Συμπυκνωμένα αιμοπετάλια: δείκτες ποιότητας

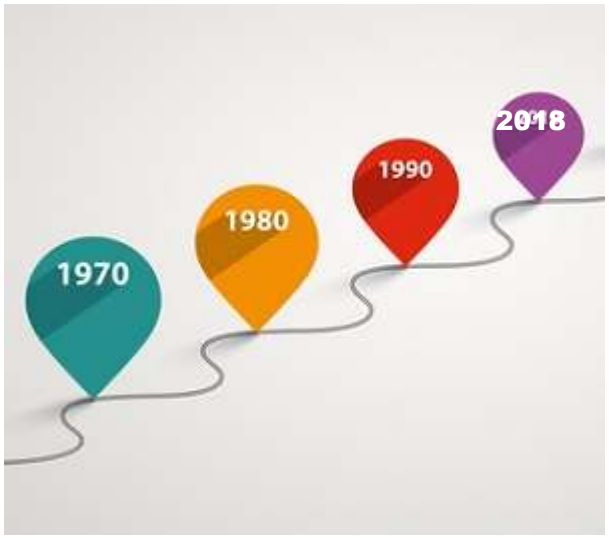
AMERICAN SOCIETY OF HEMATOLOGY 50
Conquering Blood Diseases – From Research to Patient Care

Platelet Transfusions: An Historical Perspective

Morris A. Blajchman

The existence of platelets and their possible contribution to hemostasis was described in the 1870s, but it was not until 1910 that transfused platelets were shown to reverse the risk of bleeding in thrombocytopenic patients. The first such report, by W.W. Duke, was in a 20-year-old man who had profound mucocutaneous bleeding associated with a platelet count of only 6×10^9/L. When he became moribund as the result of uncontrollable epistaxis, he was given fresh whole blood transfusions. The transfusion of a "large" amount of such blood was associated with the dramatic cessation of his bleeding, at which time his count had increased to 123×10^9/L! Because of the many obstacles that prevented the ready availability of platelets for transfusion, many years elapsed before platelet transfusions became routine practice in the treatment of thrombocytopenic patients. It was not until approximately the 1970s that the routine availability of platelet transfusions became a reality. This became possible when Drs. Scott Murphy and Frank Gardner (reported in 1969) provided evidence that platelets could be stored at 22 ± 2°C, for up to 3 days and still maintain their hemostatic function. Subsequent improvements, including the availability of improved storage containers, enabled the provision of platelets for transfusion after 5 or even 7 days of storage. At the present time, the possibility of 10-day storage looms clearly on the horizon.

Συμπυκνωμένα αιμοπετάλια



12. Platelets, Cryopreserved .....

1. Platelets, Recovered, Single Unit ....

2. Platelets, Recovered, Pooled ..

3. Platelets, Recovered, Pooled, Leucocyte-Depleted ...

4. Platelets, Recovered, Pooled, in Additive Solution ...

6. Platelets, Pooled, Pathogen-reduced ..

5. Platelets, Recovered, Pooled, Leucocyte-Depleted, in Additive Solution .....

7. Platelets, Apheresis

8. Platelets, Apheresis, Leucocyte-Depleted ..

9. Platelets, Apheresis, in Additive Solution ..

10. Platelets, Apheresis, Leucocyte-Depleted, in Additive Solution .....

11. Platelets, Apheresis, Pathogen-reduced ..

VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion

International Forum

Vox Sang. *40:* 115–12((1981)

Which are the Parameters to be Controlled in Platelet Concentrates in Order that They May be Offered to the Medical Profession as a Standardized Product with Specific Properties?

Richard H. Aster. It is clear that when platelet metabolism reduces the pH of stored platelets to the range 6.1–6.2, profound and irreversible changes in platelet ultrastructure and metabolism ensue which render platelets functionless and incapable of surviving in the circulation of a recipient [1, 2]. At a pH greater than 7.6, clumping of platelets frequently occurs. This is also associated with reduced recovery and survival of platelets posttransfusion. Clearly, then, pH is a critical variable which must be controlled. Formation of metabolites that lower pH is temperature dependent. We believe more satisfactory preservation of platelets can be achieved if temperature is restricted to the range 18–20 °C, rather than the conventional 18–22 °C [unpubl. data]. Gentle agitation of platelets is also crucial to successful preservation of platelets at room temperature, probably because mixing prevents metabolites from accumulating in high concentrations in the immediate vicinity of individual platelets. We have not been able to show that any particular type of agitation is especially advantageous.

Another index of satisfactory preservation is platelet shape. The degree to which platelets maintain their normal discoid configuration can readily be assessed by phase microscopic examination or by simple visual inspection of a platelet concentrate to determine whether it produces 'shimmering' of transmitted light. In our experience, retention of normal discoid shape is closely related to posttransfusion viability of platelets. The osmotic reversal reaction, which has been shown to correlate with platelet viability, is in effect a measure of the ability of platelets to maintain a discoid shape. Absence of discoidicity does not necessarily mean that platelets are incapable of functioning in hemostatis, at least immediately posttransfusion, as shown by the effectiveness of platelets stored for up to 24 h at 4 °C [3–5]. When platelets are to be shipped over long distances under conditions that make control of temperature and agitation difficult or impossible, we believe it is preferable to refrigerate them and transfuse within 24 h of collection.

After 3 days of storage at room temperature under conditions currently considered to be optimal, platelets exhibit profound functional abnormalities utilizing conventional in vitro tests of aggregation and release. Yet, it has been convincingly demonstrated that such platelets are capable of surviving normally [1–3] and of producing hemostatis [3–5] except, possibly, during the first few hours posttransfusion [3–5]. In at least one study, reversal of functional defects has been directly demonstrated in blood samples obtained posttransfusion [6].

These considerations suggest that certain criteria are now available to indicate when platelets will *not* function and/or survive normally posttransfusion but that no measures currently available permit one to conclude with certainty that they *will* be effective in hemostatis. Since failure to achieve a significant posttransfusion increment is

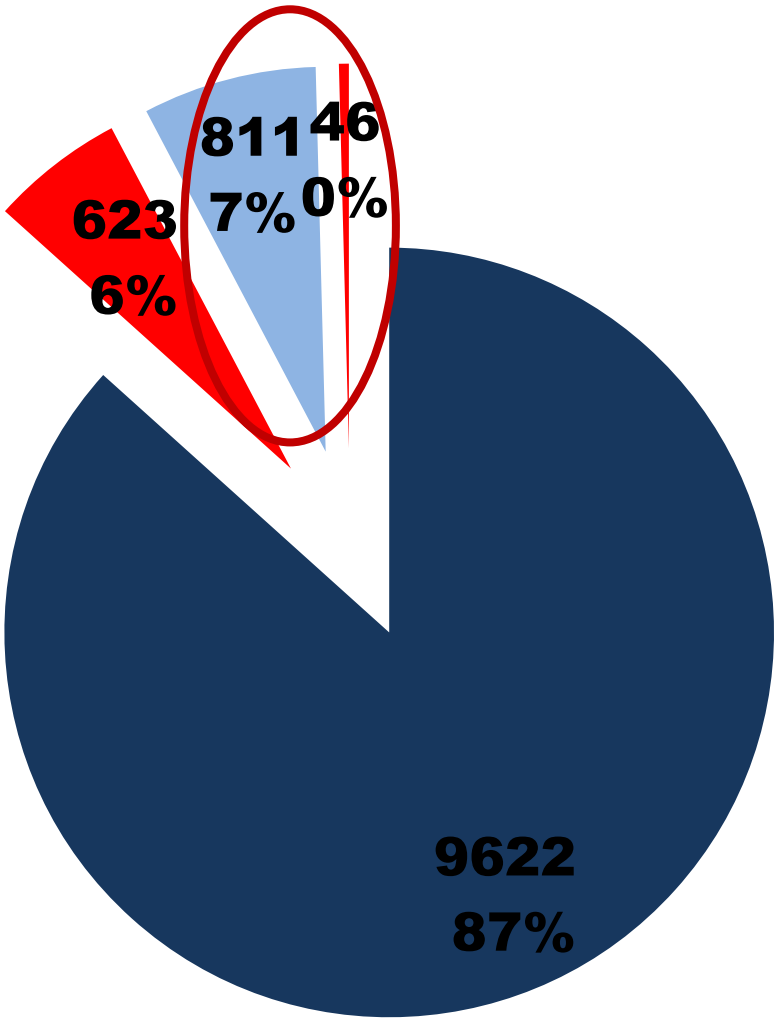
Διαπιστευτήρια

Platelet concentrates

Ιπποκράτειο Θεσσαλονίκης

Παραγωγή-Εισαγωγή

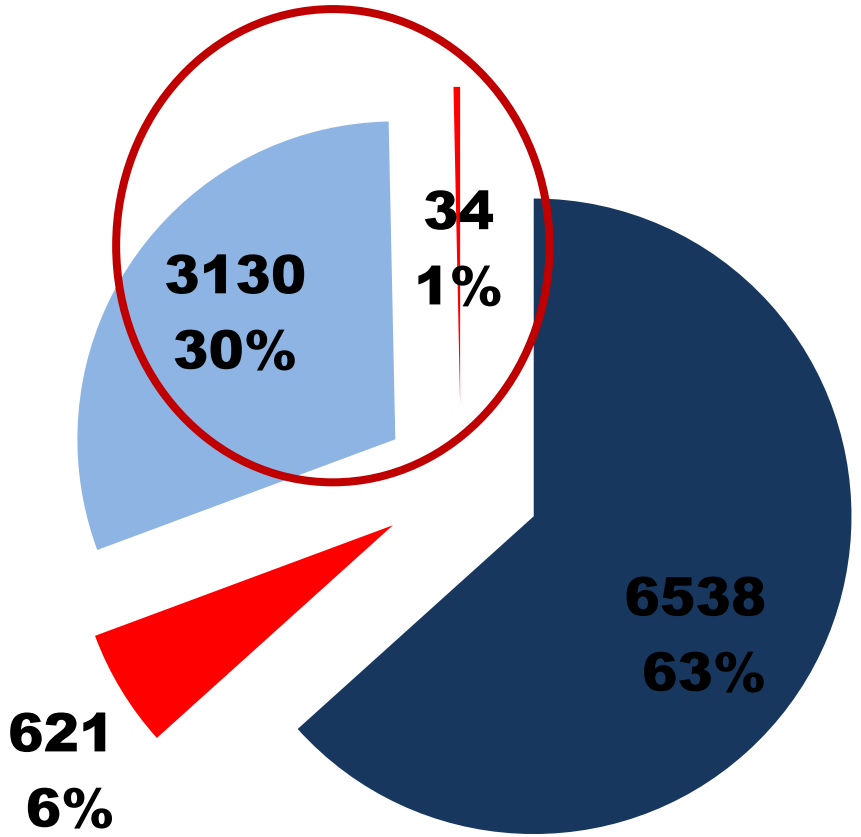
2013-2017



Ιπποκράτειο Θεσσαλονίκης

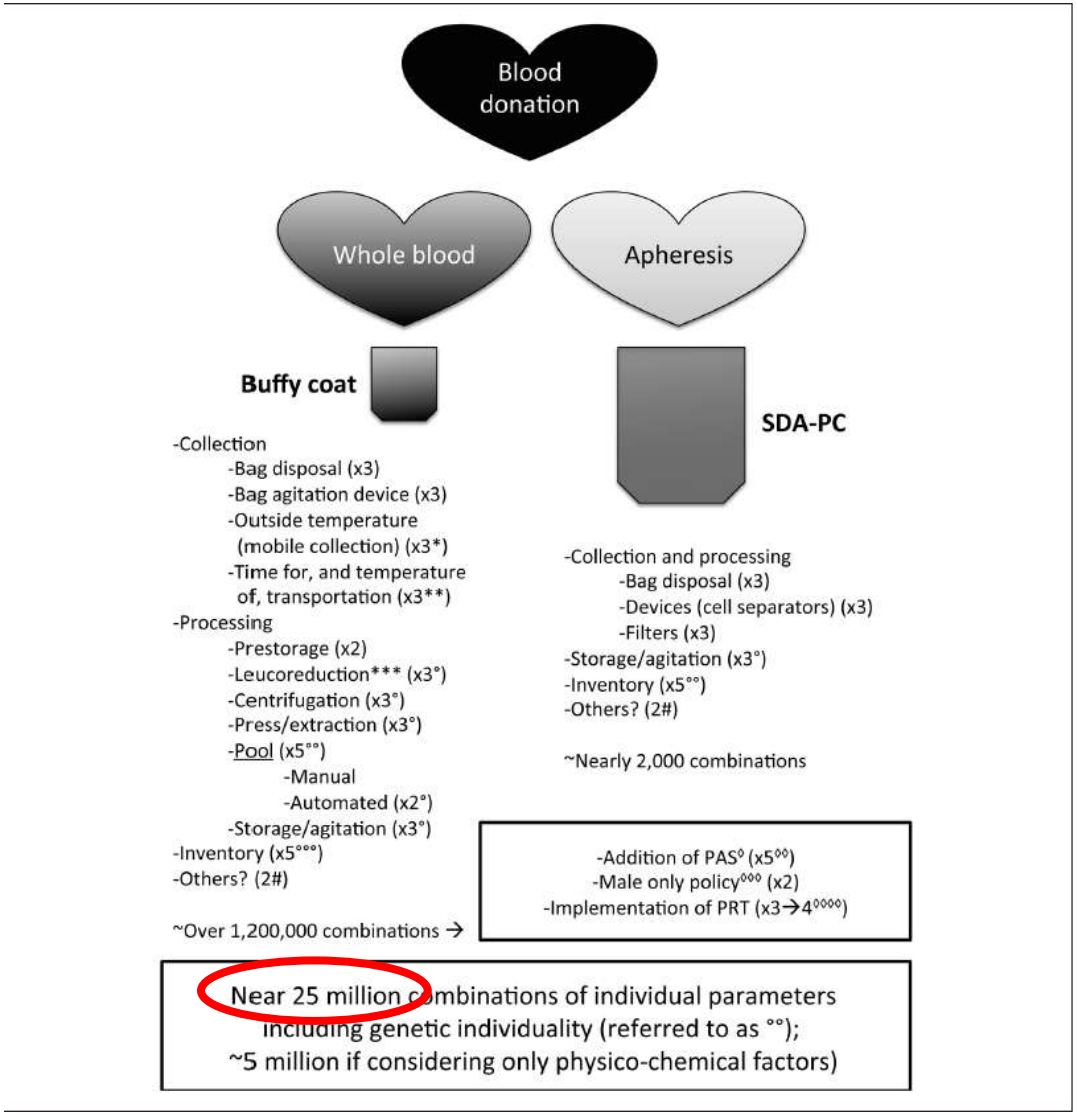
Κατανάλωση εντός/εκτός

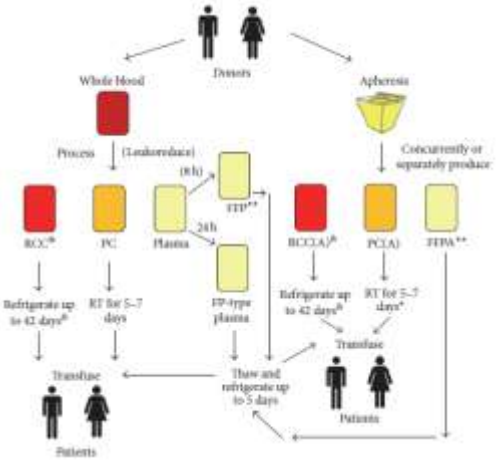
2013-2017



Improving platelet transfusion safety: biomedical and technical considerations

Olivier Garraud[1,2], Fabrice Cognasse[2,3], Jean-Daniel Tissot[4], Patricia Chavarin[3], Syria Laperche[1], Pascal Morel[5], Jean-Jacques Lefrère[1,6], Bruno Pozzetto[2], Miguel Lozano[7], Neil Blumberg[8], Jean-Claude Osselaer[4]



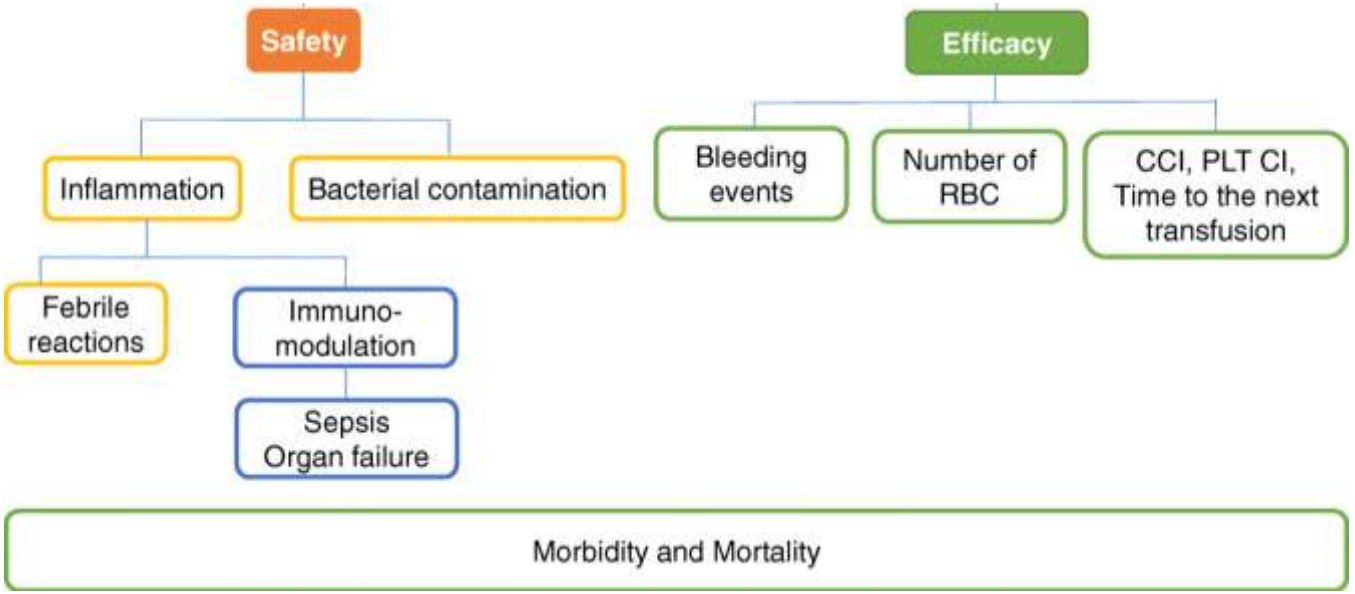


Blood Transfus 2016;

Ασφάλεια και αποτελεσματικότητα

Platelet concentrates account for near 10% of all labile blood components but are responsible for more than 25% of the reported adverse events. Besides factors

Blood Transfus 2016;



Aubron *et al. Critical Care* (2018)

EFFICACY OF PROPHYLACTIC SINGLE DONOR PLATELETS (SDP) TRANSFUSION IS RELATED TO THE TIME OF STORAGE AND NOT TO THE ABO COMPATIBILITY IN CHILDREN WITH MALIGNANCY

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[1]Ippokratio Hospital Thessaloniki, Thessaloniki, Greece

Background: The prophylactic transfusion of apheresis platelets remains the gold standard in order to avoid spontaneous bleeding in children undergoing intensive chemotherapy protocols. Due to inventory constrains, several times transfusion services are issuing ABO mismatched platelets.

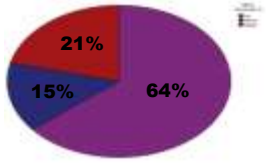
Aims: To provide descriptive data based on our centre's experience with regard to platelet increments post prophylactic transfusions in children with malignancy and investigate for factors that could be related to the effectiveness of SDP transfusion.

Methods: We retrospectively analysed data from a 3 years period (2011-2014) on the prophylactic SDP use on 48 children (25 boys/23 girls) with a median age of 7(2.5-14)years diagnosed with haematologic or solid malignancies (29 ALL, 3 AML, 4 NHL, 2 Wilms' tumor, 4 Ewing sarcoma, 3 myeloblastoma, 2 neuroblastoma and 1 rhabdomyosarcoma). Transfusion efficacy was assessed based on the corrected count increment (CCI) that takes into consideration the difference in platelet counts pre and post transfusion together with the number of platelets transfused as well as the patients' body surface area. Response was evaluated at 24 hours post transfusion and any CCI $<5x10^3$ was considered inadequate. Patient related (age, gender, disease, ABO/D, previous exposure to SDP or random platelets, status at last follow up) as well as product related (duration of storage, ABO/D, apheresis machine) factors were recorded and included in the analysis.

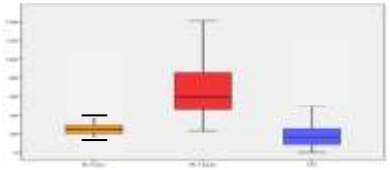
Results: In total 228 transfusions, meeting the inclusion criteria were analysed. In 146 (64%), patients received ABO identical SDPs whereas in 48 (21%) and 34 (15%) children received SDPs with major or minor ABO mismatch respectively. The mean value of CCI was 17.9 (0-66.4)$x10^3$and transfusion refractoriness was noticed in 35 SDPs administration (15%). The median SDP age was 2.59 (0.5-5) days and each child received 3(1-21) prophylactic transfusions. Previous exposure to SDP was recorded in 207 transfusions (136 with major mismatch) whereas random platelets transfusion had preceded the current transfusion in 189 cases (37 with major mismatch). In a univariate analysis a strong negative correlation was found between the time of SDP storage and the transfusion efficacy ($p<0.002$). In case of refractoriness (CCI $<5x10^3$) the mean product age was 3.35 days, significantly longer compared to that of the efficacious transfusions (2.47 days) ($p<0.003$). At the contrary the ABO compatibility between the patient and the transfused SDP did not influence the CCI (18.5, 16.7 and 17 $x10^3$forABO identical and with major and minor mismatch respectively). When CCI was analysed by the patients' ABO blood type significant differences were found between groups with patients on group B showing the modest response (CCI 12.8 $x10^3$).

Summary and Conclusions: Based on our findings, prophylactic transfusion of fresh SDPs (<48 hours) leads to bigger platelet increments while transfusion of older SDP is related to refractoriness. Interestingly enough, opposite to literature, we found no correlation between the ABO compatibility status and the SDP transfusion efficacy. This could partly be explained by the strong immunosuppression that our study population suffers due to both the underlying disease as well as the chemotherapy received. In summary for children with malignancy, should a prophylactic platelet transfusion is needed the first choice should be to provide fresh SDP ideally of the same ABO, without though firm restrictions on the use of other ABO blood types if the first are not available.

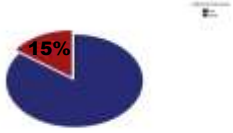
Results

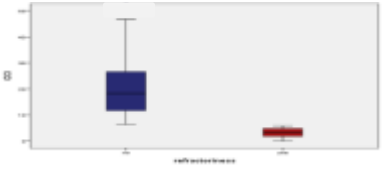


SDP-patient ABO compatibility

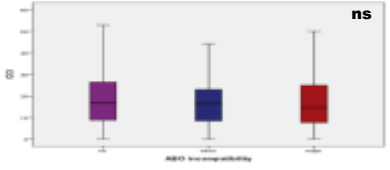


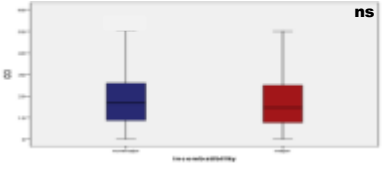
CCI (corrected count increment)



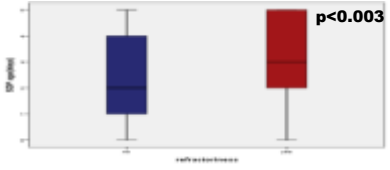


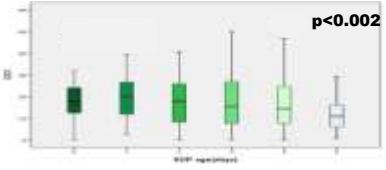
Refractoriness (CCI<5x10³ m²/μL)





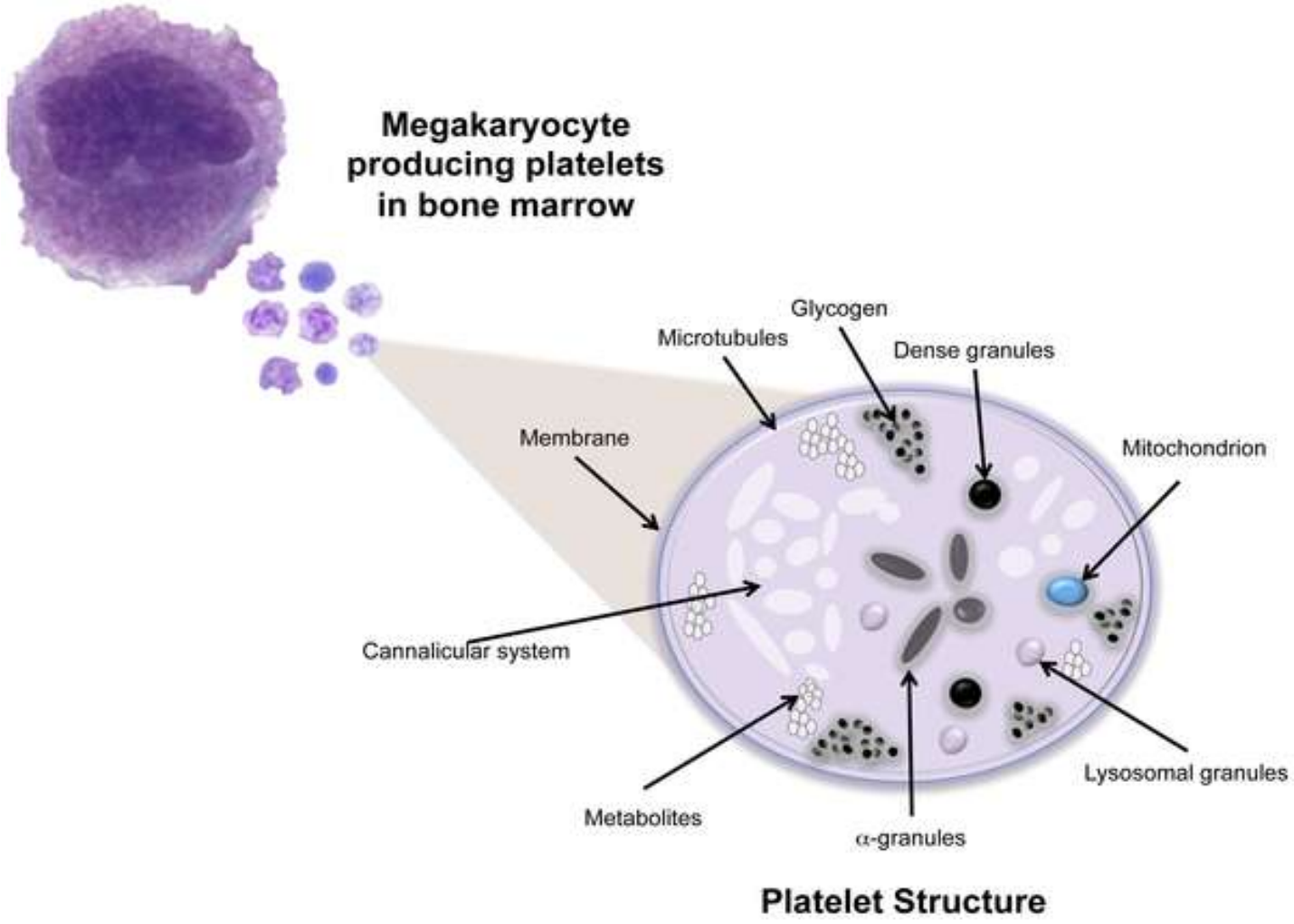
CCI by ABO compatibility





CCI by SDP storage time

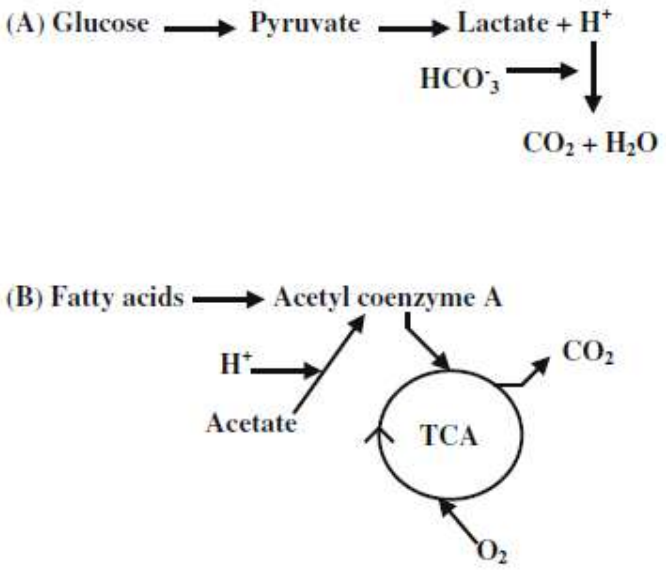
Το ευπαθές υλικό . . .



Το ευπαθές υλικό . . .

Βιοχημεία

- In the resting state
  - 15% ATP - by glycolysis
  - 85% by TCA cycle – with O2 consumption
- In the activated state
  - 50% ATP by glycolysis - increase lactate production.
- Decreased pO2 in the plastic platelet container
  - Increasing the rate of glycolysis to compensate for the decrease in ATP regeneration from the oxidative (TCA) metabolism
  - This increases glucose consumption and causes an increase in lactic acid
  - This results in a fall in pH - <6.4 after 5-7 days of storage at 22°C.
- Lactic acid is buffered by bicarbonate - When the bicarbonate buffers are depleted during PC storage
  - pH rapidly falls to less than 6.2



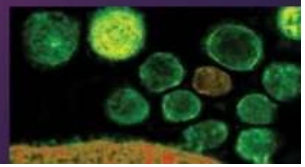
Το ευπαθές υλικό . . .

Ενεργοποίηση

- Platelets get activated following exposure to
  - foreign surfaces – plastic bag
  - low pH – metabolic alteration
  - shear stress - during component separation
- Upon activation, the platelets lose their discoid morphology and become more spherical with multiple pseudopods.
- Conformational changes in GPIIb/IIIa complex exposes binding sites for adhesive proteins (fibrinogen, vWF) resulting in platelet aggregates.

Platelet activation causes

1. Release of granular contents
   - Function -> recruitment of leucocytes and platelets
   - promote, immunity against infection
   - contribute to wound healing
   - presence of these contents in storage medium -> various transfusion reactions
2. Expression of sequestered membrane proteins (CD62, CD63) & phospholipids
   - Negatively charged phospholipids providing a surface for the prothrombinase complex (X-Va) thereby contributing to procoagulant activity

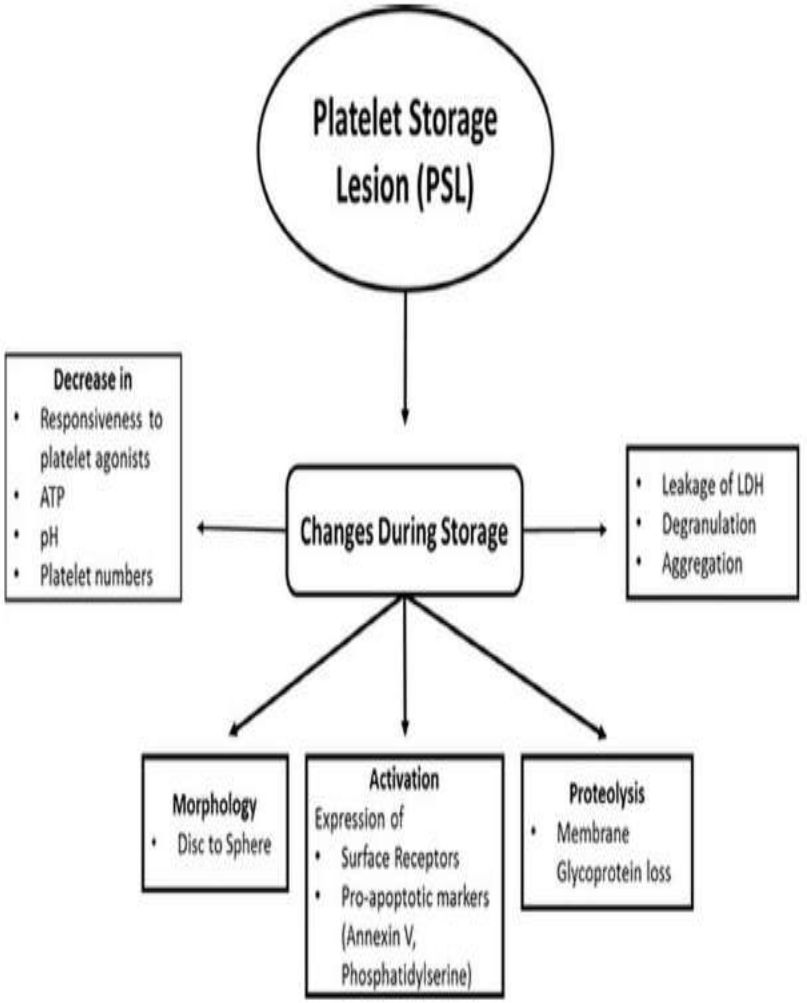


- Agitation while storage cause platelet lysis and calpain (protease) activation
- Platelet lysis
  - discharge cytosolic lactate dehydrogenase (LDH) and granular contents
  - accumulation in the storage solution
- Activation of calpain
  - degradation of cytoskeletal proteins like actin
  - generate platelet microvesicles.
- Microvesicle formation leads to decrease in mean platelet volume (MPV) and also contributes to procoagulant activity

Παρασκευή και αποθήκευση

Storage lesion

Factors	
Collection techniques	Composition of anticoagulant/ preservative solution Blood flow rate Ratio of anticoagulant Centrifugation force Resting period before resuspension
Storage conditions	Temperature and storage period of whole blood before processing and storage High cellular content Volume and composition of suspension media Final plasma concentration in storage media Type of agitation
Storage containers	Plastic bag composition Pack size and thickness of plastic Gas transfer properties of plastic Thickness of container wall
Treatment after collection	Extent of leukodepletion Extent of plasma removal UV-B irradiation γ-irradiation Cryopreservation Lyophilisation



Δείκτες ποιότητας

Αξιολόγηση της αποθηκευτικής βλάβης

- Biochemical tests - assess platelet viability
  - pH, pO_2, LDH accumulation, glucose consumption, and ATP depletion
- Assess alterations in the discoid morphology
  - Swirling phenomenon
  - decrease in MPV
- Platelet activation markers – various assays can be used
  - release of specific granular contents (β thromboglobulin, platelet factor 4)
  - changes in GP expression on platelet surface (GPIb, GPIIb, and GPIIIa)

Parameters associated with storage lesions	Parameters associated with activation	Parameters associated with aggregation
pH	Morphology	Rotation thromboelastometry (ROTEM) evaluation
Visible swirling	P-selectin	ADP
Shape change	CD-40L	Collagen
Hypotonic shock recovery	GMP-140	TRAP (thrombin receptor-activating peptide), ristocetin, and arachidonic acid response
Lactate production	GPIB, GPIX, GPIIB, GPIV, and activated IIb-IIIa (PAC-1 binding)	
Glucose consumption	CD62P and CD63	
Cytokines	Annexin V-lactadherin binding	
Microparticles		

Δείκτες ποιότητας

Οπτική επιθεώρηση

First quality parameters in blood banking

Swirling

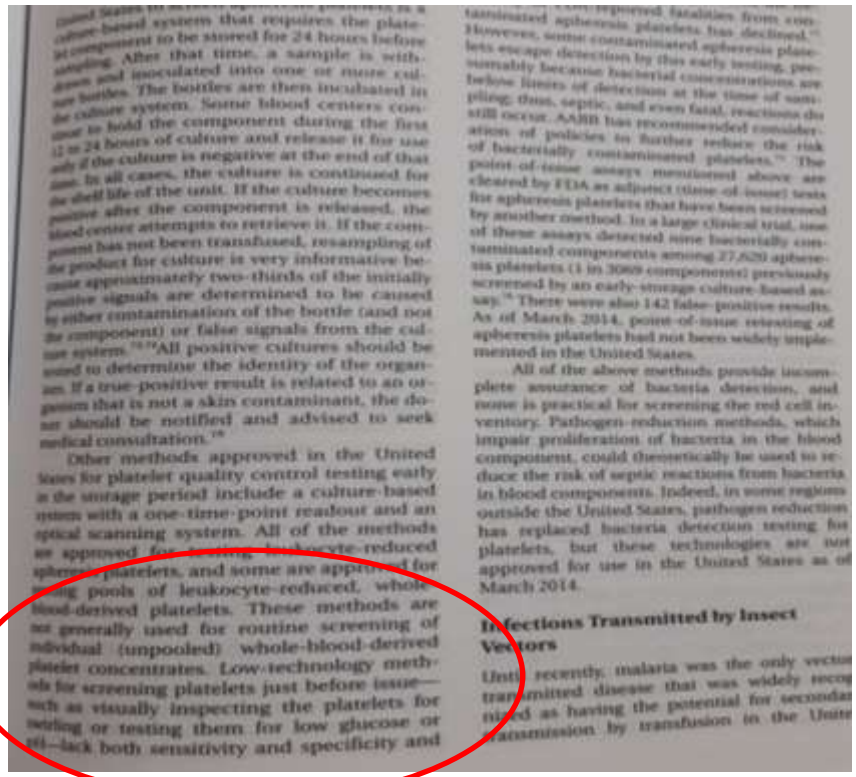
PLT morphology

PLT concentration and MPV

Platelets. 2006 Sep;17(6):393-6.

Suitability of measurement of swirling as a marker of platelet shape change in concentrates stored for transfusion.

On the day of preparation, some platelet units may contain clumps composed of platelet aggregates.[33] In routine practice, visual inspection is adequate to determine the degree of clumping subjectively and ensure that units with excessive clumping are not released for labeling. Most of the clumps seen on day 0 disappear on day 1 of storage with continuous agitation, particularly those showing light to moderate clumping.[33] The temperature at which platelets are prepared may influence clumping; platelets prepared at 24 C appear to show the least amount of clumping compared to those prepared at less than 24 C.[33] Visual inspections after the platelet concentrates are prepared have shown an absence of visible red cells in the vast majority of units, which implies that the units contain fewer than 0.4×10^9 red cells. Generally, the number of red cells in a unit of platelets does not exceed 1.0×10^9.[34]



Δείκτες ποιότητας

Βιοχημική προσέγγιση

In vitro

Blood gases

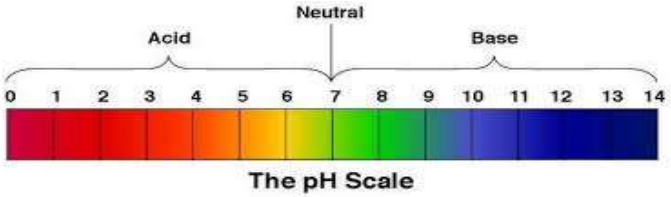
pH, pO_2, pCO_2

PLT metabolic parameters

Glucose, lactate, LDH

Δείκτες ποιότητας

Βιοχημική προσέγγιση



Storage of Platelet Concentrates at 22°C

By Scott Murphy, Seyed N. Sayar and Frank H. Gardner

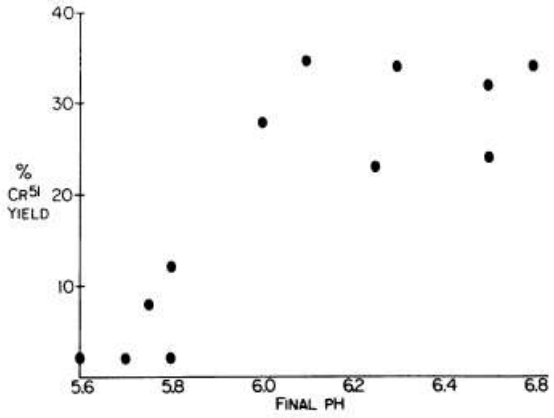
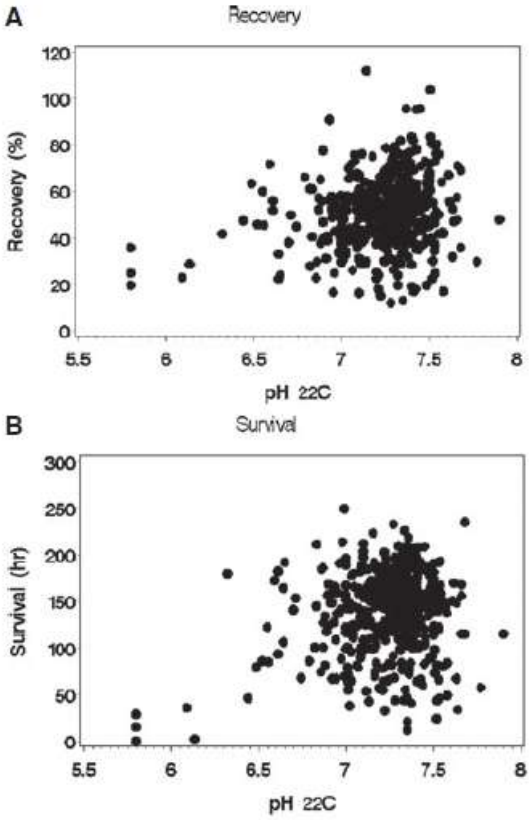


Fig. 2.—Effect of final PC pH on ^{51}Cr yield after storage at 22°C for three days. Abrupt loss of viability if pH falls below 6.0 during storage.

In vitro pH effects on in vivo recovery and survival of platelets: an analysis by the BEST Collaborative

Larry J. Dumont, James P. AuBuchon, Hans Gulliksson, Sherrill J. Slichter, M. Dean Elfath, Stein Holme, James R. Murphy, Leslie E. Rose, Mark A. Popovsky, and Scott Murphy



CONCLUSION: These data suggest that there is no relationship between in vitro pH at a $pH_{22°C}$ of at least 6.2 and in vivo PLT viability as measured by radiolabeled recovery and survival of autologous PLTs.

TRANSFUSION 2006

Δείκτες ποιότητας

Βιοχημική προσέγγιση

In vitro and in vivo evaluation of leukoreduced platelets stored for 7 days in CLX containers

TABLE 2. Biochemical, hematologic, and functional test results*

Measure	Day 1 Control	Day 1 Test	p < 0.05	Day 5, control	Day 7, test	p < 0.05
pH	7.47 ± 0.07	7.46 ± 0.09		7.31 ± 0.13	7.06 ± 0.27	†
pO_2 (mmHg)	147 ± 11	137 ± 16	†	131 ± 26	135 ± 28	
pCO_2 (mmHg)	36 ± 4	37 ± 6		25 ± 5	22 ± 6	†
HCO_3^- (mEq/L)	16 ± 2	16 ± 2		9 ± 3	6 ± 3	†
Glucose (mmol/L)	34 ± 2	34 ± 3		30 ± 2	27 ± 3	†
Lactate (mmol/L)	5.0 ± 1.2	5.2 ± 1.2		12.8 ± 2.2	18.0 ± 3.6	†
Morphology (% disks)	74 ± 8	74 ± 8		56 ± 12	48 ± 17	†
P-selectin (%)	59 ± 17	59 ± 15		61 ± 18	69 ± 16	†
Hypotonic shock response (%)	42 ± 18	49 ± 20		52 ± 15	43 ± 20	†
Extent of shape change (%)	18 ± 4	18 ± 5		17 ± 4	15 ± 2	†

TRANSFUSION 2005;

Δείκτες ποιότητας

Λειτουργική προσέγγιση

ex vivo
In vitro

ISBT Science Series
An affiliated publication to Vox Sanguinis
ISBT Science Series (2013) 8, 221–224
STATE OF THE ART 3D-S31-01

Assays for quality control of platelets for transfusion

H. Deckmyn[1] & H.B. Feys[2]
[1]Laboratory for Thrombosis Research, KU Leuven Kulak, Ghent, Belgium
[2]Transfusion Research Center, Belgian Red Cross Flanders, Brugge, Belgium

Determination of platelet reactivity *in vitro*

Hypotonic shock response (HSR)

shape change (ESC)

Systems under flow

Thromboelastography

Platelet aggregation

Flow cytometry

CD62P analysis by flow cytometry

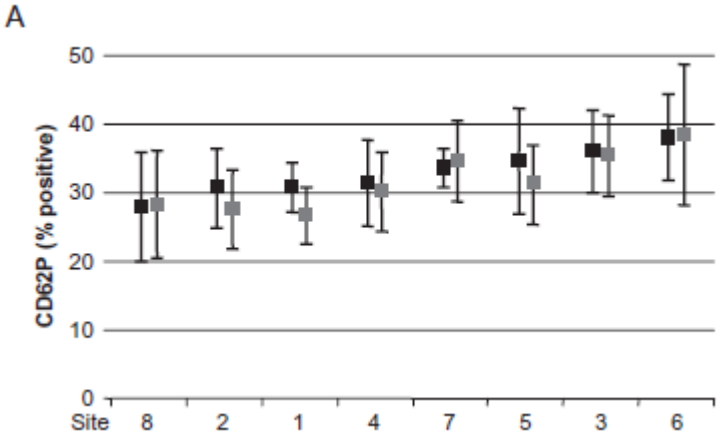
Annexin V binding, PF4, soluble CD62P, CD40L

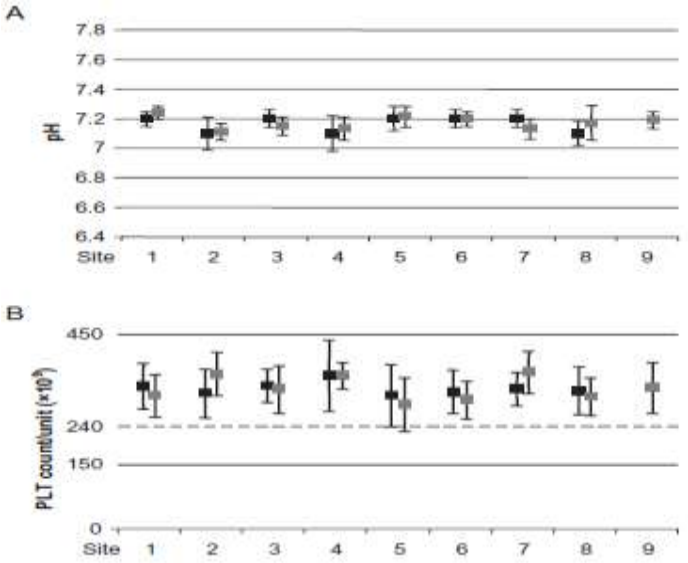
Δείκτες ποιότητας
Λειτουργική προσέγγιση

Development of a quality monitoring program for platelet components: a report of the first four years' experience at Canadian Blood Services

Elena Levin, Craig Jenkins, Brankica Culibrk, Maria I.C. Gyöngyössy-Issa, Katherine Serrano, and Dana V. Devine

Parameter (unit)	PRP-PCs		BC-PCs	
	QMP 1 (n = 106†)	QMP 2 (n = 72)	QMP 3 (n = 96)	QMP 4 (n = 108‡)
PLT concentration (×10⁹/L)	1394 ± 417	1569 ± 463	946 ± 175	947 ± 166
MPV (fL)	8.5 ± 1.0	8.4 ± 0.8	8.3 ± 0.4	8.3 ± 0.4
Morphology (score)	253 ± 24	260 ± 15	284 ± 23	299 ± 20
CD62P (%)	34.8 ± 13.0	47.1 ± 10.3	32.9 ± 6.6	31.7 ± 7.2
pH at 22°C	7.25 ± 0.11	7.15 ± 0.19	7.35 ± 0.09	7.36 ± 0.08
Lactate (mmol/L)	15.6 ± 3.2	16.1 ± 3.7	13.8 ± 1.7	13.4 ± 1.5
Glucose (mmol/L)	28.9 ± 3.1	29.1 ± 3.7	15.0 ± 1.3	14.4 ± 1.2
pO_2 (mmHg)	98 ± 26	98 ± 33	97 ± 20	87 ± 17
pCO_2 (mmHg)	31 ± 9	35 ± 11	38 ± 9	36 ± 6





TRANSFUSION 2012;52:810-818.

Δείκτες ποιότητας

Λειτουργική προσέγγιση

in vivo

In vivo platelet recovery and survival calculations

Bleeding time

$$CCI = \frac{(\text{post-transfusion platelet count}/\mu L - \text{pretransfusion platelet count}/\mu L) \times \text{body surface area } (m^2)}{\text{No. of platelets transfused} \times 10^{11}}$$

Δείκτες ποιότητας

Ασφάλεια

ex vivo
In vitro

ABO, RhD

Anti-HIV 1 & 2

HBsAg

Anti-HCV

by the FDA or validated to provide sensitivity equivalent to FDA-approved methods. None of these methods is sensitive enough to detect bacteria immediately after collection. All methods require a waiting time for bacteria contaminants to multiply before the component is sampled.

The process most commonly used in the United States to screen apheresis platelets is a culture-based system that requires the platelet component to be stored for 24 hours before sampling. After that time, a sample is withdrawn and inoculated into one or more culture bottles. The bottles are then incubated in the culture system. Some blood centers continue to hold the component during the first 12 to 24 hours of culture and release it for use only if the culture is negative at the end of that time. In all cases, the culture is continued for the shelf life of the unit. If the culture becomes positive after the component is released, the blood center attempts to retrieve it. If the component has not been transfused, resampling of the product for culture is very informative because approximately two-thirds of the initially positive signals are determined to be caused by either contamination of the bottle (and not the component) or false signals from the culture system.[73,74] All positive cultures should be tested to determine the identity of the organism. If a true-positive result is related to an organism that is not a skin contaminant, the donor should be notified and advised to seek medical consultation.[19]

Other methods approved in the United States for platelet quality control testing early in the storage period include a culture-based system with a one-time-point readout and an optical scanning system. All of the methods are approved for testing leukocyte-reduced apheresis platelets, and some are approved for testing pools of leukocyte-reduced, whole-blood-derived platelets. These methods are not generally used for routine screening of individual (unpooled) whole-blood-derived platelet concentrates. Low-technology methods for screening platelets just before issue—such as visually inspecting the platelets for swirling or testing them for low glucose or pH—lack both sensitivity and specificity and do not fulfill the AABB standard for bacteria detection.[18(p111),20,73] However, two FDA-cleared point-of-issue assays can be used for bacteria detection testing of platelet concentrates that are pooled immediately before issue.

Since the implementation of routine bacterial screening of apheresis platelets, the frequency of FDA-reported fatalities from contaminated apheresis platelets has declined.[71] However, some contaminated apheresis platelets escape detection by this early testing, presumably because bacterial concentrations are below limits of detection at the time of sampling; thus, septic, and even fatal, reactions do still occur. AABB has recommended consideration of policies to further reduce the risk of bacterially contaminated platelets.[75] The point-of-issue assays mentioned above are cleared by FDA as adjunct (time-of-issue) tests for apheresis platelets that have been screened by another method. In a large clinical trial, one of these assays detected nine bacterially contaminated components among 27,620 apheresis platelets (1 in 3069 components) previously screened by an early-storage culture-based assay.[76] There were also 142 false-positive results. As of March 2014, point-of-issue retesting of apheresis platelets had not been widely implemented in the United States.

All of the above methods provide incomplete assurance of bacteria detection, and none is practical for screening the red cell inventory. Pathogen-reduction methods, which impair proliferation of bacteria in the blood component, could theoretically be used to reduce the risk of septic reactions from bacteria in blood components. Indeed, in some regions outside the United States, pathogen reduction has replaced bacteria detection testing for platelets, but these technologies are not approved for use in the United States as of March 2014.

Infections Transmitted by Insect Vectors

Until recently, malaria was the only vector-transmitted disease that was widely recognized as having the potential for secondary transmission by transfusion in the United

Δείκτες ποιότητας

Ασφάλεια

Residual risk of bacterial contamination of platelets: six years of experience with sterility testing

TABLE 1. Bacterial contamination rates, routine PC screening: January 2010 to December 2016

Variable	Component: Buffy coat pooled PCs, N = 601,988	Component: Apheresis PCs, N = 186,737	p value
No. of initial positives	390	269	< 0.0001
Rate per 10,000	6.47	14.40	
No. of true positives	57	18	0.9473
Rate per 10,000 (% initial positives)	0.94 (14.6)	0.96 (6.7)	
No. of indeterminate results	32	29	< 0.0001
Rate per 10,000 (% initial positives)	0.53 (8.2)	1.50 (10.4)	
No. of false positives			
Machine error	228	206	< 0.0001
Rate per 10,000 (% initial positives)	3.78 (58.5)	11.03 (76.6)	
No. of false positives due to contamination	73	17	0.2854
Rate per 10,000 (% initial positives)	1.21 (18.7)	0.91 (6.3)	

TABLE 2. True-positive cultures, routine PC screening: January 2010 to December 2016

	Species identified
Gram-positive bacteria	Gram-negative bacteria
Apheresis PCs (N = 18)	
CoNS (n = 1)	*Escherichia coli* (n = 3)
Streptococcus spp. (n = 8)	*Serratia marcescens* (n = 3)
Corynebacterium spp. (n = 1)	
Bacillus (n = 1)	
Enterococcus faecium (n = 1)	
Buffy coat pooled PCs (N = 57)	
CoNS (n = 33)	*Morganella morganii* (n = 1)
Streptococcus spp. (n = 9)	*Serratia marcescens* (n = 1)
Bacillus spp. (n = 5)	*Pseudomonas aeruginosa* (n = 1)
Staphylococcus aureus (n = 4)	*Citrobacter koseri* (n = 1)
Actinomyces (n = 1)	
Enterococcus faecium (n = 1)	

TABLE 3. Bacterial contamination rates, QC sterility testing at outdate: January 2010 to December 2016

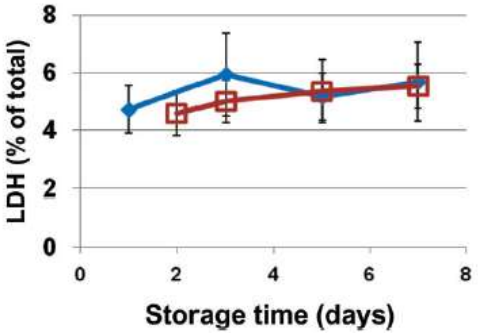
Variable	Pooled platelets, N = 8535: No.	Pooled platelets, N = 8535: Rate per 1000	Pooled platelets, N = 8535: % Initial positives	Apheresis platelets, N = 8498: No.	Apheresis platelets, N = 8498: Rate per 1000	Apheresis platelets, N = 8498: % Initial positives	p value between rate per 1000
Initial positives	72	8.4	100	121	14.2	100	0.0003
Only aerobic	8	2.1	25.0	34	4	28.1	0.0252
Only anaerobic	47	5.5	65.3	73	8.6	60.3	0.0161
Both	7	0.8	9.7	14	1.6	11.6	0.1239
p value between culture bottles		0.0003			0.0002		
True positives*	7	0.8	9.7	8	0.9	6.6	0.7897
Only aerobic	0	0	0	1†	0.1	0.8	0.4989
Only anaerobic	3‡	0.4	4.2	2§	0.2	1.7	1.0000
Both	4‖	0.5	5.6	5¶	0.6	4.2	0.7533
p value between culture bottles		0.2500			1.000		
False positives							
Machine error	53	6.2	73.6	96	11.3	79.3	0.0004
Only aerobic	13	1.5	18.1	29	3.4	24.0	0.0129
Only anaerobic	38	4.5	52.8	63	7.4	52.1	0.0118
Both	2	4.5	2.8	4	0.5	3.3	0.6901
p value between culture bottles		0.0005			0.0004		
False positives due to contamination	10	1.2	13.9	14	1.6	11.6	0.4230
Only aerobic	4	0.4	5.6	1	0.1	0.8	0.3749
Only anaerobic	5	0.6	6.9	8	0.9	6.6	0.4228
Both	1	0.1	1.4	5	0.6	4.1	0.2828
p value between culture bottles		0.7389			0.0391		
Indeterminate results	2	0.2	2.8	3	0.4	2.5	0.6868

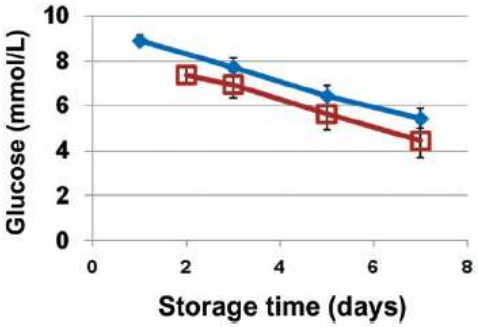
* True-positive cultures identified during QC sterility testing of outdated PCs were missed during routine PC screening and thus are categorized as "false negatives."
† CoNS (n = 1).
‡ *P. acnes* (n = 3)
§ *P. acnes* (n = 1) and CoNS (n = 1).
‖ CoNS (n = 4).
¶ *S. aureus* (n = 1) and CoNS (n = 4).

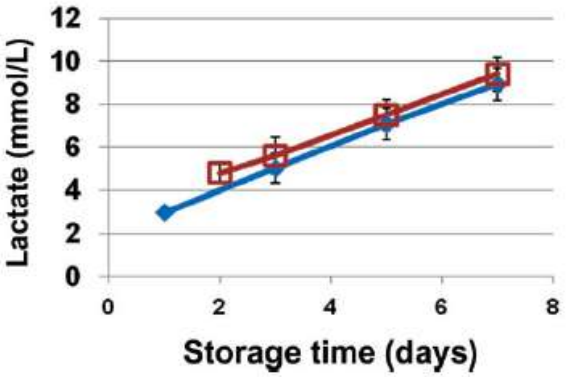
Δείκτες ποιότητας

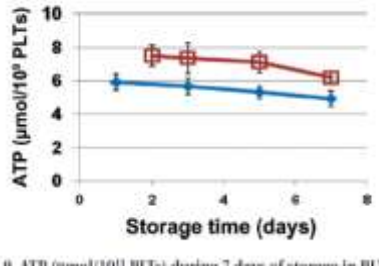
Storage of interim platelet units for 18 to 24 hours before pooling: in vitro study

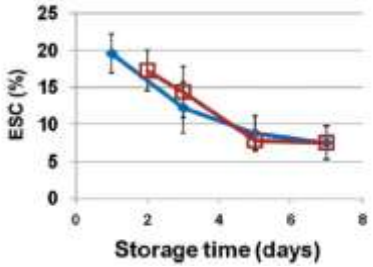
Per Sandgren, Geert van Waeg, Cat

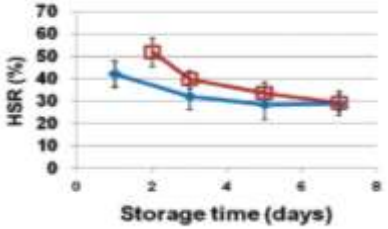


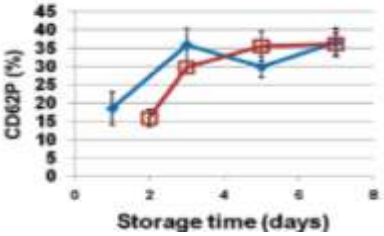


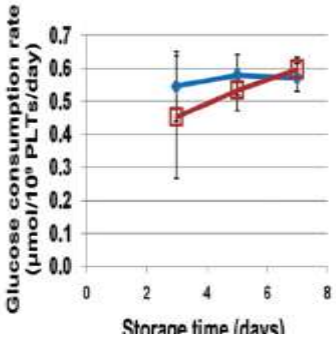


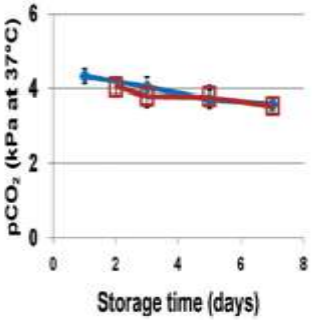


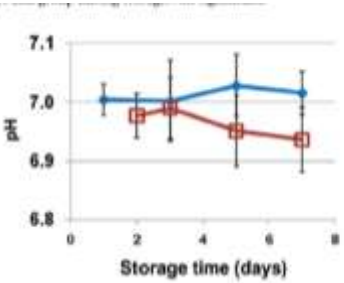












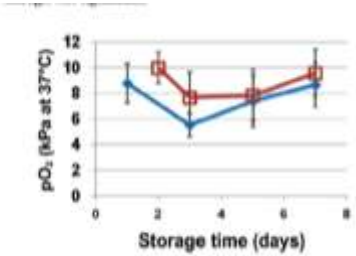


Fig. 8. Oxygen tension (kPa at 37°C) during 7 days of storage

Ποιότητα και
προσθετικά διαλύματα

	Plasma Lyte A	PAS-II (T-Sol, Baxter)	PAS-III (InterSol, Baxter)	Composol (Fresenius)	PAS-III M (SSP+, MacoPharma)
NaCl	90	116	77	90	69
KCl	5	-	-	5	5
$MgCl_2$	3	-	-	1.5	1.5
Na_3-citrate	-	10	10	11	10
NaH_2PO_4/Na_2HPO_4	-	-	26	-	26
Na-acetate	27	30	30	27	30
Na-gluconate	23	-	-	23	-

*The compositions of commercial solutions may be slightly different from basic compositions.

Platelet Additive Solutions: A Review of the Latest Developments and Their Clinical Implications

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Department of Product and Process Development, Sanquin Blood Bank, Amsterdam, The Netherlands

Review Article

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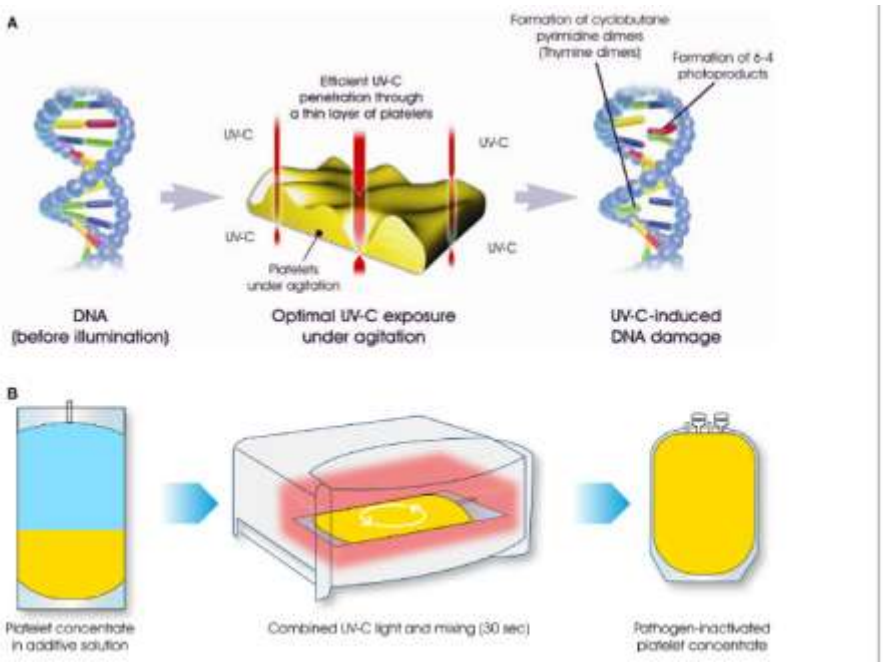
In summary, the current generation of PAS allow excellent storage of platelets during at least 7 days after collection, as shown by CCI data for PAS-E and recovery and survival data for PAS-F. PASs should be further reformulated, in order to keep the platelet quality close to that when blood is freshly collected. In addition, PASs can be used to support storage of pathogen-inactivated as well as cold-stored platelets. The current PASs probably do not require a 30% plasma carry-over [34]. With a lower percentage of plasma, it is probable that the number of transfusion reactions will further decrease. Possibly, using advanced apheresis-like technologies to produce platelet concentrates, the plasma carry-over could be driven down to only a few percent. TRALI caused by HLA antibodies thus can be prevented. Bacterial contamination of platelets in PAS may be a concern. There is not much literature, but there is a plausible explanation (bactericidal proteins in plasma), and the data that is available does show an increased risk. The risk and severity of a transfusion-transmitted bacterial infection should be weighed against the cost of e.g. introducing a post-storage bacterial screening assay. Another concern is patients undergoing massive transfusions who need clotting factors and do not tolerate dilution of their circulatory volume with PAS. However, no clinical data is available, and only under worst-case laboratory conditions an effect could be observed. Nevertheless, clinical evaluations need to be performed.

Ποιότητα και αδρανοποίηση

Pathogen Inactivation of Cellular Blood Products—An Additional Safety Layer in Transfusion Medicine



	Technology		
	INTERCEPT blood system	**MIRASOL PRT system**	**THERAFLEX UV-Platelets**
Mechanism of action	UVA plus amotosalen (alkylating agent)	UV plus riboflavin (vitamin B2 = photosensitizer)	UVC alone
Blood products	Plasma and platelets	Plasma and platelets (in development for whole blood)	Plasma and platelets (in development for RBCs)
Status	Approved in some countries	Approved in some countries	In clinical development

Ποιότητα και θερμοκρασία

Cold platelets for trauma-associated bleeding: regulatory approval, accreditation approval, and practice implementation—just the "tip of the iceberg"

One size doesn't fit all: Should we reconsider the introduction of cold-stored platelets in blood bank inventories? [version 1; referees: 2 approved]

Alessandra Berzuini, Marta Spreafico, Daniele Prati

Table 2. List of *in vitro* experiments comparing platelet storage at 4°C versus room temperature.

Authors	Journal	Year	4°C versus room temperature
Johnson *et al.*	*Transfusion*	2016	Reduction of glycolysis Increased expression of P-selectin Faster thrombin generation Faster clot formation, equal strength
Bynum *et al.*	*Transfusion*	2016	Less oxidative stress Stronger clot Increased response to aggregating agents Better aggregation in shear stress conditions
Getz *et al.*	*Transfusion*	2016	No difference in platelet content in the first 5 days of storage No difference in rotation thromboelastometry (ROTEM) pattern after 5 days of storage
Wood *et al.*	*Transfusion*	2016	Decreased expression of GPIB, GPIX, GPIIB, and GPIV (easier von Willebrand factor attack) Increased expression of P-selectin, tetraspanin, and phosphatidylserine Cytoskeleton protein modifications corresponding to activation state (proteomics) Increased expression of CD62P, CD63, and annexin V
Baimukanova *et al.*	*Transfusion*	2016	Increased aggregation potential
Reddoch *et al.*	*Shock*	2014	Increased expression of CD40 and P-selectin
	Shock	2016	Increase of intracellular free calcium Increase of dense granule release of ATP Accelerated thrombin generation More pronounced response to ADP, collagen, and TRAP (thrombin receptor-activating peptide) Faster, stronger, and more durable clot
Mondoro and Vostal	*Platelet*	2002	Increased response to ADP and epinephrine Stronger clot resistance to disaggregating agents No spontaneous aggregation
Connor *et al.*	*Transfusion*	1996	Reduced expression of GMP-140 ADP response of 250%; collagen response of 100% at more than room temperature
Triulzi *et al.*	*Transfusion*	1992	Increased expression of GMP-140
Rinder *et al.*	*Transfusion*	1990	Increased expression of GMP-140
Becker *et al.*	*Transfusion*	1983	More pronounced ADP response

CONCLUSION: In the future, pathogen-reduced (PR), PLT additive solution (PAS) CS-PLTs seem more practical due to low risks of bacterial contamination and storage-related clotting. This should make longer storage of CS-PLTs feasible (e.g., 10 days or more). With a longer shelf life, PR PAS CS-PLTs could potentially be used in a wider range of patient populations.

TRANSFUSION Volume 57, December 2017

The Re-emergence of Cold-Stored Platelets

Why is the medical community (re)-interested in cold-stored platelets?

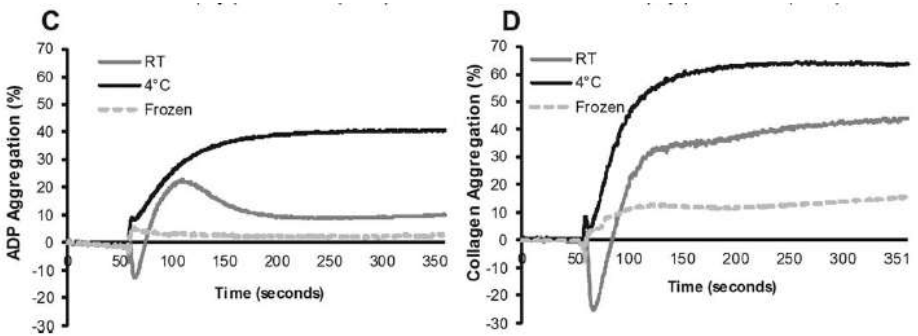
healthcare institutions should tailor two different therapeutic strategies for CS-PLTs and RT-PLTs, respectively, based on specific clinical situations.

Ποιότητα και
θερμοκρασία

Refrigeration and cryopreservation of platelets differentially affect platelet metabolism and function: a comparison with conventional platelet storage conditions

Lacey Johnson,[1] Shereen Tan,[1] Ben Wood,[1,2] April Davis,[1] and Denese C. Marks[1]

STUDY DESIGN AND METHODS: A three-arm pool-and-split study was carried out using buffy coat–derived PLTs stored in 30% plasma/70% SSP+. The three matched treatment arms were room temperature stored (20-24°C), cold-stored (2-6°C), and cryopreserved (−80°C with dimethyl sulfoxide). Liquid-stored PLTs were tested over a 21-day period, while cryopreserved PLTs were examined immediately after thawing and after 6 and 24 hours of storage at room temperature.



CONCLUSION: Cold storage and cryopreservation of PLTs led to morphologic and metabolic changes. However, storage under these conditions appears to maintain or even enhance certain aspects of in vitro PLT function.

Platelets

Cryopreservation of platelets is not widely available because the procedures for cryopreservation are complex and not routinely practiced at most blood centers. Several cryoprotectants have been described for platelet cryopreservation[72,73] However, 5% or 6% dimethyl sulfoxide (DMSO) is most commonly used, mainly for autologous platelet transfusions in patients who are refractory to allogeneic platelets. Cryopreserved platelets can be stored for at least 2 years. After thawing, the platelet recovery rate in vitro is about 75%, which may be reduced further if thawed platelets are centrifuged to remove the DMSO before transfusion. The in vivo recovery rate after transfusion of thawed, DMSO-reduced platelets is about 35% to 42%.[74] In vivo, the platelets that survive after transfusion are hemostatically effective.[75]

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Συστάσεις

EDQM
19th Edition
2017

Parameter to be checked	Requirements	Frequency of control
ABO, RhD	Grouping	All units
Anti-HIV 1 & 2	Negative by approved screening test	All units
HBsAg	Negative by approved screening test	All units
Anti-HCV	Negative by approved screening test	All units

Statistical Process Control (SPC) is a tool that enables an organisation to detect changes in the processes and procedures it carries out by monitoring data collected over a period of time in a standardised fashion. SPC became mandatory in 2005 for blood establishments in the EU (Directive 2004/33/EC). Methods and standards for the application of SPC to quality assurance of blood components need to be continuously studied and further developed. The technique can be

Recovered single unit

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 60 \times 10^9$	as determined by SPC
Residual leucocytes per final unit [a] a. prepared from buffy-coat b. prepared from PRP	a. $< 0.05 \times 10^9$ b. $< 0.2 \times 10^9$	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [b]	> 6.4	as determined by SPC

Recovered pooled

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 2 \times 10^{11}$	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^9$ per final unit	as determined by SPC
pH measured (+22°C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

a A minimum of 90 % of units tested should meet the required value.
b These requirements are deemed to have been met if 90 % of the tested units fall within the values indicated.
c All tested units must comply. Measurement of the pH in a closed system is preferable to prevent CO_2 escape. Measurement may be made at another temperature and then corrected.

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Συστάσεις

EDQM
19th Edition
2017

Recovered pooled leucocyte-depleted

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 2 \times 10^{11}$	as determined by SPC
Residual leucocytes per final unit [a]	$< 1 \times 10^6$	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [b]	> 6.4	as determined by SPC

Recovered pooled in additive solution

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 2 \times 10^{11}$	as determined by SPC
Residual leucocyte content [b]	$< 0.3 \times 10^9$ per final unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

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Συστάσεις

EDQM
19th Edition
2017

Recovered pooled leucocyte-depleted in additive solution

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 2 \times 10^{11}$	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^6$ per final unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

Recovered pooled pathogen reduced

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content per final unit [a]	$> 2 \times 10^{11}$	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^6$ per final unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Συστάσεις

EDQM
19th Edition
2017

Apheresis

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content [a]	Standard unit: minimum 2×10^{11} per unit For use in neonates or infants: minimum 0.5×10^{11} per unit	as determined by SPC
Residual leucocyte content [b]	$< 0.3 \times 10^9$ per unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

Apheresis leucocyte-depleted

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content [a]	Standard unit: minimum 2×10^{11} per unit For use in neonates or infants: minimum 0.5×10^{11} per unit	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^6$ per unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Συστάσεις

EDQM
19th Edition
2017

Apheresis in additive solution

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content [a]	Standard unit: minimum 2×10^{11} per unit For use in neonates or infants: minimum 0.5×10^{11} per unit	as determined by SPC
Residual leucocyte content [b]	$< 0.3 \times 10^9$ per final unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

Apheresis leucocyte-depleted in additive solution

HLA and/or HPA	As required	All units
Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content [a]	Standard unit: minimum 2×10^{11} per unit For use in neonates or infants: minimum 0.5×10^{11} per unit	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^6$ per unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

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Συστάσεις

EDQM
19th Edition
2017

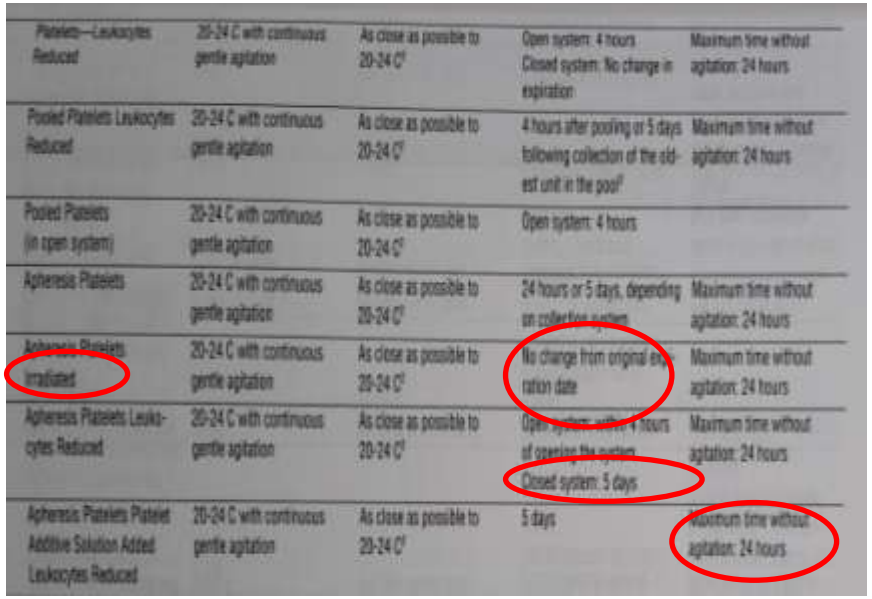
Apheresis pathogen-reduced

Volume [a]	> 40 mL per 60×10^9 of platelets	as determined by SPC
Platelet content [a]	minimum 2×10^{11} per unit	as determined by SPC
Residual leucocyte content [b]	$< 1 \times 10^6$ per unit	as determined by SPC
pH measured (+ 22 °C) at the end of the recommended shelf-life [c]	> 6.4	as determined by SPC

Platelets cryopreserved

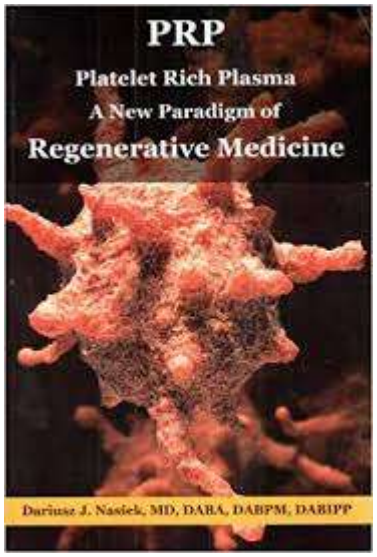
Parameter to be checked	Requirements	Frequency of control
Volume	50-200 mL	All units
Platelet content	> 40 % of the pre-freeze platelet content	All units

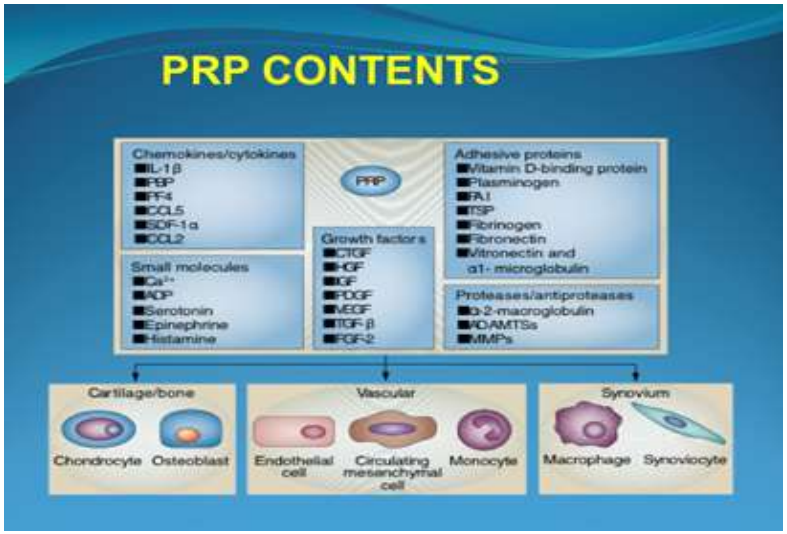
Platelets, Cryo when thawed will not swirl.



Platelets—Leukocytes Reduced	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	Open system: 4 hours Closed system: No change in expiration	Maximum time without agitation: 24 hours
Pooled Platelets Leukocytes Reduced	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	4 hours after pooling or 5 days following collection of the oldest unit in the pool[g]	Maximum time without agitation: 24 hours
Pooled Platelets (in open system)	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	Open system: 4 hours	
Apheresis Platelets	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	24 hours or 5 days, depending on collection system	Maximum time without agitation: 24 hours
Apheresis Platelets Irradiated	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	No change from original expiration date	Maximum time without agitation: 24 hours
Apheresis Platelets Leukocytes Reduced	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	Open system: within 4 hours of opening the system Closed system: 5 days	Maximum time without agitation: 24 hours
Apheresis Platelets Platelet Additive Solution Added Leukocytes Reduced	20-24 C with continuous gentle agitation	As close as possible to 20-24 C[f]	5 days	Maximum time without agitation: 24 hours

Αντισυμβατική χρήση





Ποιότητα στη μετάγγιση