ABO and Rh ISOIMMUNISATION

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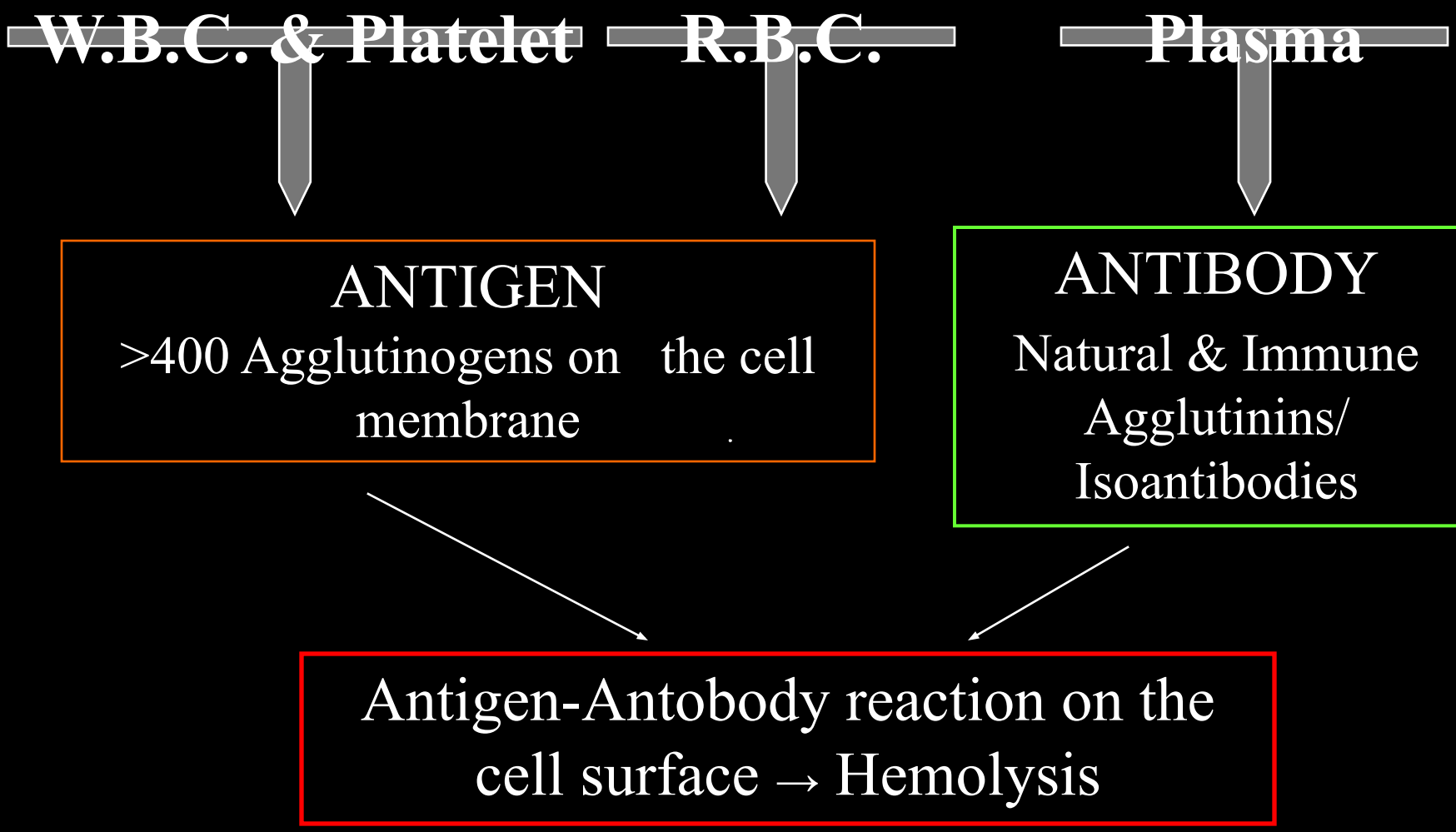
The Basics Of Blood



The Basics Of Blood

Antigens: -

- Controlled by genes at unknown No. of chromosomal loci.
- Appearance by 40 days of I.U. Life- unchanged till death.
- Also present in tissues & tissue fluids.
- Blood group system: A group of antigens controlled by a locus having a variable no of allele genes.

The Basics Of Blood

Antigens: -

- > 15 blood group systems are recognised :
  - **ABO, Rh,** Kell, Duffy, MN, P, Lewis, Lutheran, Xg, Li, Yt, Dombrock, Colton, Public antigens & Private antigens.
- Blood type- means individual antigen phenotype which is the serological expression of the inherited genes
- Most of these blood group antigens have been found to be associated with hemolytic disease.
- However– ABO & Rh account for 98%

The Basics Of Blood

Antibodies: -

Alloantibodies / Agglutinins

- Natural
  IgM
- Iso / immune antobodies
  IgG
  - Formed in response to foreign R.B.C. or soluble blood group substance.

The Basics Of Blood
Natural Antibodies: -

- Antibodies are formed against most of the major group antigens & present in almost all individuals when the antigen is absent.
- In most other minor systems, natural antibodies to the antigens are found occassionally but as their anitgenicity is low, the immune antibodies are also rare (except –Kell & Duffy)
- Mostly of them are IgM type.
- React poorly at body temp. (except anti-A & anti-B), but agglutinate R.B.C.s at 5-20°C
- Usually do not cross placenta.

The Basics Of Blood
Immune Antibodies: -

- In contrast the immune or isoantibodies are IgG.
- Best react at body temp. & readily cross placenta.
- Most antibodies are complement binding notable exceptions being Rh & MN.

Antibodies Can Be Detected by: -

a. Saline agglutination test (SAT).
b. Tests using cells suspended in colloid media.
c. Tests using enzyme-treated cells- Rh & occasional antobodies.
d. Indirect antiglobulin (Coomb's test) - wide spectrum.

- Antibodies may be Complete / Incomplete

	⇓ IgM	⇓ IgG
Detected by→	SAT	b, c, d

ABO Blood Group System

- ABO system is controlled by allelic genes A1, A2, B, O located on the long arm of chromosome 9
- The loci of ABO & H are not genetically linked
- A1 & A2 genes perform same function but have a different rate constant
- The O gene is an amorph & functionaly silent
- The H antigen is a precursor to A & B
- Secretors & nonsecretors – Se & se genes control the production of a flucosyl transferase, which controls the production of H, A & B antigens in tissues

ABO Blood Group System

Genotype (Genes)	Phenotype (Blood type)	Antigens in R.B.C.	Antibody In plasma
A_1A_1 , A_1A_2 A_2A_2, A_2O	A_1 (23-25%) A_2 (6-10%)	A_1, (H) A_2, (H)	anti-B, anti-H Anti-B, anti-A_1
BB, BO	B(8-17%)	B,(H)	Anti-A/A_1
A_1B A_2B	A_1B(3%) A_2B(1%)	A,A_1,B A,B,H	Anti-H Anti-A_1
O,O H,h	O(43-50%) Oh Bombay	H None	Anti-A,-A_1,-B Anti-A,-A_1,-B,-H

ABO System & Pregnancy

- Majorities of hemolytic diseases are due to ABO incompatibility
- Foetus inherits one gene from each parent.
  - O + O = O, O + A= O or A, O + B= O or B, O + AB= A or B.
- There is a 20% chance of ABO incompatibility of mother & foetus
- Only 5% chance of developing hemolytic disease only in type A & B infants of type O mothers, that too only of milder forms

ABO System & Pregnancy

- In foetus & newborn, RBCs have a decreased No. of H, A & B reactive sites
- The foetal immunoglobulin production is low, so the plasma contains very little of anti-A & B agglutinins
- Anti-A & B produced in the mother being natural are IgM molecules & so do not cross placenta.
- In some type O adults, much of the anti-A & B and anti-AB (a cross reacting antibody, also called anti-C) isoagglutinins are of IgG class.

ABO System & Pregnancy

- There is no adequate method of antenatal diagnosis.
- Direct Coomb's antiglobulin test may be negative in ABO haemolytic disease.
- ABO haemolytic disease is frequently seen in infants of primigravidae & the chance of recurence is 87%.
- The risk of stillbirth is not increased & no antenatal treatment is necessary.
- Only 67% of affected infants will need any treatment.

Rhesus Blood Group System

- First demonstrated by testing human blood with rabit anti sera against red cells of Rhesus monkey & classifying Rh negative & Rh positive.
- However the underlying biochemical genetics is not well understood and the genotyping & phenotyping remains little confused
- The genotype is determined by the inheritance of 3 pairs of closely linked allelic genes situated in tanderm on chromosome 9 & named as D/d, C/c, E/e (Fisher- Race theory)

Rhesus Blood Group System

- The gene ‘d’ is an amorph & has no antigenic expression. So there are only five effective antigens.
- But Weiner postulates a series of allelic genes at a single locus Rho (D), rh (C),rh (E), hr © & hr (e)
- The updated system of Rosenfield refers these antigens as – Rh1, Rh2, Rh3, Rh4, Rh5
- Subsequently less common antigens Cw, Du, Es have been found
- The foetus inherits one gene from each group as a haplotype such as sets of Cde, cde etc from each parent

Rhesus Blood Group System

- 12 sets of combinations & 78 genotypes are possible. Most frequent genotypes are –
  - Cde/cde(33%), Cde/cDe(18%), Cde/cDE(12%) cDE/cde(11%), cde/cde(15%), cdE/cde(1%), Cde/cde(1%)
- Though several Rh genotypes and phenotypes have been described, for clinical & all practical purposes it is enough to know whether one is Rh POSITIVE or NEGATIVE against anti D sera.

Rhesus Blood Group System

- Incidence of Rh negative varies in different races:
  - Mongoloids- nil, Chinese & Japanese- 1-2%, Indians-5%, Africans-5-8%, Causcasians-15-17% & Basques-30-35%.
- The antigenic expressions of these genes are dependent on an interaction between R.B.C. membrane protein & phospholipid molecules resulting in a set of antithelical epitopes, the coresponding antigens, consisting of C/c, D/d, E/e.
- The antigenic determinants form an intrinsic part of the red cell membrane protein structure.

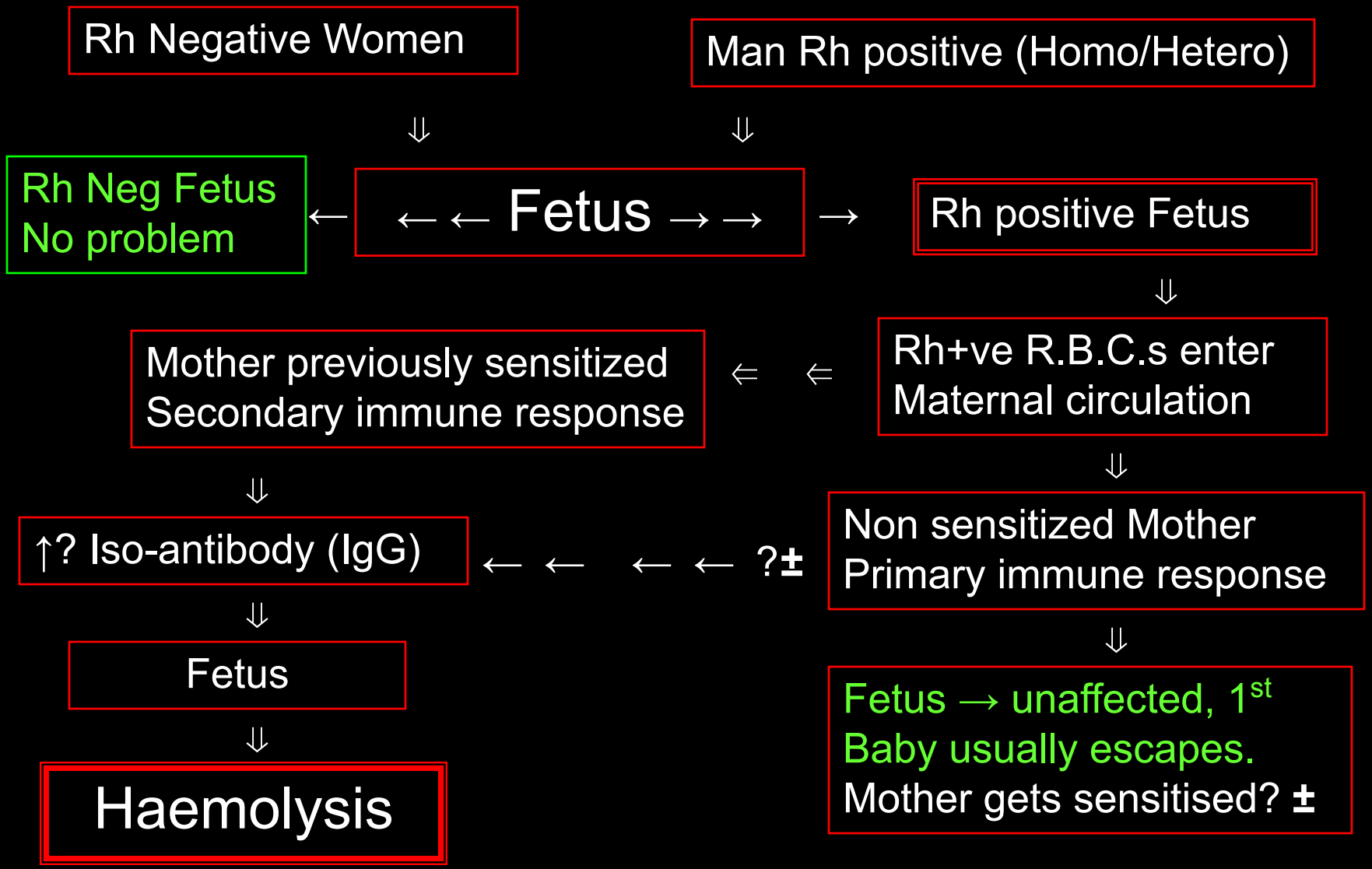
Rhesus Blood Group System

- C/c & E/e are weak antigens and impractical to match.
- ‘D’ is by far the most immunogenic in the Rh system excepting those that have the natural antibodies.
- There is a rare type of Rh negative called Rh null who lack all known Rh antigens.
- ‘D’ antigen has no natural antibody while C & E have the coresponding natural antibodies, though weak & found infrequently.

Rhesus Blood Group System

- A single transfusion of + ve blood to a – ve person has a 50% chance of forming anti Rh D antibodies (IgG)
- Anti Rh antibodies are of three categories-
  - 1st order – saline / bivalent / complete antibodies
  - 2nd order - albumin active / univalent / incomplete antibodies
  - 3rd order – atypical / antiglobulin active / incomplete antibodies

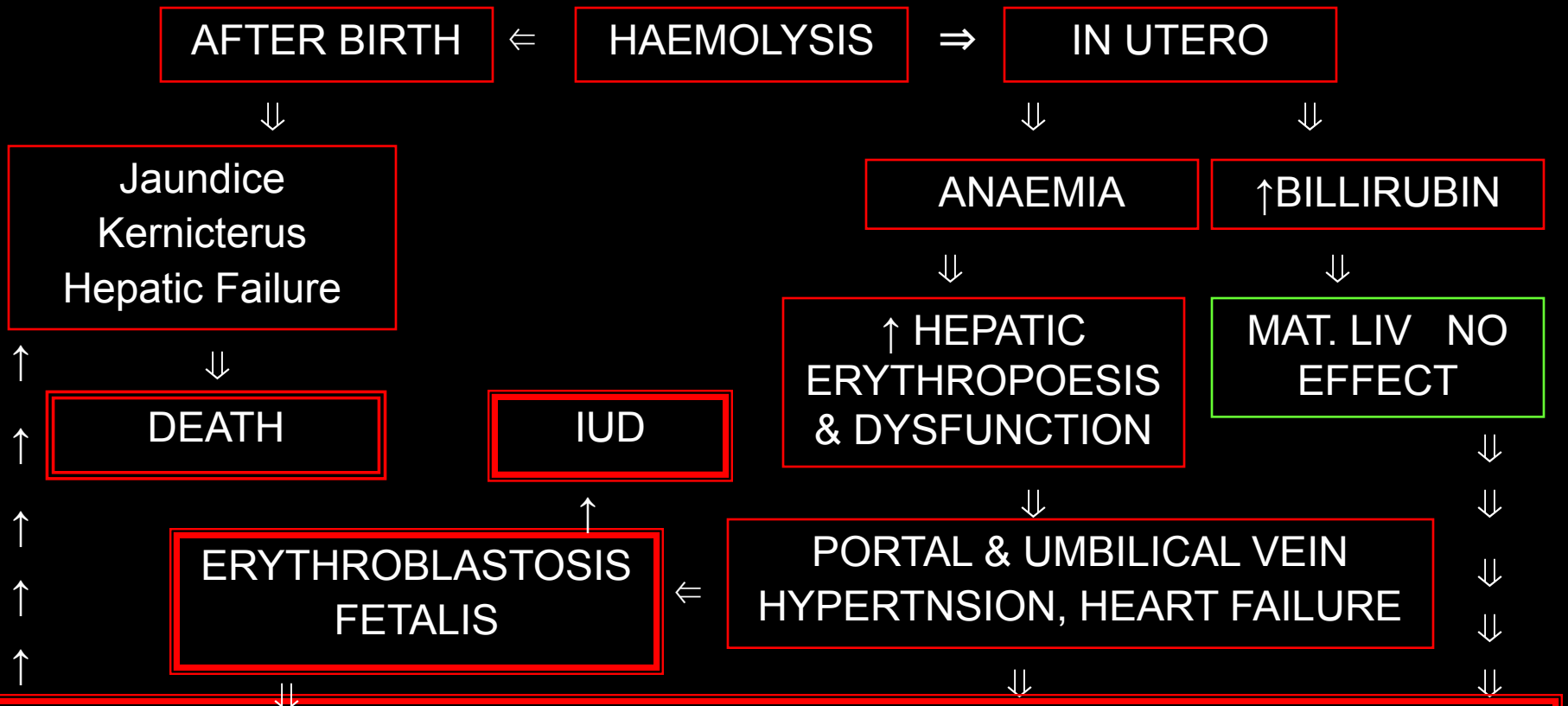
Pathogenesis Of Rh Iso-immunisation



Pathogenesis Of Rh Iso-immunisation

- Chances of T.P.H/F.M.H. are only 5% in 1st trimester but 47% in 3rd trimester, many conditions can increase the risk.
- Chances of primary sensitization during 1st pregnancy is only 1-2%, but 10 to 15% of patients may become sensitized after delivery.
- ABO incompatibility and Rh non-responder status may protect.
- Amount of antibodies that enter the fetal circulation will determine the degree of haemolysis

Pathology Of Iso-immunisation



BIRTH OF AN AFFECTED INFANT - Wide spectrum of presentations. Rapid deterioration of the infant after birth. May contiune for few days to few months. Chance of delayed anaemia at 6-8 weeks probably due to persistance of anti Rh antibodies.

Prevention of Rh Incompatibility

- Premarital counseling? Ambitious?
- Proper matching of blood particularly in women before childbearing.
- Blood grouping must for every woman, before 1st pregnancy.
- Rh+ve Blood transfusion- 300mcg Immunoglobulin (minimum).
- Proper management of unsensitised Rh negative pregnancies.

Management of Unsensitised Pregnancy

- Blood typing at 1st visit, If negative husband's typing. If husband is also negative then no treatment
- If husband is positive, if possible, Homo/Hetero?
- Do Indirect Coomb's test of mother –
  - Negative-good.
  - Repeat ICT at 28 weeks – Negative- ICT at 35 weeks - Negative- Observe
  - Positive→ Sensitised - 300mcg Rh immunoglobulin

Management of Unsensitised Pregnancy

- In Abortion, Ectopic, CVS-
  - Pregnancy < 12 weeks- 50mcg Anti D
  - Pregnancy >12 weeks- 300mcg Anti D
- APH, IUD, Amniocentesis, Abdominal trauma, Foetal-maternal hemorrhage -300mcg Anti D
- At birth- cord blood for ABO & Rh typing
- Baby Rh negative – Be happy

Management of Unsensitised Pregnancy

- If Rh positive- Test mother's blood for ICT & Infant's for DCT
  - Negative or weakly reactive- 300mcg immunoglobulin
  - Positive – Sensitised–Hb & Bilirubin Estimation of the infant -Treat the infant
- ?Prophylactic Anti D administration during antenatal period to all negative mothers at 28weeks and again at 34 / 36 weeks.

Management of Sensitized Pregnancy

- Causes of sensitization-
  - Misinterpretation of maternal Rh type
  - Rh +ve blood transfusion
  - Unprotected preg. & labour
  - Inadequate dose / improper use of IgG on previous occasions
  - Immunization to cross-reacting antigen

Management of Sensitized Pregnancy

- Careful planning during antepartum, intrapartum & neonatal period
- Father's blood type & Rh antigen status
- Knowledge of maternal antibody titer to the specific antigen
- Intrauterine foetal monitoring with repeated ultrasound examination, cordocetesis / amniocentesis

Management of Sensitized Pregnancy

- Fetus Rh Negative: - Observation
- Fetus Rh Positive: -
  - Intrauterine transfusion of ‘Rh Neg’ blood as indicated
  - Timely delivery any time after 32 weeks
  - Management of the infant up to 8 weeks
- In cases of severely sensitized women, consider medical termination of pregnancy and sterilization .

THANK YOU