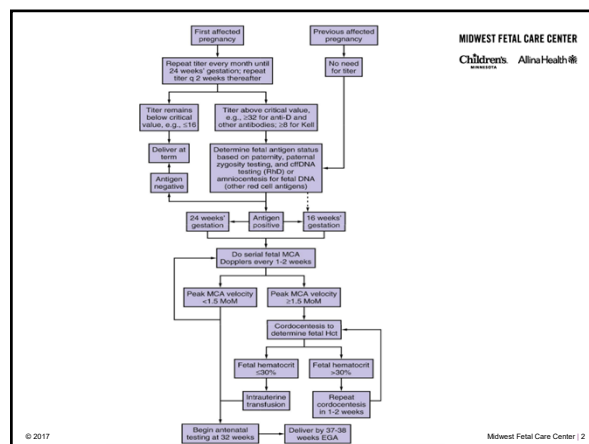


Hemolytic Disease of the Fetus and Newborn (AKA ALLOMMUNIZATION)

Saul Snowise, M.D.

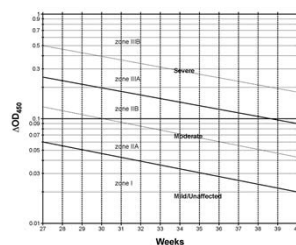
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History

- 1950's 15% of affected gestations resulted in stillbirth
- Correlation by Bevis and Walker between amniotic fluid levels of bilirubin and postnatal kernicterus
- Liley curve decreased perinatal mortality from 22% to 8.7% from 1958 - 1962



History

- Liley introduced concept of intra-peritoneal transfusion for most severely affected cases
- First successful IUT in 1963
- Over next 6 years
 - 275 procedures
 - 67 stillbirths
 - 21 neonatal deaths
 - 51 survivors (37%)



Pathogenesis

- RBCs express antigens by 30 days of gestation
- Feto-maternal hemorrhage during birth main factor
- Exposes mother to foreign antigen = **ALLOIMMUNIZATION**

Unprovoked	Provoked
Idiopathic-spontaneous	Termination of pregnancy
Delivery	Amniocentesis
Spontaneous abortion	Chorionic villus sampling
Ectopic pregnancy	Cordocentesis
Abruption	External cephalic version
Antepartum hemorrhage	Fetal intervention - fetoscopy, shunt, drainage
	Trauma
	Manual removal of placenta

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Pathogenesis

Maternal Response

- Innate immune system identifies/destroys foreign cells
- Foreign antigens presented to the humoral immune system
- B lymphocytes respond rapidly to future exposure with IgG Antibodies

Fetal Response

- How much antibody is made
- Can it cross the placenta
- Does the fetus react to it

Extravascular hemolysis

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MCA-PSV prior to 18 Wks

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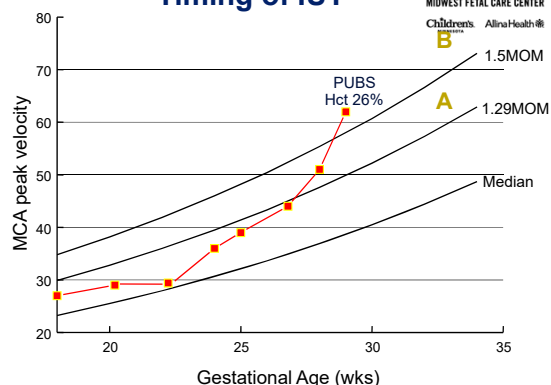
Nomogram of predicted MCA PSV at the 5th, 10th, 90th and 95th percentiles and 1.5 MoM for 11 to 18 weeks gestational age

GA, wk	MCA PSV, cm/s					
	5 th	10 th	50 th	90 th	95 th	1.5 MoM
11	3.2	5.2	10.7	15.2	19.5	16.1
12	4.5	6.5	12.1	16.9	21.2	18.2
13	5.8	7.8	13.6	18.5	22.8	20.3
14	7.1	9.0	15.0	20.2	24.5	22.4
15	8.4	10.3	16.4	21.8	26.1	24.5
16	9.8	11.5	17.8	23.4	27.7	26.7
17	11.1	12.8	19.2	25.1	29.4	28.8
18	12.4	14.1	20.6	26.7	31.0	30.9

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Adapted from Tongson et al. J Ultrasound Med 2007; 26:1013-7 19

Timing of IUT



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Intrauterine Transfusion

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Setting

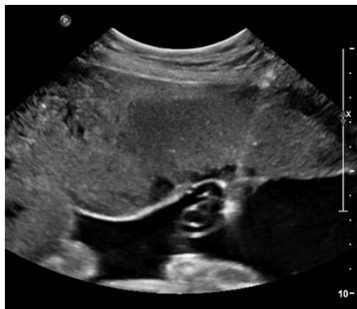
- In/close to OR
- Sedation anesthesia
- Prophylactic Abx, tocolysis

Fetal Site

- Placental cord insertion
- Hepatic portion of the umbilical vein
- Free loop
- Intraperitoneal
- Intracardiac

Medications

- Vecuronium 0.1mg/kg
- Fentanyl 2mcg/kg



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Intrauterine Transfusion

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Amount to Transfuse

- $EFW \times 0.02 = \text{volume of PRBCs to increase the Hct by 10\%}$
 - Based on donor Hct of 75-80%
 - No more than 4 fold increase in Hct

Transfusion Interval

- MCA-PSV vs Empiric interval
- MCA-PSV $>1.69\text{MoM}$
- Hgb decreases;
 - 0.4mg/dL/day after 1st IUT
 - 0.3mg/dL/day after 2nd IUT
 - 0.2mg/dL/day after 3rd IUT

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Intrauterine Transfusion

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Complications

- Fetal bradycardia
- 2% emergency cesarean
- Infection 0.3%/procedure
- PPROM 0.1%/procedure
- Bleeding, fetal needle injuries, arterial spasm, alloimmunization

Delivery

- Last IUT at 34w6d
- 7-10 days of phenobarbital
- Delivery at 37-38 weeks
- C/sec for routine obstetric indications

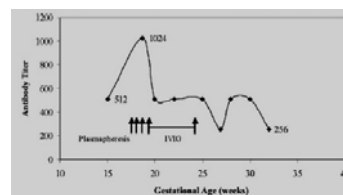
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Trevel et al. Am J Obstet Gynecol 2005;192:478-82 23

Immunomodulation

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- Intravenous access "difficult" prior to 18 weeks
- 30-60% of maternal IgG antibodies cross the placenta by 12 weeks of gestation
- Intraperitoneal transfusions can be used, but can we delay the passage of antibodies into the fetal compartment?
- Plasmapheresis followed by weekly IVIG 1g/kg has been shown to delay the timing of first transfusion and improve outcomes



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Ruma et al. Am J Obstet Gynecol 2007;196:133e1-138e6 24

