Coag et Plasmaphérèse

F Parquin
Groupe de Transplantation Pulmonaire
Hôpital Foch
Suresnes

Pas de conflit d'intérêt

Changes in coagulation factors, complement, immunoglobulins, and immune complex concentrations with plasma exchange

TRANSFUSION 1982;22:54–58.

R. L. VOLKIN, T. W. STARZ, A. WINKELSTEIN, R. K. SHADDUCK, J. H. LEWIS, U. HASIBA, AND J. A. SPERO

EP centrifugation

Table 2. *Coagulation Factors 48 Hours After Three Plasma Exchanges (Three patients)*

	Preexchange*	Postexchange*	Per cent Decrease
PT (seconds)	11.5 ± 1.7	11.1 ± 0.3	
APTT (seconds)	32.4 ± 2.9	29.2 ± 2.5	
Fibrinogen (mg/dl)	253 ± 33	125 ± 30	51
Factor			
II (units/ml)	0.82 ± 0.13	0.67 ± 0.15	18
V (units/ml)	1.35 ± 0.09	1.06 ± 0.22	21
VII (units/ml)	0.85 ± 0.22	0.78 ± 0.33	8
VIII (units/ml)	1.82 ± 0.72	1.42 ± 0.22	22
IX (units/ml)	1.30 ± 0.66	1.20 ± 0.25	8
X (units/ml)	0.79 ± 0.06	0.76 ± 0.04	4
XI (units/ml)	0.90 ± 0.22	0.69 ± 0.18	23
XII (units/ml)	0.63 ± 0.11	0.44 ± 0.13	30
Fletcher Factor (units/ml)	1.02 ± 0.39	0.61 ± 0.23	40

* Values are means ± 1 SEM for individual coagulation factors before and following three plasma exchanges. The only significant disease was observed in fibrinogen levels ($p < 0.05$).

Wood L J Clin Apheresis 1986

Therapeutic Apheresis: A Review of Complications and Recommendations for Prevention and Management

Michele H. Mokrzycki[1]* and Rasheed A. Balogun[2]

Journal of Clinical Apheresis 26:243–248 (2011)

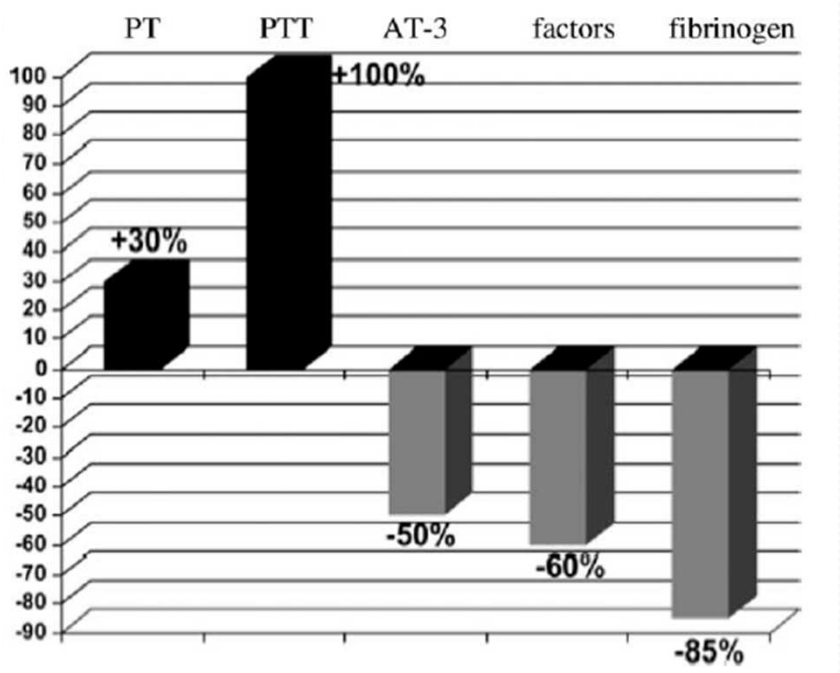
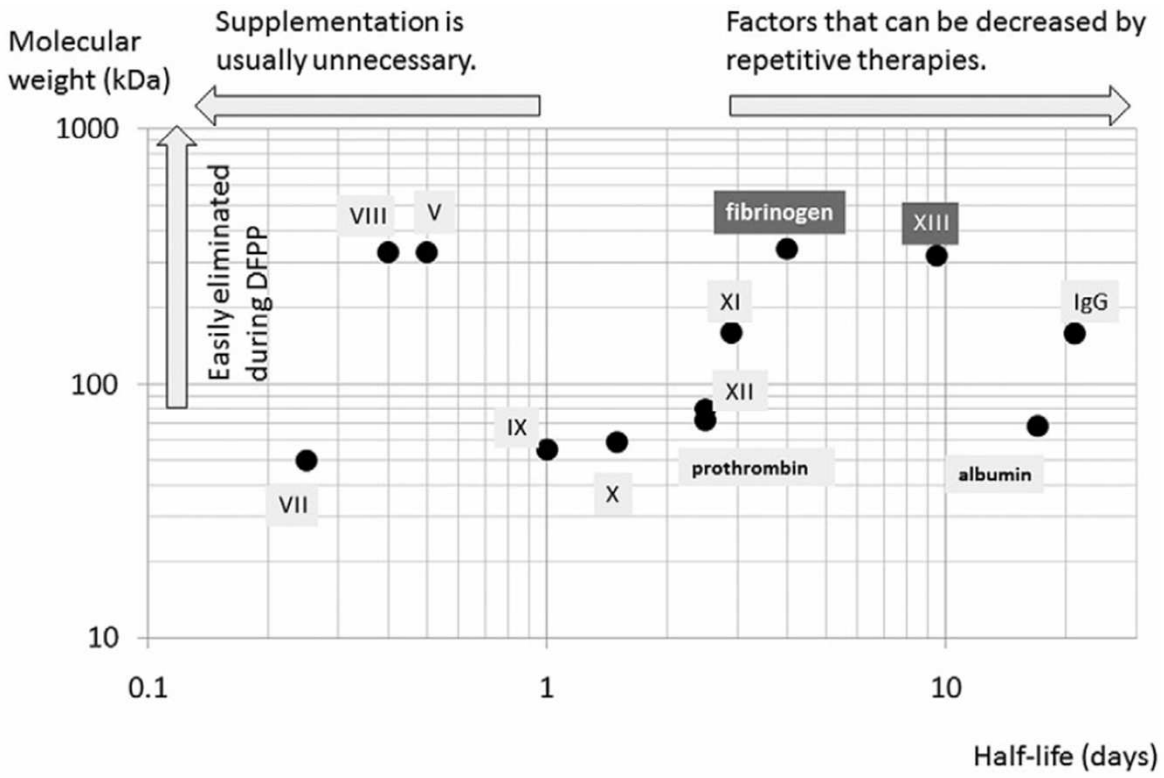


Fig. 2. Alterations in coagulation after TPE using albumin replacement.

Theoretical Basis of Pathogenic Substance Removal During Plasmapheresis

Therapeutic Apheresis and Dialysis 15(5):421–430

Norio Hanafusa



DFPP

FIG. 7. Half-lives and molecular weights of coagulation factors. Many coagulation factors have molecular weights larger than or almost equal to that of albumin and are removed by double filtrate plasmapheresis (DFPP). The half-lives of fibrinogen and factor XIII are long compared with the schedule of therapy. Such factors can be decreased through repeated therapy.

Fibrinogen Reduction and Bleeding Complications in Plasma Exchange, Immunoadsorption and a Combination of the Two

Simon Zöllner[a] Eleonore Pablik[b] Wilfred Druml[a] Kurt Derfler[a] Andrew Rees[c]
Peter Biesenbach[a]

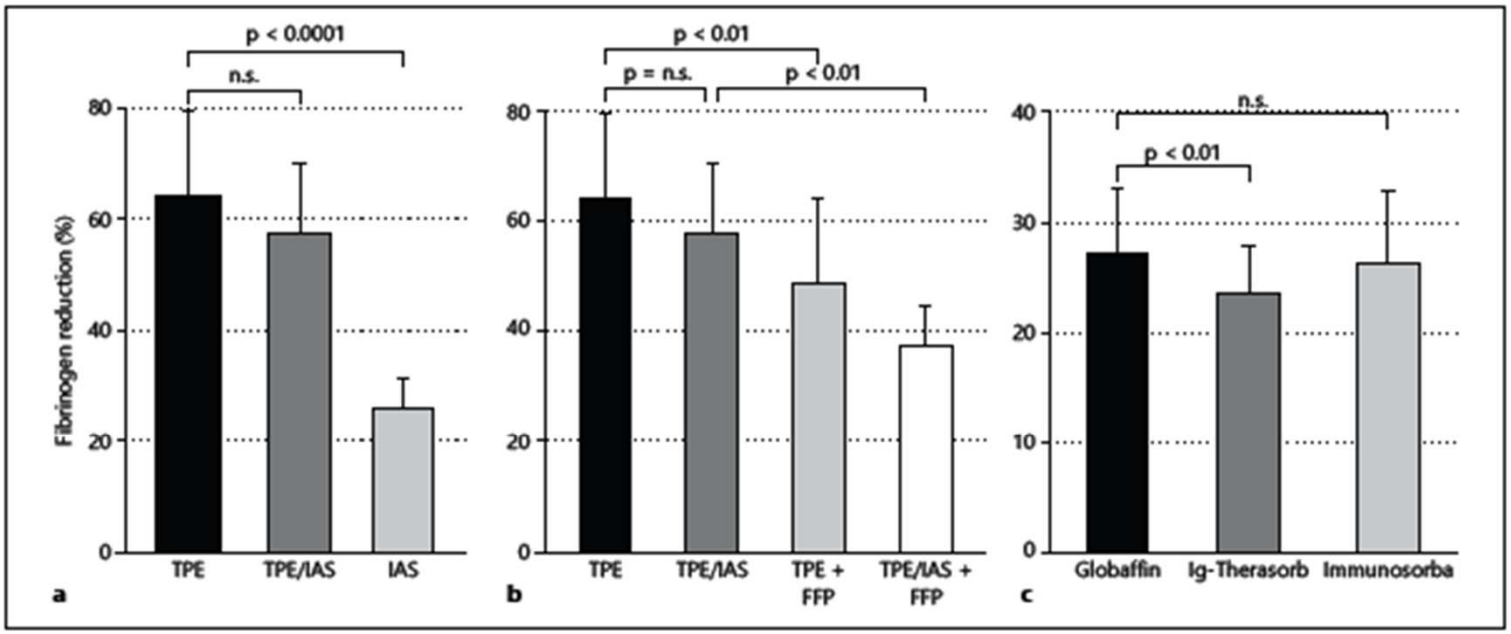
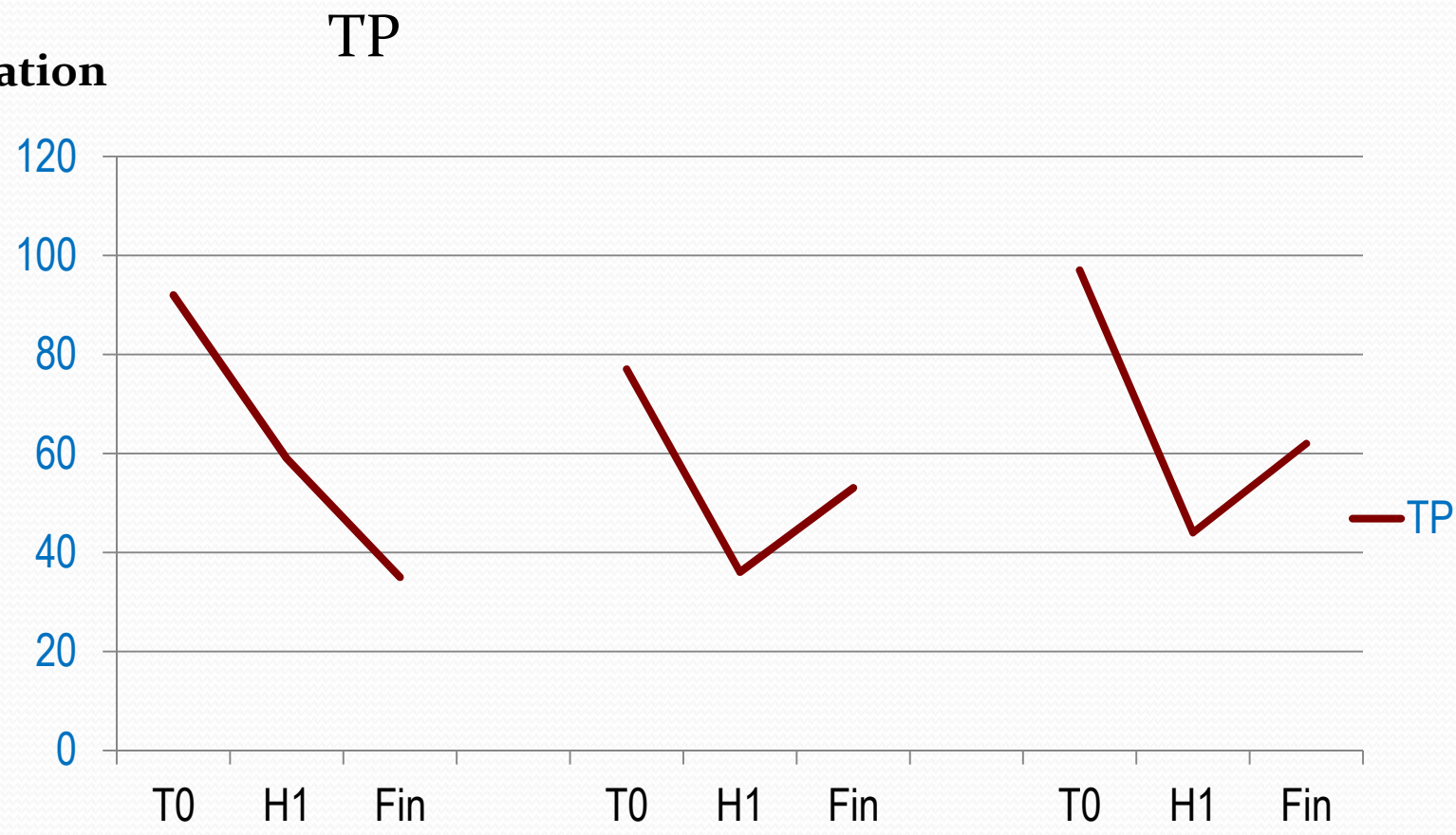


Fig. 1. Fibrinogen reduction in apheresis. Data presented in percentage and standard deviation. TPE = Therapeutic plasma exchange; IAS = immunoadsorption; TPE/IAS = combined treatment of TPE and IAS; TPE + FFP = TPE with addition of 2–4 units of fresh frozen plasma.

Coagulation disorders (1)

centrifugation

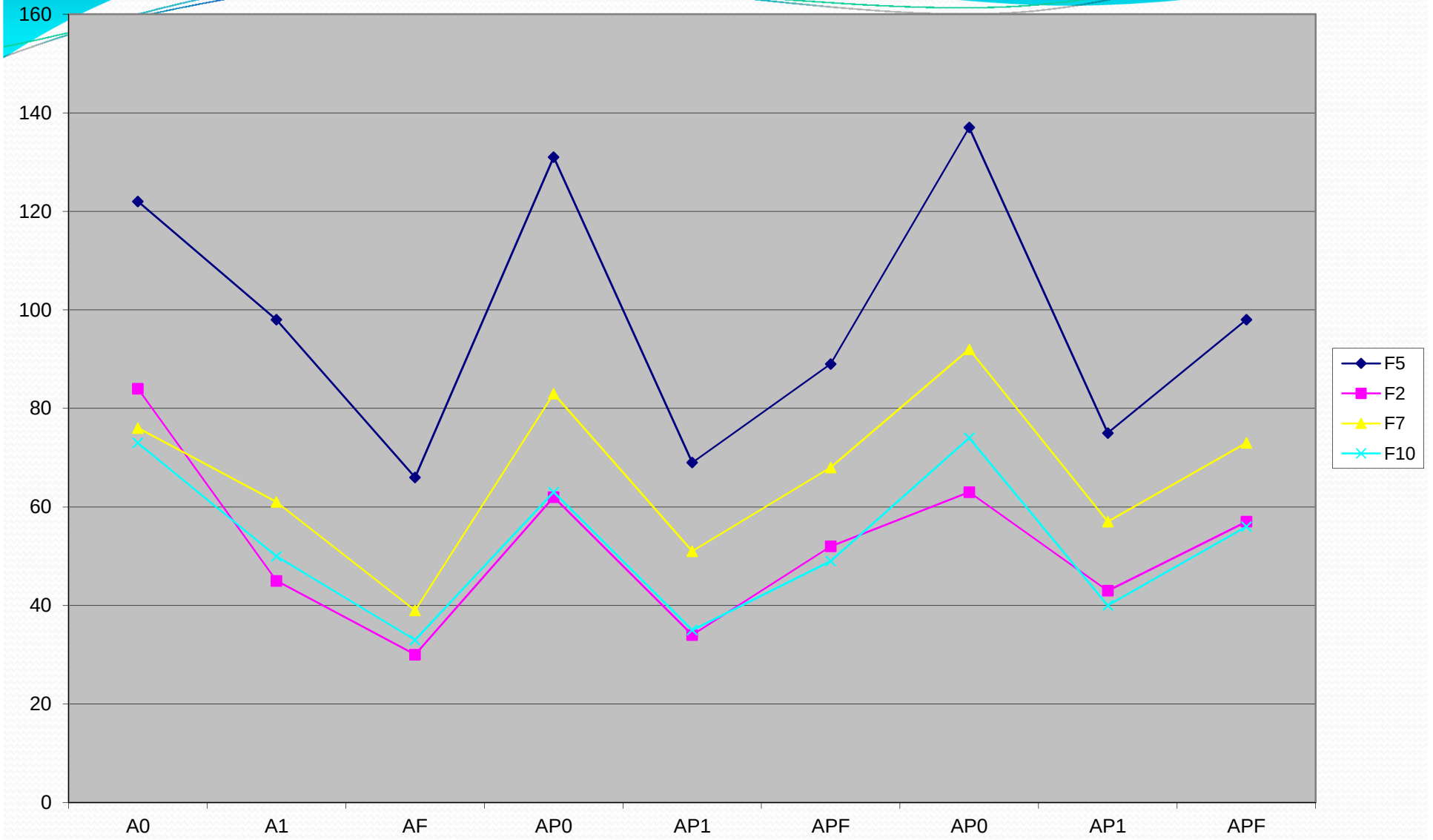


EP N° 1
100% Albu

EP N° 2
50% Albu
50% PVI

EP N° 3
50% Albu
50% PVI

COFACTEURS



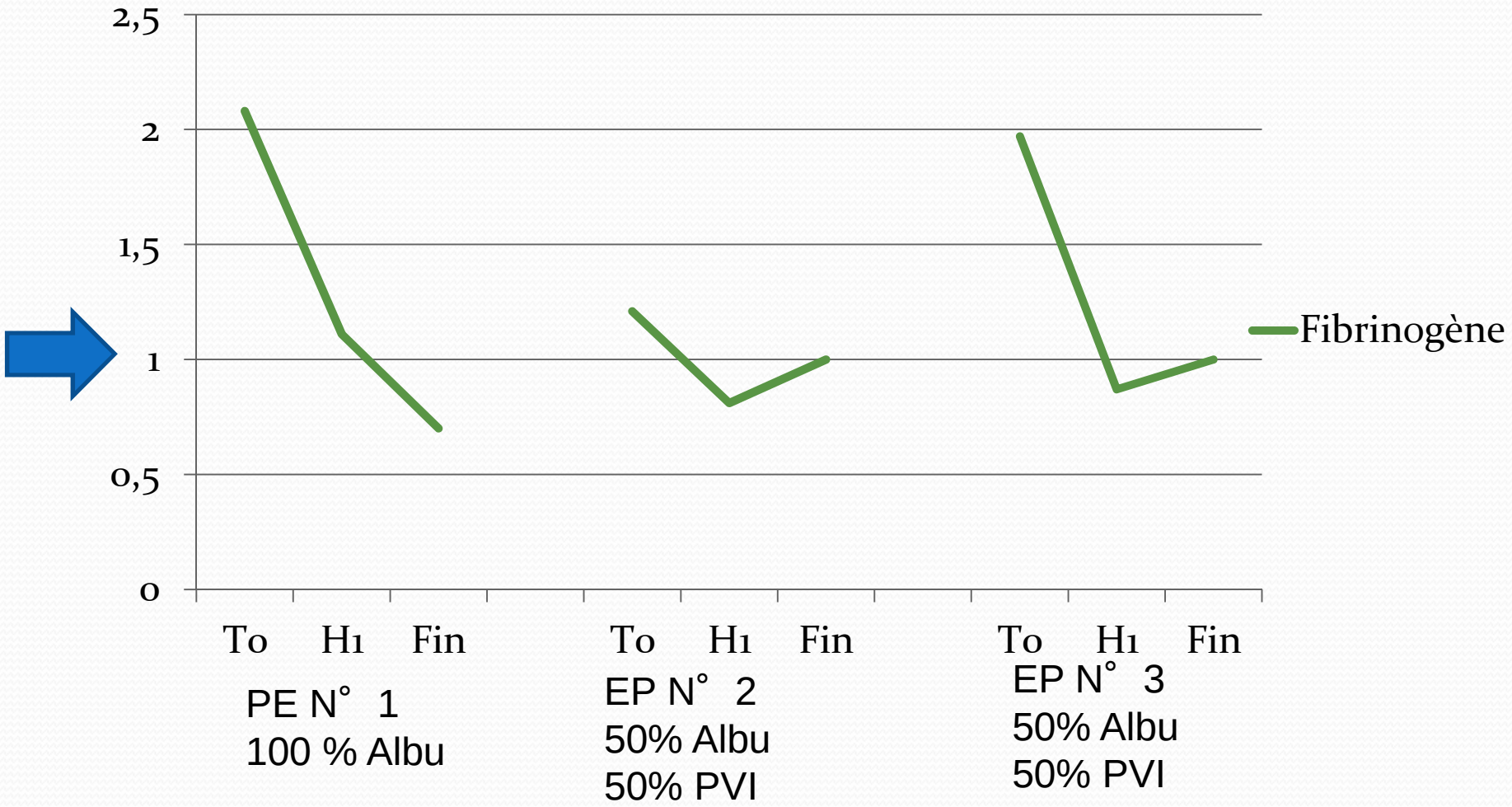
EP 1 100% Albu

EP 2 : 50% Albu, 50% PFC

EP 3 : 50% Albu, 50% PFC

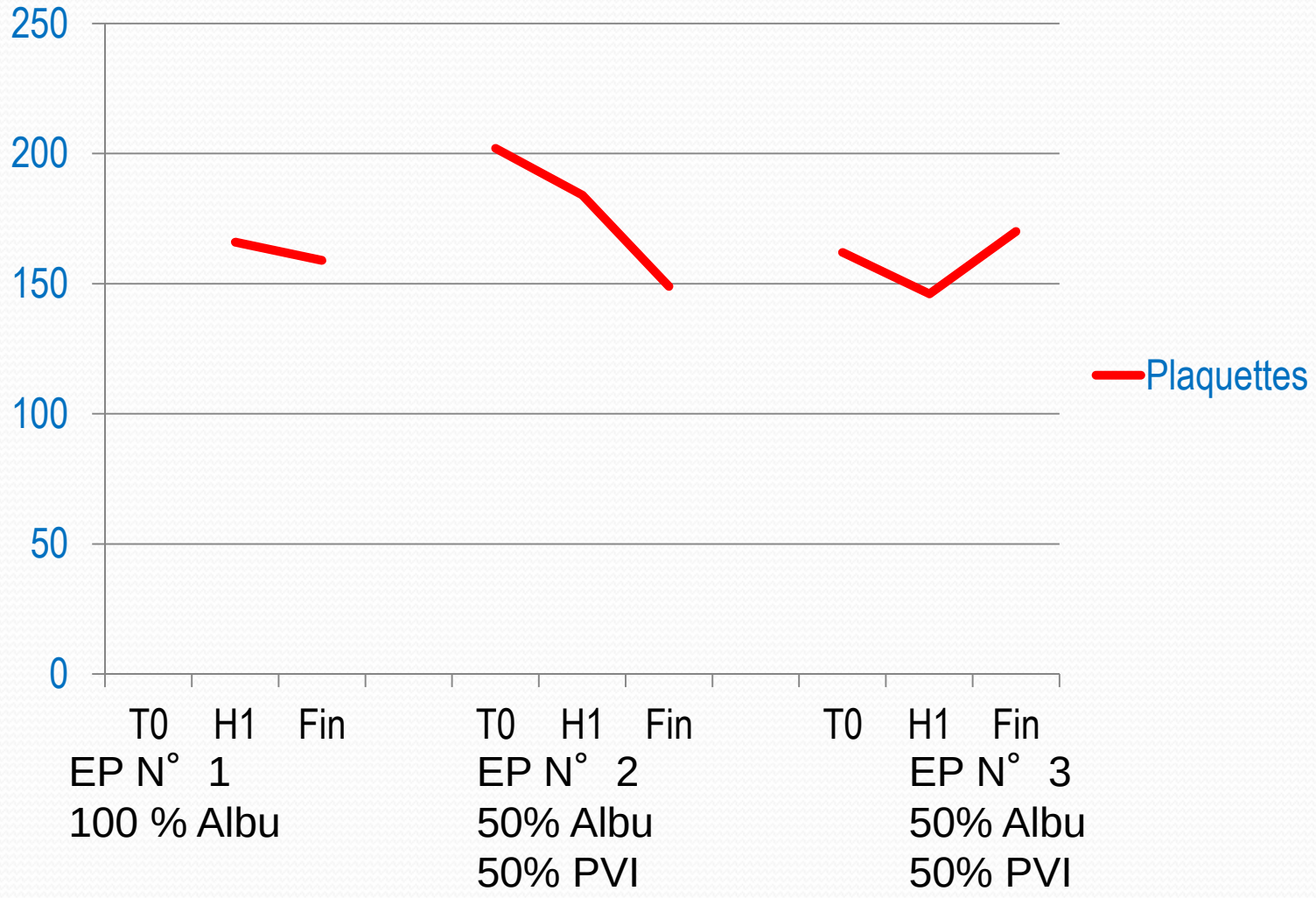
Coagulation disorders (2): FIBRINOGEN +++

centrifugation



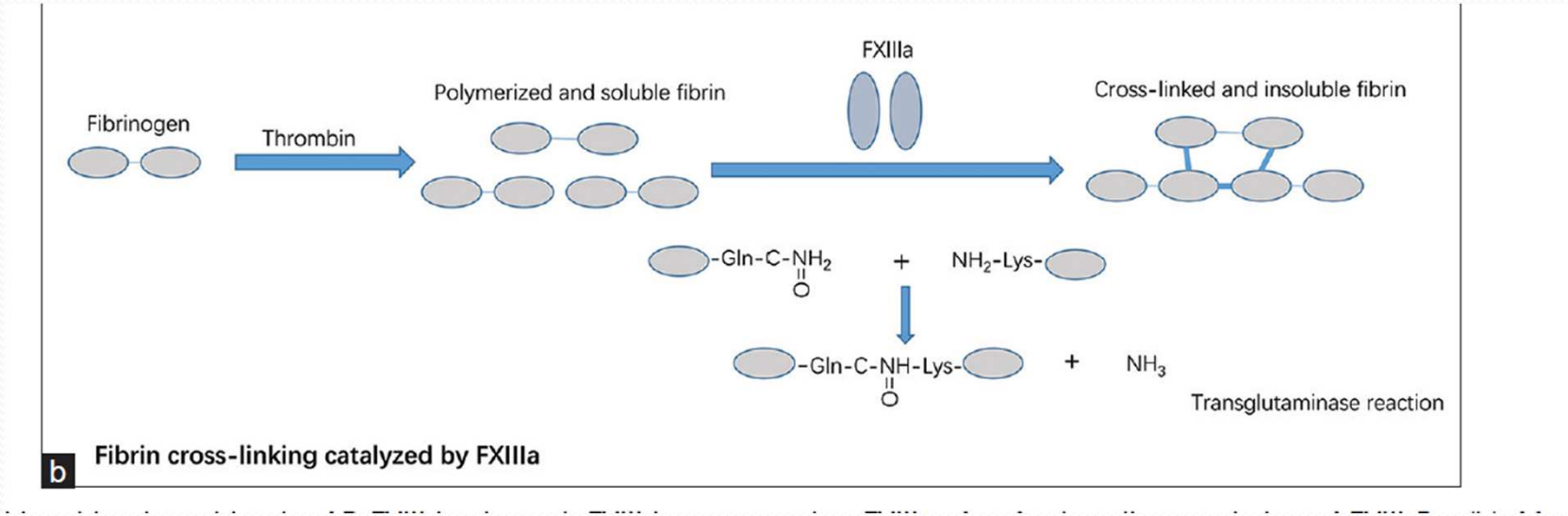
fibrinogen may take between 2.5 to 4 days for recovery to pretreatment level (Wood et al J Clin Apheresis 1986; 3:124-8)

Coagulation disorders (3)



Facteur XIII

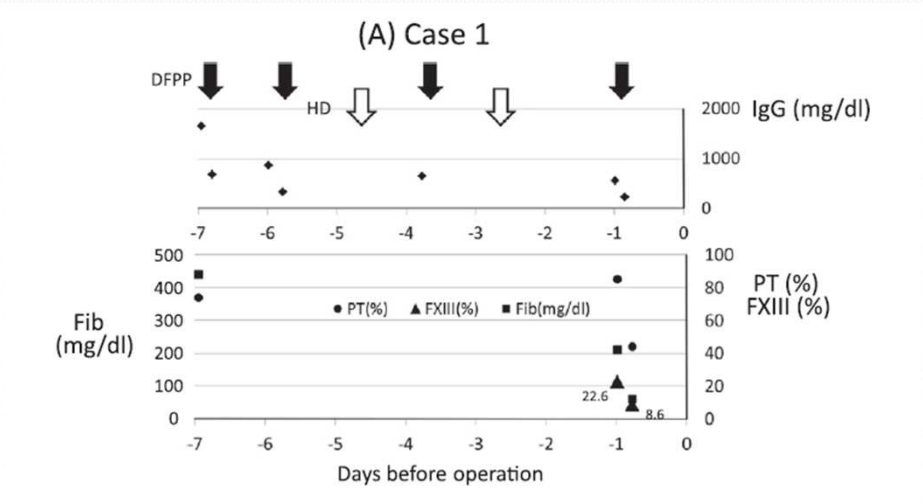
- PM 320 Kd
- Demi vie longue env 10 jours
- Cofacteur stabilisant de la fibrine

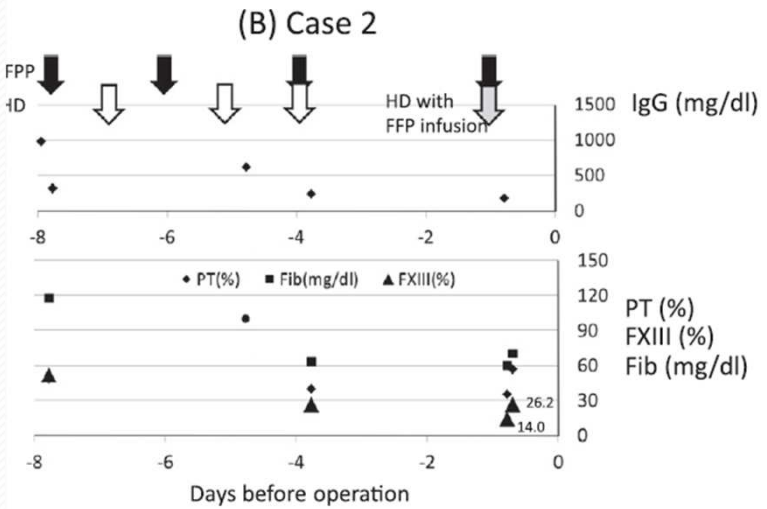


The effect of different apheresis modalities on coagulation factor XIII level during antibody removal in ABO-blood type incompatible living related renal transplantation

Norio Hanafusa [a,*], Yoshifumi Hamasaki [b,c], Hiroo Kawarasaki [d], Ryo Kido [b], Yugo Shibagaki [d], Akira Ishikawa [e], Yutaka Enomoto [c], Toshiro Fujita [b], Eisei Noiri [a], Masaomi Nangaku [a,b]

Transfusion and Apheresis Science 49 (2013) 254–258





Facteur XIII suite

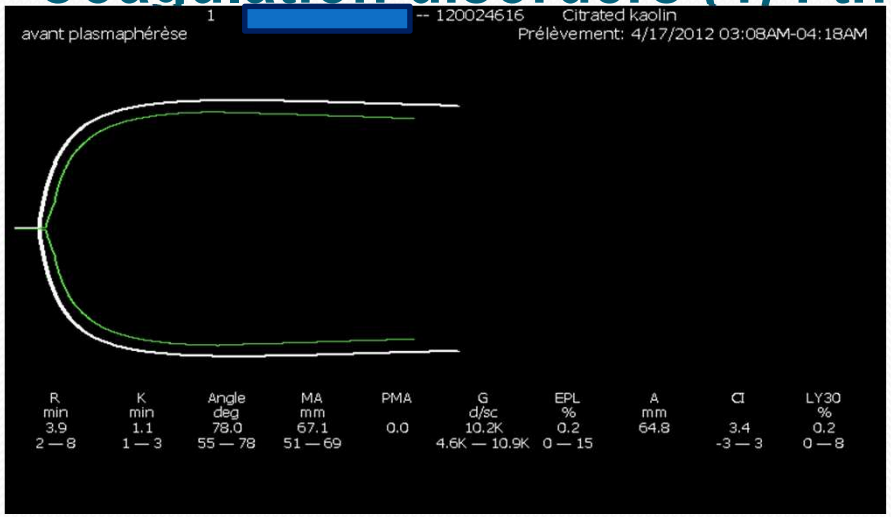
- Niveau < 10 % associé à des saignements graves neuro
- Travaux japonais sur DFPP en greffe rénale ABO incompatible *(Hanafusa N Transfusion and apheresis Sci 2013)*
- Travaux sur déficits en F XIII
  - FXIII concentrate and recombinant FXIII-A are available for prophylaxis; a 4 weekly
  - dose of 35 to 40 U/kg is recommended and a trough level of greater than 5% FXIII activity should be aimed for
  - During surgical procedures, the target should be higher than 50% FXIII activity.

COMMENT MESURER ?

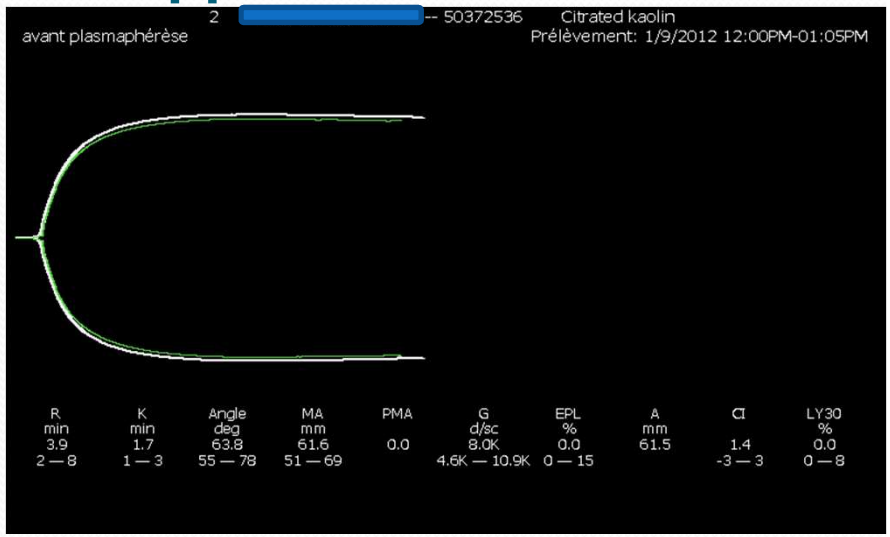
Cas particulier TP EP périopératoire

- Transplantation pulmonaire :
  - 1 chirurgie hémorragique , parfois très hémorragique
  - 2 péridurale thoracique très importante pour la gestion de l'analgésie post opératoire
  - 3 durée d'ischémie facteur de risque de DPG
- Indication EP pré opératoire : immunisation HLA
- 1 EP pré op immédiat réalisé en SSPI
- Discussion avec anesthésistes et chir
  - Centrifugation, voie centrale, 1,2 MP, citrate
  - Coag doit être normale en fin de procédure
  - Evaluation plus poussée de la coag
    - TP TCA fibrinogène et TEG

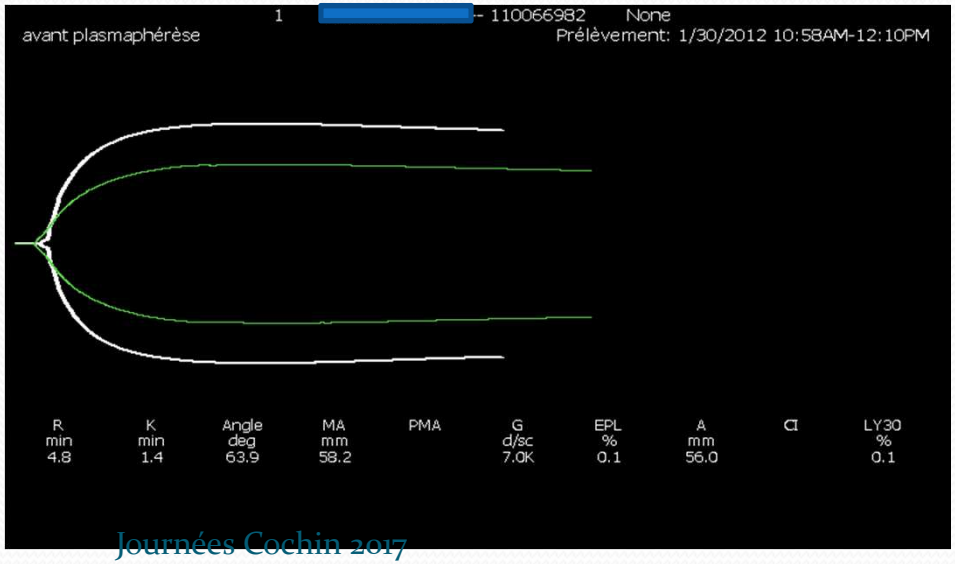
Coagulation disorders (4) : the TEG approach



100% PFC



50%albumine, 50% PFC



100% albumine

Dr François données personnelles

TEG thromboélastogramme

- Examen ancien 1948, normé depuis 2005 seulement
- Utilisé surtout en chirurgie hépatique et cardiaque pour gérer la transfusion de produits sanguins
- Explore l'ensemble de la coagulation et la fibrinolyse
- Technique semi automatisée

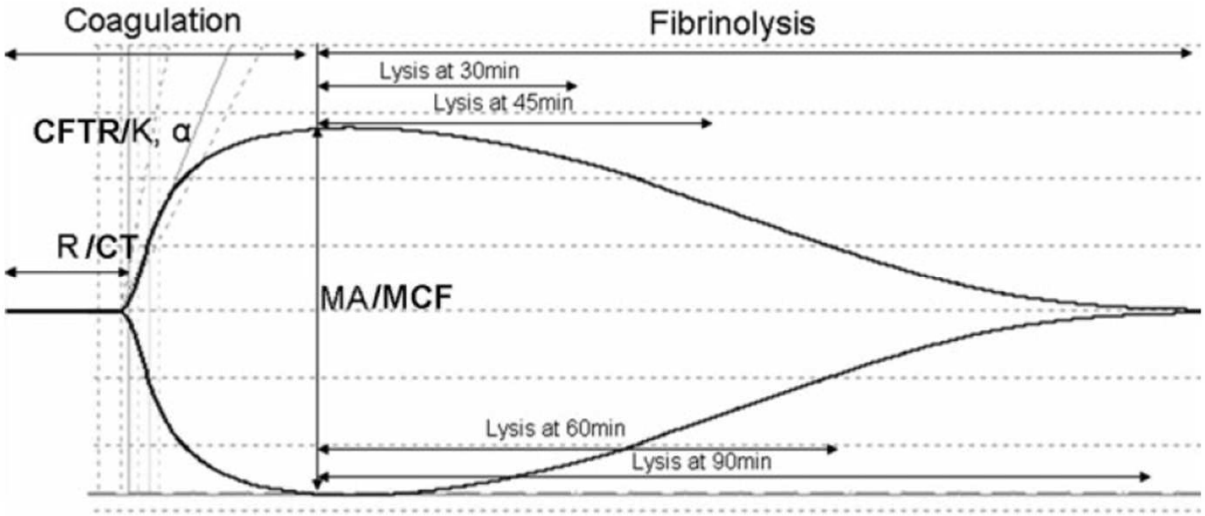
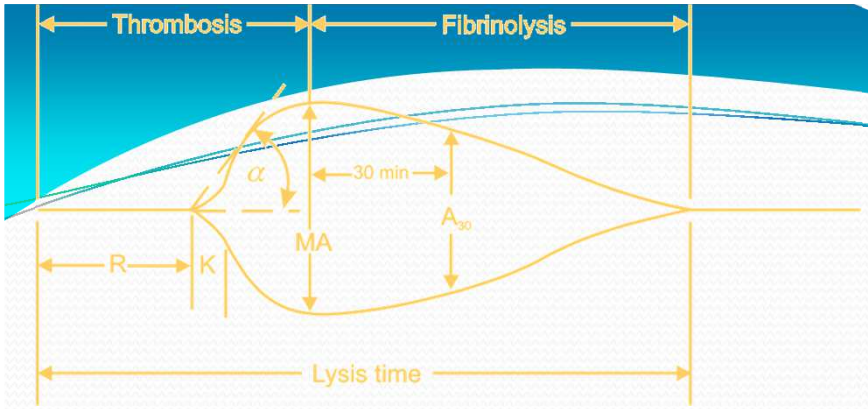


Figure 1 A thromboelastograph showing various test parameters.



Tracé TEG®

Temps de coagulation, partie enzymatique	R	R est le temps de latence qui s'écoule entre le moment où le sang est placé dans le TEG ® et le début de la formation de la fibrine (MA=2mm de hauteur)
Cinétique formation caillot et formation filaments fibrine	α	L'angle α reflète la rapidité (cinétique) de l'accumulation de fibrine et de son maillage, c'est-à-dire la vitesse de renforcement du caillot
	K	Le temps K mesure le temps nécessaire pour obtenir 20mm de hauteur.
Solidité du caillot, accumulation plaquettes	MA	MA, ou Maximum Amplitude, est directement fonction des propriétés dynamiques maximales d'interaction entre la fibrine et les plaquettes via leurs récepteurs IIb/IIIa. Ce paramètre reflète la rigidité maximale du caillot
	G	Transformation de MA en dynes/cm², coefficient de viscoélasticité G = 5000 * MA / (100 - MA)
Stabilité du caillot, lyse	LY30 EPL	LY30 mesure le rythme de réduction de l'amplitude dans les 30 minutes qui suivent l'obtention de l'MA. Ce paramètre reflète la stabilité du caillot.

2 techniques TEG et ROTEM

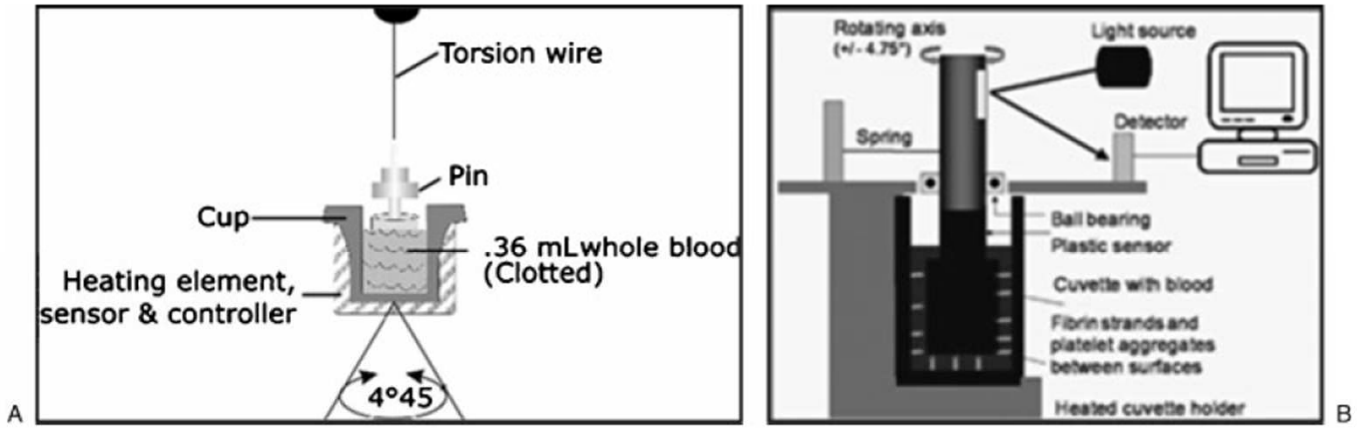


Figure 2 The mechanism of thromboelastography using (A) the TEG (Haemonetics Corp., Braintree, MA) and (B) the ROTEM (Tern International GmbH, Munich, Germany).

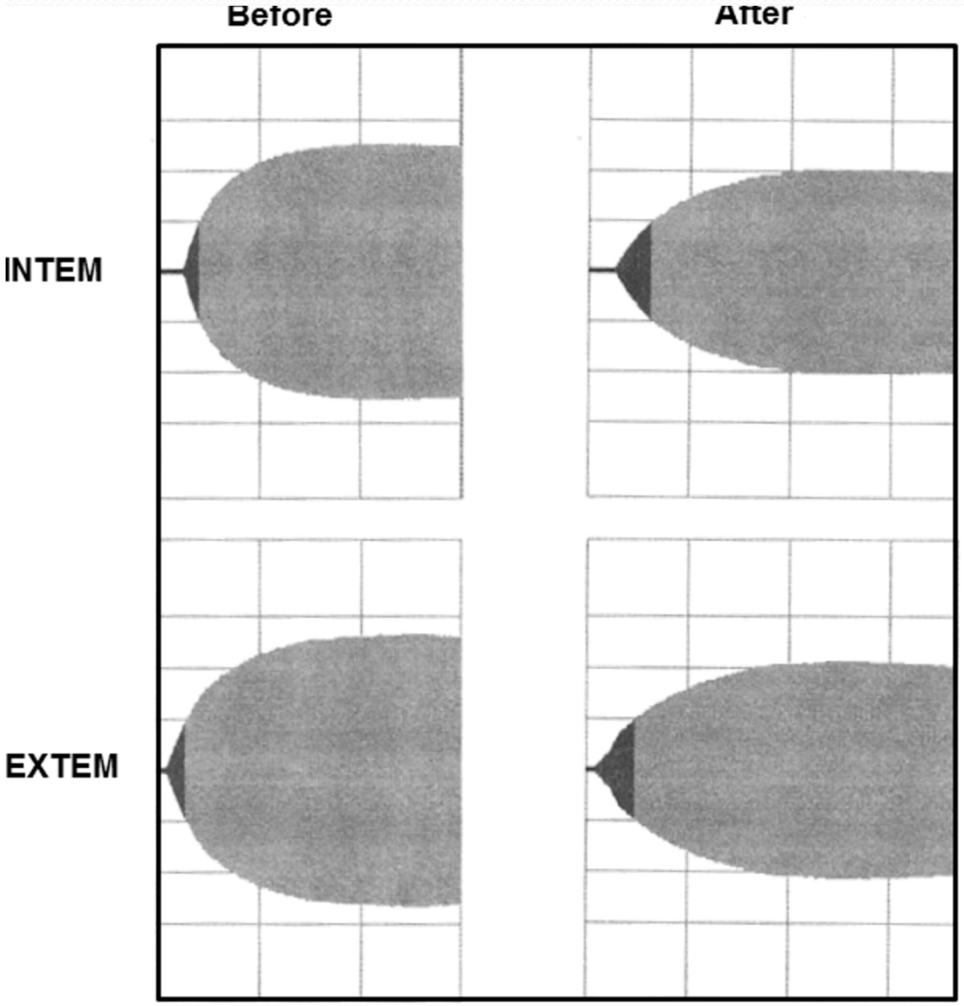
Table 1 Thromboelastography Parameters

Clot Formation Phase	TEG Parameter	ROTEM Parameter
Initial fibrin formation	R (reaction time)	CT (clot time)
Rate of clot development	K α (angle)	CFT (clot formation time) α (angle)
Maximum clot strength	MA (maximum amplitude)	MCF (maximum clot firmness)
Clot lysis	LY30 (percentage lysis at 30 minutes)	ML (maximum lysis)

Assessment of Hemostasis after Plasma Exchange Using Rotational Thrombelastometry (ROTEM)

Gerold Thölking[1]*, Rolf Mesters[2], Ralf Dittrich[3], Hermann Pavenstädt[1], Philipp Kümpers[1], Stefan Reuter[1]

PLOS ONE | DOI:10.1371/journal.pone.0130402 June 29, 2015



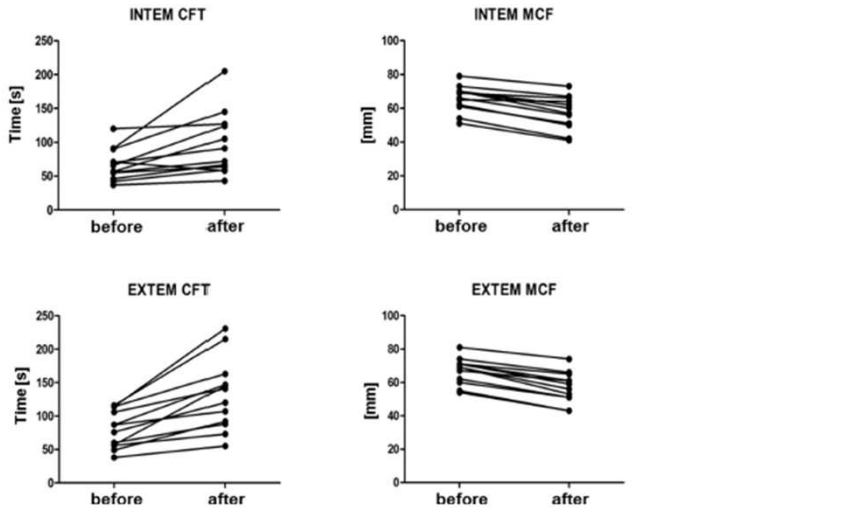


Fig 4. Clot-formation time (CFT) and maximum clot firmness (MCF) of all patients before and after TPE. INTEM and EXTEM analyses revealed a significant prolonged CFT (P = 0.0144 and P = 0.002, respectively) and reduced MCF (P = 0.0057 and P = 0.0058, respectively).

doi:10.1371/journal.pone.0130402.g004

Albumine 100 %

Coagulation profile after plasma exchange using albumin as a replacement solution measured by thromboelastometry

A. Blasi,[1] J. Cid,[2] J. Beltran,[3] P. Taurà,[3] J. Balust[3] & M. Lozano[2]

Vox Sanguinis (2016) 110, 159–165

Table 3 Laboratory assays and TEM parameters, before PE, after PE and before the next PE

	Before PE	After PE	% of variation (average)	% of determinations outside the ranges after PE	Before next PE	% Recovery (related to values after previous PE)	% of determinations outside the ranges before next PE
Standard Coagulation Test							
PT (%)	86 (81–98)	49 (43–52)	−49 (−54 to −41)	31	85 (78–92)	48 (41–51)	0
Platelets ($\times 10^9$/l)	129 (92–175)	126 (92–154)	0 (−9–5)	30	125 (90–165)	−1 (−7–11)	26
Fibrinogen (g/l)	1·4 (1·1–2·6)	0·7 (0·5–0·9)	−67 (−64 to −58)	69	1·3 (1·0–1·6)	46 (37–64)	15
TEM							
CT (seconds)	86 (74–122)	152 (112–193)	62 (35–84)	87	92 (75–135)	−32 (−61 to −7)	5
MCF (mm)	48 (39–60)	36 (29–46)	−23 (−29 to −21)	81	49 (40–50)	12 (6–25)	57
LY60 (%)	100 (97–100)	100 (97–100)	0 (0–1)	0	100 (97–100)	0 (0–1)	0
fibTEM (mm)	7 (5–15)	4 (3–6)	−50 (−62 to −27)	87	6 (5–9)	33 (0–50)	47

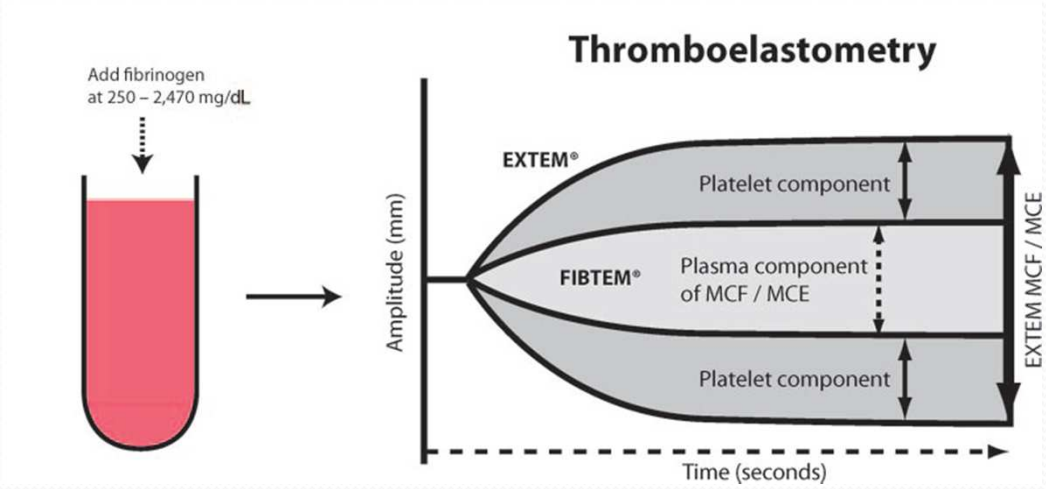
Values are given as a median and interquartile range. PT, prothrombin time; PE, plasma exchange; CT, clotting time; CFT, clot formation time; MCF, maximum clot firmness; LY60, lysis at 60 min.

T rénaux 1,3 MP Albumine 5%

The Effects of Fibrinogen Levels on Thromboelastometric Variables in the Presence of Thrombocytopenia

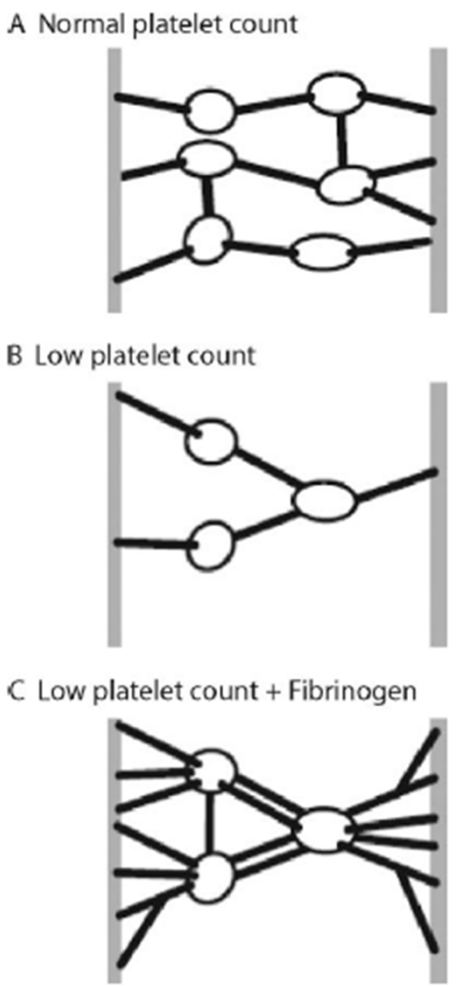
Thomas Lang, MD*† **BACKGROUND:** The binding of fibrinogen and fibrin to platelets is important in

(Anesth Analg 2009;108:751–8)

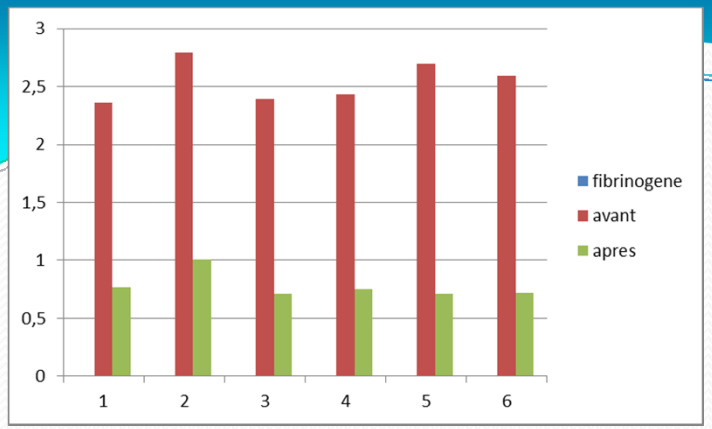


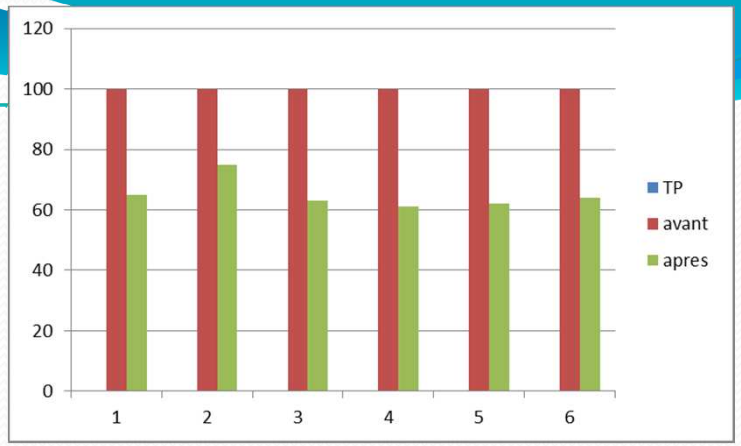
Fibrinogen supplementation *ex vivo* increases clot firmness comparable to platelet transfusion in thrombocytopenia†

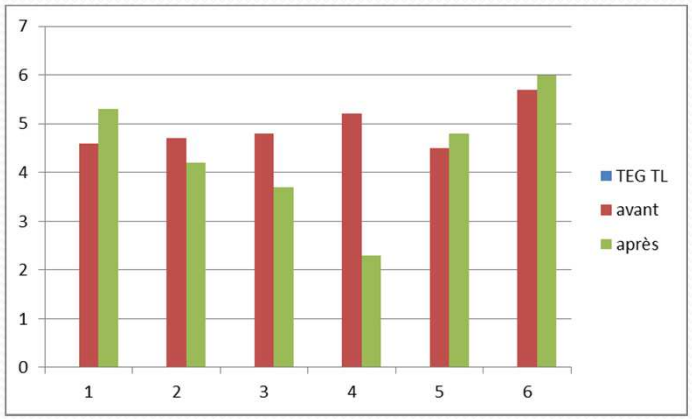
British Journal Of Anaesthesia, 117 (5): 576–82 (2016)

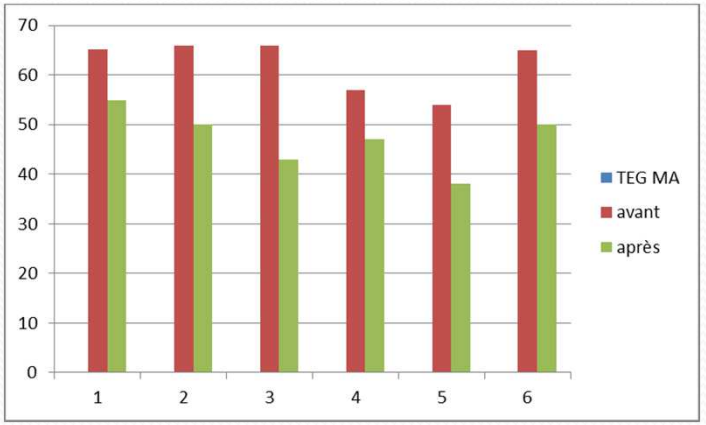


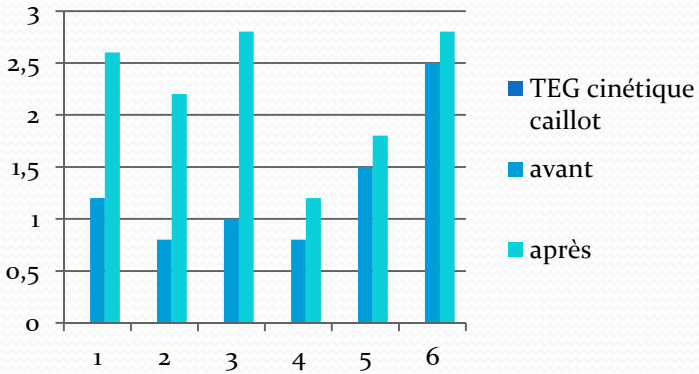
Quelques exemples



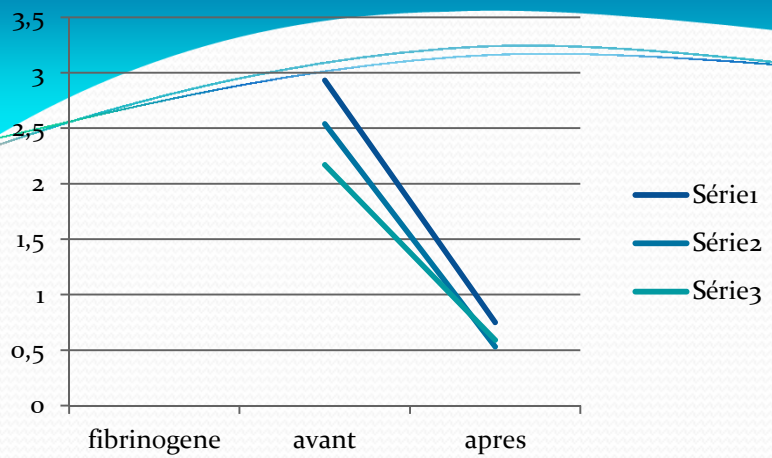


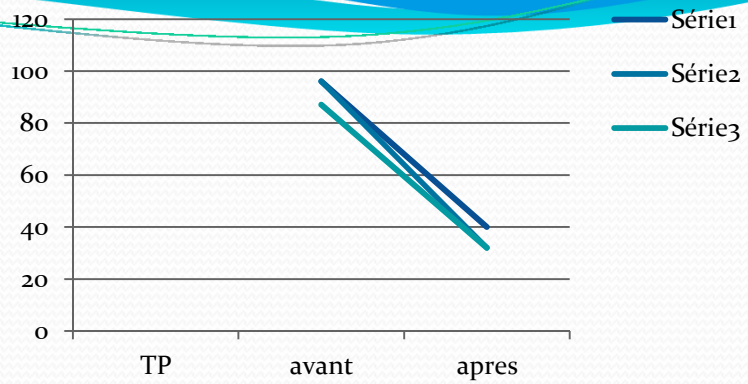


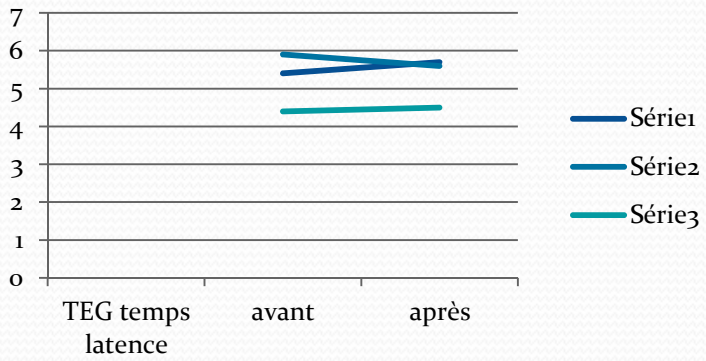


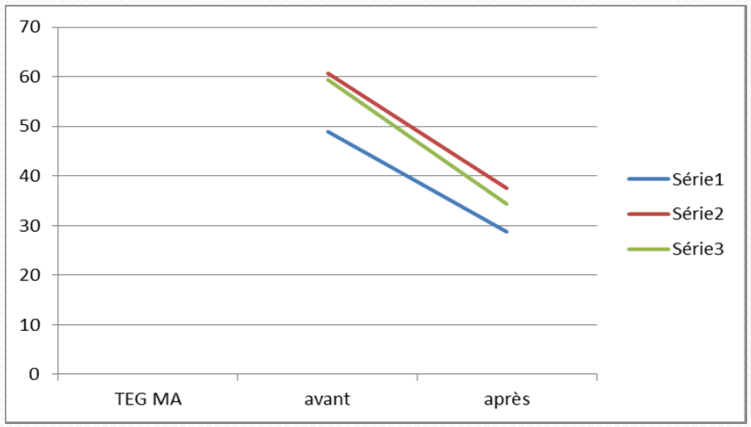


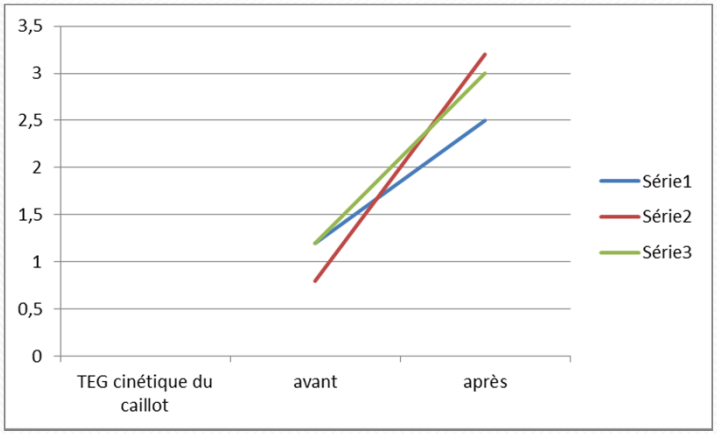
M F
Transplanté rénal
Récidive Syndrome néphrotique post TR
DFPP 1,6 MP citrate



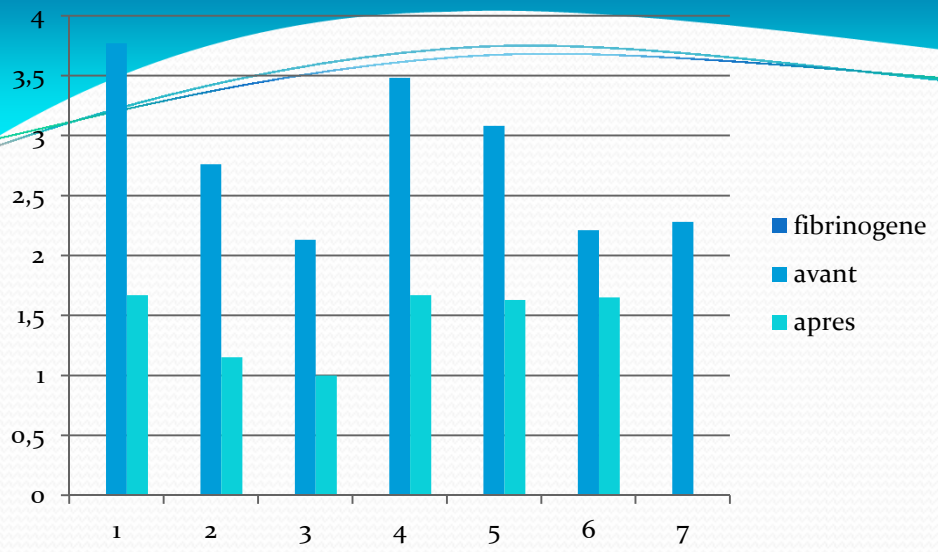


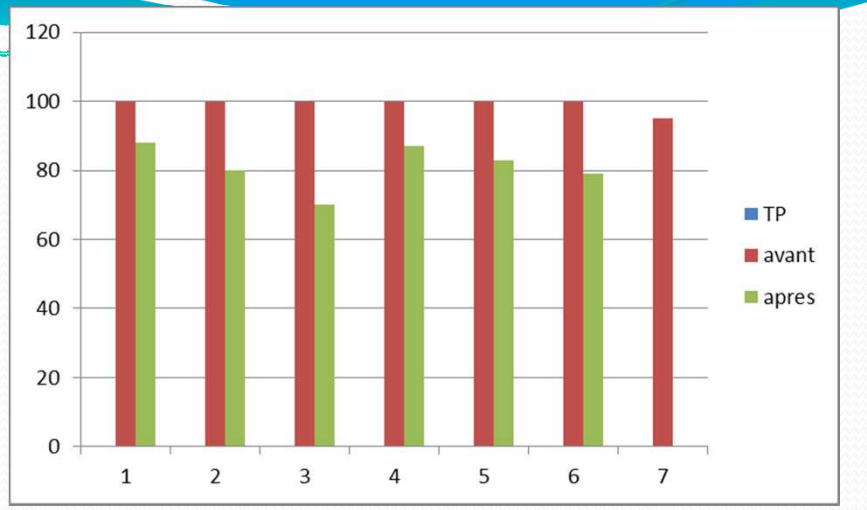


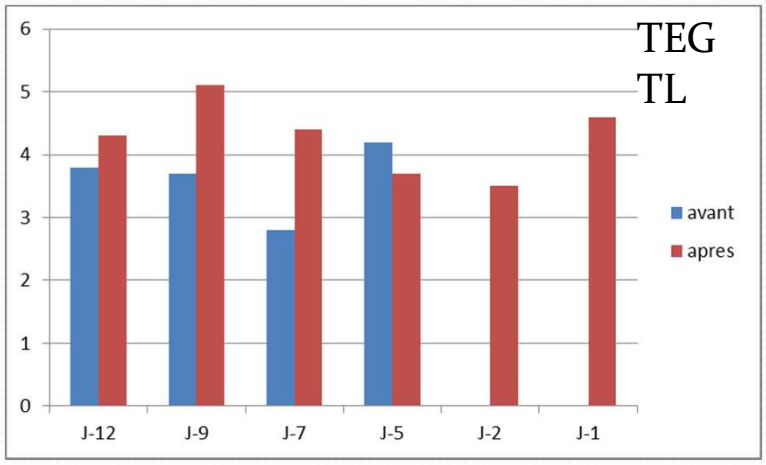


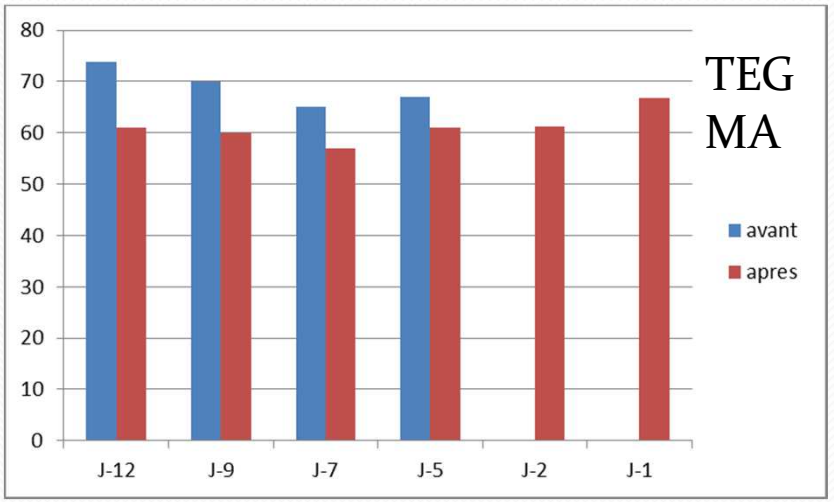


M O
T rénale
Récidive HSF
Optia 1,4 MP









M MD transplantation, rénale
DV ABO incompatible

Mais

- Rebond hypercoagulabilité à H6
  - The citrate effect ? Evolution Fib/fib ag
    - (Yamada et al Transfusion 2016)
  - Evolution fibrinolyse
  - Cinétique des facteurs différente
- Retentissement clinique
  - Quelques rares cas de thrombose EP entre H6 et H9

TABLE I. Adverse Events in Therapeutic Plasma Exchange Procedures

Category	Symptoms	Incidence (%)
Common adverse events		**<10%**
Hypocalcemia	Parasthesias	1.5–9.0
Hypovolemia	Hypotension	0.4–4.2
	Muscle cramps	0.4–2.5
	Headaches	0.3–5.0
Anaphylactoid	Urticaria	0.7–12
	Rigors	1.1–8.8
Rare adverse events		**~ 1.5%**
Cardiac	Myocardial ischemia/ infarction/shock	0.03–1.5
	Arrhythmia	0.1–0.7
Pulmonary	Respiratory arrest/ pulmonary edema	0.2–0.3
	Pulmonary embolism	0.1
Hematologic	Thrombosis/hemorrhage	0.2–0.7
Infectious	Hepatitis	0.7
	Other infection	0.3
Neurologic	Seizures	0.03–0.4
	Cerebrovascular ischemia	0.03–0.1
Pyrogenic	Hyperthermia	0.7–1.0

Adapted from Kaplan AA, American Journal of Kidney Diseases, 2008. (Ref. 12).

Quelles solutions ?

ESPACER les EP ttes les 48 h

- sous surveillance de la coag +++
- Avantage
  - Récupération souvent satisfaisante si foie nl
  - Uniquement si risque hémorragique faible
- Inconvénient
  - Non réalisable dans les pathologies graves
  - CI si risque hémorragique élevé en particulier périopératoire ou geste invasif

IA

Immunoadsorption Versus Therapeutic Plasma Exchange. Will Fibrinogen Make the Difference?

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Blood Purif 2014;38:158–159

TABLE 1. *Patient characteristics and the reduction of coagulation factor XIII (F13) and immunoglobulin G (IgG) during a session*

	Age	Sex	Primary disease	Modality	Sessions	Post/pre ratio (F13)	Post/pre ratio (IgG)	Fractional decrease of F13 to IgG
Case 1	71	F	MG	IAPP	1	0.660	0.721	0.916
Case 2	52	M	DCM	IAPP	2	0.702 ± 0.049	0.751 ± 0.028	0.965 ± 0.063
Case 3	51	M	DCM	IAPP	4	0.761 ± 0.067	0.772 ± 0.020	0.985 ± 0.087
Case 4	51	F	MG	DFPP	2	0.341 ± 0.011	0.456 ± 0.013	0.748 ± 0.044
Case 5	74	F	Paraneoplastic syndrome	DFPP	7	0.290 ± 0.096	0.276 ± 0.015	0.789 ± 0.075
Case 6	38	M	Stiff person syndrome	DFPP	5	0.256 ± 0.017	0.371 ± 0.012	0.689 ± 0.048
Case 7	42	M	MG with MuSK antibody	DFPP	14	0.266 ± 0.040	0.405 ± 0.035	0.649 ± 0.083

Values were expressed in average ± standard deviation. The fractional decrease of F13 was calculated as the division of the post/pre ratio of F13 by that of IgG. The number of sessions signifies sessions in which the values for FXIII were determined both before and after the session. DCM, dilated cardiomyopathy; DFPP, double filtration plasmapheresis; IAPP, immunoadsoption plasmapheresis; MG, myasthenia gravis.

Hanafusa Therap Apher and Dialysis 2013

Selective plasma exchange

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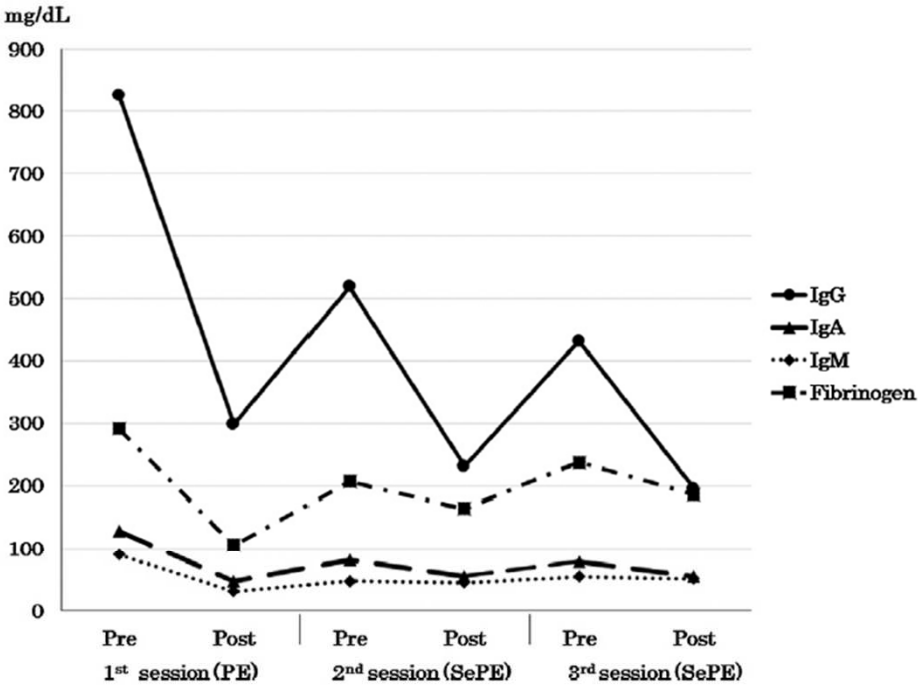

Fig. 4. Removal dynamics of IgG, IgA, IgM, and fibrinogen by a combination of PE and SePE. The combination of PE and SePE involves three plasmapheresis sessions, in which PE was performed in the first session and SePE was performed in the second and third sessions on alternate days. Pre and post indicate the concentrations before and immediately after each plasmapheresis session, respectively. PE, plasma exchange; SePE, selective plasma exchange; IgG, immunoglobulin G; IgA, immunoglobulin A; and IgM, immunoglobulin M.

Modified from Miyamoto S and Ohkubo A et al. *Therap Apher Dial.* 2016;20:342–7.

DFPP
Séparateur pore
0,03 micron

Corriger les troubles de coag

- PFC
  - Avantages troubles de coag bien corrigés
  - Inconvénients
    - Réactions allergiques
    - Infections VHE, autres virus
  - En pratique souvent à partir du troisième EP 500 à 750 ml
- Fibrinogène
  - Ne prend pas en compte les autres facteurs
  - Hors AMM
  - Quelle dose ?

Conclusion

- Troubles de l'hémostase sont dominés par la baisse du **fibrinogène** et du facteur XIII
- Le TEG permet d'avoir une vision globale de la coagulation : modification surtout MA et cinétique du caillot liés au fibrinogène +++
  - Utile en pré opératoire ou avant tout geste hémorragique
- Que faire?
  - Espacer les séances d'EP /48 h
  - PFC selon risque hémorragique
  - Autres techniques IA, SePE