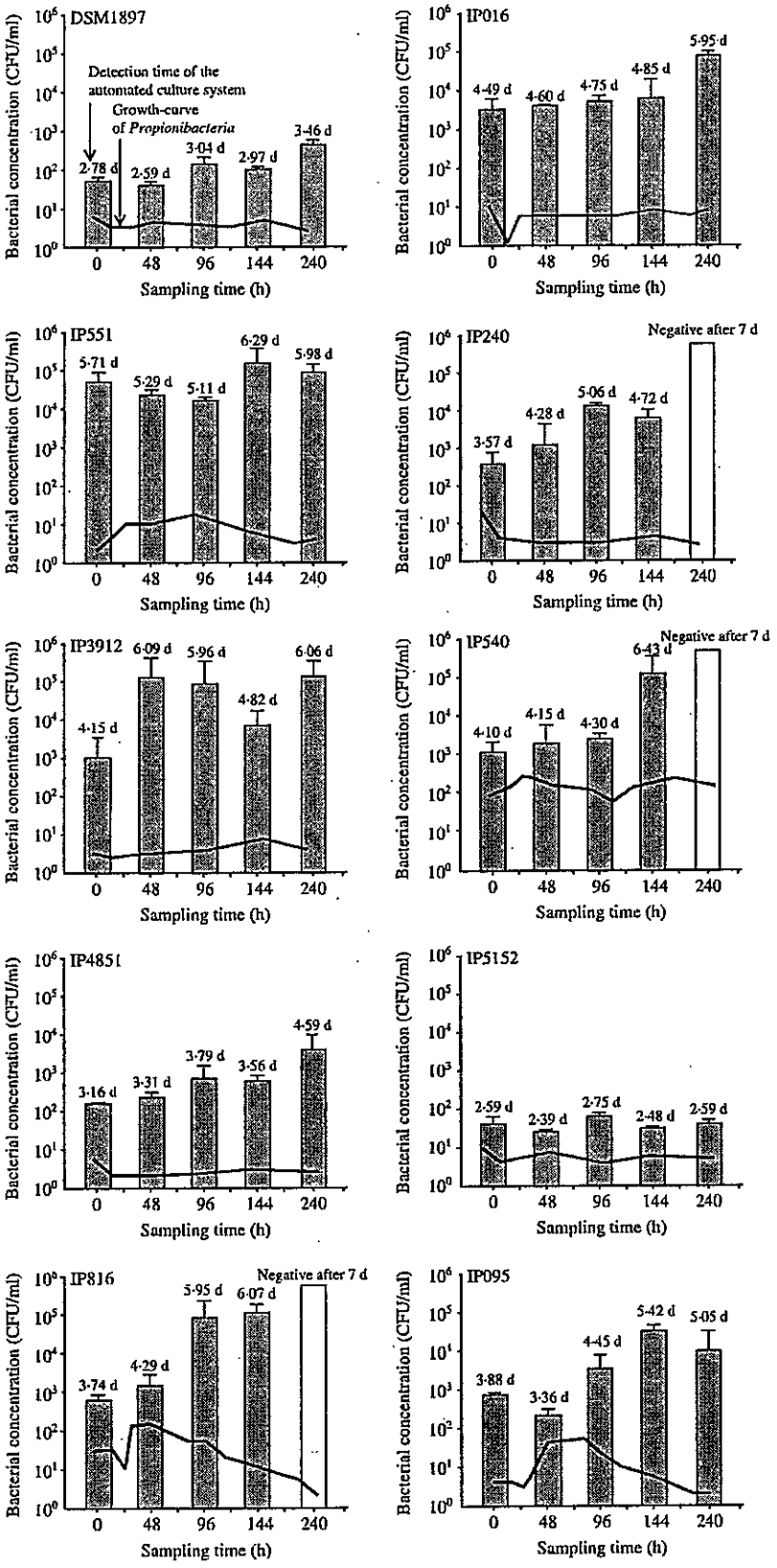

Fig. 2 Bacterial proliferation of *Propionibacterium* species in platelet concentrates (PCs) during storage and microbiological monitoring using an automated culture system. One single apheresis-derived PC unit was spiked with approximately 1–100 CFU/ml of *Propionibacterium* species and stored at 22 °C. Samples were taken in duplicate before inoculation (negative control) and at different times (0, 48, 96, 144 and 240 h after inoculation), enumerated by plating culture (line indicates the bacterial growth representing the bacterial load at the time of sampling) and inoculated into the anaerobic culture bottles for microbiological monitoring using an automated culture system (median times to first positive culture of the BacT/Alert detection is displayed in bars). d, days.

culture system, depending on the bacterial load in the PCs and growth characteristics of the strain. The BacT/Alert automated culture system detected all 10 *Propionibacterium* strains in the mean time of 2·59 to 5·71 days by sampling immediately after inoculation. During culture of inoculated PCs, all samples, with the exception of samples of IP240, IP540 and IP016, taken 240 h after inoculation were detected. Corresponding to the bacterial titres, the time to detection remained nearly constant (DSM1897, IP5152 and IP551) or slightly increased (IP540, IP016, IP240, IP3912, IP4851, IP816 and IP095) when samples were taken during the 10-day storage. Samples that did not react after 7-day incubation due to sampling error (samples of IP540, IP240 and IP816 after 240 h of storage) were subcultured for bacterial verification and considered sterile. Furthermore, no positive signal was recorded by the culture system for samples taken from unspiked PCs during incubation for up to 7 days.

Discussion

Contamination during blood donation or processing and subclinical infections in blood donors have all been implicated as sources of bacterial contamination in PCs [26]. Nevertheless, the predominant organisms implicated in platelet bacterial contamination are part of the human skin flora, including *Staphylococci*, *Corynebacterium* species and *Propionibacterium* species [3]. Coring of skin during the phlebotomy process may facilitate the entrance of bacteria into the collection bag [11]. In various studies, *P. acnes* was the most frequently implicated organism of bacterial contamination of PCs, but to date the clinical significance is debatable [8,14,27,28]. Thus, the principal objectives of this study were to discuss the meaning and appraisal of *Propionibacteria* detection at the end of storage using automated culture for platelet bacteria screening. Therefore, we simulated the bacterial contamination of PCs with 10 *Propionibacterium* species and monitored their growth characteristics in PCs during a 10-day storage at 22 °C. Although the bacterial contamination of apheresis products at collection may be as low as 1 to 10 CFUs per bag (0·003–0·03 CFU/ml) [17], it is common practice to perform *in vitro* experiments with an inoculum ensuring growth (1–100 CFU/ml) [29]. The results of our study agree to the findings of Mohr and colleagues [30] and show that *Propionibacterium* species do not proliferate under platelet storage conditions and therefore do not reach the level considered clinically significant (10^5 CFU/ml) [31]. These kinetics contribute to a very low bacterial concentration at the time of transfusion particularly considering that all implicated PCs were transfused within the first 3 days after donation, which is common practice in hospitals we serve. Hence, even the most sensitive assay based on the cultivation of bacteria misses *Propionibacteria* due to sampling error or detects *Propionibacteria* too late (5–7 days after PC preparation), when blood products have already been transfused. Therefore, sampling error and low rates of bacterial growth make it difficult to prevent transfusion of PCs contaminated with this organism [2].

Until today, different bacterial screening methods for the detection of bacterial contamination of PCs have been developed to reduce the risk of bacterial transmission by blood products [11]. But, to date none of these preventive methods is sufficient for the perfect preventive screening or detection of contaminated units. As shown in this study, *Propionibacterium* species may be missed or were detected most frequently in PCs with culture-based methods when blood products have already been transfused because of low bacterial numbers [6]. Inoculating anaerobic bottles in automated culture systems can detect these bacteria after 3- to 7-day incubation. Therefore, it must be pointed out that not all bacteria have the pathogenic capacity or growth characteristics to develop clinically significant inocula during the time period of platelet storage [32]. Nevertheless, automated bacterial screening methods based on carbon dioxide production or oxygen consumption as a function of bacterial growth have been regarded as the gold standard due to the high sensitivity with a stated detection limit of 1 CFU/ml [2,33–35]. Nonetheless, the use of the anaerobic culture bottle, in addition to the aerobic bottle, has a number of advantages. Most importantly, it enables detection of obligate anaerobes that have been implicated in transfusion-associated bacterial sepsis [21]. The need for detection of these organisms, however, requires clarification because of their slow growth and impaired survival [11]. In this study, we have shown that the growth of different bacterial species can vary widely in PCs. Similar data have been reported by others [25,30,36–39].

To approach this problem, we reviewed the medical records of six patients that received PCs tested positive for *P. acnes*. All patients neither showed symptoms of febrile transfusion complications, nor evidence of an inflammatory event associated with transfusion. Most patients transfused were under antibiotic therapy because of other infectious disease prior to transfusion. Therefore, our findings cannot be interpreted unequivocally. In moving forward, systematic studies of the outcome of patients transfused with *P. acnes*-contaminated PCs are needed. Although *P. acnes* is associated with serious infections like brain abscesses, osteomyelitis, endophthalmitis after intraocular surgey and lens implantation, subdural empyema, cerebal shunt infection and infective endocarditis [40], no correlation to transfusion transmission due to contaminated PCs has been reported and only a few cases have been described in transfusion-related sepsis [41–43]. As shown in our sterility testing study, in all cases of putative contaminated PC units, *P. acnes* was not isolated from the patients, and a cause-and-effect relation was not confirmed.

Moreover, Macauley *et al.* reported that eight units in which *P. acnes* was detected in the initial cultures were

transfused, but without adverse reactions associated to the unit [44]. In any event, transfusion-related clinical syndromes from PCs transfusion are often difficult, if not impossible to prove [43]. The lack of signs for transmissions of a bacterial infection is consistent with the assumption of either a low bacterial load or limited pathogenicity [10].

Therefore, further studies are needed to clarify the clinical significance of transfusion-transmitted bacterial infection in regard to *P. acnes*, taking into account that many recipients of PCs are immunosupressed or neutropenic. Studies of clinical syndromes including endocarditis, postcraniotomy infections, arthritis and spondylodiscitis, endophthalmitis and pansinusitis caused by *P. acnes* are currently being performed to confirm its pathogenic potential and clinical significance [15,45].

In conclusion, depending on the species and inoculums, differences in bacterial growth in PCs are often observed. Bacterial contamination of blood components may not always result in bacterial multiplication, because some organisms may not be able to survive the storage conditions due to autosterilization in the blood component. Other strains of bacteria may survive in the unit in low numbers but not multiply. In this study, we demonstrated that *P. acnes* is a frequent contaminant of blood components in platelet bacteria screening. But, due to its slow growth, the levels of bacteria in blood components may be too low to result in sepsis upon transfusion. However, optimized growth conditions using automated culture in platelet screening offers such species the opportunity to grow and be detected at the end of storage, but these conditions do not reflect the real storage and growth conditions of PCs.

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No. 18

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2007. 12. 13	該当なし	

一般的名称	(製造承認書に記載なし)	研究報告の公表状況	WHO, Epidemic and Pandemic Alert and Response (EPR). Available from: URL: http://www.who.int/csr/don/2007_12_09/en/index.html	公表国 中国
販売名(企業名)	合成血「日赤」(日本赤十字社) 照射合成血「日赤」(日本赤十字社) 合成血-LR「日赤」(日本赤十字社) 照射合成血-LR「日赤」(日本赤十字社)			

研究報告の概要

○鳥インフルエンザ―中国における状況―最新情報5
中国保健省は江蘇省におけるH5N1鳥インフルエンザの新たなヒト症例を報告した。この症例は12月6日に国立研究所にて感染が確認された。
患者は52歳の男性で、12月2日にH5N1感染のため死亡した24歳の男性の父親である。患者と密接な接触があった者であり、当局が医学的観察を行っていた。発症は12月3日で、直ちに治療のため病院に送られた。
12月9日までに中国では27例が確定され、17例が死亡例だった。

報告企業の意見	今後の対応
中国江蘇省において、H5N1鳥インフルエンザのため死亡した患者の父親がH5N1に感染、発症したとの報告である。	日本赤十字社では家禽に高病原性トリインフルエンザの流行が認められた場合、当該飼養農場の関係者や防疫作業従事者の献血制限を行っている。新型インフルエンザが流行した場合、献血者減少につながることも予想される。今後も引き続き情報の収集に努める。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「日赤」
合成血-LR「日赤」
照射合成血-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

46

MedDRA/J Ver.11.0J

JRC2007T-090

World Health Organization

Avian influenza – situation in China - update 5

9 December 2007

The Ministry of Health in China has reported a new case of human infection with the H5N1 avian influenza virus in Jiangsu Province. The case was confirmed by the national laboratory on 6 December.

The 52-year old male is the father of the 24-year old man who died from H5N1 infection on 2 December 2007. He is one of the close contacts placed under medical observation by national authorities. He developed symptoms on 3 December and was sent immediately to hospital for treatment.

Of the 27 cases confirmed to date in China, 17 have been fatal.