GROUP QUESTION SHEET *(included with Booklet "A")*

This sheet should be filled out as a group effort. Any differences of opinion should be noted.

1. Complete the following Table as fully as possible from data received. Give phenotypes *and* genotypes when possible. Put parentheses around genotypes.

	ABO	Isoagglu-tinins	Rh	MNSs	Direct Coombs	Indirect Coombs
Mother						
Mr. Smith						
Child at birth						
Child at 9 months						

2. Why was the baby sick shortly after birth? (Give a diagnosis and describe the pathogenesis of the disease.)

3. What immediate measures would you have taken after the child was born?

4. Why is there a difference between the data on the baby at birth and at 9 months of age?

5. Could this child's disease have been prevented? How?

6. Check the boxes in the following chart that represent *unnecessary* laboratory tests that were performed (*i.e.* tests whose outcomes were not in question).

	ABO	Isoagglu-tinins	Rh	MNSs	Direct Coombs	Indirect Coombs
Mother						
Mr. Smith						
Child at birth						
Child at 9 months						

Now compare your group's answers with the Correct Group Answers.

CORRECT GROUP ANSWERS ARE ON THE LAST TWO PAGES OF BOOKLET "B".

DO NOT LOOK AT THEM OR REMOVE THEM UNTIL YOUR GROUP HAS COMPLETED DISCUSSING AND ANSWERING THE GROUP QUESTIONS.

CORRECT GROUP ANSWERS *(included with Booklet "B")*

CORRECT GROUP ANSWERS ARE ON THE NEXT TWO PAGES

DO NOT LOOK AT THEM OR REMOVE THEM UNTIL YOUR GROUP HAS COMPLETED DISCUSSING AND ANSWERING THE GROUP QUESTIONS.

CORRECT GROUP ANSWERS *(with Booklet "B")*

1.

	ABO	Isoagglu-tinins	Rh	MNSs	Direct Coombs	Indirect Coombs
Mother	O (OO)	Anti-A Anti-B	- (-/-)	MSs (MMSs)	-	+
Mr. Smith	A (AA or AO)	Anti-B	+ (+/- or +/+)	MNS (MNS S)	-	-
Child at birth	O (OO)	None	+ (+/-)	MS (MMSS)	+	*Not done*
Child at 9 months	O (OO)	Anti-A Anti-B	+ (+/-)	MS (MMSS)	-	-

2. Debbie was suffering from erythroblastosis fetalis. She is Rh+ and has IgG antibody on her RBCs, as indicated by the positive direct Coombs test. Her mother is Rh- with demonstrable antibody to the Rh antigen, as we deduced from the positive indirect Coombs test and a previous history of stillbirths. This indicates that the mother has become sensitized to the Rh(D) antigen, has produced IgG anti-D antibodies, and those crossed the placenta and destroyed the baby's RBCs. The RBC destruction in erythroblastosis fetalis mainly takes place in the liver and spleen, where the IgG-opsonized RBC are taken up by macrophages and broken down (extravascular hemolysis). This results in marked anemia and mobilization of young red cell precursors to the peripheral blood (erythroblasts and reticulocytes, panels A and B respectively, in the figures corresponding to this child's hemogram). Intracellular lysis of RBC results in the release of large amounts of unconjugated bilirubin. While the baby is in the womb, bilirubin crosses the placenta and is conjugated by the mother's liver. When the baby is born, he(she) is unable to conjugate bilirubin, due to the lack of hepatic β-glucuronyl transferase. This results in accumulation of unconjugated bilirubin, which is not soluble in water and not easily eliminated. On the other hand, unconjugated bilirubin is lipophylic and the blood-brain barrier membrane of the newborn is not yet well formed and allows diffusion of bilirubin into the brain, where its deposition can cause irreversible damage (kernicterus).

3. In severe cases of erythroblastosis fetalis, the baby is given an Rh- RBC transfusion in utero. In other cases, exchange transfusions are given at birth. Plasmapheresis may also be used to reduce the levels of bilirubin. In less severe cases, placing the baby under a UV light may result in significant breakdown of unconjugated bilirubin.

4. At birth, the baby had no A or B isoagglutinins, as it was to be expected from her blood type (O). This is because at this time he had not yet been exposed to intestinal bacteria with cross-reactive polysaccharides that are responsible for the induction of anti-A and anti-B isoagglutinins. At nine months of age Debbie had the normal complement of isoagglutinins.

5 Giving Rh- mothers antibody to Rh antigen (RhO[D] Immune Globulin, Rhogam) at the 28th week of pregnancy and immediately after they deliver can prevent Rh diseases. Rhogam administration inhibits the maternal antibody response to Rh and thereby protects her next baby from erythroblastosis fetalis. It was believed that Rhogam would act by blocking the Rh antigens in the baby's red cells and preventing maternal sensitization. However, this scenario seems rather unlikely, particularly if one considers that the antibody administered at the 28^{th} week bind fetal red cells (it can cross the placenta, if no fetal red cells have reached maternal circulation) will be eliminated very quickly. Thus, prolonged protection by the postulated mechanism until week 40 is highly unlikely. There are recent papers concerning the therapeutic effect of intravenous immunoglobulin (IVIg), used as an immunotherapeutic agent for some autoimmune diseases, which suggest that IVIg works by cross-linking antigen receptors and Fc II receptors on the B cell membrane. This appears to downregulate B cell activity, and perhaps even causes apoptotic death of the B cells, which in turn would lead to decreased autoantibody synthesis. A similar mechanism may be operational with Rhogam - the B cell would "see" the Rh antigen through the antigen receptor, and the rhogam antibody bound to the RBC would interact with Fc γIIR, thus causing B cell downregulation. If a mother is known to be sensitized to Rh and the father is Rh+, amniocentesis followed by PCR can determine whether the baby is Rh+. If so, it becomes clear that the baby is at risk for the development of hemolytic disease, and measures (including intrauterine transfusion of O, Rh- RBC) can be taken to minimize the clinical consequences.

6. “Unnecessary” or superfluous laboratory tests are indicated by letters in the table, with explanations below:

	ABO	Isoagglu-tinins	Rh	MNSs	Direct Coombs	Indirect Coombs
Mother					a	
Mr. Smith					b	b
Child at birth		c				
Child at 9 months	d		d	d	e	e

a. The mother was not anemic, and the question was not whether she had antibody on her RBCs but whether she was making antibody to her baby's RBCs.

b. The father's antibody to RBCs is irrelevant, and there was no reason to suspect he was anemic.

c. Newborns do not have isoagglutinins.

d. There is no reason to expect the baby's RBC antigens to change.

e. There is no reason to now expect the baby to be having any trouble.

When you have finished reviewing these answers, each student should answer the questions on the posttest.