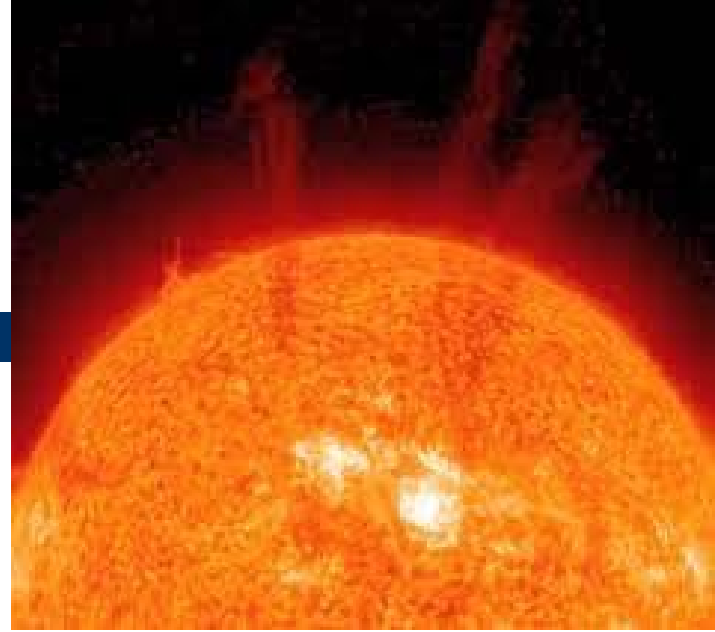
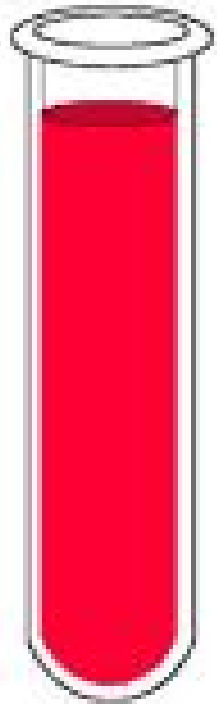




Namaste مرحبا **Willkommen** Bem Vindo Selamat Datang
 Bienvenidos Namaste Bienvenue Croeso Welcome Bienvenidos أهلا وسهلا
 Benvenuti Welkom **Welcome** Croeso Namaste
 Bienvenue Bienvenidos مرحبا أهلا وسهلا أهلا وسهلا
 Selamat Datang **Bienvenue** Welcome Willkommen Croeso Bem Vindo
 Willkommen **Benvenuti** Willkommen Selamat Datang Croeso
 добре дошъл **Benvenuti** Willkommen Benvenuti
 καλώς ήλθατε

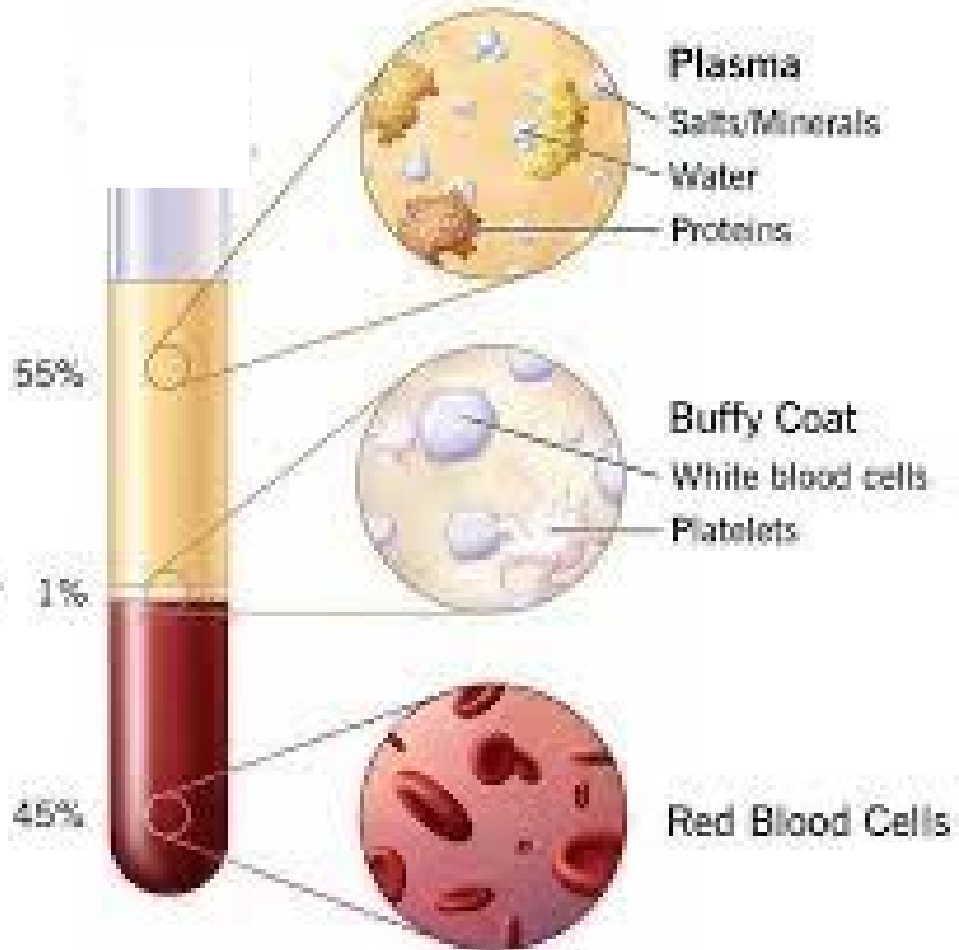


- **Plasma (state of matter):**
matter with electrons ripped away from atoms - forming an ionized gas. (usually superheated)



Whole blood

Centrifugation →



Plasma

Salts/Minerals

Water

Proteins

55%

Buffy Coat

White blood cells

Platelets

1%

45%

Red Blood Cells

Plasma therapy

- **Plasma transfusion**
- **Plasmapheresis/ TPE**

Plasma therapy

- **Plasma transfusion**

**Replace different plasma components
(coag factors, etc, circulating
complement regulators)**

Rosenberg & Urevitch

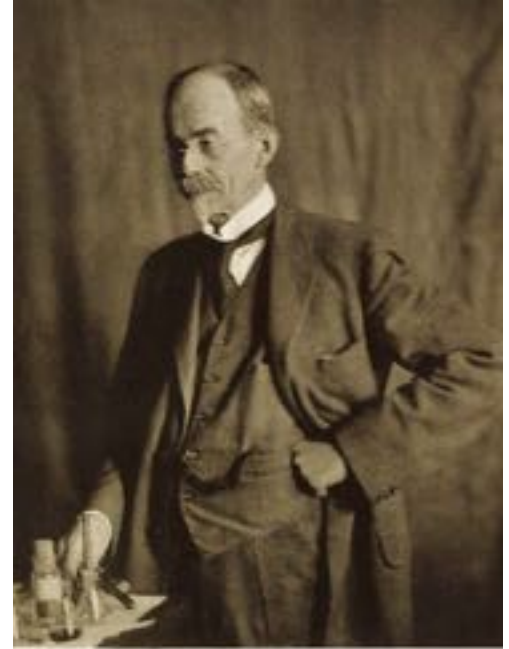
- ***1913, Published 1914***

“For the question regarding washing of blood outside the body and the vitality of red blood cells.”

Russki Vrach.

John Abel *et al.*

Plasma removal with return of
corpuscles (plasmapheresis).
The Journal of Pharmacology
and experimental therapeutics
Vol. V. No. 6, July, 1914



John J. Abel

By Doris Ulmann (1882-1934) -
<http://www.photogravure.com/>



Plasmapheresis

ἀφαίρεσις

- Apharesis (GK)
- Take away, remove

Plasma

removal & replacement

PE

Why would you want to remove plasma?



Why would you want to remove plasma?

Containing a substance

- **Acutely toxic/ harmful/ pathological**
- **Can be efficiently removed**

(think of antibodies)

بس ہترجع تانی؟

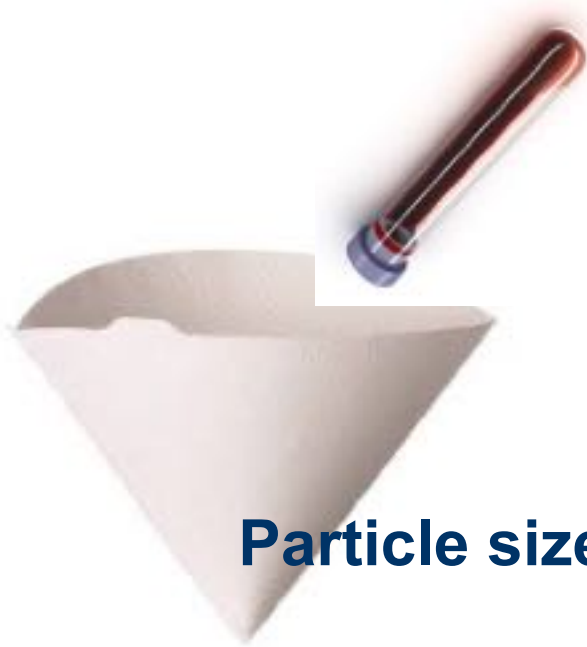
Relation to HUS?

- **FFP can restore functional circulating complement regulatory proteins, as well as ADAMTS-13**
- **Large volume transfusions may be difficult during AKI**
- **Removal of antibodies, abnormal factors & activation products**

American Society for Apheresis (ASFA) The Apheresis Applications Committee



Cat I	<i>1st line therapy alone or with other therapy</i>	TTP aHUS, Factor H AB
Cat II	<i>2nd line alone/ with other therapy</i>	
Cat III	<i>decision-making individualized</i>	aHUS, complement factor mutations
Cat IV	<i>suggested ineffective or harmful</i>	typical diarrhea- associated HUS

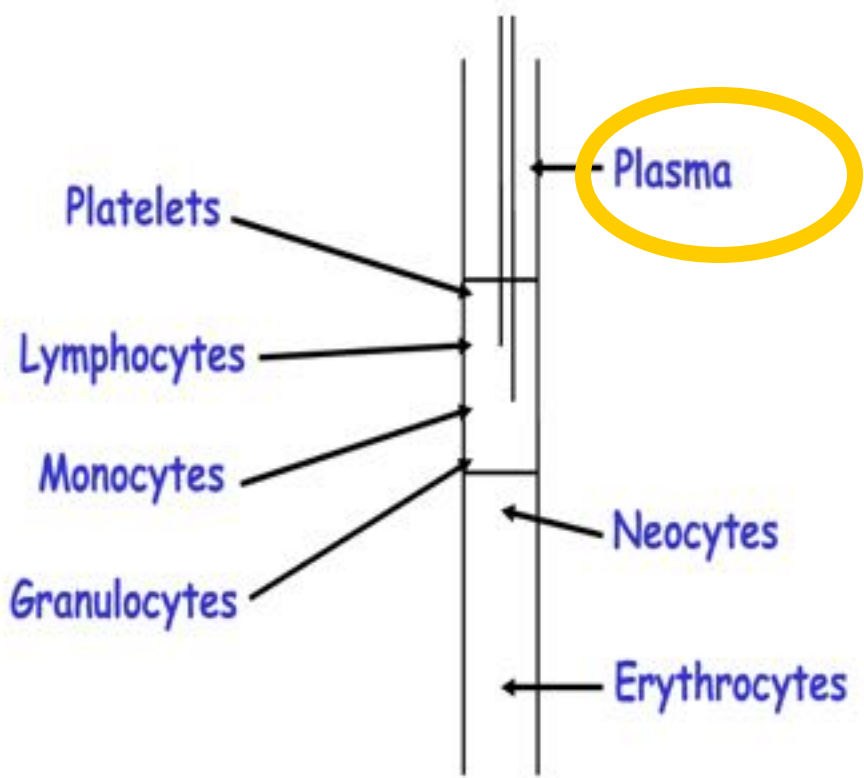


Particle size

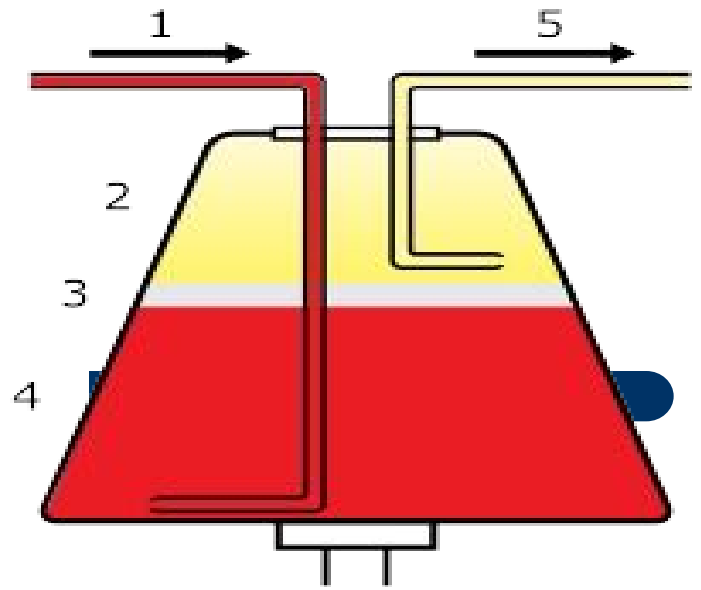


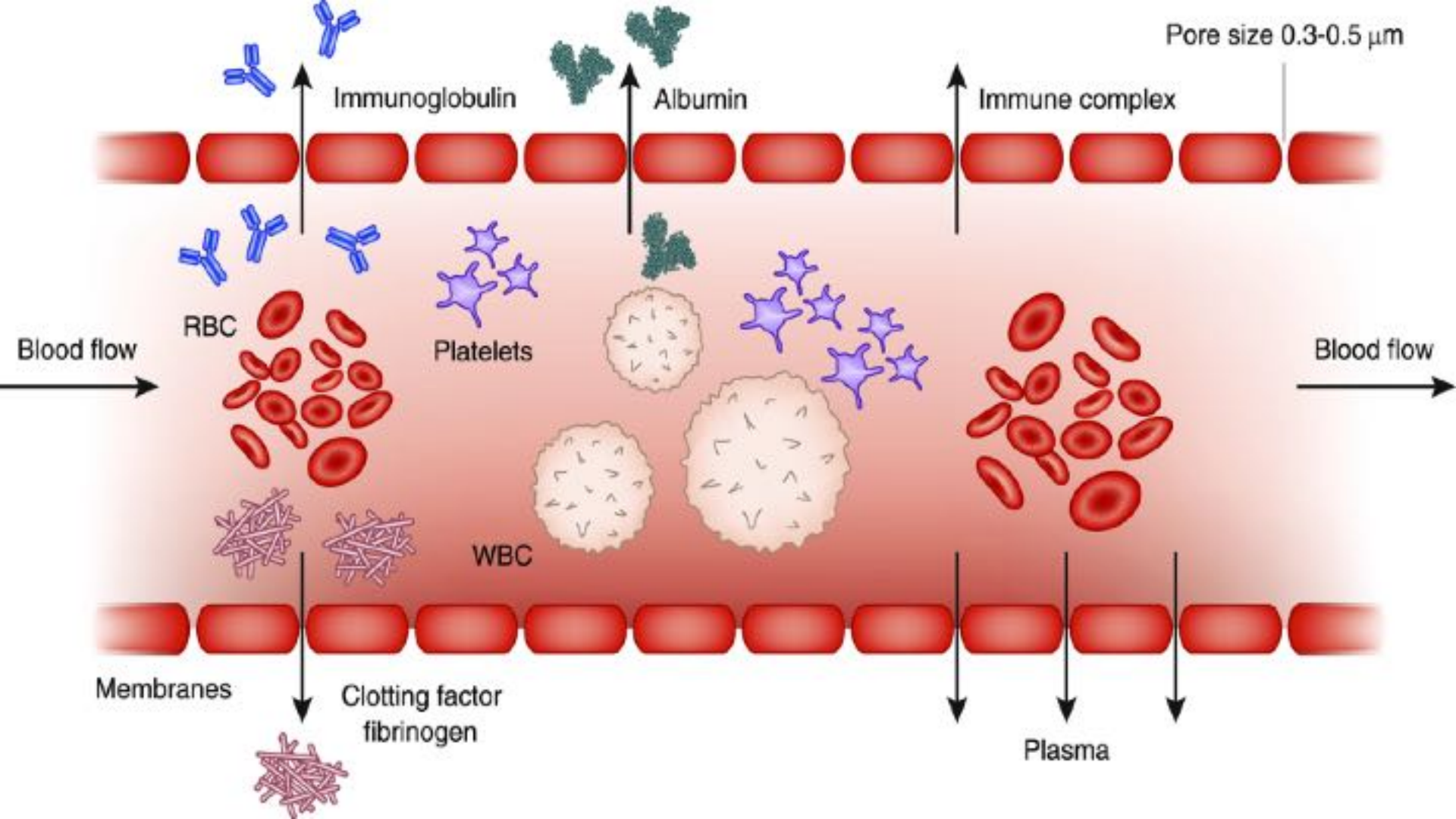
Specific gravity

Blood Components Separated by Centrifugation




- Citrate
- Discard plasma → Replacement
- Repeat cycle







Membrane filtration (MPS)

- **Continuous flow**
 - **Volume change only during priming/ return**
 - **The ability to perform downstream secondary filtration**
- 

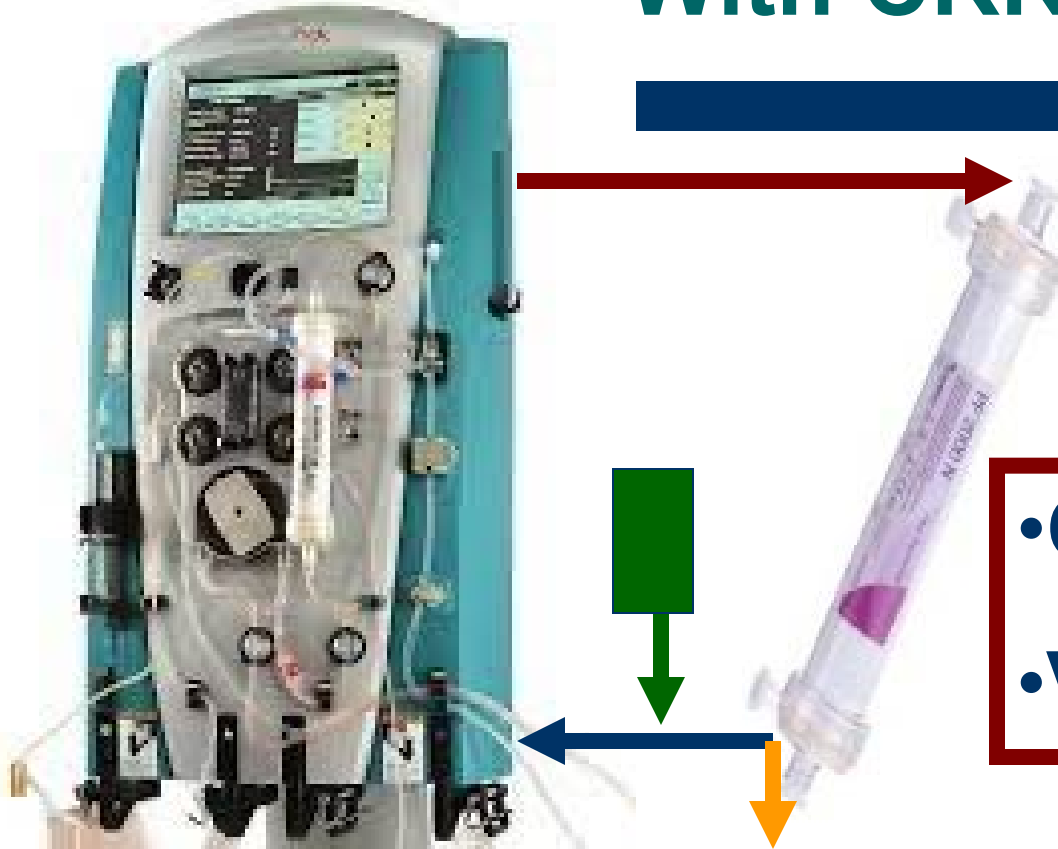
With standard HD equipment



- Intense monitoring
- UF/ substitution separate
- Vol. errors & lags

**NOT volumetrically
controlled**

With CRRT equipment



- CVVH-like
- Volume controlled

Separation	Centrifuge	Membrane
Blood flow	Lower	Higher
Access	Periph./ Central	Central
Anticoagulation	High citrate	Any or none
Circulation	Cycles	Continuous
Equipment	Specific	HD or CRRT
Other therapies	Cell apheresis	Dialysis Double filtration
Cost & experience		

Plasmapheresis prescription

- **REMOVAL** **how much?**
- **REPLACEMENT** **with what?**
- **FREQUENCY** **with what?**
- **DURATION** **with what?**

Plasmapheresis prescription

- **REMOVAL** **how much?**
1PV=62%, 1.5PV=75%, More ↓ efficiency
- **FREQUENCY** **repeat Q1-2d**
- **DURATION** **arbitrary 5+x, taper**

Plasmapheresis prescription

- **REMOVAL** 1-1.5x PI Vol
- **REPLACEMENT** FFP, 5%alb, NS
- **FREQUENCY** repeat Q1-2d
- **DURATION** arbitrary 5+x, taper

Guideline for the investigation and initial therapy of diarrhea-negative hemolytic uremic syndrome

**Gema Ariceta • Nesrin Besbas • Sally Johnson •
Diana Karpman • Daniel Landau • Christoph Licht •
Chantal Loirat • Carmine Pecoraro • C. Mark Taylor •
Nicole Van de Kar • Johan VandeWalle •
Lothar B. Zimmerhackl •
The European Paediatric Study Group for HUS**

PE for aHUS

- **Complement disorders are the most common. Most will benefit from PE**
- **aHUS can rapidly progress to ESKD**
- **Treatment started within 24h of diagnosis as aHUS, Empirical before subgroup identified**
- **TTP mortality ↓ 90% to 10% with early PI. Therapy**

- **Children >6Mo age (arbitrary) with diarrhea or bloody diarrhea: establish cause**
- **Confirm a suspected invasive pneumococcal infection**
- **Regard all others as atypical**
- **A low C3 indicates complement dysregulation but normal C3 cannot exclude**

Diagnosis of HUS
Atypical presentation (see step one)

Exceptions²

Plasmapheresis within 24 hours of diagnosis
Exchange 1.5 x plasma volume (60-75ml/kg) per session
Replace with fresh frozen plasma or Octaplas®¹

Repeat plasmapheresis daily x 5
Then 5 sessions per week for 2 weeks
Then 3 sessions per week for 2 weeks

Withdrawal³
Alternative diagnosis
Complication of plasmapheresis
Early remission

Assess outcome at day 33
Go to step 4

Exclusions/ reservations

- **Confirmed Shiga-E.coli infection**
- **Highly suspected condition not requiring PE**
Sibling with ADAMTS-13 mutation
(transfusion)
- **Cobalamin C disorder**
(hypotonia – megaloblastic an.)
- **Consider procedure requirements**



- **“The dosage, frequency and duration are all arbitrary, but are influenced by the experience of the authors and rare published cases”**

Hematological remission:

- **Platelets $> 150 \times 10^9/L$ for 2 wks**
- **No evidence of hemolysis
(LDH, frag RBCs)**

Independent of renal function

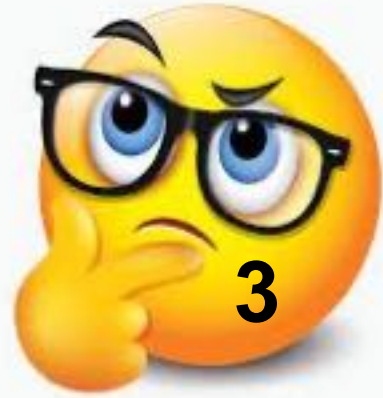
Early outcome end-point (d33)



- The guideline does NOT address further management for those who do/ or do not attain remission
- Recognizing that subgroup confirmation may not be available then

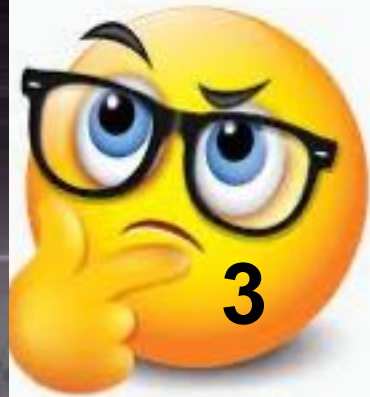
- 
- 
- ***Long-term PE/ transfusion?***

- ***What about transplantation?***



We're now in 2023

- **We have modern complement inhibitors**



Plasma therapy should no longer be the first line for confirmed aHUS, except

- **When eculizumab is not available**
- **In cases with antiFH-AB**

PI transfusion (without PE) will only help when just factor replacement is needed

Turk J Pediatr. 2021

The Turkish Journal of Pediatrics 2021; 63: 986-993
<https://doi.org/10.24953/turkjpeg.2021.06.006>

Original Article

Could plasma based therapies still be considered in selected cases with atypical hemolytic uremic syndrome?

Sare Gülfem Özlü¹, Bora Gülhan², Özlem Aydoğ³, Emine Atayar⁴, Ali Delibaş⁵,



Available online at www.sciencedirect.com

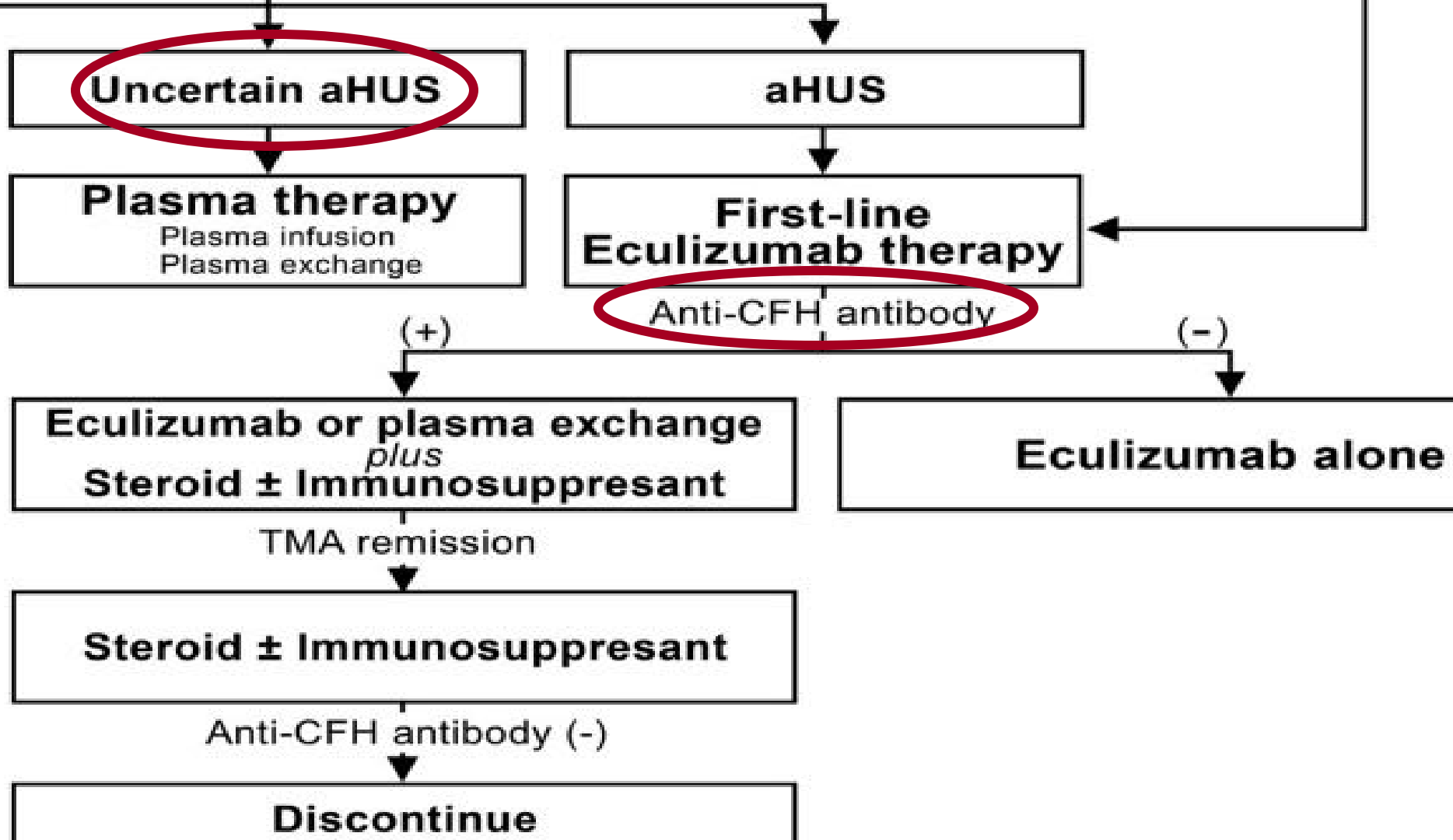
ScienceDirect

journal homepage: www.jfma-online.com

Clinical Practice

Atypical hemolytic uremic syndrome: Consensus of diagnosis and treatment in Taiwan

Min-Hua Tseng ^a, Shih-Hua Lin ^b, Jeng-Daw Tsai ^c,



Indian Guidelines *Bagga et al., 2019*

- **Start PE**
- + **Induction with oral steroids and IV CPA (preferred) or IV RTX for aFH-Ab**
- **Taper PE once hematological remission**
- **Maint PRD-MMF 1 year, monitor AB**
- **ECULIZUMAB suggested for failure of remission with PE, life-threatening seizures, cardiac emergencies, PE complications**

