

# *Plasma and RBC Exchange for Erythropoietic Protoporphyrria*

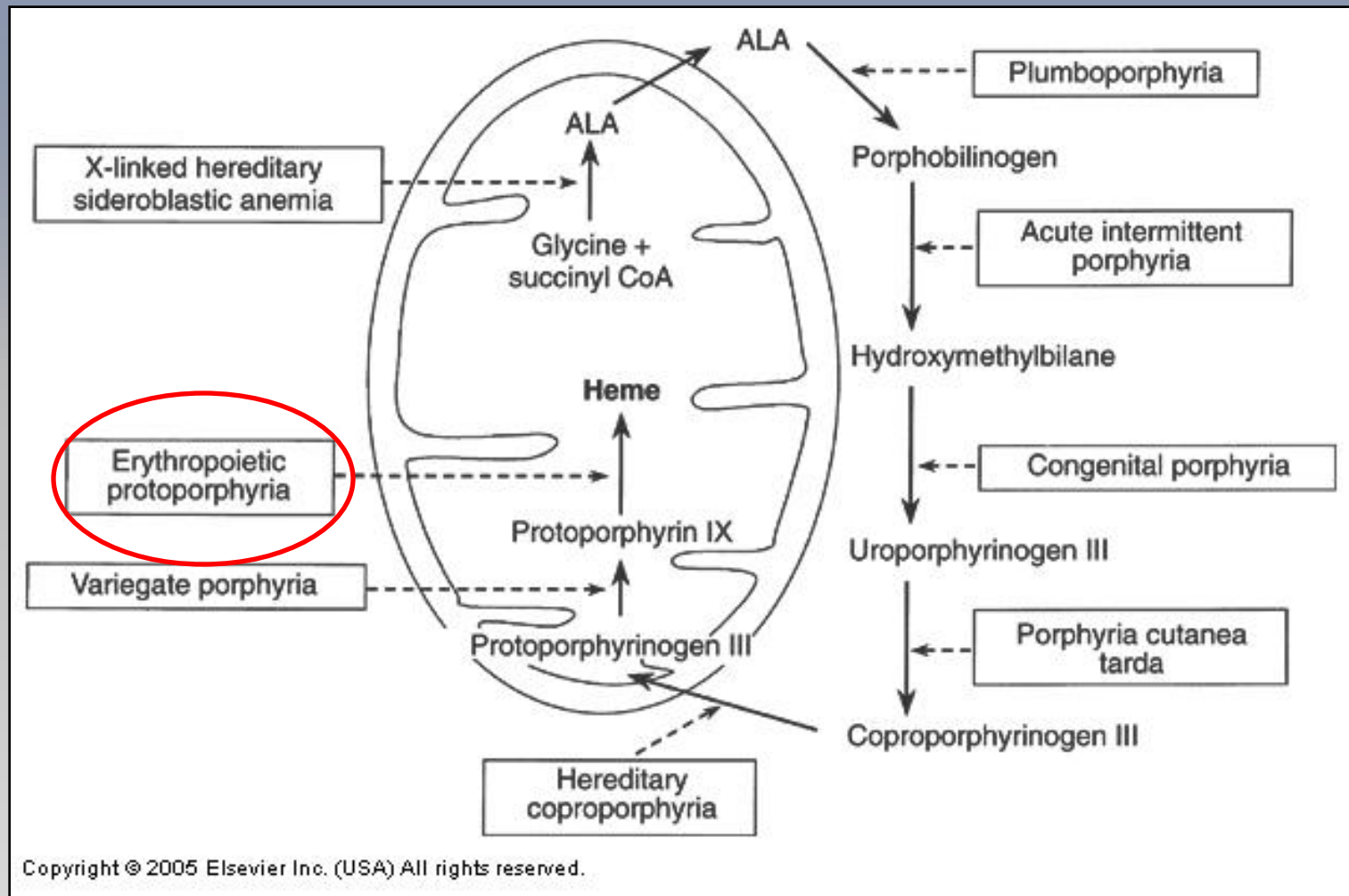
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# Background

- Erythropoietic Protoporphyrin (EPP) rare disease characterized by altered heme synthesis
- PSBC consulted for therapeutic options in a patient with EPP presenting with acute liver failure
- Prior experience with TPE and RCE showed some benefits
- Rationale for using TPE and RCE

# Heme Synthesis and Porphyrrias



# EPP

- **Pathophysiology**

- Prevalence: 1:75,000 to 1:200,000
- Ferrochelatase deficiency
- Autosomal/recessive inheritance
- Protoporphyrin in RBC and stools
- Multiple Triggers: sun exposure, drugs
  - Estrogens, barbiturates, sulfonamides, others

- **Clinical Manifestations**

- Anemia
- Axonal Neuropathy
- Skin
- Liver

# Mechanism of disease in EPP

Excess plasma protoporphyrin → Bile → Insoluble

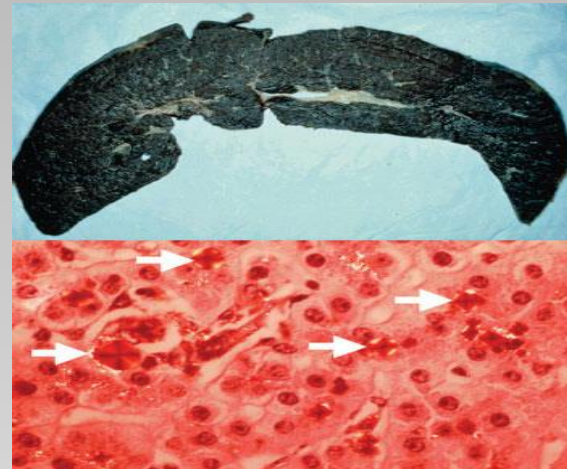
↓  
Light  
Skin → Free radicals

↓  
Hepatobiliary disease

- Cholelithiasis
- Mild
- Progressive
- Terminal phase



*The Korean Journal of Hepatology 2010 ; 16 : 83 - 88*



*Liver Transplantation, 2005: Vol 11, No 12: 1590-1596*

# Case: Ms. LM

- 50 year old female
- Admitted for abdominal pain, jaundice and altered liver function
- EPP since age 5 - skin manifestations
- Past surgical history
  - Cholecystectomy (30 years)
  - Recent history of knee surgery: Acetaminophen intake: 4 - 6 g/day
- Plasma protoporphyrin: 521 ug/dL (<1)
- RBC protoporphyrin: 3906 ug/dL(<80)
- Liver biopsy
  - Crystal deposition
  - Cholestatic liver injury
  - Absence of cirrhosis or necrosis

# Treatment Options

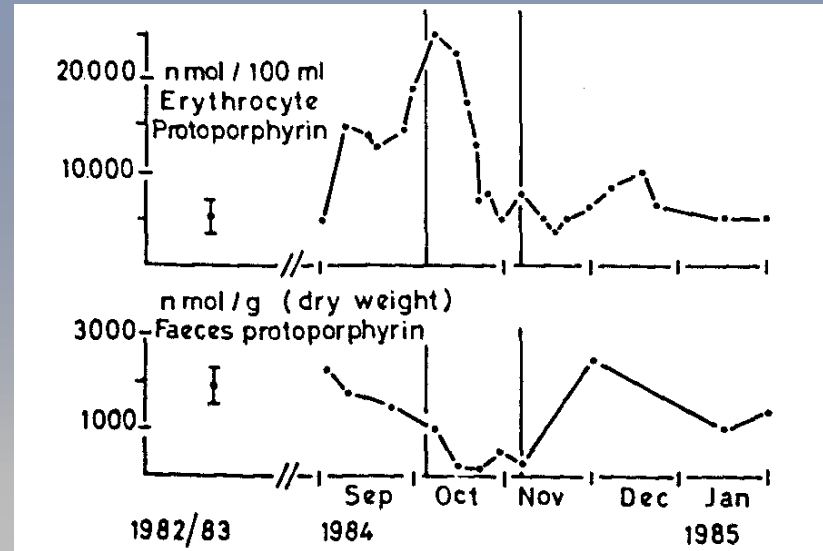
Goal of Therapy	Treatment
Oxidative stress, skin	$\beta$ -carotene
↑ Excretion protoporphyrin	Ursodeoxycholic acid Cholestyramine
↓ Production protoporphyrin	Hypertransfusion Hematin infusion
↓ Plasma protoporphyrin	TPE Hemodialysis RCE
Glutathione redox system	NAC infusion
Replace ferrochetalase enzyme	Hematopoietic Progenitor Cell transplant
Replace liver function	Liver transplant

# Published Experience: TPE and RCE for PPE

## Van Wijk - 2 cases 1988

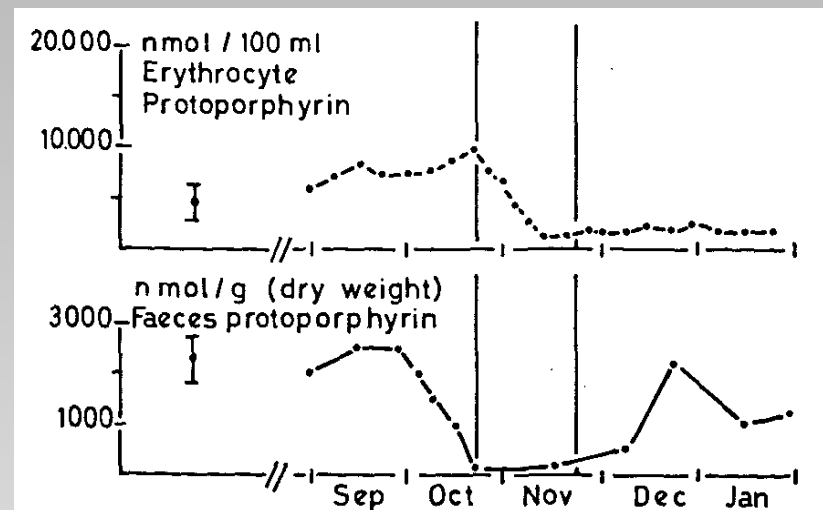
Patient A, 31 F

- Liver cirrhosis, jaundice
- RCE, 6 procedures in 3 weeks
- RBC transfusion, Hb >9
- Clinical and laboratory improvement.



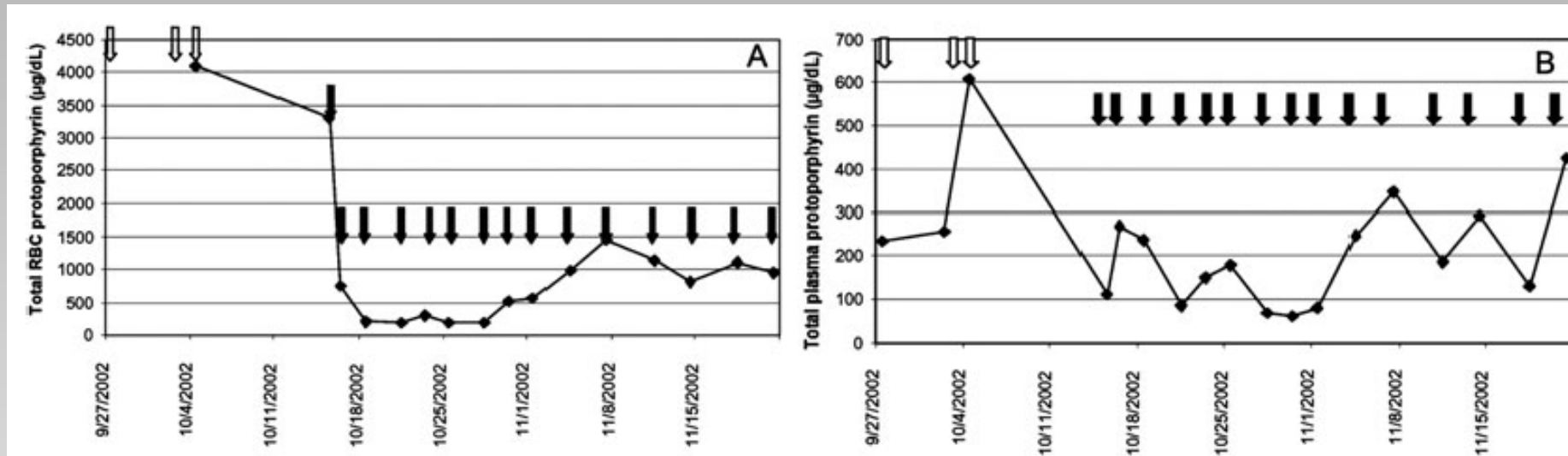
Patient B, 20 M

- Liver cirrhosis, jaundice
- RCE and transfusion therapy
- Clinical and Laboratory improvement.



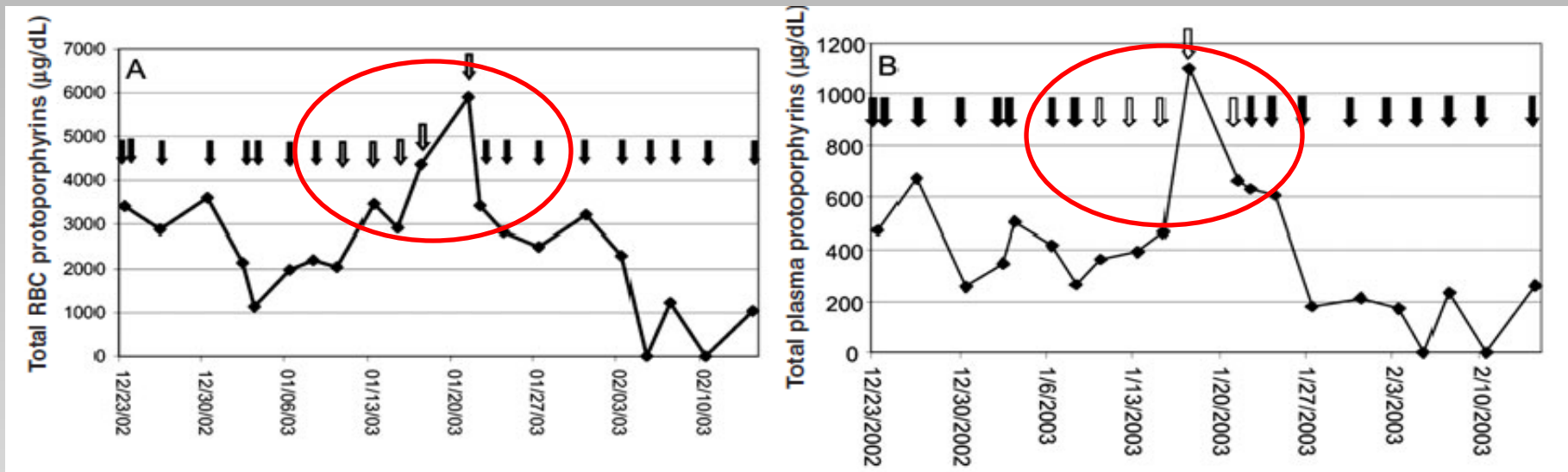
# Published Experience: TPE and RCE for PPE Eichbaum - 2005

- Patient 1
- 59 M, s/p liver transplant, progressive liver failure
- Treatment:
  - 4 x 1 volume plasma exchange, Albumin replacement
  - RCE x 18 (6 weeks) (Target fraction 25%, Hct 35%)
- Laboratory improvement but not clinical recovery



# Published Experience: TPE and RCE for PPE Eichbaum - 2 cases 2005 cont.

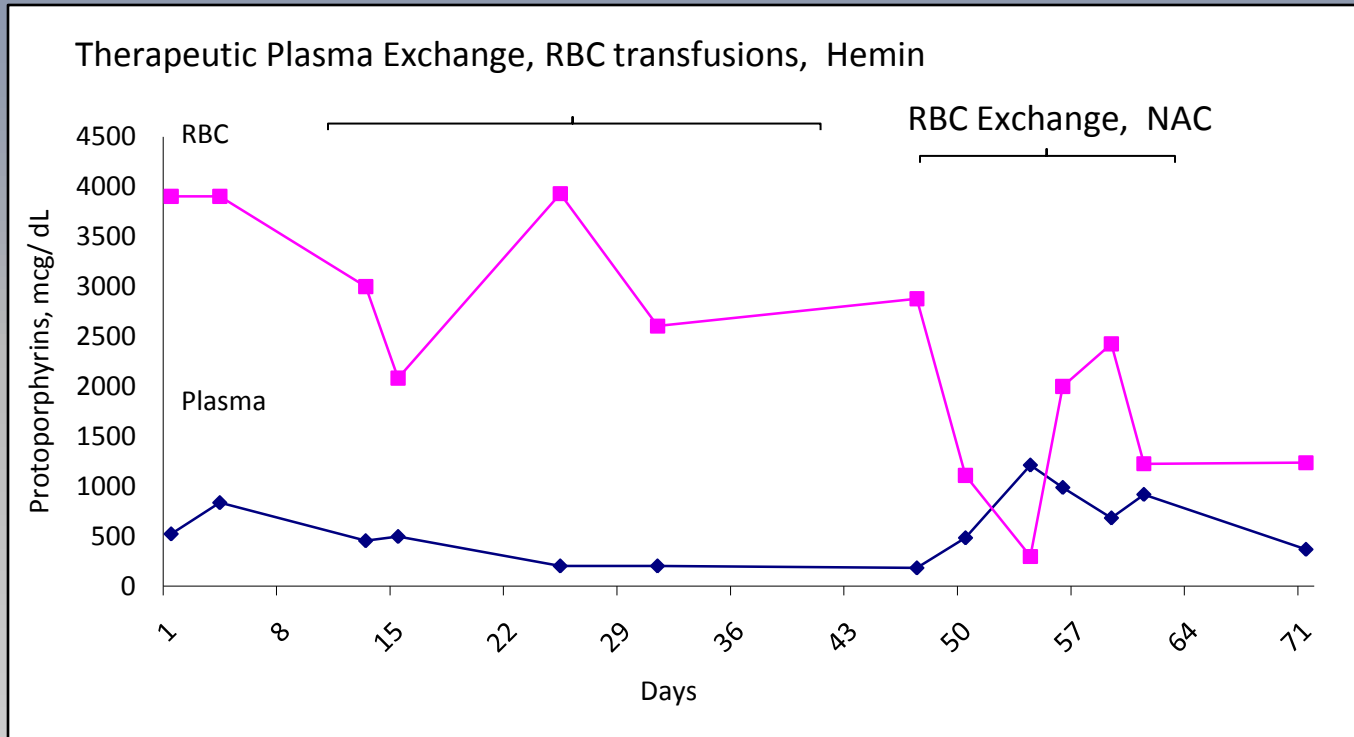
- Patient 2
- 39 F, progressive liver failure
- Initial treatment with TPE and hematin
- Switched to RCE x 17 (8 weeks)
- Laboratory improvement without clinical recovery



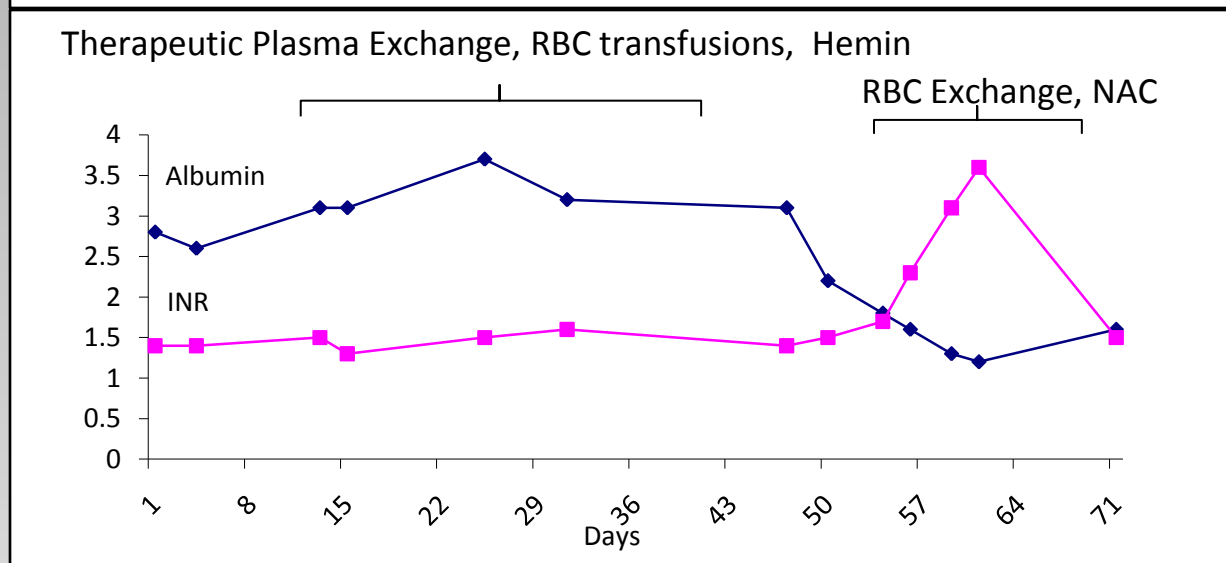
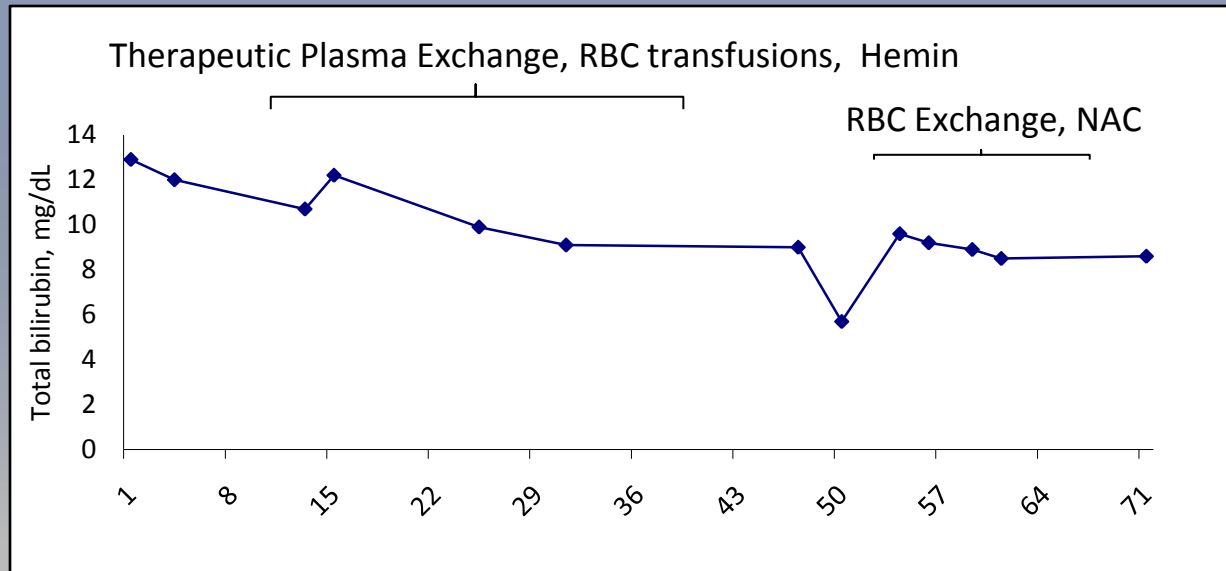
# Case: Ms. LM - Treatment

- NAC, Ursodeoxycholic acid, Cholestyramine
- Hemin infusion and hypertransfusion
- TPE
  - Central access
  - 20 procedures in 4 weeks
  - 50% FFP replacement
- RBC exchange
  - 6 procedures in 2 weeks
  - Remaining fraction 25%
  - Hematocrit 35%
  - ~ 8 units of RBC per exchange

# Ms. LM: Treatment response



# Ms. LM: Liver function



# Acetaminophen Induced Acute Liver Failure

- What role did acetaminophen play in patient?
  - Glutathione depletion occurs with acute overdose of acetaminophen -> toxic metabolites
  - No specific data in patients with EPP
- TPE exchange in Acetaminophen OD -> no or little benefit

# Conclusions

- Multiple triggers for EPP related hepatic failure
- Unknown contribution of acetaminophen toxicity
- Mild efficacy of RCE in lowering protoporphyrin levels  
-> cost effective?
- No clinical or laboratory improvement after RCE->  
advanced liver disease?
- Potential benefits before transplant

# Acknowledgements

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Thanks

Questions?