Diedrich B, Remberger M, Shanwell A, et al.
A prospective randomized trial of prophylactic platelet transfusion trigger of 10x10^9/L versus 30x10^9/L in allogeneic hematopoietic progenitor cell transplant recipients

On the basis of previous studies, the trigger for platelet transfusion therapy has been set at 20x10^9 platelets/L, as it has been shown that severe haemorrhages rarely occur in patients with a count above this limit. In allogeneic hematopoietic progenitor cell transplant (HPCT) recipients, the conditioning regimen (high-dose chemotherapy, total body irradiation) destroys the patient’s haematopoiesis and, thus, transfusions of blood components are frequently needed during the pancytopenic period. The impact of lowering the trigger for prophylactic platelet transfusions is still a matter of debate. The aim of the by Diedrich et al., carried out in Stockholm at the Karolinska University Hospital, was to compare prophylactic platelet transfusion trigger levels of 10x10^9 platelets/L (T10) and less than 30x10^9/L (T30), regarding the number of platelet and red blood cell (RBC) transfusions given and the incidence of haemorrhagic events (WHO grades 2-4) in allogeneic HPCT recipients. These data were recorded in 166 HPCT recipients, randomly assigned to receive prophylactic platelet transfusions if their platelet counts fell below T10 (79 patients) or below T30 (87 patients). All platelet concentrates were ABO-matched; 85% of them were prepared by the buffy-coat system and 15% were apheresis-derived. Time of engraftment of white blood cells, absolute neutrophil count, and the number of RBC transfusions were not significantly different between the two groups. The number of platelet concentrates transfused in group T10 (median 4 units) was obviously lower than that in group T30 (median 10 units; p<0.001), but no significant differences were found regarding clinical outcome variables (bacteraemia, graft-versus-host disease, hospital stay, death, and survival) or in the median total number of RBC transfusions given. The incidence and type of bleeding episodes were also comparable (18% in group T10 and 15% in group T30). No deaths were attributed to haemorrhages. In conclusion, a prophylactic platelet transfusion trigger level of 10x10^9 platelets/L was found to be safe and results in several advantages: i) avoidance of undesirable side effects (fever, shivering, allergic reactions, sepsis from bacterial contamination, infectious disease transmission, immunisation with subsequent platelet refractoriness); ii) reduction of the shortage of platelet concentrates; iii) lower costs.

Akiba J, Umemura T, Alter HJ, et al.
SEN virus: epidemiology and characteristics of a transfusion-transmitted virus

SEN virus (SEN-V) is a blood-borne virus discovered in 1999 by investigators at DiaSorin Biomolecular Research Institute (Saluggia, Italy) during investigations of a viral cause of post-transfusion hepatitis not due to HBV, HCV or to any other of the known human hepatitis viruses. This type of hepatitis is currently referred to as "non-A-to-E hepatitis". The name SEN-V was derived from the initials of the first patient in whom this virus was identified. The virus has 8 strains, designated from A to H: strains D and H appear to be associated more frequently with non-A-to-E hepatitis. The prevalence of SEN-V in otherwise healthy people varies markedly by geographic region: 1.8% in USA, from 10 to 22% in Japan, 15% in Taiwan, 5% in Thailand, from 8 to 17% in Germany, 24% in Greece, and at least 13%
in Italy. Transmission of SEN-V by transfusion has been reported: the virus was detected in 86 of 286 (30%) previously uninfected surgical patients who received blood components but in only 3 of 97 (3%) untransfused patients. The prevalence is high in haemophiliacs (from 42 to 68%) and among haemodialysis patients (from 13 to 68%). The prevalence among patients with acute non-A-to-E hepatitis is 33 to 92% of cases, while SEN-V has been detected in 36 to 69% of people with a chronic form of hepatitis. Transmission by haemotherapy has been confirmed by detection of greater than 99% strain homology between SEN-V in donor and pertinent recipient sera. Concurrent infections with SEN-V and HIV-1, HBV or HCV have been reported in some countries (USA, Italy, Germany, and Japan) and these observations can reflect their blood-borne transmission. Although the virus was discovered during an investigation of causes of post-transfusion hepatitis, there is no solid evidence so far that SEN-V infection either causes hepatitis or worsens the course of a coexistent liver disease. Research on SEN-V has decreased in recent years both because of a lack of such evidence and also because the DiaSorin company ceased working on SEN-V, after it was acquired by another firm. Nevertheless, SEN-V appears to be transmitted by transfusion, and further studies might reveal more about its role in the future.

Factors affecting the formation of white particulate matter in red blood cell components
Transfusion 2005; 45:1127-32.

It is well known that whole blood and red blood cell components can contain biological material named white particulate matter (WPM). The Department of Transfusion Medicine at NIH in Bethesda (MD, USA) carried out a study to identify factors contributing to the formation of WPM. Whole blood was collected from 18 healthy donors (9 men and 9 women); approximately 450mL was drawn from each donor into 63mL of anticoagulant. Three different types of collection sets were used, and the donors were randomly assigned to have their blood collected into one of the three bag sets. One set was from a lot that had been recalled because implicated in the frequent development of WPM, one set was of the same type and manufacturer as the previous, but from a lot not recalled and the third set tested was made by a second manufacturer. Six units were collected into each type of collection set. Immediately after the collection, each whole blood (WB) unit was divided equally into four bags of the same type as the collection bag, except that the anticoagulant had been removed. These bags were labelled A, B, C, and D and stored for 4 hours, two (A and B bags) at room temperature and two (C and D bags) at +4 °C. After storage, red blood cell concentrates (RBC) were prepared from each quarter-unit, two (A and C bags) by heavy centrifugation (5,000xg) and two (B and D bags) by light centrifugation (2,000xg). Plasma was removed and preservative solution (AS-1 for the first two bag types, and AS-3 for the third collection set type) was added and mixed. WB and RBC were visually inspected for WPM at various intervals: WB over the 4 hours of storage and RBC over 1 hour. Each WB unit was inspected at 15-minutes intervals for the first hour and then every 30 minutes for the following 3 hours. Each unit of RBC was inspected every 15 minutes for 1 hour. The presence of WPM was scored as type I (small material, starry sky), type II (large material, waxy), type III (atypical bubbles, oily) and type IV (large yellow-white oil slick). No WPM was detected in divided WB units during the 4 hours of storage, nor in the RBC immediately after centrifugation, but, after 1 hour of storage, WPM was detected in divided RBC from 9 of the 18 donors. Overall, 72 RBC were prepared from the 18 initial units and WPM was detected in 25 of these 72 components (35%). The 36 RBC prepared by heavy centrifugation were more likely to contain WPM than the 36 prepared by light centrifugation (50% vs 19%; p<0.02). The incidence of WPM was similar among components stored at room temperature or at +4 °C. Donors of RBC with WPM had higher total cholesterol levels than donors of components without WPM (p<0.04), but there was no difference in triglyceride levels between the two groups. Platelet counts also affected WPM formation: in fact, donors of RBC with WPM had higher platelet counts than those whose donations did not contain WPM. Interestingly, WPM disappeared from some units after 2 or 3 days of storage. In conclusion, these results suggest that WPM will be found in many RBC inspected very shortly after preparation, but that it disappears in most cases after 3 days of storage. Several studies have shown that WPM is removed by leucoreduction filters. The composition of the WPM was not identified, but it is more likely to occur in components that are centrifuged at high speed and to be present in blood collected from donors with higher cholesterol levels.
Yazer MH, Triulzi DJ

Use of a pH meter for bacterial screening of whole blood platelets

Transfusion 2005; 45: 1133-7

Since March 2004, the AABB has required all Transfusion Services in the USA to detect and limit bacterial contamination of platelet components. It is well known that this contamination is a leading cause of transfusion-related morbidity and mortality. Multiple techniques of bacterial detection have been advanced, ranging from the simplest method to sophisticated automated culture systems. At the Institute for Transfusion Medicine of Pittsburgh University (PA, USA) a handheld pH meter was used as a surrogate test for bacterial contamination, as it had been found that, when micro-organisms proliferate dangerously, the pH value decreases below 7.0. Given the large volume of whole blood platelet concentrates (WBP) issued by the Centre, the pH method was used for screening the 37,060 concentrates prepared during a 5-month period (from May to September 2004). Four hundred and five WBP (1.1%) had a pH value of less than 7.0 and were quarantined, along with their red blood cell concentrates (RBC) and plasma. Within 24 hours of detection of the low pH, a 4 to 8mL aliquot was cultured in an automated system for 5 days. Four WBP were culture-positive (1% of the 405 WBP that failed pH screening). In one case Staphylococcus aureus was isolated from the WBP unit after 4 hours of culture and from the associated RBC unit after 45.6 hours. Diphtheroids, coagulase-negative Staphylococcus, and B. subtilis were isolated from the other three culture-positive WBP, but none was found in the associated RBC. The white blood cell and platelet counts in 56 WBP that failed pH screening were compared to those in 56 WBP with acceptable pH values: the former contained, on average, more than twice the number of white blood cells (2.83x10^3 ±3.26/µL vs 1.19x10^3 ±0.77/µL; p<0.0007) and approximately 13% more platelets (1.359.82x10^3 ±346.83/µL vs 1.199x10^3 ±312,60/µL; p<0.05). In conclusion, pH screening of WBP at issue prevents transfusion of contaminated blood components (RBC and platelet concentrates). Higher white cell and platelet counts probably explain the low pH not due to bacterial contamination.

Chen Q, Flegel WA

Random survey for RHD alleles among D+ European persons


The Department of Transfusion Medicine at the University Hospital in Ulm (Germany) has provided another relevant contribution to knowledge regarding the Rh system and, in particular, the genetics of the D antigen. It is widely known that this antigen is the most important blood group determinant encoded by a protein. The anti-D antibody is still the leading cause of haemolytic disease of the newborn and is also involved in haemolytic transfusion reactions and in warm autoimmune haemolytic anaemia. Following the cloning of both RH genes in the early 1990s, the number of distinct RHD alleles known has steadily increased and now exceeds 100. Variant D occurs more frequently in Africans and the Ulm group has recently (Blood 2002; 100: 306-11) described five new RHD alleles, encoded by a RHD gene cluster, dubbed DAU ("D of African origin", in German "D afrikanischer Ursprung"): from DAU-0 to DAU-4. At present, from a phylogenetic point of view, there are four known D clusters: DIVa cluster; weak D type 4 cluster; DAU cluster and Eurasian D cluster. Chen and Flegel performed a survey among 1,000 south-western German random blood donors in order to gauge the variety of RHD alleles in a D+ European population. Blood samples were collected from 500 ccDee, 250 CcDee, and 250 ccDEe donors. All 1,000 DNA samples were also sequenced for RHD exon 5. Fifteen aberrant RHD alleles were found among the 500 ccDee donors and two among the 250 CcDee donors. No aberrant RHD alleles were found among the ccDEe samples. A new aberrant RHD allele was discovered and named DAU-5. Nucleotide sequencing of RHD exon 5 revealed three novel alleles, dubbed DUC-1, DQC, and DUC-2. Weak D type 4 was detected more frequently than expected (in eight ccDee donors), whereas the population frequencies of the other RHD alleles confirmed the published estimates. From a clinical point of view, DAU-5 is clearly relevant, as it expressed a partial D phenotype and, consequently, carriers should be transfused with D- products. The situation for DCQ is probably similar, but because this allele was masked by a regular D antigen no specific pattern could be established and transfusion recommendations should await further characterization. The other two new RHD alleles, namely DUC-1 and DUC-2, expressed a normal D epitope pattern and should be regarded as a normal D for clinical purpose. In summary, in the course of molecular screening among a very limited European D+ population, 20 people were found to carry aberrant RHD alleles: four of these alleles are new and
probably sporadic and, therefore, it can be concluded that the variety of RHD alleles within the European population may be larger than previously thought.


Vox Sang 2005; 88: 289-303

Viral testing using nucleic acid technology (NAT) was first introduced in Europe in 1995 by the plasma industry. The rationale was founded on the relevance of NAT testing of blood donations in reinforcing transfusion safety by detecting acute viral infections in the "window phase", not discovered by current serological screening methods. Subsequently, several European countries have implemented NAT for blood screening. In order to obtain information on this development in blood screening, the Editorial Board of Vox Sanguinis organized, in 2002, the first International Forum on this subject. Eleven countries replied to the questionnaire: the USA, Australia (AUS), Japan (J), Austria (A), Finland (FIN), France (F), Germany (D), Great Britain (GB), Italy (I), Ireland (IRL), and the Netherlands (NL). At that time, hepatitis C virus (HCV) infection was the greatest concern, and all 11 countries had given priority to HCV NAT. Five countries (USA, AUS, D, F, NL) also performed testing for HIV-1 RNA, while one Blood Centre in Germany (Frankfurt) tested donor blood samples for HBV, too. Since then, rapid developments have taken place in NAT screening, and a larger number of blood donations have been tested using NAT. Therefore, it was of interest to have an update at the end of 2003, and a new questionnaire was sent to experts in 26 countries. Eighteen countries contributed to this second International Forum: fourteen from Europe. A, Belgium (B), D, F, FIN, GB, Greece (GR), I, NL, Norway (N), Slovenia (SLO), Spain (E), Sweden (S), and Switzerland (CH) and four from outside Europe: AUS, Canada (CDN), Hong Kong (HK), and the USA. Screening for HCV NAT is mandatory in fourteen countries (A, AUS, B, CH, CDN, D, E, F, GB, I, N, NL, SLO, SLO, USA) and recommended in three (FIN, GR, HK), while S has not, to date, introduced NAT technology. NAT testing for HIV-1 is mandatory in only six countries (AUS, B, CDN, F, NL, USA), but it is used in some (but not in all) laboratories in A, CH, D, GB, GR, HK and I. FIN plans to introduce HIV NAT this year (2005), while E, N, SLO and S do not use this test. Three different types of NAT (for HCV and HIV) were used. AUS, B, GR, and HK (equivalent to 23%) use exclusively the Chiron Procleix HIV-1/HCV TMA assay, CDN, CH, FIN, N, NL and SLO (35%) the Roche Ampliscreen and 23% (F, GB, I, USA) used both technologies in a proportion of 30% vs 70% in favour of Roche, except for USA, where this proportion was reversed. Three countries (A, D, E; equivalent to 19%) used an in-house technique in combination with one or the two commercial assays. Pool sizes ranged from single to 48 donations in the Chiron system, 8 to 96 for Roche, and 48 to 96 when in-house techniques were used. The sensitivity levels was expressed in IU/mL, but also in genome equivalents/mL or in copies mL, so they resulted very heterogeneous and could not be compared. The specificity rates ranged from 97 to 100%.

The observed yield of HCV NAT tests ranged from 0 in SLO (but the number of tested samples [327,174] was small) to 5.34 per 106 donations in FIN. All participants detected fewer cases than predicted, except for the USA (37% more cases than expected). Collating European data, a yield of 0.93 per 106 donations was obtained, which is 4 times lower than that observed in the USA, and 2.5 times lower than in the Pacific area. The observed yield for HIV is very limited. In the 10 European countries screening (on a mandatory or voluntary basis) for this marker, the gain ranged from 0 (B, CH, E, GB, GR, NL) to 1.8 per million in Italy. There was no significant difference between observed and predicted yields. Collating European data, the HIV NAT positive rate was 0.37 (13/36 million donations), which was very similar to that in the USA and AUS (0.31); however, the yield rate in HK was markedly higher (3.7). As regards HBV, the use of NAT screening is controversial. With the exception of A, D and E (where this test is so far performed in only three Blood Centres), HBV NAT has not been implemented in any of the other countries of the questioned experts. Systematic NAT screening is under consideration in CDN, E, GR and HK: these countries have the highest predicted residual risk rate per HBV infection, ranging from 7.5 (GR) to 200 (HK) HBsAg-positive blood donations per million. Experts agreed that the use of NAT HBV testing could not replace individual screening for HBsAg. Four countries (CH, I, SLO, USA) provided further interesting information about the implementation and the use of NAT screening in their reality and these contributions are included separately in the Forum. The Italian draft was written by Velati and Zanetti and reports the data of a survey promoted since 2001 (up-dated to 2003: see also Blood Transfus 2003; 1: 368-78). In conclusion, the investigation showed that the overall HIV NAT yield was concordant with the prediction, while the HCV NAT yield seemed lower than predicted. Clinical interest in HBV NAT seems low, at present.
Cooling LL, Kelly K, Barton J, et al.  
Determinants of ABH expression on human blood platelets  
Blood 2005; 105: 3356-64

ABH determinants are expressed on a variety of platelet membrane glycoproteins and glycosphingolipids. From a clinical point of view, transfusion of ABH-incompatible platelets can be associated with decreased recovery, shortened survival, and an increased incidence of platelet HLA-immune refractoriness. ABH incompatibility can act synergistically with HLA incompatibility to further decrease post-transfusion recovery and survival. For these reasons, it is strongly recommended that ABH-compatible platelets be transfused, when available. This paper, regarding a study carried out in the USA by researchers from the Universities of Michigan and Iowa, reports a large-scale analysis of individual apheresis platelet donors in order to identify factors affecting platelet ABH expression. Factors examined in 166 group A donors were age, sex, A1/A2 subgroups, and Lewis phenotype. These variables were compared with ABH expression on platelet and red blood cell membranes, as determined by flow cytometry, Western blotting, and glycosphingolipid analysis. The Authors chose to focus on group A platelets donors, because the A/O major mismatch is more likely to adversely affect the transfusion response and because of the higher likelihood of this mismatch, given the distribution of group A and group O in the general population. Samples from group O and group B donors were included as controls. The A antigen on platelet membranes, glycoproteins, glycosphingolipids was linked to an A1 red cell phenotype. Using a combination of flow cytometry, glycosphingolipid analysis, and Western blotting, the Authors confirmed that donor A1/A2 status is the greatest predictor of platelet ABH expression. Overall, there was a nearly 100% concordance between an A1 blood group phenotype and presence of A antigen on platelet membranes, glycoproteins, and glycosphingolipids. ABH was identified on both glycoproteins and glycosphingolipids, independently of secretor status, indicating endogenous synthesis. ABH expression was consistent over time in single donors, suggesting that the relative density of ABH antigens on A1 is a specific, heritable trait. In contrast, platelet ABH varied significantly among donors (from 0% to 87%). As regards sex and age, ABH expression on platelets is higher in female donors, particularly in older female donors (>50 years; p=0.05), suggesting a relationship with falling hormone levels during the menopause. The expression of blood group A on platelet glycoproteins and glycosphingolipids is dictated by A1 subtype and is independent of Lewis phenotype. Another surprising finding was the linear co-expression of A and H antigens on platelets, unlike on red blood cells, which express A and H inversely. ABH A2 donors were typed as "O compatible" platelets by all three methods; really, they possess a "Bombay-like" phenotype, as they lack both A and H determinants on platelets. This is a remarkable discovery, as platelet concentrates from such donors can be used in patients undergoing A/O ABH major mismatch allogeneic progenitor cell transplantation: A2 platelets are, in fact, compatible with both the recipient (group O platelets) and donor (group A plasma).