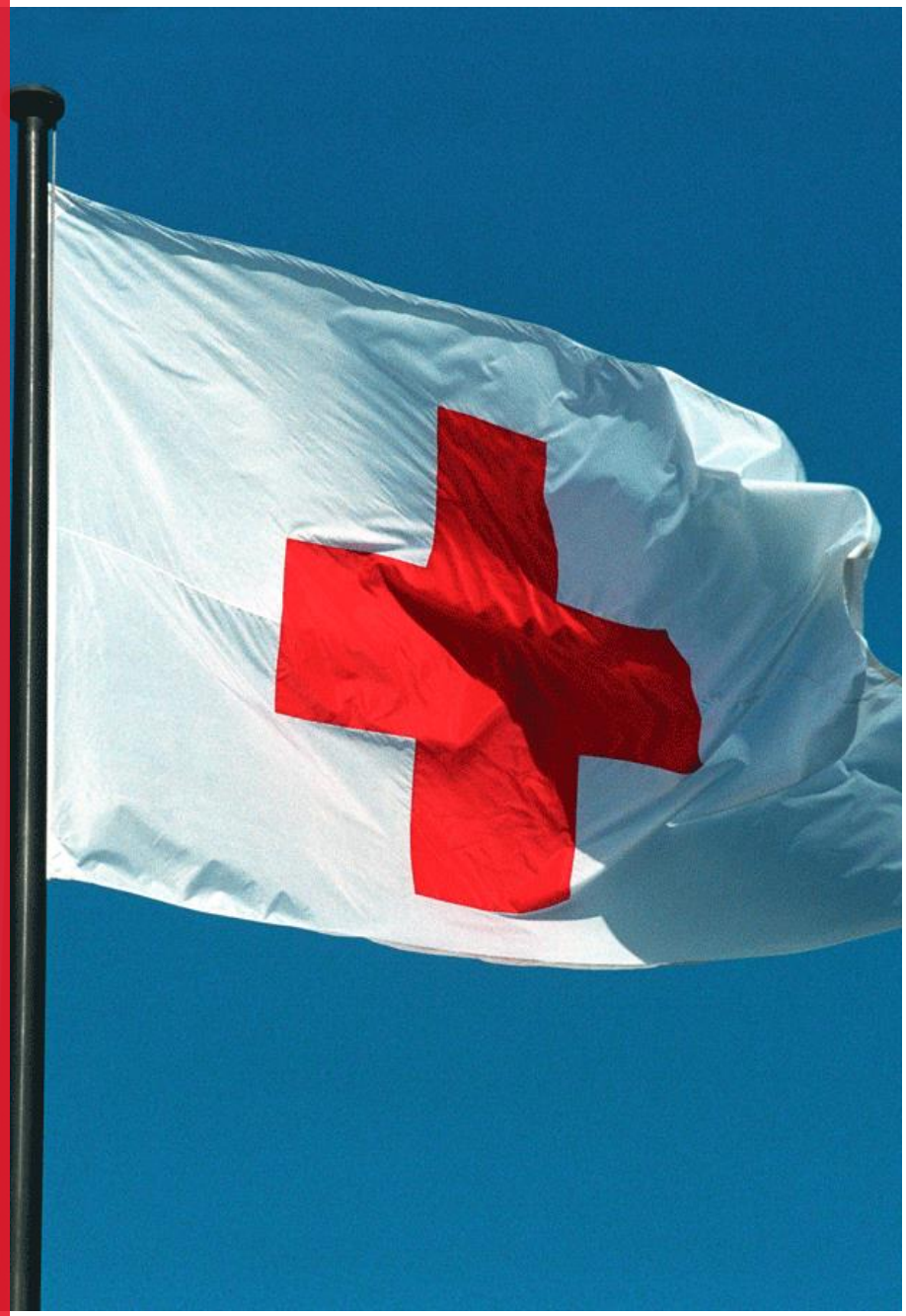
American Red Cross

It’s Not Easy Being Green…

F. Bernadette West MD
ARC CT/RI region



Disclosures

Nothing relevant to the discussion today.

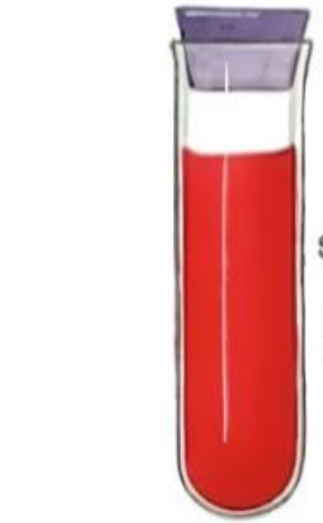
Objectives

- State the general steps in plasma collection and manufacturing.
- List plasma contents and products.
- Discuss reasons for plasma color variations.

ARC Distributions in FY18

- Total Distributions - 6,534,254 blood products
- RBCs - 4,420,895
- Platelets
  - SDP 892,071
  - RDP 21,160
  - PSP 14,516
- Plasma - 973,492
- Cryo - 72,173
- Cryo Pools - 139,936

Plasma contents

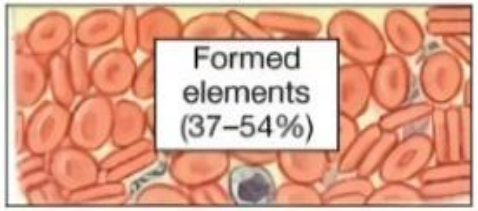


Sample of whole blood

consists of

Plasma (46–63%)

+



Formed elements (37–54%)

PLASMA COMPOSITION	
Plasma proteins	7%
Other solutes	1%
Water	92%
Transports organic and inorganic molecules, formed elements, and heat	

PLASMA PROTEINS	
Albumins (60%)	Major contributors to osmotic pressure of plasma; transport lipids, steroid hormones
Globulins (35%)	Transport ions, hormones, lipids; immune function
Fibrinogen (4%)	Essential component of clotting system; can be converted to insoluble fibrin
Regulatory proteins (<1%)	Enzymes, proenzymes, hormones

OTHER SOLUTES	
Electrolytes	Normal extracellular fluid ion composition essential for vital cellular activities. Ions contribute to osmotic pressure of body fluids. Major plasma electrolytes are Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, HPO_4^{2-}, SO_4^{2-}
Organic nutrients	Used for ATP production, growth, and maintenance of cells; include lipids (fatty acids, cholesterol, glycerides), carbohydrates (primarily glucose), and amino acids
Organic wastes	Carried to sites of breakdown or excretion; include urea, uric acid, creatinine, bilirubin, ammonium ions

(b)

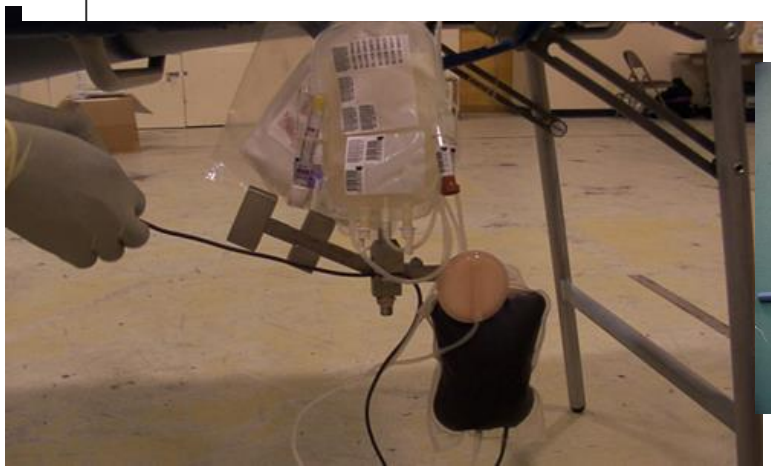
Plasma for transfusion

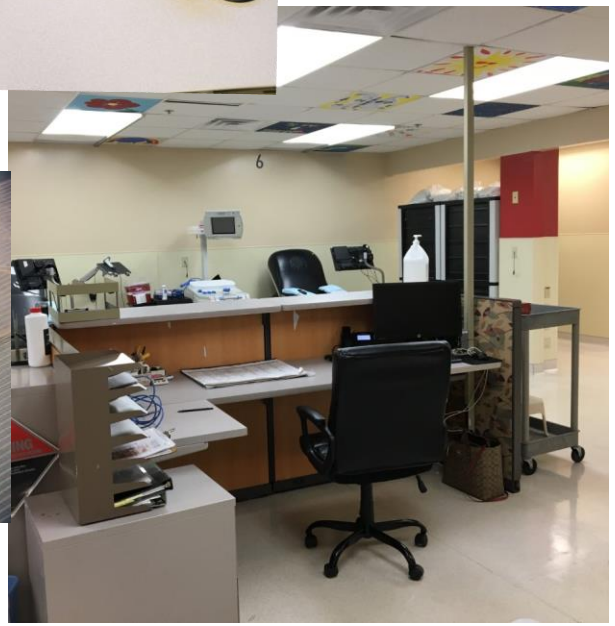
- *Plasma intended for transfusion* must meet all FDA blood donor requirements, mostly in 21 CFR § 630
- FDA's Five layers of safety.
  - History, mini-physical; Deferral lists; Donor testing; Quarantine of units until all testing / any other issues are completed; Problem and deficiency investigaiton to ensure quality.
- **Separated from a whole blood (WB) donation.**
- **Collection by apheresis methods.**

Where it starts

Full-Length Donor History Questionnaire (DHQ)

	Yes	No
Are you		
1. Feeling healthy and well today?	❑	❑
2. Currently taking an antibiotic?	❑	❑
3. Currently taking any other medication for an infection?	❑	❑





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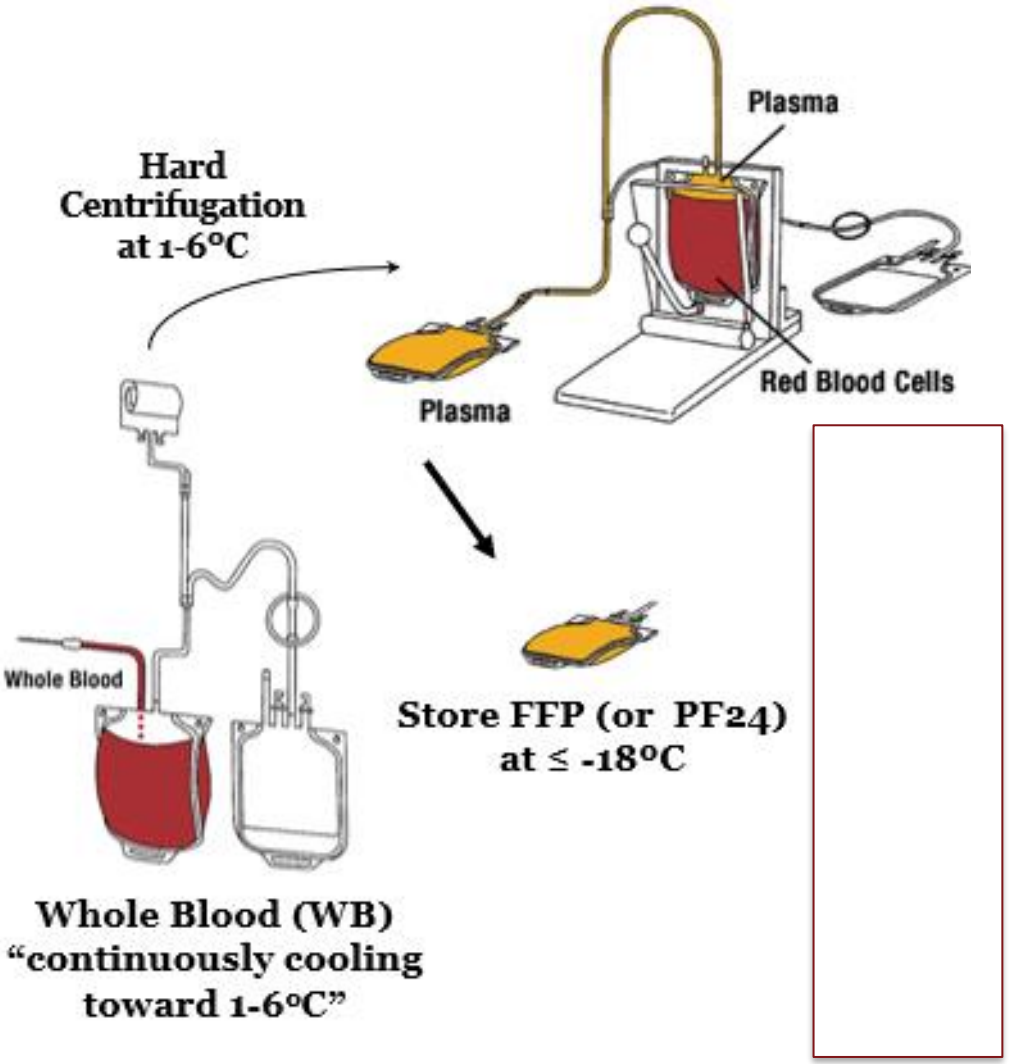
Manufacturing



Process Flow

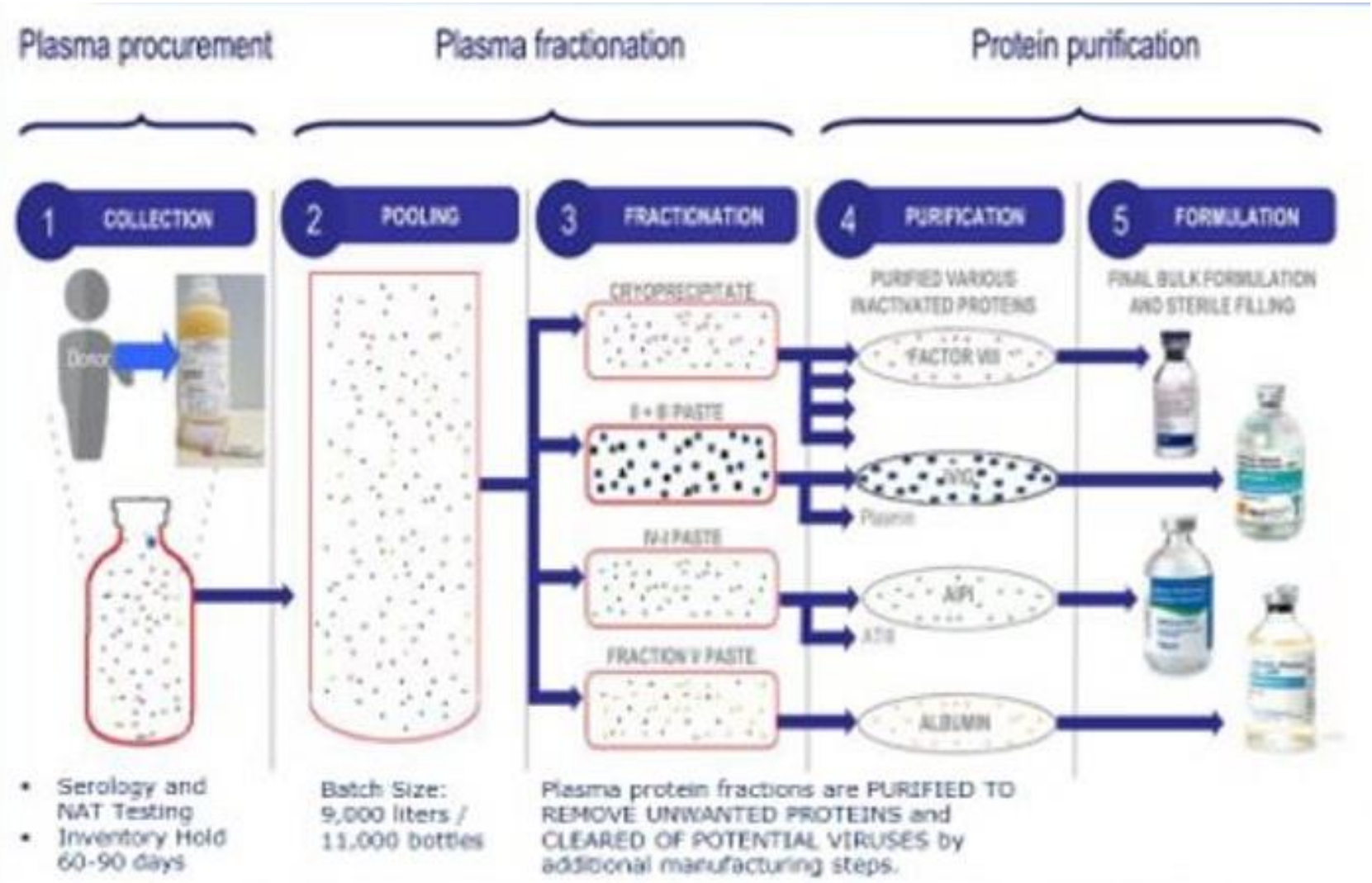
Some Plasma Components

- Fresh Frozen Plasma (WB or APH) frozen at –18C or colder by 8hrs of collection.
- FP24 (WB or APH) frozen at –18C from 8-24hrs after collection.
- Thawed Plasma (from frozen)
- Plasma cyroprecipitate reduced (cryo supernatant)
- Liquid Plasma (WB) for MTP, never-frozen.

Source Plasma

- *Plasma intended for fractionation* must meet requirements, mostly in 21 CFR § 640.60
  - Collection by apheresis methods at Source Plasma centers.
  - *Relatively small amount from as recovered plasma (TRALI-risk)*, from blood centers.

Source Plasma



Plasma for Transfusion (or not)

Yellow color

- Carotenoids
- Bilirubin
- Hemoglobin
- Iron transferrin

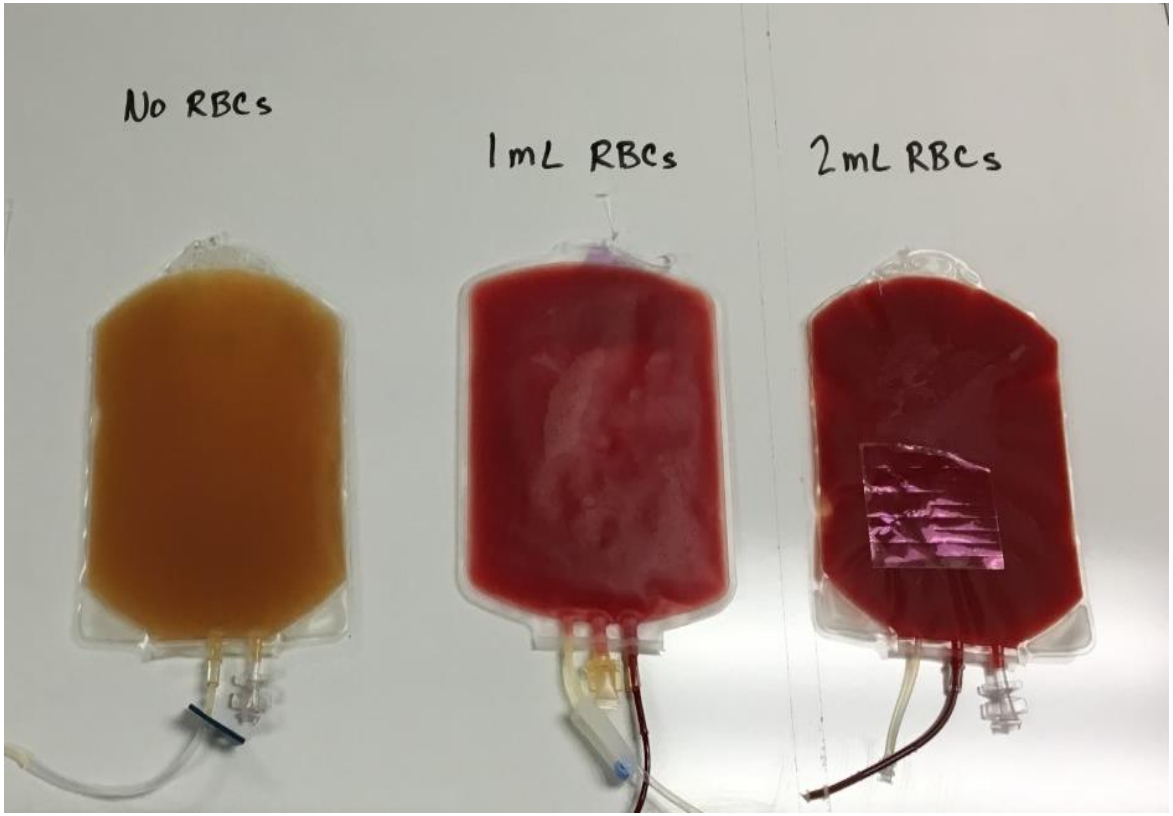


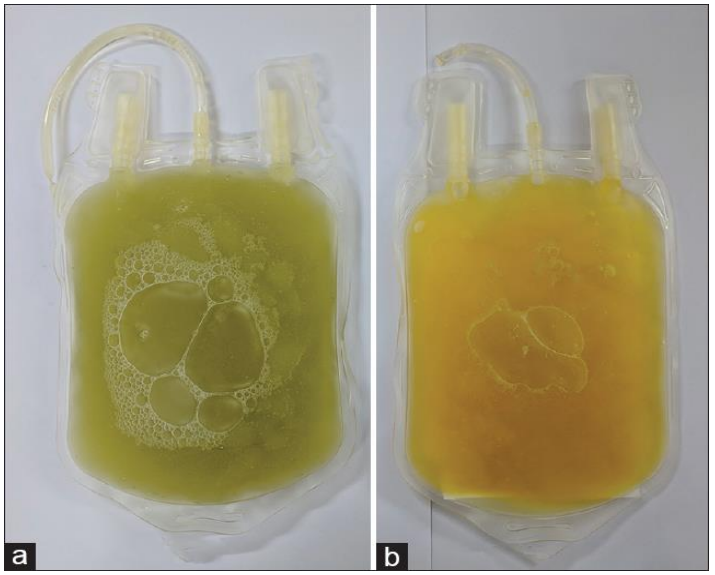
Image by Dr. Mary Berg, UCDenver Dept of Lab Med.

Green plasma

Fig. 1. The green plasma unit on the *right*, shown with a typical yellow unit.

Green Plasma revisited , Anesthesiology, 2009.

- Normal variant
- OCP usual cause
- OK to transfuse!



Mani A, Poornima A P, Gupta D. Greenish discoloration of plasma: Is it really a matter of concern?. Asian J Transfus Sci 2019;13:1-2

Patient

- 32 y/o female, BMI 44, dx RA
- 7.15 admit for UTI / E.coli sepsis, AKI, home 7.22.21
- 7.24 admit for septic shock, AKI. restart IVAbx.
  - Petechial rash,
- 7.25 resp.distress --> emergent intubation-->ECMO
- 7.28 deterioration, normal ADAMTS-13, began plasma exchange, CRRT, ritux, methylpred, HUS/TMA?
- 7.29 eculizumab started.
- 8.5. CXR showed improved aeration. Off ECMO. normal LV RV heart per echo, continue CRRT

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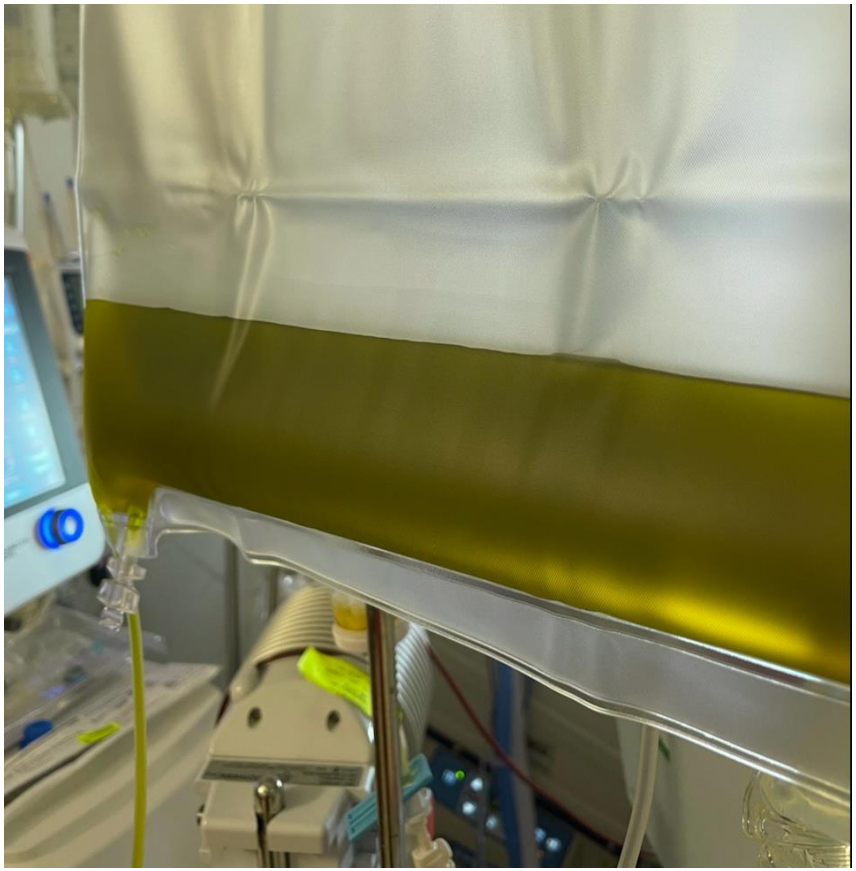
July 29

Plasma exchange waste bags



possible CAUSES of green-colored plasma

- Bacterial infection, esp.gram-negative cryophilic spp such as *Pseudomonas*
  - Pyocyanin or pyoverdin contaminants
- Some drugs, sulfonamides (sulfhemoglobin)
- **Methylene blue dye used in surgery**

Fig. 1. Green serum following blood collection and centrifugation.

Kuriloff DB, Sanborn KV. Rapid intraoperative localization of parathyroid glands utilizing methylene blue infusion. Otolaryngol Head Neck Surg 2004;131:616 – 22.

Part 2

- FDA approved birth control pill Enovid on May 9, 1960.
- Increased reports of green tint to plasma was noted (worldwide) and investigated.

CÆRULOPLASMIN AND GREEN PLASMA

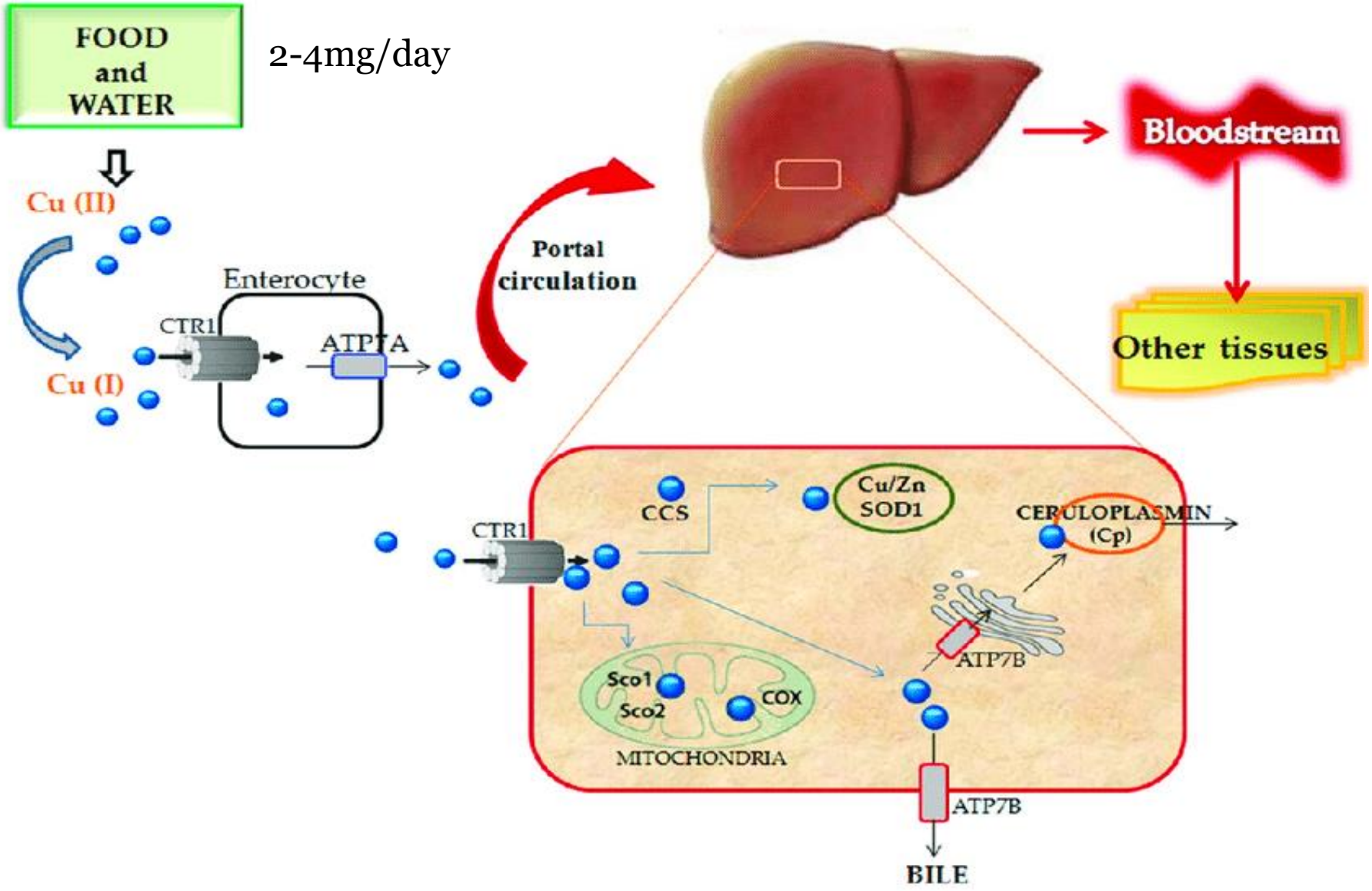
- Dr. Tovey and Professor Lathe
- Green plasma in 1 of 6 women on oral contraceptives
- Elevated total copper content

TABLE I—PLASMA-TOTAL-COPPER LEVELS IN VARIOUS GROUPS

	Group	No. of subjects	Mean plasma-total-copper level (μg./100 ml.)	Standard deviation	Significance of differences
A	*Normal men, aged 24–42*	17	106·9	±12·5	..
B	*Normal women in reproductive life, aged 20–38*	14	124·2	±24·7	B *v.* A P<0·02
C	*Women taking oral contraceptive tablets, aged 19–42*	16	215·8	±27·1	C *v.* B P<0·001
	Normal pregnant women:				
D	2–10 weeks after L.M.P.	3	154·0	±14·8	..
E	11–20 weeks after L.M.P.	13	165·9	±35·5	E *v.* B P<0·01
F	21–30 weeks after L.M.P.	12	220·4	±37·2	F *v.* B P<0·001
G	31–40 weeks after	12	225·9	±47·5	G *v.* B

Ceruloplasmin

- Ceruloplasmin is a ferroxidase enzyme made by hepatocytes
  - Function: Transport (dietary) copper (90%)
- Acute phase reactant (increases in inflammatory conditions and cell injury)
  - Increased in: Leukemia, lymphoma, carcinoma, primary biliary cirrhosis, SLE, RA.
  - Gram-negative cryophilic bacterial infection (pseudomonas)
    - Also inc.in: pregnancy, estrogen, OCP w/progesterone.
    - Consider 'female' cancers with increased estrogen states.
    - Low in Menkes syndrome, protein loss, malabsorption, advance liver dz, Wilson dz, hepatitis / cirrhosis, other. (look for increased free copper levels).



Antonucci L et al. NAF liver disease and nutritional implications. Nutrients 9. 2017

The NEW ENGLAND JOURNAL of MEDICINE

IMAGES IN CLINICAL MEDICINE

Bright Green Serum

A 49-YEAR-OLD WOMAN WAS ADMITTED TO THE hospital for evaluation of abdominal pain. Her hospital course was complicated by contrast-medium–induced renal failure requiring dialysis. She subsequently underwent resection of an adnexal mass, 16 cm in diameter. Four hours after surgery, the patient was found to have bright green serum that persisted for 4 days. Intraoperative angiography with a fluorescent dye (total dose, approximately 800 mg) and a Wood's lamp had been used to evaluate mesenteric-vessel viability. Although this dye normally clears rapidly from the blood, it persisted in this patient owing to the acute renal failure. The mass was diagnosed as colon cancer, which was found to be metastatic. The patient died from complications of the cancer 7 months later.

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62.03 Green Plasma Has a Superior Hemostatic Profile Compared with Standard Color Plasma

- Noted less MOF and improved survival pre-menopausal females.
- Pilot study to evaluate the hemostatic potential and capacity of green plasma compared to standard color plasma. N=12.
- Green plasma overall more hypercoagulable (TEG sutdies)

	Control plasma %	Green plasma %	P value
FII	96	107	0.0004
FVII	106	124	0.149
FXI	101	121	0.025

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[1]University Of Texas Health Science Center At Houston,Acute Care Surgery/Surgery,Houston, TX, USA

Back to our patient

- ID testing all negative. Covid-19 negative
- Ceruloplasmin levels: 7.30.2021 14.8 mg/dL (19.0-39.0 mg/dL)
- Blood cx all negative.
- Never on OCP. Not pregnant.
- Was it just RA?
- Copper levels? Not done.
- No sulfonamide drugs
- Occult malignancy?

Summary

- **Yellow** and **blue** make **green.**
- Green plasma is generally safe.
- Green color in plasma is ***usually*** due to the following:
  - Being in an estrogenic state, usually OCP related
  - Elevated ceruloplasmin levels, drug or gram-negative cryophilic infection.
- In patient settings consider the above plus the following:
  - RA, SLE, carcinomas, liver failure, etc.
- Unfortunately, during the patient's hospital stay the reason for her green plasma was not determined.

- Thank You!