 52, 67, 86, 93, 97, 102, 135, 137). Eleven of 13 clinical studies, which have been conducted either retrospectively or prospectively, suggest that transfusion is significantly and independently related to an increased risk of bacterial infection (67, 136). As expected, all 13 studies

demonstrated that transfusion was associated with infection of wounds, incisions, or burns. However, more significantly, 11 of 12 studies also established the association between transfusion and the occurrence of infections distal to the site of injury, suggesting a generalized rather than a specific response (136). In a prospective clinical study by Jensen and colleagues, the presence of donor leukocytes and platelets in transfused blood was highly correlated with increased incidence of bacterial infection of patients undergoing colorectal surgery (67). In addition, patients who received whole blood had significantly impaired natural killer cell function compared with untransfused patients (67). Finally, in seven of eight studies, there was a dose response between the number of components transfused and the incidence of infection (136).

In the above studies, infection rates following transfusion ranged from 8 to 57%. Therefore, infections that are a consequence of immunosuppression from blood transfusion appear to be much more common than sepsis caused by blood components containing bacteria.

CONCLUSION

The frequency of patient sepsis attributable to transfusion of bacterially contaminated blood components appears to be very low but is similar to or less than that of transfusion-associated hepatitis C virus infection, which is transmitted in approximately 1 of 2,000 to 6,000 tested units (79) and which is frequently asymptomatic. It is significantly greater than that for infection with the human immunodeficiency and hepatitis B viruses, which are reported to transmit infections in 1 in 225,000 and 1 in 200,000 of all tested units, respectively (37). Although it is not clear whether published data on assessment of contamination levels by culture of routine components are accurate, the data do imply that the risk could be significantly greater than that measured by patient observation. In fact, transient fever during or following transfusion is not uncommon, but most cases are attributed to the patient's immune response to transfused leukocytes. The true incidence and the range of outcomes from bacterial contamination of blood products are poorly characterized. Consequently, more information is needed.

Several potential interventions for reducing the incidence of sepsis have been discussed. Careful attention to the process of phlebotomy itself should reduce the frequency of contamination by environmental and skin surface organisms, although it is evident that it may not be possible to sterilize organisms that reside below the most superficial levels of the donor's skin. It does not appear likely that effective donor health history screening procedures can be developed to identify individuals with low levels of bacteremia. Although not rigorously evaluated, it appears that the risk/benefit ratio for the addition of antibiotics to blood components may not be favorable. Further reduction in the storage time of erythrocytes or platelets is logistically difficult and could impact the availability of blood components. The efficacy of leukodepletion filters for the prevention of sepsis awaits further study. These and other approaches were considered in public meetings of the Blood Products Advisory Committee to the FDA. The FDA's concluding assessments presented at that meeting were in general accordance with these comments. They did, however, recommended further efforts to educate hospital professionals to recognize and respond promptly and appropriately to adverse signs in recipients during transfusion.

Perhaps the most promising approach considered for the reduction or prevention of transfusion-associated sepsis is the use of tests to detect bacteria directly in blood components shortly before their infusion. There is much potential for the application of modern techniques in biotechnology to the development of simple, accessible, and effective test procedures for bacteria in blood.

REFERENCES

1. **Aber, R. C.** 1990. Transfusion-associated *Yersinia enterocolitica*. Transfusion **30:**193–194.
2. **Ali, A. M., D. Elder, H. Richardson, and M. A. Blajchman.** 1987. Sterility verification to allow prolonged safe storage of apheresis platelet concentrates, abstract 1156. Blood **70:**325a.
3. **Anderson, K. C.** 1993. Current trends: evolving concepts in transfusion medicine. Bacterial contamination of platelets. Transfus. Sci. **14:**159–162.
4. **Anderson, K. C., M. A. Lew, B. C. Gorgone, J. Martel, C. B. Leamy, and B. Sullivan.** 1986. Transfusion-related sepsis after prolonged platelet storage. Am. J. Med. **81:**405–411.
5. **Arduino, M. J., L. A. Bland, M. A. Tipple, S. M. Aguero, M. S. Favero, and W. R. Jarvis.** 1989. Growth and endotoxin production of *Yersinia enterocolitica* and *Enterobacter agglomerans* in packed erythrocytes. J. Clin. Microbiol. **27:**1483–1485.
6. **Arnow, P. M., L. M. Weiss, D. Weil, and N. R. Rosen.** 1986. *Escherichia coli* sepsis from contaminated platelet transfusion. Arch. Intern. Med. **146:**321–324.
7. **AuBuchon, J. P., and C. Pickard.** 1993. White cell reduction and bacterial proliferation. Transfusion **33:**533.
8. **Balligand, G., Y. Laroche, and G. Cornelis.** 1985. Genetic analysis of virulence plasmid from a serogroup 9 *Yersinia enterocolitica* strain: role of outer membrane protein P1 in resistance to human serum and autoagglutination. Infect. Immun. **48:**782–786.
9. **Badon, S. J., R. D. Fister, and R. G. Cable.** 1989. Survival of *Borrelia burgdorferi* in blood products. Transfusion **29:**581–583.
10. **Barrett, B. B., J. W. Andersen, and K. C. Anderson.** 1993. Strategies for the avoidance of bacterial contamination of blood components. Transfusion **33:**228–234.
11. **Bell, A. R., and H. A. Ludlam.** 1992. Contamination of blood cultures during venepuncture: fact or myth? Postgrad. Med. J. **68:**388–389.
12. **Bettigole, R., D. Amsterdam, and J. Levin.** 1989. Death from bacterially contaminated transfusion, abstract 1462. Blood **74**(Suppl.):383a.
13. **Bjune, G., T. E. Ruud, and J. Eng.** 1984. Bacterial shock due to transfusion with *Yersinia enterocolitica* infected blood. J. Infect. Dis. **16:**411–412.
14. **Blajchman, M. A., and A. M. Ali.** 1992. Bacteria in the blood supply: an overlooked issue in transfusion medicine, p. 213–228. *In* S. J. Nance (ed.), Blood safety: current challenges. American Association of Blood Banks, Bethesda, Md.
15. **Blajchman, M. A., J. H. Thornley, H. Richardson, D. Elder, C. Spiak, and J. Racher.** 1979. Platelet transfusion-induced *Serratia marcescens* sepsis due to vacuum tube contamination. Transfusion **19:**39–44.
16. **Braine, H. G., T. S. Kickler, P. Charache, P. M. Ness, J. Davis, C. Reichart, and A. K. Fuller.** 1986. Bacterial sepsis secondary to platelet transfusion: an adverse effect of extended storage at room temperature. Transfusion **26:**391–393.
17. **Bray, B. M.** 1987. Risk of infection from water bath blood warmers. Anaesthesia **42:**778–779.
18. **Brecher, M. E., G. Bopthe, and A. Kerr.** 1993. The use of a chemiluminescence-linked universal bacterial ribosomal RNA gene probe and blood gas analysis for the rapid detection of bacterial contamination in white cell-reduced and nonreduced platelets. Transfusion **33:**450–457.
19. **Bruining, A., and C. C. M. de Wilde-Beekhuizen.** 1975. A case of contamination of donor blood by *Yersinia enterocolitica* type 9. Medikon **4:**30–31.
20. **Buchholz, D. H., J. P. AuBuchon, E. Snyder, S. Edberg, V. Piscitelli, R. L. Kandler, C. Pickard, and P. Napychank.** 1991. Leukocyte depletion and bacterial proliferation in blood components, abstract S233. Transfusion **31S:**63S.
21. **Buchholz, D. H., J. P. AuBuchon, E. L. Snyder, R. Kandler, S. Edberg, V. Piscitelli, C. Pickard, and P. Napychank.** 1992. Removal of *Yersinia enterocolitica* from AS-1 red cells. Transfusion **32:**667–672.

22. **Buchholz, D. H., G. M. Young, N. R. Friedman, J. A. Reilly, and M. R. Mardiney, Jr.** 1973. Detection and quantitation of bacteria in platelet products stored at ambient temperature. Transfusion **13:**268–275.
23. **Buchholz, D. H., V. M. Young, N. R. Friedman, J. A. Reilly, and M. R. Mardiney, Jr.** 1971. Bacterial proliferation in platelet products stored at room temperature. N. Engl. J. Med. **285:**429–433.
24. **Bufill, J. A., and P. S. Ritch.** 1989. *Yersinia enterocolitica* serotype O:3 sepsis after blood transfusion. N. Engl. J. Med. **320:**810.
25. **Casewell, M. W., N. G. P. Slater, and J. E. Cooper.** 1981. Operating theatre water-baths as a cause of *Pseudomonas* septicaemia. J. Hosp. Infect. **2:**237–240.
26. **Chambers, R. W., H. T. Foley, and P. J. Schmidt.** 1969. Transmission of syphilis by fresh blood components. Transfusion **9:**32–34.
27. **Chongokolwatana, V., M. Morgan, J. C. Faegin, M. R. Jacobs, and R. Yomtovian.** 1993. Comparison of microscopy and a bacterial DNA probe detecting bacterially contaminated platelets, abstract S191. Transfusion **33S:**50S.
28. **Collins, P. S., J. M. Salander, J. R. Youkey, B. M. Elliot, G. J. Collins, Jr., H. J. Donohue, and N. M. Rich.** 1985. Fatal sepsis from blood contaminated with *Yersinia enterocolitica*: a case report. Milit. Med. **150:**689–692.
29. **Cordle, D., J. A. Koepke, and F. P. Koontz.** 1990. The sterility of platelet and granulocyte concentrates collected by discontinuous flow centrifugation. Transfusion **20:**105–107.
30. **Cover, T. L., and R. C. Arber.** 1989. *Yersinia enterocolitica*. N. Engl. J. Med. **321:**16–24.
31. **Cunningham, M., and J. D. Cash.** 1973. Bacterial contamination of platelet concentrates stored at 20°C. J. Clin. Pathol. **26:**401–404.
32. **Davis, J. P., M. Moser, R. H. Hucheson, T. G. Betz, M. H. Wilder, L. A. Wintermeyer, B. J. Francis, and H. D. Donnell, Jr.** 1988. *Yersinia enterocolitica* bacteremia and endotoxin shock associated with red blood cell transfusion—United States 1987–1988. Morbid. Mortal. Weekly Rep. **37:**577–578.
33. **Dawes, L. G., C. Aprahamian, R. E. Condon, and M. A. Malangoni.** 1986. The risk of infection after colon injury. Surgery **100:**796–801.
34. **Dellinger, E. P., S. D. Miller, M. J. Wertz, M. Grypma, B. Droppert, and P. A. Anderson.** 1988. Risk of infection after open fracture of the arm or leg. Arch. Surg. **123:**1320–1327.
35. **Dellinger, E. P., M. R. Oreskovich, M. J. Wertz, V. Hamasaki, and E. S. Lennard.** 1984. Risk of infection following laparotomy for penetrating abdominal injury. Arch. Surg. **119:**20–27.
36. **Department of Health and Human Services and Food and Drug Administration.** 1986. Septic reactions after platelet transfusions, p. 151–241. *In* Blood products, sixteenth meeting, vol. I. Transcripts. Baker, Hames and Burkes Reporting, Inc., Washington, D.C.
37. **Dodd, R. Y.** 1992. The risk of transfusion-transmitted infection. N. Engl. J. Med. **327:**419–421.
38. **Douglas, D., J. M. Sorace, and T. Kickler.** 1987. Beta-hemolytic *Streptococcus* contamination of a platelet unit. Transfusion **27S:** 512.
39. **Elrick, J.** 1988. A case study—fatal gram-negative shock following blood transfusions. *Yersinia* News (Melbourne) **5:**1–2.
40. **Farmer, J. J., B. R. Davis, and F. W. Hickman.** 1976. Detection of *Serratia* outbreaks in hospital. Lancet **ii:**455–459.
41. **Feng, P., S. P. Keasler, and W. E. Hill.** 1992. Direct identification of *Yersinia enterocolitica* in blood by polymerase chain reaction amplification. Transfusion **32:**850–854.
42. **Fenwick, S. G., and A. Murray.** 1991. Detection of pathogenic *Yersinia enterocolitica* by polymerase chain reaction. Lancet **337:** 496–497.
43. **Fernandez, M. C., and J. E. Menitove.** 1989. Blood transfusion and post operative infection in orthopaedic patients, abstract S190. Transfusion **29S:**53S.
44. **Foreman, N. K., W. C. Wang, E. J. Cullen, Jr., G. L. Stidham, T. A. Pearson, and J. L. Shenep.** 1991. Endotoxic shock after transfusion of contaminated red blood cells. Pediatr. Infect. Dis. J. **10:**624–626.
45. **Galloway, S. J., and P. D. Jones.** 1986. Transfusion acquired *Yersinia enterocolitica*. Aust. N. Z. J. Med. **16:**248.
46. **George, C. D., and P. J. Morello.** 1986. Immunologic effects of blood transfusion upon renal transplantation, tumor operations and bacterial infections. Am. J. Surg. **152:**329–337.
47. **Gibaud, M., P. Martin-Dupont, M. Dominguez, P. Laurentjoye, B. Chassaing, and B. Leng.** 1984. Septicémie à *Pseudomonas fluorescens* aprés transfusion de sang contaminé. Presse Med. **13:**2583–2584.
48. **Goddard, D., S. I. Jacobs, and S. M. Manohitharajah.** 1973. The bacteriological screening of platelet concentrates stored at 22°. Transfusion **13:**103–106.
49. **Goldman, M., and M. A. Blajchman.** 1991. Blood product-associated bacterial sepsis. Transfus. Med. Rev. **5:**73–83.
50. **Gong, J., C. F. Högman, A. Hambraeus, C. S. Johansson, and L. Eriksson.** 1993. Transfusion-transmitted *Yersinia enterocolitica* infection. Vox Sang. **65:**42–46.
51. **Gottlieb, T.** 1993. Hazards of bacterial contamination of blood products. Anaesth. Intensive Care **21:**20–23.
52. **Graves, A., W. G. Cioffi, A. D. Mason, Jr., et al.** 1989. Relationship of transfusion and infection in a burn population. J. Trauma **29:**948–952.
53. **Grossman, B. J., P. Kollins, P. M. Lau, J. L. Perreten, R. J. Bowman, S. Malcolm, and W. M. Palko.** 1991. Screening blood donors for gastrointestinal illness: a strategy to eliminate carriers of *Yersinia enterocolitica*. Transfusion **31:**500–501.
54. **Halpin, T. J., S. Kilker, and J. Epstein.** 1992. Bacterial contamination of platelet pools—Ohio, 1991. Morbid. Mortal. Weekly Rep. **41:**36–37.
55. **Heal, J. M., and H. J. Cohen.** 1991. Do white cells in stored blood components reduce the likelihood of posttransfusion bacterial sepsis? Transfusion **31:**581–583.
56. **Heal, J. M., M. E. Jones, J. Forey, A. Chaudhry, and R. L. Stricof.** 1987. Fatal *Salmonella* septicemia after platelet transfusion. Transfusion **27:**2–5.
57. **Heal, J. M., S. Singal, E. Sardisco, and T. Mayer.** 1986. Bacterial proliferation in platelet concentrates. Transfusion **26:**388–390.
58. **Heesemann, J., C. Keller, R. Morawa, N. Schmidt, H. J. Siemens, and R. Laufs.** 1983. Plasmids of human strains of *Yersinia enterocolitica*: molecular relatedness and possible importance for pathogenesis. J. Infect. Dis. **147:**107–115.
59. **Heltberg, O., F. Skov, P. Gerner-Smidt, H. J. Kolmos, E. Dybkjaer, E. Gutschik, D. Jerne, O. B. Jepsen, M. Weischer, W. Frederiksen, and H. Sorensen.** 1993. Nosocomial epidemic of *Serratia marcescens* septicemia ascribed to contaminated blood transfusion bags. Transfusion **33:**221–227.
60. **Hogan, J., B. Curry, M. Brecher, G. Boothe, M. Kemper, A. Pineda, V. Halling, G. Tegtmeier, S. Henderson, R. Yomtovian, and V. Chongokolwatana.** 1993. Detection of bacterially contaminated platelet units with an all-bacterial DNA probe test, abstract S152. Transfusion **33S:**40S.
61. **Högman, C. F., H. Fritz, and L. Sandberg.** 1993. Posttransfusion *Serratia marcescens* septicemia. Transfusion **33:**189–191.
62. **Högman, C. F., J. Gong, L. Eriksson, A. Hambraeus, and C. S. Johansson.** 1991. White cells protect donor blood against bacterial contamination. Transfusion **31:**620–626.
63. **Högman, C. F., J. Gong, A. Hamnraeus, C. S. Johansson, and L. Eriksson.** 1992. The role of white cells in the transmission of *Yersinia enterocolitica* in blood components. Transfusion **32:**654–657.
64. **Honig, C. L., and J. R. Bove.** 1980. Transfusion-associated fatalities: review of Bureau of Biologics reports 1976–1978. Transfusion **20:**653–661.
65. **Jacobs, J., D. Jamaer, J. Vandeven, M. Wouters, C. Vermylen, and J. Vandepitte.** 1989. *Yersinia enterocolitica* in donor blood: a case report and review. J. Clin. Microbiol. **27:**1119–1121.
66. **Janot, C., M. E. Briquel, F. Steiff, and J. C. Burdin.** 1989. Infectious complications due to transfusion acquired *Yersinia enterocolitica*. Transfusion **29:**372–373.
67. **Jensen, L. S., A. J. Andersen, P. M. Christiansen, P. Hokland, C. O. Juhl, G. Madsen, J. Mortensen, C. Moller-Nielsen, F. Hanberg-Sorensen, and M. Hokland.** 1992. Postoperative infection and natural killer cell function following blood transfusion in

patients undergoing elective colorectal surgery. Br. J. Surg. **79:** 513–516.
68. **Jeppsson, B., S. Lindahl, S. Ingemansson, S. Kornhall, and S. Sjövall.** 1984. Bacterial contamination of blood transfusion: an unusual cause of sepsis. Acta Chir. Scand. **150:**489–481.
69. **Kahn, R. A., and L. J. Flinton.** 1974. The relationship between platelets and bacteria. Blood **44:**715–721.
70. **Kahn, R. A., and R. L. Syring.** 1975. The fate of bacteria introduced into whole blood from which platelet concentrates were prepared and stored at 22 or 4°C. Transfusion **15:**363–367.
71. **Kapperud, G., H. J. Skarpeid, R. Solberg, and T. Bergan.** 1985. Outer membrane proteins and plasmids in different *Yersinia enterocolitica* serogroups isolated from man and animals. Acta Pathol. Microbiol. Immunol. Scand. Sect. B **93:**27–35.
72. **Katz, A. J., and R. C. Tilton.** 1970. Sterility of platelet concentrates stored at 25°C. Transfusion **10:**329–330.
73. **Katz, L., J. L. MacPherson, and T. F. Zuck.** 1992. Yersinia and blood donation. Transfusion **32:**191.
74. **Kemper, M., and K. Kuramoto.** 1993. Rapid detection of bacterial contamination in blood and blood components, abstract S196. Transfusion **33S:**51S.
75. **Khabbaz, R. F., P. M. Arnow, A. K. Highsmith, L. A. Herwaldt, T. Chou, W. R. Jarvis, N. W. Lerche, and J. R. Allen.** 1984. *Pseudomonas fluorescens* bacteremia from blood transfusion. Am. J. Med. **76:**62–68.
76. **Kim, D. M., M. E. Brecher, L. A. Bland, T. J. Estes, R. A. Carmen, and E. J. Nelson.** 1992. Visual identification of bacterially contaminated red cells. Transfusion **32:**221–225.
77. **Kim, D. M., M. E. Brecher, L. A. Bland, T. J. Estes, S. K. McAllister, S. M. Aguero, R. A. Carmen, and E. J. Nelson.** 1992. Prestorage removal of *Yersinia enterocolitica* from red cells with white cell-reduction filters. Transfusion **32:**658–662.
78. **Kim, D. M., T. J. Estes, and M. E. Brecher.** 1992. WBC filtration, blood gas analysis and plasma hemoglobin in Yersinia enterocolitica contaminated red cells, abstract S156. Transfusion **32S:**41S.
79. **Kleinman, S., H. Alter, M. Busch, P. Holland, G. Tegtmeier, M. Nelles, S. Lee, E. Page, J. Wilber, and A. Polito.** 1992. Increased detection of hepatitis C virus (HCV)-infected blood donors by a multiple-antigen HCV enzyme immunoassay. Transfusion **32:** 805–813.
80. **Kora, S., H. Kuroki, T. Kido, N. Katsurada, and M. Sado.** 1993. Mechanism of leukocyte removal by porous material, p. 119–129. *In* S. Sekiguchi (ed.), Clinical application of leukocyte depletion. Blackwell Scientific Publications, Oxford.
81. **Lian, C. J., W. S. Hwang, and C. H. Pai.** 1987. Plasmid-mediated resistance to phagocytosis in *Yersinia enterocolitica*. Infect. Immun. **55:**1176–1182.
82. **Lian, C. J., and C. H. Pai.** 1985. Inhibition of human neutrophil chemiluminescence by plasmid-mediated outer membrane proteins of *Yersinia enterocolitica*. Infect. Immun. **49:**145–151.
83. **Mallin, W. S., D. T. Reuss, J. W. Bracke, S. C. Roberts, and G. L. Moore.** 1973. Bacteriological study of platelet concentrates stored at 22° and 4°C. Transfusion **13:**439–442.
84. **Martinez, R. J.** 1983. Plasmid-mediated and temperature-regulated surface properties of *Yersinia enterocolitica*. Infect. Immun. **41:**921–930.
85. **McCarthy, L. R., and J. E. Senne.** 1980. Evaluation of acridine orange stain for detection of microorganisms in blood cultures. J. Clin. Microbiol. **11:**281–285.
86. **Miholic, J., M. Hudec, E. Domanig, H. Hiertz, W. Klepetko, F. Lackner, and E. Wolner.** 1985. Risk factors for severe bacterial infections after valve replacement and aortocoronary bypass operations: analysis of 246 cases by logistic regression. Ann. Thorac. Surg. **40:**224–228.
87. **Mollaret, H. H.** 1989. Le choc septique transfusionnel du a *Yersinia enterocolitica*. Apropos de 19 cas. Med. Malad. Infect. **4:**186–192.
88. **Morduchowicz, G., S. Pitlik, D. Huminer, M. Alkan, M. Drucker, J. B. Rosenfeld, and C. S. Block.** 1991. Transfusion reactions due to bacterial contamination of blood and blood products. Rev. Infect. Dis. **13:**307–314.
89. **Morrell, R. M., Jr., and B. L. Wasilauskas.** 1992. Tracking laboratory contamination using a *Bacillus cereus* pseudoepidemic as an example. J. Clin. Microbiol. **30:**1469–1473.
90. **Morrow, J. F., H. G. Braine, T. S. Kickler, P. M. Ness, J. D. Dick, and A. K. Fuller.** 1991. Septic reactions to platelet transfusions. A persistant problem. JAMA **266:**555–558.
91. **Muder, R. R., Y. C. Yee, J. D. Rihs, and M. Bunker.** 1992. *Staphylococcus epidermidis* bacteremia from transfusion of contaminated platelets: application of bacterial DNA analysis. Transfusion **32:**771–774.
92. **Munro, R., and A. Lye.** 1990. *Yersinia enterocolitica* bacteraemia after blood transfusion. Med. J. Aust. **152:**280.
93. **Murphy, P., J. M. Heal, and N. Blumberg.** 1991. Infection or suspected infection after hip replacement surgery with autologous or homologous blood transfusions. Transfusion **31:**212–217.
94. **Murray, A. E., C. A. Bartzokas, A. J. N. Shepherd, and F. M. Roberts.** 1987. Blood transfusion-associated *Pseudomonas fluorescens* septicemia: Is this an increasing problem? J. Hosp. Infect. **9:**243–248.
95. **Myhre, B. A., S. H. Demainew, R. N. Yoshimori, E. Nelson, and R. A. Carmen.** 1985. pH changes caused by bacterial growth in contaminated platelet concentrates. Ann. Clin. Lab. Sci. **15:**509–514.
96. **Myhre, B. A., L. J. Walker, and M. L. White.** 1974. Bacterial properties of platelet concentrates. Transfusion **14:**116–123.
97. **Nichols, R. L., J. W. Smith, D. B. Klein, D. D. Trunkey, R. H. Cooper, M. F. Adinolfi, and J. Mills.** 1984. Risk of infection after penetrating abdominal trauma. N. Engl. J. Med. **311:**1065–1070.
98. **Nightingale, S. L.** 1991. Possibility of *Yersinia enterocolitica* bacteremia due to transfusion. JAMA **266:**190.
99. **Nolte, F. S., J. M. Williams, R. C. Jerris, J. A. Morello, C. D. Leitch, S. Matushek, L. D. Schwabe, F. Dorigan, and F. E. Kocka.** 1993. Multicenter clinical evaluation of a continuous monitoring blood culture system using fluorescent-sensor technology (BACTEC 9240). J. Clin. Microbiol. **31:**552–557.
100. **Oka, S., K. Maeda, T. Nishimura, and N. Yamawaki.** 1993. Mechanism of leukocyte removal with fibers, p. 105–118. *In* S. Sekiguchi (ed.), Clinical application of leukocyte depletion. Blackwell Scientific Publications, Oxford.
101. **Opelz, G., D. P. S. Sengar, M. R. Mickey, and P. I. Terasaki.** 1973. Effect of blood transfusions on subsequent kidney transplants. Transplant Proc. **5:**253–259.
102. **Ottino, G., R. De Paulis, S. Pansini, G. Rocca, M. V. Tallone, C. Comoglio, P. Costa, F. Orzan, and M. Morea.** 1987. Major sternal wound infection after open-heart surgery: a multivariate analysis of risk factors in 2579 consecutive operative procedures. Ann. Thorac. Surg. **44:**173–179.
103. **Pai, C. H., and L. DeStephano.** 1982. Serum resistance associated with virulence in *Yersinia enterocolitica*. Infect. Immun. **35:**605–611.
104. **Pepersack, F., T. Prigtogyne, J. P. Butzler, and E. Yourassowsky.** 1979. *Campylobacter jejuni* post-transfusional septicaemia. Lancet **ii:**911.
105. **Pepper, D. S.** 1976. Frozen red cells. Clin. Hematol. **6:**53–67.
106. **Phillips, P., L. Grayson, K. Stockman, and J. Hansky.** 1984. Transfusion-related *Pseudomonas* sepsis. Lancet **i:**879.
107. **Pietersz, R. N. I., H. W. Reesink, W. Pauw, W. J. A. Dekker, and L. Buisman.** 1992. Prevention of *Yersinia enterocolitica* growth in red-blood-cell concentrates. Lancet **340:**755–756.
108. **Portnoy, D. A., S. L. Moseley, and S. Falkow.** 1981. Characterization of plasmids and plasmid-associated determinants of *Yersinia enterocolitica* pathogenesis. Infect. Immun. **31:**775–782.
109. **Punsalang, A., J. M. Heal, and P. J. Murphy.** 1989. Growth of gram-positive and gram-negative bacteria in platelet concentrates. Transfusion **29:**596–599.
110. **Radcliffe, J. H., M. A. Denham, C. Gaydos, and M. B. Simpson, Jr.** 1978. Bacteriological sterility of washed deglycerolized red blood cells after 72 hours storage. Transfusion **18:**365–366.
111. **Reik, H., and S. J. Rubin.** 1981. Evaluation of the buffy-coat smear for rapid detection of bacteremia. JAMA **245:**357–359.
112. **Rhame, F. S., R. K. Root, J. D. MacLowry, T. A. Dadisman, and J. V. Bennett.** 1973. *Salmonella* septicemia from platelet transfusions: study of an outbreak traced to a hematolgenous carrier of *Salmonella cholerae-suis*. Ann. Intern. Med. **78:**633–641.
113. **Richards, C., J. Kolins, and C. D. Trindade.** 1992. Autologous

transfusion-transmitted *Yersinia enterocolitica*. JAMA **268:**1541–1542.
114. **Risseeuw-Appel, I. M., and F. C. Kothe.** 1983. Transfusion syphilis: a case report. Sex. Transm. Dis. **10:**200–201.
115. **Robins-Browne, R. M.** 1993. Removal of *Yersinia enterocolitica* from red-blood-cell concentrates. Lancet **341:**250.
116. **Sande, M. A., and G. L. Mandell.** 1990. Antimicrobial agents. The aminoglycosides, p. 1104–1108. *In* L. S. Goodman and A. G. Gilman (ed.), The pharmacological basis of therapeutics. Pergamon Press, New York.
117. **Sayers, M. (chairman).** 1991. May 9 Minutes to the 32nd meeting of the Blood Product Advisory Committee. Food and Drug Administration, Bethesda, Md.
118. **Sazama, K., Ober, Kaler, Grimes, and Shriver.** 1989. Transfusion deaths: the second decade of mandatory FDA reporting, abstract S121. Transfusion **29S:**36S.
119. **Schifman, R. B., and A. Pindur.** 1993. The effect of skin disinfection material on reducing blood culture contamination. Am. J. Clin. Pathol. **99:**536–538.
120. **Schmitt, J. L., P. Bataille, B. Coevoert, F. Eb, G. Laurans, A. Fournier, and J. Orfila.** 1982. Septicémie à *Yersinia enterocolitica* avec choc, insuffisance rénale et oedème pulmonaire lésionnel mortel après transfusion dans le post-partum. Med. Malad. Infect. **13:**197–199.
121. **Scott, J., F. E. Boulton, J. R. W. Govan, R. S. Miles, D. B. L. McClelland, and C. V. Prowse.** 1988. A fatal transfusion reaction associated with blood contaminated with *Pseudomonas fluorescens*. Vox Sang. **54:**201–204.
122. **Shahar, E., B. S. Wohl-Gottesman, and L. Shenkman.** 1990. Contamination of blood cultures during venepuncture: fact or myth. Postgrad. Med. J. **66:**1053–1058.
123. **Shayegani, M., L. M. Parsons, A. L. Waring, J. Donhowe, R. Goering, W. A. Archinal, and J. Linden.** 1991. Molecular relatedness of *Staphylococcus epidermidis* isolates obtained during a platelet transfusion-associated episode of sepsis. J. Clin. Microbiol. **29:**2768–2773.
124. **Sherburne, B., A. McCullough, W. H. Dzik, and P. DeGiroiami.** 1991. Bacterial proliferation in platelet concentrates is unaffected by pre-storage leukocyte depletion, abstract 1391. Blood **78** (Suppl.):350a.
125. **Silver, H., A. C. Sonnenwirth, and L. D. Beisser.** 1970. Bacteriologic study of platelet concentrates prepared and stored without refrigeration. Transfusion **10:**315–316.
126. **Soendjojo, A., M. Boedisantoso, M. I. Ilias, and D. Rahardjo.** 1982. Syphilis d'emblée due to a blood transfusion. Br. J. Vener. Dis. **58:**149–150.
127. **Stenhouse, M. A. E., and L. V. Milner.** 1982. *Yersinia enterocolitica*. A hazard in blood transfusion. Transfusion **22:**396–398.
128. **Stenhouse, M. A. E., and L. V. Milner.** 1992. A survey of cold-growing Gram-negative organisms isolated from the skin of prospective blood donors. Transfus. Med. **2:**235–237.
129. **Stossel, T. P.** 1975. Phagocytosis: recognition and ingestion. Semin. Hematol. **12:**83–116.
130. **Strand, C. L., R. R. Wajsbort, and K. Sturmann.** 1993. Effect of iodophor vs iodine tincture skin preparation on blood culture contamination rate. JAMA **269:**1004–1006.
131. **Stubbs, J. R., R. L. Reddy, S. A. Elg, E. H. Perry, L. L. Adcock, and J. McCullough.** 1991. Fatal *Yersinia enterocolitica* (serotype O:5,27) after blood transfusion. Vox Sang. **61:**18–23.
132. **Surgenor, D. M., E. L. Wallace, S. H. S. Hao, and R. H. Chapman.** 1990. Collection and transfusion of blood in the United States 1982–1988. N. Engl. J. Med. **322:**1646–1651.
133. **Szymanski, I. O.** 1985. Sterility of single-donor apheresis platelets. Transfusion **25:**290.
134. **Tabor, E., and R. J. Gerety.** 1984. Five cases of *Pseudomonas* sepsis transmitted by blood transfusions. Lancet **i:**1403.
135. **Tartter, P. I.** 1988. Blood transfusion and infectious complications following colorectal cancer surgery. Br. J. Surg. **75:**789–792.
136. **Tartter, P. I.** 1989. Immune consequences of blood transfusion in the surgical patient. Surg. Immun. **1:**13–19.
137. **Tartter, P. I., R. M. Driefuss, A. M. Malon, T. M. Heimann, and A. H. Aufses.** 1988. Relationship of postoperative septic complications and blood transfusions in patients with Crohn's disease. Am. J. Surg. **155:**43–47.
138. **Taylor, M. C., T. Keane, and F. R. Falkner.** 1984. *Pseudomonas putida* in transfused blood. Lancet **ii:**107.
139. **Tertti, R., E. Eerola, O. P. Lehtonen, T. H. Ståhlnerg, M. Viander, and A. Toivanen.** 1987. Virulence-plasmid is associated with the inhibition of opsonization in *Yersinia enterocolitica* and *Yersinia pseudotuberculosis*. Clin. Exp. Immunol. **68:**266–274.
140. **Thorpe, T. C., M. L. Wilson, J. E. Turner, J. L. DiGuiseppi, M. Willert, S. Mirrett, and L. B. Reller.** 1990. BacT/Alert: an automated colorimetric microbial detection system. J. Clin. Microbiol. **28:**1608–1612.
141. **Thuillier, M., and M. C. Gandrille.** 1969. Accidents transfusionnels dus à du sang contaminé par des bacilles à pigment jaune. Rev. Fr. Transfus. **12:**477–480.
142. **Tipple, M. A., L. A. Bland, J. J. Murphy, M. J. Arduino, A. L. Panlilio, J. J. Farmer III, M. A. Tourault, C. R. MacPherson, J. E. Menitove, A. J. Grindon, P. S. Hohnson, R. G. Strauss, J. A. Bufill, P. S. Ritch, J. R. Archer, O. C. Tablan, and W. R. Jarvis.** 1990. Sepsis associated with transfusion of red cells contaminated with *Yersinia enterocolitica*. Transfusion **30:**207–213.
143. **Triulzi, D. J., J. M. Heal, and N. Blumberg.** 1990. Transfusion-induced immunomodulation and its clinical consequences, p. 1–34. *In* S. T. Nance (ed.), Transfusion medicine in the 1990's. American Association of Blood Banks, Arlington, Va.
144. **Van Lierde, S., G. R. Fleisher, S. A. Plotkin, and J. M. Campos.** 1985. A case of platelet transfusion-related *Serratia marcescens* sepsis. Pediatr. Infect. Dis. **4:**293–295.
145. **Wagner, S. J.** Unpublished observations.
146. **Wagner, S. J., L. I. Friedman, and R. Y. Dodd.** 1991. Bactericidal effects of gentamicin against *Yersinia* spiked into ADSOL red cells, abstract S46. Transfusion **31S:**S16.
147. **Wagner, S. J., D. Robinette, and R. Dodd.** 1993. Factors affecting *Yersinia enterocolitica* (serotype O:8) viability in deliberately inoculated blood. Transfusion **33:**713–716.
148. **Walker, R. H. (ed.).** 1990. Technical manual, 10th ed., p. 420–421, 628. American Association of Blood Banks, Arlington, Va.
149. **Wenz, B., E. R. Burns, and L. F. R. Freundlich.** 1992. Prevention of growth of *Yersinia enterocolitica* in blood by polyester fiber filtration. Transfusion **32:**663–666.
150. **Wenz, B., D. Ciavarella, and L. Freundlich.** 1993. Effect of prestorage white cell reduction on bacterial growth in platelet concentrates. Transfusion **33:**520–523.
151. **Wilkinson, T. J., B. M. Colls, S. T. Chambers, and R. B. Ikram.** 1991. Blood transfusion acquired *Yersinia enterocolitica* sepsis: two cases. N. Z. Med. J. **104:**121–122.
152. **Woernle, C. H., R. E. Hoffman, J. D. Smith, M. T. Osterholm, F. E. Thompson, C. M. Sewell, T. J. Halpin, G. R. Istre, and R. Hutcheson.** 1991. Update: *Yersinia enterocolitica* bacteremia and endotoxin shock associated with red blood cell transfusions—United States 1991. Morbid. Mortal. Weekly Rep. **40:**176–178.
153. **Wolf, C. F. W., P. Javidian, M. Olenich, G. Halverson, M. James, and K. Krieger.** 1993. Fatal *Serratia liquifaciens* septic shock after transfusion of contaminated red blood cells (adenine-saline added): report of a case, abstract S151. Transfusion **33S:**40S.
154. **Wrenn, H. E., and C. E. Speicher.** 1974. Sterility of 400 single units stored at room temperature. Transfusion **14:**171–172.
155. **Wright, D. C., I. F. Selss, K. J. Vinton, and R. N. Pierce.** 1985. Fatal *Yersinia enterocolitica* sepsis after blood transfusion. Arch. Pathol. Lab. Med. **109:**1040–1042.