Isoimmunization

An Introduction to Antibodies and Pregnancy

by Monique Kinney
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Part 1: An overview of Isoimmunization

What is Isoimmunization (Iso)?
Isoimmunization (also called alloimmunization), occurs when a woman’s immune system is sensitized to foreign blood cell antigens. This causes the woman to make antibodies that cross the placenta and destroy baby's blood cells.

During pregnancy, some of the mother's antibodies are transported across the placenta and enter the fetal circulation. This is necessary because newborns have only a primitive immune system, and the presence of maternal antibodies helps them survive while their immune system matures. A downside to this protection is that by targeting fetal blood cells, maternal antibodies can also cause HDN.

Blood production in the fetus begins at about 3 weeks, and the baby's blood cells can have antigens on the red cell membrane as early as 38 days after conception.

Antibody? Antigen? What’s my body doing again?
Antigen – foreign protein on red blood cells of dad or baby
Antibody – made by mom to defend her body from the antigen
Antigens are foreign. Antibodies defend the body.

How it works
Dad makes the E antigen and passes it to baby. When baby’s blood and mom’s blood mix, mom’s blood finds the foreign antigen and makes antibodies to defend her body. This is called sensitization. The antibodies then find the foreign cells and destroy them in a process called hemolysis (hemo = cell, lysis = death). The next time mom’s sensitized body finds the E antigen, her antibodies are primed and ready to attack the foreign cells. So when mom has baby #2, who has dad’s E antigen, her antibodies cross the placenta and attack the baby’s blood.

How did I become sensitized?
The most common ways maternal sensitization occurs are:
- Blood transfusion
- Birth
- Abortion
- Ectopic Pregnancy
- Fetomaternial hemorrhage
- Placental abruption
- Amniocentesis
- Chorionic villus sampling
- Percutaneous umbilical blood sampling
- External cephalic version (trying to turn a breech baby)
- Manual removal of the placenta (instead of spontaneous delivery of the placenta)

Why is Iso dangerous?
Isoimmunization is dangerous because the antibodies can cross the placenta during pregnancy and if the fetus is positive for the specific antigens, the fetal red blood cells are destroyed. This can result in anemia, hemolytic disease of the newborn (HDN), fetal hydrops (sometimes fatal), and more.
Possible Outcomes
If you are sensitized, it is not a death sentence for your baby, and it does not mean you cannot have additional children. Advancements in fetal surveillance and treatment allow for successful outcomes for most of the affected fetuses. For the Rh D- woman, the drug Rhogam has reduced the risk of sensitization to less than 1% of susceptible pregnancies. Because of this other alloantibodies have increased in relative importance. These include antibodies to other antigens of the Rh blood group system (ie, c, C, e, E) and other atypical antibodies known to cause severe anemia, such as anti-Kell (ie, K, k), anti-Duffy (ie, Fy\(^a\)), and anti-Kidd (ie, Jk\(^a\), Jk\(^b\))\(^1\).

How do I know if I have an antibody?
There is only one way to know if you have an antibody, you have to get tested. Routine antibody screening is done in the US on all pregnancies (unless refused) as part of the basic prenatal blood work.

What do I do? Where do I start?
Start by keeping a binder or folder. Use this to write down all your questions (and the doctor's answers). No question is silly. It is important that you are informed and able to actively participate in your care and advocate for your baby. Ask for copies of all your test results and keep them in your folder. Don't forget to get a copy of each ultrasound report and MCA scan (complete with all the PSV values, not just the highest or lowest). This way you can see how things are changing and how baby is doing. This is also helpful if you have to have multiple doctors. Sometimes things don't always get passed along between offices, so it is very important to have your own record. It is also a great place to put keepsakes such as ultrasound photos, bracelets, etc. Consider having someone come with you to tests and appointments for support or to drive you home after procedures.

You also need to get a medical alert card for your wallet or a medical alert bracelet. Mine says “Transfusion Alert: Anti-E”. This is important even after you're not pregnant. If you are ever in an accident or unconscious and need blood, you do not want to have a life threatening transfusion reaction. Some blood banks, hospitals, or doctor's offices will provide them for you. There are also multiple places online where you can order a bracelet, or in the pharmacy section of our local Meijer, there is a USB medical alert card that you can put your entire medical record, not just your antibody status. Some cell phones have an In Case of Emergency or ICE section where you can write your antibody status and include emergency contact information for your MFM too. I've attached a printable medical alert card in the appendix.
Part 2: Prenatal Testing

Basic Prenatal Blood Work – What it Includes
For me, my basic prenatal blood work (performed at Borgess Hospital in Michigan, USA) included:

Blood type ABO type and Rh type to find out what my blood type is (for me it is O+).
Antibody screen aka Indirect Coomb’s test (not to be confused with the Direct Coomb’s that is run on baby after birth). This came back positive so they ran an antibody ID panel.
The Antibody ID panel came back positive for Anti-E for me. They ran 2 more tests, a test looking for the antigen E, and another test called an antibody titer.
The antibody ID panel, antigen test, and the titer are all isoimmune specific tests. If you don’t test positive for an antibody, you won’t have these tests run.

Complete Blood Count (CBC). This checks for how many white and red blood cells you have in general. It also measures Hemoglobin (Hgb), Hematocrit (Hct), and a couple other things. This and the tests that follow are not iso related, but are done to check the general health of the person.
An automated differential checking how many of each specific white blood cells I had.
The last part of the blood test was for immunology. They wanted to make sure I was indeed immune to rubella. Rubella can cause serious problems if a pregnant woman is exposed to Rubella and is not immune to it.
They also tested my urine to see if I was pregnant, had blood cells, mucus, bacteria, protein, sugar, etc. being secreted in my urine.

The most important parts of the blood test for the pregnant woman concerned about Isoimmunization are the blood type (ABO and Rh), Antibody screen, Antibody ID panel, Antigen ID panel, and the Titer.

No antibody found
A negative Indirect Coombs Test (also called an indirect agglutination test) means that your blood is compatible with the baby’s blood or that sensitization has not yet occurred (yay!). It checks to make sure that the pregnant woman has not developed antibodies against any potential antigen-positive blood of her baby. If sensitization has not occurred, in the case of Rh-D negative women, it can be prevented by a shot of Rhogam. See Interventions – Rhogam. This test should be repeated each pregnancy.

Antibody found
A positive Indirect Coombs test result means that your blood is incompatible. If you have a positive indirect Coombs test, it means you have already been sensitized and there are antibodies floating around in your blood. In this case, an identification panel and the antibody titer test should be done. The mother can be tested early in pregnancy to check the blood type of her baby by amniocentesis or free floating fetal DNA. If the baby has antigen-positive blood, the mother will be watched closely throughout the pregnancy to prevent problems to the baby’s red blood cells. If the mother declines in-utero antigen testing for the baby, she will still be monitored closely throughout the pregnancy just as if the baby was antigen positive.
There are many antigens. There is the Rhesus (Rh) group which includes D, c, C, e, E, and is the most clinically relevant (Note: no d antigen, pronounced “little d” exists so you will not find an Anti-d antibody.). However the non-Rh groups such as Kell, MNS, and Kidd have become increasingly more important as the incidence of Rh-D sensitization has decreased. Sensitization with Rh antibodies (c, C, e, E) is still responsible for the largest proportion of hemolytic disease in the newborn (HDN), followed by Anti-K, anti-D, anti-E, anti-Fya, anti-Jka⁴.

Once you know which antibodies you have, you can find out if they are associated with hemolytic disease of the newborn (HDN). If an antibody is associated with HDN, additional blood testing occurs. While not all antibodies are included in the table below, these are some of the most common.

**Antibodies NOT Associated with HDN⁴**

- Duffy: Fyᵇ
- Kidd: Jkᵇ
- Lewis: Leᵃ, Leᵇ
- Lutheran: Luᵃ, Luᵇ
- Wright: Wrᵇ
- Batty
- Becker
- Berrens
- Coᵃᵇ
- Evans
- G
- Gonzales
- Hil
- Hunt
- Hut
- Jobbins
- Jrᵃ
- Mur
- P
- Rm
- Ven
- Vw
- Xgᵃ
- Ytᵇ

**Antibodies Associated with HDN⁴**

- Diego: Diᵃ, Diᵇ
- Duffy: Fyᵃ
- Kell: K₁, Kpᵃ, k, Jsᵃ, Jsᵇ
- Kidd: Jkᵃ
- MNS: M, S, s, N
- Rh: D, c, C, Cʷ, e, E
- Wright: Wrᵃ
In the case of Anti-E antibodies, it is advisable to retest at 28 weeks to be sure that Anti-c has not developed.

**Additional blood work**

*Paternal blood work*

Once an antibody that has been associated with HDN has been found in Mom’s blood, Paternal testing takes place to see what chance the baby or future children from the couple have of being affected. At our lab this was called the Rh Phenotype test and they only checked to see how many of the genes he had for the specific antigen (E) matching my antibody (Anti-E).

If Dad is heterozygous (E/e), then there is a 50% chance that the baby or future babies will be affected by that specific antibody. In this case, the fetus can be tested in utero or after birth. They may also say that he has tested positive for both the E antigen and the e antigen.

If Dad is homozygous dominant (E/E) then there is a 100% chance of the baby and future children being affected by that specific antibody. They may also say he tested positive for the E antigen and negative for the e antigen.

If Dad is homozygous recessive (e/e) then there is a 100% chance of the baby and future children NOT being affected by that specific antibody. They may also say that he tested negative for the E antigen and positive for the e antigen.

**Testing Baby**

There are 3 ways that the baby can be tested to see if they have the specific antigens.

1. **Amniocentesis** is the test that is most commonly done while baby is still in the womb. See Prenatal Testing – Amniocentesis

2. **Free floating fetal DNA.** There are small pieces of fetal DNA floating around in Mom’s blood stream. In some places (not common practice everywhere), a simple blood test drawn from Mom can tell about some of baby’s antigens. Unfortunately, cell-free fetal DNA testing for determining the genotype for other red blood cell antigens such as E and Kell is not yet available in United States.

3. **Direct Coombs test** is the test that is done after birth. It is done for the babies of all sensitized mothers, and is especially important if amniocentesis or free floating fetal DNA testing was refused. See Post-Delivery Blood Testing – Direct Coombs.

More blood work for mom – maternal titers
What is it?
Titors are a measure of expressing the concentration. Your titors will help tell you how much of the antibodies are in your blood.

When is it done?
Depending on doctor preference, titors are done monthly, biweekly, or weekly. Some doctors will only do titors at the beginning and at the end, and will treat baby as affected, especially in the case of an already affected pregnancy. When you have your prenatal blood work, if your indirect Coombs test comes back positive, the lab should automatically titer it for you.

Where is it done?
Titors are done in the lab.

Why is it done?
Titors are done to help tell the doctor about how many antibodies are in your system, however they are not an effective monitoring tool when you have already had an affected baby, or in the case of some antibodies.

How is it done?
A simple blood draw is all that is needed for titors. Usually only 1 vial of blood is taken.

How often is it done?
Titors are drawn anywhere from once or twice per pregnancy, to monthly, biweekly, or weekly. It depends on the doctor's preference.

What do the numbers mean?
Your titors will come as a ratio. Such as 1:less than 1, 1:2, 1:4, 1:8, 1:16, 1:32, 1:1024, etc. This tells you how many times they need to dilute the blood to get rid of the antibodies. The higher the second number, the more likely baby is to be affected.
Large differences in titer can be seen in the same patient between different laboratories, and a newer gel technique produces higher titer results than the older tube method. Therefore, standard tube methodology should be used to determine critical titer, and a change of more than 1 dilution represents a true increase in maternal antibody titer.5

When to get additional monitoring
You should have additional monitoring whenever you hit critical titer (1:16 for most antibodies, 1:8 for Kell), have a rise in titors, or have an antibody for which titors are not an accurate indicator of anemia.

Ultrasound Testing

What is it?
Ultrasound is an imaging test that uses sound waves to create a picture of how a baby is developing in the womb. It is also used to check the female pelvic organs during pregnancy.

When is it done?
Ultrasound can be done at any point in the pregnancy.

Where is it done?
Ultrasound can be done almost anywhere. It is frequently done in the doctor's office and doesn't require a special trip to the hospital.

Why is it done?
Ultrasound is used early on to establish correct gestational age. This is important for determining what the correct normal lab values are for the baby (amniotic fluid bilirubin levels, size of the baby, etc.). It is also used early to confirm a normal pregnancy, determine the baby's age, look for problems, such as ectopic pregnancies or the chances for a miscarriage, determine heart rate, look for twins, and to identify problems with the organs (placenta, uterus, cervix, ovaries). Later on, ultrasounds are used to detect ascites and fetal hydrops. Ascites is the buildup of fluid in the space between the lining of the abdomen and abdominal organs. Fetal Hydrops is the end stage of hemolytic disease of the newborn where the baby has 1/3 normal hemoglobin or less. Both are severe complications from the antibodies and require immediate treatment.

How often is it done?
How often an ultrasound is done depends on the type of ultrasound, and what the doctor is looking for. A simple dating ultrasound, or general anatomy ultrasound is only done once. Doppler ultrasounds or biophysical profile ultrasounds are done more frequently (every couple of days if needed).

How is it done?
Ultrasound is a non-invasive, painless procedure. You will lie on your back on an exam table. The person performing the test will spread a gel on your abdomen and place a wand in the gel. The gel helps the wand transmit sound waves that will bounce off the baby to create a picture on the ultrasound machine. If it is very early in pregnancy, a vaginal ultrasound may be done. The procedure is the same, except that a slim wand is inserted into the vagina.

What do the numbers mean?
Your doctor will go over any numbers with you. Depending on the type of ultrasound you have, there are a variety of number possibilities.

What risks are there?
While most doctors agree that ultrasound is safe, it does carry some slight risks that you should be aware of. For most women with ISO, these risks are nowhere close to the very real risk of the baby dying if not treated appropriately.

Ultrasounds can cause problems with high heat, cavitation, and acoustic streaming. When fetuses move away from the stream of high-frequency sound waves, they may be feeling vibrations, heat or both. As the FDA warned in 2004, "ultrasound is a form of energy, and even at low levels, laboratory studies have shown it can produce physical effect in tissue, such as jarring vibrations and a rise in temperature." What this means is that the baby does
feel the ultrasound waves as vibrations and/or heat. Depending on the energy, they can also be heard by both mom and baby.

Tissues of the central nervous system are sensitive to damage by physical agents, such as heat and ultrasound. Exposure to pulsed spectral Doppler ultrasound can significantly heat biologic tissue because of the relatively high intensities used and the need to hold the beam stationary during examinations. This has significant implications for sensitive neural tissue such as that exposed during spectral Doppler flow studies of fetal cerebral vessels. The amount of ultrasound-induced intracranial heating increases with gestational age and the development of fetal bone; pulsed spectral Doppler ultrasound can produce biologically significant heating in the fetal brain; the rate of heating near bone is rapid, with approximately 75% of the maximum heating occurring within 30 s; blood flow has minimal cooling effect on ultrasound-induced heating of the brain when insonated with narrow focused clinical beams; the threshold for irreversible damage in the developing embryo and fetal brain is exceeded when a temperature increase of 4 degrees C is maintained for 5 min; an ultrasound exposure that produces a temperature increase of up to 1.5 degrees C in 120 s does not elicit measurable electrophysiologic responses in fetal brain; for some exposure conditions, the thermal index (TI), as used in the FDA-approved output display standard, underestimates the extent of ultrasound-induced intracranial temperature increase.

There is also some correlation between Intrauterine Growth Retardation (IGR) and repeated ultrasound usage. In a study between two groups of women, one group (1415 women) had 1 ultrasound at 18 weeks, the others (1419) had 5 ultrasounds total, beginning at 18 weeks. The intensive group had a significantly higher intrauterine growth restriction which showed up as birth weights less than 10th percentile, and birth weights less than 3rd percentile. A follow up study was done on these children. Examinations were done at 1, 2, 3, 5, and 8 years of age on children born without congenital abnormalities and from singleton pregnancies (intensive group n=1362, regular group n=1352). The follow-up rate at 1 year was 85% (2310/2714) and at 8 years was 75% (2042/2714). By 1 year of age and thereafter, physical sizes were similar in the two groups. There were no significant differences indicating deleterious effects of multiple ultrasound studies at any age as measured by standard tests of childhood speech, language, behaviour, and neurological development. INTERPRETATION: Exposure to multiple prenatal ultrasound examinations from 18 weeks gestation onwards might be associated with a small effect on fetal growth but is followed in childhood by growth and measures of developmental outcome similar to those in children who had received a single prenatal scan.

MCA Doppler Assessment
What is it?
A special type of doppler ultrasound, called a Middle Cerebral Artery (MCA) scan, is used to detect fetal anemia. This is a doppler assessment of peak velocity in mid cerebral artery.

When is it done?
MCA scans are done before 35 weeks because after 35 weeks there is a higher risk of getting a false positive (saying baby is anemic when he actually isn't). However, new data suggests that MCA scans may be accurate enough to use up to 37 weeks.

Where is it done?
MCA scans can be done anywhere ultrasound scans are done as long as the machine (and technician) are capable.

Why is it done?
It is done to detect fetal anemia.

How often is it done?
How often an MCA is done depends on each individual case. We started out with one per month, but when our MoM numbers went up (see 'What do the numbers mean?'), we had one every 2 days. Some doctors do them every 2 weeks, every week, or twice a week, depending on your MoM values.

How is it done?
MCA scans are done on your belly just like any other ultrasound. There is a certain angle that the technician needs to get to measure the blood flow in the correct artery of the brain. You will probably see red or blue on the screen since the colors indicate blood flow. Not all technicians are as skilled as others, or as the doctor. You can have different numbers from different techs at the same time. It is always a good idea to go with the numbers from the most experienced person (frequently the doctor). They will usually take an average of 3-5 readings to make sure they get a full picture.

What do the numbers mean?
With an MCA scan, you will get PSV values. Ask for them if they aren't given, or look at the screen during the scan. These PSV values are then plugged into a formula to find your MoM number. You can get a great calculator here:
http://www.perinatology.com/calculators/MCA.htm
A MoM of 1 is normal. 1.5 is generally considered anemic. More charts and data can be found in the section on Fetal Anemia.
After an intrauterine transfusion (IUT) the characteristics of fetal blood are altered because adult red cells are smaller and less rigid and they display an increased tendency for erythrocyte aggregation. Therefore it became pertinent to examine the usefulness of MCA PSV following IUT. But applying a change in the established cutoff level for MCA PSV from 1.50MoM (multiples of the median) in the fetus never transfused to 1.69MoM in previously transfused fetus may be of help.\textsuperscript{16}

What risks are there? 
There are no additional risks with an MCA scan. It is important to note that MCA scans are not fully accurate after a transfusion. It is not uncommon to get false high readings after a transfusion. See the section on Fetal Anemia for more information. There is also a greater chance of getting a false high MoM if the baby is moving or over 35 weeks.

An excellent resource can be found at https://www.scotblood.co.uk/media/101703/pregnant_women_with_red_cell_antibodies_record_of_care.pdf
This is a collection of documents you can use to keep track of your own care. Print it out and take it with you to all appointments. It has places to record titers, PSV and MOM values, and more.

\textbf{Biophysical Profile} 
What is it? 
A Biophysical profile (BPP) is a part of the ultrasound that can be added on if the doctor chooses. It takes 30 minutes and looks at 4 main areas: breathing, gross body movements, muscle tone, and amniotic fluid.

When is it done? 
Biophysical profiles can be done any time after the age of viability (24 weeks), but usually do not begin until after week 32\textsuperscript{7}.

Why is it done? 
A biophysical profile is used to evaluate and monitor a baby's health. The goal of a biophysical profile is to prevent pregnancy loss and detect fetal hypoxia — when the baby is deprived of an adequate oxygen supply — early enough so that the baby can be delivered and not sustain permanent damage\textsuperscript{7}. Since this is always a risk with ISO pregnancies, most women will have at least one done.

How often is it done? 
Biophysical profiles can be done once during pregnancy, or more frequently depending on each individual case. Some doctors have them done once a month, every week or twice a week near the end of pregnancy.

How is it done? 
A Biophysical profile is done just like a regular ultrasound, except they look for a couple of extra things and assign a score to the baby.
What do the numbers mean?
There are 8 points possible, 2 points are assigned for each category. It is an all or nothing score (2 points or 0 points).
Breathing: 1 or more episodes of fetal breathing lasting at least 30 seconds.
Gross Body Movement: 3 or more discrete body or limb movements.
Fetal Tone: One or more episodes of active extension and flexion of an extremity or opening and closing of the hand.
Amniotic Fluid Volume: A 2 x 2 centimeter pocket of amniotic fluid is present.
In this case, a perfect score is 8. Some places add on an extra category to give a possibility of 10 points. If so, they are adding a Non Stress Test (NST).
NST: 2 or more heart rate increases of at least 15 beats per minute. Each increase lasts 15 seconds or more and is seen with movement.

8 to 10 points means that your baby is healthy. A score of 6 to 8 points means that you may need to be retested in 12 to 24 hours. A score of 4 or less may mean the baby is having problems. Further testing will be recommended. A low score may mean that you need extra monitoring, early, or immediate delivery.

Nonstress Test (NST)
What is it?
A nonstress test is a monitoring tool where they put 2 “buttons” on mom's belly to monitor heart rate and uterine contractions. It is basically just monitoring baby's heart rate for an extended amount of time, usually about 20-30 minutes.

When is it done?
Non-stress tests can be done anytime after 26 weeks.

Where is it done?
NSTs are done in the doctor's office or hospital.

Why is it done?
NSTs are done to monitor baby's heart rate and to see if the baby is reactive or if additional tests are needed to check on baby's health.

How often is it done?
Depending on the doctor and situation, NSTs can be done every 3 days, or only when decreased movement is noticed.

How is it done?
Two sensors are put on the belly and secured with 1 or 2 bands. The sensors are hooked up to a machine that will print out a graph with baby's heart rate, mom's heart rate, baby's movements, and uterine contractions.

What do the numbers mean?
If the line is relatively flat, it is considered nonreactive. This is sometimes referred to as baby sleeping. They will try and wake baby up by having mom drink juice or eat something. They
can also use a buzzer on the belly to startle the baby and get movement. In order to pass the NST (reactive), you need 2 or more heart rate increases of at least 15 beats per minute. Each increase lasts 15 seconds or more and is seen with movement.

In the photos below, the baby's heart rate is the top line, mom's heart rate is the faint middle line, the dotted line is the baby's movement (more visible in the reactive picture), and the bottom line is the uterine contractions.

**Nonreactive or asleep**

**Reactive**

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Additional Info
Because iso babies can gradually become anemic, they can compensate for the anemia. This makes it so that it is possible for baby to still pass an NST and still be anemic. It's important to always pay attention to movement, and notify your care provider and/or labor and delivery if you notice decreased movement.

**Amniocentesis**
What is it?
Amniocentesis (amnio) is a procedure where they remove some of the fluid from around baby for testing.

When is it done?
Amniocentesis is usually done between 14 and 20 weeks, but can be done earlier or later in ISO cases.

Where is it done?
Amniocentesis is usually done in the hospital, but some doctor's offices and outpatient facilities are able to do it as well.

Why is it done?
Amniocentesis is done to check baby's blood type and to check for antigens. It is also used to measure the level of bilirubin and to check for lung maturity before delivery.

How often is it done?
Amniocentesis is usually done only once. Occasionally a second amnio will be done to check for lung maturity if early delivery is needed.

How is it done?
The doctor will perform an ultrasound to see where the baby is and to guide the needle. He will clean your abdomen and insert a thin, hollow needle into the uterus. A syringe will be used to take a small amount of fluid and the needle will be removed. You will need to stay still during the procedure. You may notice a stinging sensation or some cramping. The procedure usually takes about 20-30 minutes. Afterwards, baby will be monitored for a few minutes to check on heart rate. Talk with your doctor to find out about any physical restrictions and warning signs to watch for.14

What do the numbers mean?
There are 2 different curves used to plot the values for bilirubin.
Lily Curve – there are 2 versions of the liley curve. The original was for after 27 weeks, however since the bili tends to peak at 23-25 weeks' gestation in unaffected fetuses, a modified zone was developed5.
Queenan curve - “Another curve was developed by Queenan for management of pregnancies before 27 weeks' gestation. A recent comparison of the curves found the Queenan curve to be superior to the Liley curve in overall sensitivity, specificity, and accuracy.”5

[Graphs of Lily and Queenan curves]

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What risks are there?
Amniocentesis has replaced chorionic villus sampling (CVS) in ISO cases. It is considered safer, has a lower risk of increasing antibodies, and more accurately addresses the information that doctors need to know. Amniocentesis carries some risks include miscarriage (1 in 300-500 in the 2nd trimester, possibly higher if done earlier), needle injury (if baby moves into the path of the needle), leaking amniotic fluid, sensitization (if negative for antibodies) or increase in antibodies, and infection. For some women, the risks of amniocentesis are not worth it. It is possible to work with your doctor to have additional monitoring and treat the pregnancy as if it was affected by ISO.
Part 3: Prenatal Complications

Fetal Anemia
What is it?
Fetal anemia is when the baby is anemic (not enough blood). If the baby is too anemic, a blood transfusion is needed.

How is it found?
You can find out if baby is anemic by having an MCA scan and looking at the numbers from that, or from taking a sample of the baby's blood (in utero), and checking the hemoglobin level. With an MCA scan, you will get PSV values. Ask for them if they aren't given, or look at the screen during the scan. These PSV values are then plugged into a formula to find your MoM number. You can get a great calculator here: http://www.perinatology.com/calculators/MCA.htm
A MoM of 1 is normal. 1.5 is generally considered anemic.

The chart below uses PSV values and gestational ages.

Slopes for peak systolic velocity in middle cerebral artery (MCA) for normal fetuses (dotted line), mildly anemic fetuses (thin line), and severely anemia fetuses (thick line).^5

This chart shows with the MoM values.
MCA-PSV (cm/s) versus gestational age. Lines indicate MoM values and anemia range. MoMs between 1.29 and 1.5 can indicate mild anemia. MoM over 1.5 indicates moderate to severe anemia.  

An excellent resource can be found at https://www.scotblood.co.uk/media/101703/pregnant_women_with_red_cell_antibodies_record_of_care.pdf
This is a collection of documents you can use to keep track of your own care. Print it out and take it with you to all appointments. It has places to record titers, PSV and MoM values, and more.

After an intrauterine transfusion (IUT) the characteristics of fetal blood are altered because adult red cells are smaller and less rigid and they display an increased tendency for erythrocyte aggregation. Therefore it became pertinent to examine the usefulness of MCA PSV following IUT. But applying a change in the established cutoff level for MCA PSV from 1.50MoM (multiples of the median) in the fetus never transfused to 1.69MoM in previously transfused fetus may be of help.  

What is the treatment?
The only treatment for fetal anemia is a transfusion. This can be done by an intrauterine transfusion (IUT) if the baby is too young to be delivered (see the section on Prenatal Intervention: Intrauterine Transfusion for more information), or with immediately delivery and transfusion after birth. IUTs are repeated every time baby shows signs of anemia, but usually last for about 2-3 weeks.

What is the best outcome?
Two of the best outcomes involve baby not being anemic enough to need treatment, or making it to delivery with the help of IUTs. Just because you make it to delivery though, does not mean you're out of the woods. ISO babies are at risk of developing late onset anemia from 3 – 12 weeks old, so it is important to have your baby's hemoglobin levels checked until they are at least 12 weeks old. Some babies need checked longer, especially if they have had IUTs. In this case, you may be assigned a neonatologist, or hematologist who will follow your baby closely.
What is the worst outcome?
Untreated fetal anemia is almost always fatal. Even with treatment, it is still possible for the baby to die.

**Fetal Maternal Hemorrhage**

What is it?
Fetal Maternal Hemorrhage (FMH) is when the baby's blood comes out into the mother's bloodstream. This can be a big problem, especially for ISO, because the more of the baby's blood that the mother's body sees, the more antibodies are made. It can cause a jump in titers or additional stress for baby. It can also cause fetal anemia since the blood has left the baby and entered the mother.

How is it found?
Symptoms are subtle and nonspecific. Decreased fetal movement is the only symptom known without additional testing. The Kleihauer–Betke test (KBT for short) measures the amount of fetal blood in mom's bloodstream. FMH can also be diagnosed by flow cytometry, using anti-fetal hemoglobin antibodies (anti-HbF).\(^{17}\)

What is the treatment?
Treatment options include immediate C-section delivery if near term (compromised placenta may not stand up to labor), or possibly an IUT.

What is the best outcome?
In patients who are not yet sensitized to anti-D, Rhogam will be administered. For all others, if not enough blood has been lost to cause anemia, monitoring is all that is needed.

What is the worst outcome?
If anemia needing treatment is detected, an IUT or delivery with transfusion will occur. If not detected, FMH can cause fetal death. FMH accounts for nearly 14% of unexplained fetal deaths and 3% of all fetal deaths.

**Additional Information**
FMH has been demonstrated to occur in as many as 75% of pregnancies, with the frequency increasing as gestation advances and with most cases occurring during delivery. If transplacental passage of fetal erythrocytes is suspected, the rosette screening test is used to determine the presence of a fetomaternal hemorrhage. When a large hemorrhage is suspected, the Kleihauer-Betke test is used to quantify the volume of hemorrhage so that an appropriate dose of anti-D IgG can be administered. Hemorrhage volumes sufficient to cause alloimmunization are produced in 15-50% of births. This volume of fetal blood, which, in more than 50% of intrapartum cases can be as small as 0.1 mL and in rare cases can exceed 30 mL, varies depending on the degree of maternal immune response.\(^{17}\)

As many as 30% of Rh D–negative individuals have been shown to not become alloimmunized, even when challenged with large volumes of Rh D–positive blood.\(^{17}\)
Hemolytic Disease of the Newborn

What is it?
Hemolytic Disease of the Newborn (HDN) is the technical term for what is happening with the baby. Heme = blood, lysis = destruction. It's literally the destruction of the baby's blood cells.

How is it found?
HDN is found through the additional monitoring all mom's with ISO should have. It will be seen with things like rising MoM values, rising titers (not always accurate, MoM should always be relied upon first), worsening biophysical profile, decreasing hemoglobin levels, and evidence of hydrops on the ultrasound.

Indicators for severe hemolytic disease of the newborn (HDN) include mothers who have had previous children with hemolytic disease, rising maternal antibody titers, rising amniotic fluid bilirubin concentration, and ultrasonographic evidence of fetal hydrops (eg, ascites, edema, pleural and pericardial effusions, worsening biophysical profile, decreasing hemoglobin [Hb] levels).

What is the treatment?

Mild hemolytic disease accounts for 50% of newborns with positive direct antibody test results. Most of these newborns are not anemic (cord hemoglobin [Hb] >14 g/dL) and have minimal hemolysis (cord bilirubin < 4 mg/dL). Apart from early phototherapy, they require no transfusions. However, these newborns are at risk of developing severe late anemia by 3-6 weeks of life. Therefore, monitoring their Hb levels after hospital discharge is important.

Moderate hemolytic disease accounts for approximately 25% of affected neonates. Moderate hemolytic disease of newborn is characterized by moderate anemia and increased cord bilirubin levels. These infants are not clinically jaundiced at birth but rapidly develop unconjugated hyperbilirubinemia in the first 24 hours of life. Peripheral smear shows numerous nucleated RBCs, decreased platelets, and, occasionally, a large number of immature granulocytes. These newborns often have hepatosplenomegaly and are at risk of developing bilirubin encephalopathy without adequate treatment. Early exchange transfusion with type-O Rh-negative fresh RBCs with intensive phototherapy is usually required. Use of IVIG in doses of 0.5-1 g/kg in a single or multiple dose regimen have been able to effectively reduce need for exchange transfusion.

Severe hemolytic disease accounts for the remaining 25% of the alloimmunized newborns who are either stillborn or hydropic at birth. The fetal hydrops is predominantly caused by a capillary leak syndrome due to tissue hypoxia, hypoalbuminemia secondary to hepatic dysfunction, and high-output cardiac failure from anemia. About half of these fetuses become hydropic before 34 weeks' gestation and need intensive monitoring and management of alloimmunized gestation as described earlier. Mild hydrops involving ascites reverses with IVTs in only 88% of cases with improved survival but severe hydrops causing scalp edema and severe ascites and pleural effusions reverse in 39% of cases and are associated with poor survival.

What is the best outcome?
With proper treatment, baby can make it to delivery. Depending on the intensity of HDN, there will be different care needed after birth.
What is the worst outcome?
Untreated HDN is almost always fatal, especially in severe cases. It can cause problems after birth if the infant is not treated properly. Titers are not an accurate indicator of HDN, so additional monitoring must be used to check the severity and effects on baby.

**Ascites**
What is it?
Ascites is the buildup of fluid in the space between the lining of the abdomen and abdominal organs. Ascites is a sign of anemia that has gone on to fetal hydrops and must always be taken seriously with swift treatment.

How is it found?
Ascites is found by ultrasound or when examining the baby after birth.

What is the treatment?
Ascites can be treated before birth with an IUT, or after birth by inserting a tube into the belly to remove large volumes of fluid (called a paracentesis). Ascites can be treated before birth with an IUT, or after birth by inserting a tube into the belly to remove large volumes of fluid (called a paracentesis).

What is the best outcome?
With an IUT, ascites can resolve, but the baby must be monitored closely and care must be taken to avoid anemia and hydrops. Repeated IUTs will probably be needed.

What is the worst outcome?
If untreated, ascites can lead to death.

**Fetal hydrops**
What is it?
Hydrops is the end stage of Hemolytic Disease of the Newborn. It is fetal heart failure.

How is it found?
Signs of hydrops will be detectable on an ultrasound, and may be discovered during your MCA scans. Some women also have decreased movement, or no fetal movement. Signs like hepatomegaly, increased placental thickness, and polyhydramnios often precede the development of hydrops (fetal heart failure).

What is the treatment?
IUT or immediate delivery with exchange transfusion are the only treatments.

What is the best outcome?
After delivery, expect a NICU stay, but with proper care, baby can recover.

What is the worst outcome?
If untreated, it is fatal.
Part 4: Prenatal Interventions

There are a variety of interventions that are possible to help ISO babies. Here are some of the more common ones:

**Rhogam**
What is it?
Rhogam is anti-D Immune globulin. It is a shot that can prevent Rh D- women from becoming sensitized\(^1\).

When is it done?
Rhogam is done at 28 weeks, and again within 72 hours of delivery (birth, miscarriage, abortion), amniocentesis, or hemorrhage.

Where is it done?
Rhogam can be given at the hospital or the doctor's office.

Why is it done?
Rhogam is done to prevent sensitization. If your blood type is A-, AB-, B- or O-, you will be given Rhogam to attempt to prevent ISO from happening in the first place. Approximately 17% of Rh D–negative women who deliver an Rh D–positive fetus become sensitized if Rhogam is not administered appropriately.\(^17\) Once you are sensitized however (once they detect anti-D antibodies in your blood), Rhogam does no good and can throw off important test results.

How often is it done?
Rhogam is usually done twice per pregnancy. If you get pregnant again, and aren’t sensitized, you will need to get Rhogam again (even if pregnancy ends in miscarriage or abortion).

How is it done?
The doctor or nurse will give you a shot in either the arm or the butt. Some offer the choice, others prefer the butt because the muscle is larger and it is believed to absorb the medication better.

Because Rhogam has reduced the risk of sensitization to less than 1% of susceptible pregnancies, other antibodies have increased in relative importance. These include antibodies to other antigens of the Rh blood group system (ie, c, C, e, E) and other atypical antibodies known to cause severe anemia, such as anti-Kell (ie, K, k), anti-Duffy (ie, Fy\(^a\)), and anti-Kidd (ie, Jk\(^a\), Jk\(^b\)).

**IUT**
What is it?
An IUT is an Intrauterine Transfusion. It is a blood transfusion for the baby while they are still inside of you. Doctor's usually have great results with IUTs. About 75% of babies with hydrops survive, while more than 90% of babies without hydrops survive\(^19\).

When is it done?
IUTs are generally done between 18 and 35 weeks. Sometimes an IUT can be done as early as 16 weeks, but it is very difficult to do before 18 weeks. After 35 weeks, there is more risk with doing an IUT compared with delivery and a transfusion after birth\textsuperscript{20}.

Where is it done?
IUTs are done in the hospital. Usually in a surgical suite.

Why is it done?
An IUT is done to prevent baby from dying. When the baby is anemic, they do not have enough red blood cells for their body to work properly. Just like how we would die if we lost too much blood, the baby is losing too much blood and needs a transfusion.

How often is it done?
IUTs are done anytime the baby is anemic (not just for ISO). For most doctors, an IUT will be done any time a baby's MoM reaches 1.5 or higher. Some doctors also do them on a schedule since the baby will need more blood as it grows (which is approximately every 3 weeks). Many doctors use a formula to calculate how long the blood will last based on starting and ending counts. How often an IUT is done depends on each individual case and the doctor. Ask your doctor when he thinks an IUT will need to be performed, and how often.

How is it done?
IUT procedures vary by doctor and hospital. In general, you can expect:
- Sedation for you and baby (sometimes paralytic for baby to prevent injury)
- Pain medication and anesthesia to numb the area
- The doctor will use an ultrasound to guide the needle into the umbilical cord of the baby and to monitor his health. If the baby is under too much stress, the procedure will be stopped and further action may be taken.
- Once the needle is in, a sample of baby's blood will be taken and the hemoglobin (or sometimes hematocrit) will be checked. This is called a cordocentesis or percutaneous umbilical cord blood sampling (PUBS for short), and tells the doctor how anemic the baby is and how much blood will be needed.
- Once the amount of blood is decided, the doctor gives that exact amount to the baby and takes a final hemoglobin reading to see how successful the transfusion was.
- The needle is removed and it is off to recovery to rest and wait for the medications to wear off. The doctor will probably continue to monitor baby for a few hours before sending you home. Some doctors prefer an overnight stay, while others do not.
- Depending on the doctor, you may be asked to be on bed rest, or reduced activity for a day or two before resuming your normal routine.

What do the numbers mean?
Normal hemoglobin increases from about 10 to 11 g/dL at 17 weeks, to about 14 to 15 g/dL at term. If baby's hemoglobin is 2 g/dL lower than normal, he is considered mildly anemic, 2-7 g/dL lower is considered moderately anemic, and anything 7 g/dL or more below normal is considered severely anemic\textsuperscript{20}.

Additional Information
IUTs suppress the bone marrow. This means that baby will not make as many red blood cells. In many ways this is good because there will not be baby’s own blood to be attacked by the antibodies. Instead, it will be donor blood that will be safe from attack. Because the bone marrow is suppressed, ISO babies are at risk for late onset anemia. Additional tests after birth will be used to closely monitor baby.

Note: If your baby has had IUTs, the state required newborn blood screening may be off (it may be testing donor blood and not baby’s blood), and should be repeated at 1 year of age.

**Plasmapheresis**
What is it?
Plasmapheresis is the removal of the blood plasma. It is then replaced with antibody free plasma or a plasma substitute.

When is it done?
Plasmapheresis is usually done at 12 weeks.

Where is it done?
Plasmapheresis can be done in the hospital, outpatient infusion center, or doctor’s office.

Why is it done?
Plasmapheresis is done to remove the antibodies from the body. Because antibodies are found in the blood plasma, removing the plasma removes the antibodies. The fewer antibodies there are, the less baby will be attacked. Plasmapheresis does not remove the blood itself. Blood is returned to the patient. Once the antibodies are removed, plasmapheresis is usually followed with IVIG to block any remaining antibodies from crossing the placenta and to keep antibody production down.

How often is it done?
Frequency varies by case, but generally it is done 3 times the first week. This will hopefully remove a majority of the antibodies from Mom's system.

How is it done?
An IV or port is placed in a good artery. This will remove the plasma. A machine separates the plasma from the blood. The blood and replacement plasma will be returned through a second needle placed in the arm or foot.\textsuperscript{32}

**IVIG**
What is it?
IVIG stands for intravenous immunoglobulin. It is a product made from human blood plasma.

When is it done?
IVIG is usually done between 12 and 20 weeks.\textsuperscript{5} It is also sometimes used after birth to treat high bilirubin.\textsuperscript{31} Occasionally doctors will use IVIG when doing an IUT, but this is rare. There was also one case report of giving IVIG to the baby at 30 weeks with anti-M.
Where is it done?
IVIG can be administered at the hospital, outpatient infusion center, doctor's office, or sometimes at your home.

Why is it done?
IVIG blocks some of the receptors in the placenta and makes it so that the antibodies cannot cross over to the baby. It also makes it so that you will produce less antibodies because your body sees IVIG as an antibody and decides that it doesn't need to make any more.\(^5\)

How often is it done?
IVIG is usually done once per week.\(^5\)

How is it done?
IVIG is administered slowly through an IV, or possibly a port depending on how often you need to receive treatment. It can cause side effects like headache, nausea, vomiting, fever and fatigue. Many women report getting multi-day headaches from the IVIG. Your doctor can sometimes give you something for the pain.

Note: Some women have an allergic reaction to the IVIG. If this is the case, talk with your doctor about trying a different brand. Some women have no reaction when they switch brands.

**Erythropoietin**

What is it?
Erythropoietin is a hormone produced by the kidneys. It promotes the formation of red blood cells by the bone marrow. It can be made in a laboratory and used as a treatment for anemia.\(^35\)

When is it done?
Erythropoietin can be done prenatally, or after birth. It appears to be most effective after 24 weeks gestation.\(^34\).

Where is it done?
Erythropoietin can be administered at the hospital, outpatient infusion center, or doctor's office.

Why is it done?
Erythropoietin is done to help prevent late onset anemia. Especially in IUT babies, the bone marrow is suppressed, causing low levels of erythropoietin, and red blood cells are not being made. Erythropoietin is given to decrease the need for a transfusion.\(^33\)

How often is it done?
Varies by doctor.

How is it done?
Erythropoietin is administered slowly through an IV, or possibly a port depending on how often you need to receive treatment.

**Phenobarbital**
What is it?  
Phenobarbital is a narcotic and sedative drug.

When is it done?  
Phenobarbital is taken in the last couple of weeks of pregnancy.

Where is it done?  
Phenobarbital can be taken at home.

Why is it done?  
Phenobarbital improves liver function. When blood cells break down, they turn into bilirubin, which is removed by the liver. Getting the liver to mature faster can help reduce the amount of bilirubin and reduce jaundice.

How often is it done?  
Phenobarbital is typically taken 3 times per day for the last 10 days of pregnancy (assuming planned induction/delivery date).

How is it done?  
Phenobarbital is a pill you swallow.

**Steroid Shots**
What is it?  
Steroid shots are an injection of corticosteroids, a synthetic form of natural human steroids.

When is it done?  
Steroid shots are usually done between 25 and 33 weeks, but may be done later depending on situation.  

Where is it done?  
Steroid shots can be given in the hospital or doctor's office.

Why is it done?  
Steroid shots are done to help baby's lungs mature more quickly. This reduces the risk of complications and death from prematurity.

How often is it done?  
Steroid shots are done in “courses”. One course is 2 injections given about 24 hours apart.

How is it done?  
A shot is given into the arm, leg, or butt.
Early delivery
What is it?
Early delivery is when the baby is delivered prior to 38 weeks. This happens when it's in the best interest of the baby to be outside of the womb, instead of inside (and under attack) any longer.

When is it done?
Early delivery can occur at any time once the age of viability, 24 weeks, is reached.

Where is it done?
Early delivery happens in the hospital, preferably one with a high level NICU. It generally involves a c-section, but not always. In which case, you will be taken to a surgical suite.

Why is it done?
Early delivery happens when the baby is in too much distress. It can happen if you go into labor and it cannot be stopped, or if you have complications from an IUT. It can also happen if baby's health is deteriorating too quickly, or in cases of a hemorrhage. Regardless of why it happens, there will be an entire team of doctors closely watching your little one and giving him the treatment he needs.

It is always a good idea to talk with your doctor about the possibility of an early delivery to find out what his criteria for an early delivery is, and what the plan would be. If possible, try to tour the hospital's birthing area and the NICU. Knowing your way around and meeting some of the highly trained staff can go a long way towards reassuring you and taking off some of the stress/fear of the unknown.
Part 5: Delivery

You made it! Baby is here (almost). Here are some things to keep in mind when delivering an ISO baby. If you haven't already, it is helpful to keep a notebook and write down all your questions (and the doctor's answers) about birth and the hospital's processes. Also, make sure they will have antigen negative blood ready for baby. If you've got anti-Kell, baby needs kell negative blood. If he needs a transfusion, you don't want to wait several hours and risk brain damage while they find blood.

Induction
Depending on the severity of your ISO, and other factors in your pregnancy, you may be scheduled for an induction. These can occur at any number of weeks, but are typically 32-37 weeks. There are a variety of methods used for induction. Ask your doctor for additional resources, what the procedures are, and any other questions you may have.

Delayed Cord Clamping
Delayed cord clamping is a practice where the umbilical cord is not immediately clamped or cut after birth. The delay time can range from a few minutes up to half an hour. Generally the cord will be limp, pale, and no longer pulsing when clamped. Up to 1/3 of the baby's blood is in the placenta at the time of birth. Delayed clamping allows the baby to get his extra blood back from the placenta. Keep in mind though that with the blood comes the antibodies too.

Our MFM recommended it. Our ISO case was not severe, and there was greater benefit to our baby getting the extra blood than the risk from the extra antibodies. He did have a significant drop in his hemoglobin levels (3 whole points), but because he had his extra blood, it was not low enough to need a transfusion. Some MFM recommend against it. In severe cases of ISO, your antibodies will do more harm than the good the extra blood will do. In this case, it is preferable to give the baby a transfusion with clean donor blood than to give him blood with more antibodies. Talk with your doctor and decide what is best for you and your baby.

Vaginal Birth
Even if you have ISO, you can still have a vaginal birth. For us, it meant there was an entire team of people in the delivery room (9+), including a midwife, obstetrician, neonatologist, some people from the special care nursery, lab tech, and several nurses. Talk with your doctor and see what they recommend, and who they recommend be present. Blood needs to be drawn at birth, so have someone, such as your support person, make certain that it is done. Since it is not commonly done everywhere, it can be easy for delivery personnel to forget to do the immediate drawn.

Cesarean Birth
Cesarean sections, C-sections for short, can happen at any time for ISO babies. Talk with your doctor about a contingency plan for if you need a C-section, who will be present, what will happen with the baby, will you get to hold him/her, etc. Delayed cord clamping is also possible with a C-section. Keep in mind that a C-section is still major surgery and you will...
probably feel out of sorts for a few days. It's a good idea to have some extra help with moving, caring for the baby (and other children), housework, etc.

**Special Care/NICU**

Regardless of how you deliver your baby, an infant born to an isoimmunized mother shows clinical signs based on the severity of the disease. The typical diagnostic findings are jaundice, pallor, enlarged liver and/or spleen (hepatosplenomegaly), and fetal hydrops in severe cases. The jaundice typically manifests at birth or in the first 24 hours after birth with rapidly rising unconjugated bilirubin level. Occasionally, conjugated hyperbilirubinemia is present because of placental or hepatic dysfunction in those infants with severe hemolytic disease.⁵

For this reason, you should talk to your doctor about delivering in, or near, a hospital with a NICU or special care team equipped to take care of the baby. One of the worst things is to be stuck at one hospital while your baby is sent to another hospital (possibly hours away), without you. We have 2 hospitals in my town, one with a NICU, and one without. I chose to deliver at the one without the NICU, but I was informed beforehand that if my baby needed a transfusion or special care, the baby would be transferred, but I may not be (depending on how busy the hospital was).
Part 6: After Birth Blood Testing – All About Baby

Make sure it is microtesting. It is common that the cumulative blood loss due to specimens taken during the first week of life equals or exceeds the neonate’s circulating blood volume. It is, therefore, imperative to try to minimize the blood lost due to sampling by using, for example, diagnostic tests based on micro methods that require less blood and by not withdrawing more blood than strictly necessary for the analyses required.  

To get an idea of how much blood your baby has, see the chart below.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Blood Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature infants</td>
<td>100 mL/kg</td>
</tr>
<tr>
<td>Term newborns</td>
<td>85-90 mL/kg</td>
</tr>
<tr>
<td>Greater than 1 month</td>
<td>80 mL/kg</td>
</tr>
<tr>
<td>Greater than 1 year</td>
<td>70 mL/kg</td>
</tr>
</tbody>
</table>

Note: If your baby has had IUTs, the state required newborn blood screening may be off (it may be testing donor blood and not baby’s blood), and should be repeated at 1 year of age.

**Direct Coombs test**

What is it?

Also called the Direct Antiglobulin Test (DAT)

The direct antiglobulin test (DAT) is performed to determine whether an anemic patient with evidence of hemolysis has isoimmune hemolytic anemia. If baby has a positive direct coombs test, there are antibodies already bound to and attacking the red blood cells. These antibodies can be removed from the RBC and each specific antibody can be identified. While the indirect coombs test shows if Mom is making antibodies and has them floating around loose in her blood, the direct coombs test shows if the antibodies are present in the baby’s blood and bound to the red blood cells.

When is it done?

This test should be run at birth.

Where is it done?

This test will usually be done in the hospital.

Why is it done?

This test is done to see if there are any of mom's antibodies bound to and attacking the baby's blood.

How is it done?

This test can be done by taking blood from the umbilical cord or through a heel stick.

How often is it done?

For iso babies, this test is usually only performed once at birth.
What do the results mean?
A negative Direct Coombs means that there are not antibodies bound to the baby's blood. A positive Direct Coombs means that there are antibodies attacking the baby's blood. A positive result will mean that your baby needs additional testing and monitoring.

Additional Information
Occasionally, especially with IUTs, the baby may have a negative direct coombs. In this case, an indirect coombs may be run to see if there are antibodies in the blood that aren't bound and attacking the cells. Indirect coombs should also be run in the case of anti-C/anti-c.

Hemoglobin
What is it?
Hemoglobin is a protein in red blood cells that carries oxygen. A blood test can tell how much hemoglobin you have in your blood. It is usually abbreviated Hb or Hgb and is measured in grams per deciliter. It is usually done as part of a complete blood count (CBC).

When is it done?
Hemoglobin should be tested at birth, and frequently thereafter.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
Hemoglobin is checked to make sure that the baby is not anemic.

How is it done?
This test can be done by taking blood from the umbilical cord or through a heel stick.

How often is it done?
How often hemoglobin is checked depends on each case. Usually it is checked every 1-2 days in the hospital, or if baby is showing symptoms of being anemic. If baby's Hgb is dropping, more frequent checks will be needed. As baby gets older, less frequent checks are usually needed. Because ISO babies are at risk for developing late onset anemia, hemoglobin levels should be checked until at the baby is at least 12 weeks old.

What do the results mean?

Selected Normal Pediatric Laboratory Values – Hemoglobin

<table>
<thead>
<tr>
<th>Age</th>
<th>Females (g/dL)</th>
<th>Males (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>12.7-18.3</td>
<td>14.7-18.6</td>
</tr>
<tr>
<td>6 months – 2 years</td>
<td>10.4-12.4</td>
<td>10.3-12.4</td>
</tr>
</tbody>
</table>

The calculated minimum acceptable hemoglobin concentration is 6 g/dl for children and adults, 12 g/dl for preterm infants and 11 g/dl for full-term neonates at birth. The minimum
hemoglobin concentration should be 2 g/dl higher in patients who require increased oxygen or suffer from other serious disorders. Because of how the baby deals with oxygen, the minimum value of 12 g/dl or 11g/dl decreases by approximately 1 g/dl each week for 5 or 6 weeks until the minimum of 6g/dl for children and adults is reached.\textsuperscript{25}

If numbers are high
If the hemoglobin is above 10 g/dL (in the absence of specific risk factors related to the patient’s clinical characteristics) there is no need to transfuse red blood cells. Hemoglobin should still be checked regularly.

If numbers are low
Depending on how low the numbers are, treatment may be non urgent or urgent. If non-urgent, the baby will be monitored to see if he will start to make his own blood cells and recover from anemia on his own. If treatment is urgent, a blood transfusion will be performed.

Subjects with Hb concentrations below 6 g/dL almost always require transfusion therapy. In stabilized patients with Hb values between 6 and 10 g/dL, the decision whether to transfuse is based on an evaluation of clinical status; patients with values above 10 g/dL rarely require transfusion.

Indications for transfusion: Hemoglobin concentration of 4 g/dL or less (or hematocrit 12%), whatever the clinical condition of the patient or Hemoglobin concentration of 4-6 g/dl (or hematocrit 13-18%) if any the following clinical features are present: Clinical features of hypoxia, Acidosis (usually causes dyspnoea), Impaired consciousness\textsuperscript{27}

Additional Information
You should be wary of giving your ISO baby iron supplements. Most ISO babies have normal or high iron levels and serious damage or death can occur if they are given iron supplements. \textbf{Unless the Ferritin level is specifically tested, do not give iron.}

\textbf{Hematocrit}
What is it?
Hematocrit is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells\textsuperscript{28}. It is abbreviated HCT or Htc, and may be done as part of a complete blood count (CBC).

When is it done?
Hematocrit should be tested at birth, and frequently thereafter.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
Hematocrit is checked to make sure that the baby is not anemic.
How is it done?
This test can be done by taking blood from the umbilical cord or through a heel stick.

How often is it done?
How often hematocrit is checked depends on each case. Usually it is checked every 1-2 days in the hospital, or if baby is showing symptoms of being anemic. If baby's hematocrit is dropping, more frequent checks will be needed. As baby gets older, less frequent checks are usually needed. Because ISO babies are at risk for developing late onset anemia, hematocrit levels should be checked until at least 12 weeks old.

What do the results mean?

Selected Normal Pediatric Laboratory Values - Hematocrit

<table>
<thead>
<tr>
<th>Age</th>
<th>Females (%)</th>
<th>Males (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>37.4-55.9</td>
<td>43.4-56.1</td>
</tr>
<tr>
<td>6 months – 2 years</td>
<td>31.2-37.2</td>
<td>30.9-37.0</td>
</tr>
</tbody>
</table>

If numbers are high
Great, a transfusion may not be needed, but the hematocrit levels should still be checked regularly until at least 12 weeks of age. It should also be remembered that patients with acute hemorrhage can have normal, or even high, Htc values until the plasma volume is restored; the clinical evaluation of the patient in this situation is, therefore, extremely important.

If numbers are low
Depending on how low the numbers are, treatment may be non-urgent or urgent. If non-urgent, the baby will be monitored to see if he will start to make his own blood cells and recover from anemia on his own. If treatment is urgent, a blood transfusion will be performed.

Indications for transfusion: Hematocrit 12%, whatever the clinical condition of the patient or Hematocrit 13-18% if any the following clinical features are present: Clinical features of hypoxia, Acidosis (usually causes dyspnoea), Impaired consciousness. Some doctors will transfuse at 20-25% for symptomatic anemia, while others will transfuse at 20% for asymptomatic anemia.

After transfusion, the hematocrit goal will be >25% for anemia with symptoms, and >20% for anemia without symptoms.

**Ferritin**

What is it?
Ferritin is a protein that carries iron. Most of the body’s iron is bound to ferritin. A blood test can tell how much ferritin you have in your blood. A high ferritin level means baby may be in danger of an iron overdose. Most iso babies have a normal or high ferritin level depending on if they had IUTs. IUTs are done with adult blood cells that are very rich in ferritin. It is very important even if baby has not had a transfusion that you not give iron supplements or vitamins with iron in them until you have the ferritin level tested.
When is it done?
Ferritin is tested at request. It is not part of a normal blood draw unless the provider is looking for additional causes of anemia.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
Ferritin is checked to find out the baby’s iron levels and to rule out iron deficiency anemia.

How is it done?
This test can be done by taking blood from the umbilical cord, or through a vein.

How often is it done?
How often ferritin is checked depends on each case. Most of the time the doctor will only draw it once unless the levels are really high.

What do the results mean?

<table>
<thead>
<tr>
<th>Age</th>
<th>Ferritin ng/mL</th>
<th>Ferritin mcg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>25-200</td>
<td>25-200</td>
</tr>
<tr>
<td>1 to 5 months</td>
<td>50-200</td>
<td>50-200</td>
</tr>
</tbody>
</table>

If numbers are high
High ferritin levels (over 1,000 ng/mL) can mean a large buildup of iron in the body. With iso babies, this is usually called acquired hemochromatosis, and can be caused by multiple transfusions. Too much iron in the body’s organs can affect how the organ works.

If numbers are low
Low ferritin levels generally mean that anemia is iron deficiency anemia and can be helped with iron supplements.

Additional Information
You should be wary of giving your ISO baby iron supplements. Most ISO babies have normal or high iron levels and serious damage or death can occur if they are given iron supplements. Unless the Ferrin level is specifically tested, it is best to avoid them. It is especially important to avoid them until the transfusion window has closed. You will also want to check on the amount of iron in formula if you formula feed. Try to choose a no or low iron formula.

**Reticulocyte Count**
What is it?
A reticulocyte count (retic) is a blood test that measures how fast specific red blood cells (RBCs), called reticulocytes, are being made by the bone marrow and released into the blood.
When is it done?
Retic should be tested at birth, and frequently thereafter.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
This test is done to see how well the bone marrow is working at making red blood cells and to check to see if treatment for anemia is working. For example, a higher reticulocyte count means that treatment to reverse the anemia is working.

How is it done?
This test can be done by taking blood from the umbilical cord or through a heel stick.

How often is it done?
How often retic is checked depends on each case. Usually it is checked every 1-2 days in the hospital, or if baby is showing symptoms of being anemic. If baby's retic is dropping, or not increasing properly, more frequent checks may be needed. As baby gets older, less frequent checks are usually needed.

What do the results mean?
The retic is given as the percentage of RBCs that are reticulocytes. The normal range can vary from lab to lab, but this is a general guide. Newborns have a normal reticulocyte count of 2.5% to 6.5%. In normal babies, this value drops within 2 weeks to 0.5% to 2.0%. In ISO babies, it is normal for the retic to remain higher for longer as the baby combats anemia.

If numbers are high
A high retic means more red blood cells are being made by the bone marrow.

If numbers are low
A low retic means that fewer RBCs are being made. Retic can be low after baby has had an IUT. It is actually beneficial for babies to have a retic of 0 at certain times. This is when you have replaced the baby's blood with donor blood, and do not want the baby making any more of his own blood cells until after he is delivered and can have an exchange transfusion to get rid of the antibodies. If there are none of the baby's blood cells, then there is nothing for the mother's antibodies to attack. It can take a while for babies to begin to make their own red blood cells after delivery, so the retic will be checked closely for several weeks.

Bilirubin test
What is it?
The bilirubin test is how they will monitor baby's bilirubin (bili) and decide how to treat the baby.

When is it done?
Bilirubin should be tested at birth, and frequently thereafter.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
The bilirubin test is done to see how much bilirubin is in the baby's system. Bilirubin can build up with the destruction of red blood cells, and can cause brain damage.

How is it done?
This test can be done by taking blood from the umbilical cord or through a heel stick. Occasionally a device called a bilichek can be used to check the bilirubin by scanning the infant's forehead. Some doctors do not believe the bilichek is accurate enough for babies with ISO and prefer the blood draws. Others will use a mixture of both, alternating heel sticks with the bilichek.

How often is it done?
Bilirubin should be checked immediately after birth and as frequently as every 4 hours afterwards. If the levels aren't too high, your doctor may do every 12 hours until discharge, and then daily for the first week or two. Bilirubin tends to peak around day 4 or 5 with ISO babies. One thing to watch out for, is rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended. Bilirubin levels will still be checked periodically by the doctor for the first month or so of baby's life (weekly or biweekly after treatment ends).

What do the results mean?
Below is the common bilirubin graph. First determine your baby's age in hours, then plot your results.
You can also use the tools at http://bilitool.org/ to plug in your baby's information.

Bilirubin comes as 3 parts: total serum bilirubin, indirect bilirubin (sometimes called unconjugated), and direct bilirubin (conjugated). Healthy term infants may tolerate serum bilirubin levels of 25 mg/dl. Infants are more prone to the toxic effects of bilirubin if they have any of the following: acidosis, prematurity, septicemia, hypoxia, hypoglycemia, asphyxia, hypothermia, hypoproteinemia, exposure to drugs that displace bilirubin from albumin, or hemolysis (ISO). For ISO babies (and all babies with at least one of the risk factors above), use the values listed under the complicated.

TOTAL bilirubin should be used when judging baby. DO NOT subtract the direct (conjugated) from the total. This is an old practice and is not recommended by the American Academy of Pediatrics.

Phototherapy should be started anytime there's a positive coombs test and the cord blood is more than 3.5 mg/dL.

If numbers are high
This is the transfusion graph. First determine your risk. If you are having a sensitized pregnancy, you are either medium or high risk. Then determine your baby's age and plot their numbers. If at birth your bili levels are already over 14, there's a good chance you're headed for an exchange transfusion.

The following are indications for exchange transfusion:
- Severe anemia (Hb < 10 g/dL)
- Cord bilirubin > 4 mg/dL.
- Rate of bilirubin rises more than 0.5 mg/dL despite intensive phototherapy
- Severe hyperbilirubinemia[59]
- Serum bilirubin-to-albumin ratio exceeding levels that are considered safe⁵

IVIG has been shown to reduce the need for an exchange transfusion.

If levels are high, phototherapy and supportive treatment should begin immediately because jaundice severe enough to lead to kernicterus (permanent brain damage), may develop. The goal of therapy is to prevent the concentration of indirect bilirubin from reaching neurotoxic levels.

If numbers are low
Great! You’re probably good to go but the bilirubin levels will still be checked periodically by the doctor for the first month or so of baby’s life.

Additional Information
Bilirubin tends to peak around days 4-6 with ISO babies. One thing to watch out for, is rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended.

Don't delay on bilirubin treatment because it can cause irreparable brain damage and Kernicterus. See the sections on Jaundice and Kernicterus in part 7. One of the complications of bilirubin is Bronze Baby Syndrome (part 7).

**Neutrophil Count**
What is it?
The neutrophil count is how they will monitor baby's neutrophils and decide how to treat the baby.

When is it done?
The neutrophil count should be tested at birth, and every 1-2 weeks depending on numbers.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
Up to half of all iso babies develop isoimmune neonatal neutropenia (INN)\(^38\). This test checks to make sure that baby is not neutropenic.

How is it done?
Neutrophil counts are done from a blood sample. Frequently they are part of a CBC, but check with your doctor or lab to make sure.

How often is it done?
It is done every 1-2 weeks depending on numbers. If checking baby for late onset anemia, it would be easy to check the neutrophil count at the same time. Low neutrophil count can persist for up to 28 weeks.

What do the results mean?
Below are two tables for the range of neutrophils in term and preterm infants.\(^41\)

**Normal Laboratory Values for Neonates – Term**

<table>
<thead>
<tr>
<th>Values</th>
<th>Cord</th>
<th>1-12 hours</th>
<th>12-24 hours</th>
<th>3-10 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutro x 10(^9)/L</td>
<td>6-26</td>
<td>6-28</td>
<td>5-21</td>
<td>1.5-10</td>
</tr>
</tbody>
</table>

**Normal Laboratory Values for Neonates – Preterm**
<table>
<thead>
<tr>
<th>Value</th>
<th>Birth</th>
<th>12 hours</th>
<th>24 hours</th>
<th>1 week</th>
<th>2 weeks</th>
<th>1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutro x 10^9/L</td>
<td>6-26</td>
<td>6-28</td>
<td>5-21</td>
<td>1.5-10</td>
<td>1-9.5</td>
<td>1-9</td>
</tr>
</tbody>
</table>

If numbers are high
Your baby is not neutropenic.

If numbers are low
Neutropenia is defined as an absolute neutrophil count (ANC) of less than 1.5 (x10^9/L)

Additional Information
Neutropenia resolves within 11 weeks, but can persist as long as 28 weeks.

**Platelet Count aka Thrombocyte count**

What is it?
The platelet count is how they will monitor platelets and decide how to treat the baby.

When is it done?
The platelet count should be tested at birth, and every 1-2 weeks depending on numbers.

Where is it done?
This test is usually done in the hospital or at a laboratory.

Why is it done?
Iso babies are at risk of developing isoimmune thrombocytopenia. This risk is higher if baby had to have IUTs.

How is it done?
Platelet counts are done from a blood sample. Frequently they are part of a CBC, but check with your doctor or lab to make sure.

How often is it done?
It is done every 1-2 weeks depending on numbers. If checking baby for late onset anemia, it would be easy to check the platelet count at the same time.

What do the results mean?
Thrombocytopenia is defined as a platelet count of less than 150 x 10^9/L. This value is the same regardless of age.

If numbers are high
Your baby is not thrombocytopenic.

If numbers are low
Thrombocytopenia is defined as a platelet count of less than 150 x10^9/L.
**Newborn Blood Screening**

What is it?
The newborn blood screening is a required test to check for dangerous medical conditions.

When is it done?
This test is done sometime after birth and before discharge.

Where is it done?
This test is usually done in the hospital.

Why is it done?
This test is required by law in the USA.

How is it done?
A heel stick is done and drops are placed on a card to be sent for testing.

How often is it done?
Usually once, BUT if you baby has had transfusions, IUT or post birth, it is advisable to retest at 1 year old.

What do the results mean?
Here’s the interesting part - if you’ve had IUTs or post birth transfusions (before the newborn screen), your baby has donor blood. The newborn screening isn’t just testing your newborn’s blood, but the blood of all the donors for all the transfusions. You can redo the newborn testing at 4 months, but in cases of severe antibodies with multiple post birth transfusions, waiting until 1 year old is good to make sure that all the donor blood is out of baby’s system.
Part 7: After Birth Complications

Anemia
What is it?
Fetal anemia is when the baby is anemic (not enough blood). If the baby is too anemic, a blood transfusion is needed.

How is it found?
You can find out if baby is anemic by blood draws to check the hemoglobin or hematocrit level.

Selected Normal Pediatric Laboratory Values – Hemoglobin

<table>
<thead>
<tr>
<th>Age</th>
<th>Females (g/dL)</th>
<th>Males (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>12.7-18.3</td>
<td>14.7-18.6</td>
</tr>
<tr>
<td>6 months – 2 years</td>
<td>10.4-12.4</td>
<td>10.3-12.4</td>
</tr>
</tbody>
</table>

Selected Normal Pediatric Laboratory Values - Hematocrit

<table>
<thead>
<tr>
<th>Age</th>
<th>Females (%)</th>
<th>Males (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>37.4-55.9</td>
<td>43.4-56.1</td>
</tr>
<tr>
<td>6 months – 2 years</td>
<td>31.2-37.2</td>
<td>30.9-37.0</td>
</tr>
</tbody>
</table>

What is the treatment?
The treatment for anemia is a transfusion. Depending on what symptoms baby is showing, some doctors will choose to delay transfusion to give the baby time to make more of his own blood cells. Transfusions are done through an IV into the arm, umbilical cord, or head. While this may be distressing for mom to watch, it is easier on the baby.

IRON IS NOT AN ACCEPTABLE TREATMENT FOR AN ISO BABY. The anemia faced by an iso baby is caused by red blood cell destruction, not iron deficiency. Many iso babies have normal or even high levels of iron and can be easily overdosed and killed from supplements. Your baby should never be given iron supplements without having his ferritin levels checked. Normal Ferritin levels are 25-200 ng/mL.

What is the best outcome?
After treatment, many babies begin doing much better. ISO babies are at risk of developing late onset anemia from 3 – 12 weeks old, so it is important to have your baby's hemoglobin levels checked until they are at least 12 weeks old. Some babies need checked longer, especially if they have had IUTs. In this case, you may be assigned a neonatologist, or hematologist who will follow your baby closely.

What is the worst outcome?
Untreated anemia can be fatal. Even with treatment, it is still possible for the baby to die.
Jaundice
What is it?
Jaundice is the buildup of bilirubin in the bloodstream. It can occur from a variety of causes, but the red blood cell destruction from iso can be very severe.

How is it found?
You can find out if baby is jaundice by blood draws to check the bilirubin level.

Bilirubin tends to peak around days 4-6 with ISO babies. One thing to watch out for, is rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended.

What is the treatment?
The treatment for jaundice is phototherapy and possibly a transfusion. Depending on what symptoms baby is showing, some doctors will choose to delay transfusion to give the baby time to take care of things himself. Transfusions are done through an IV into the arm, umbilical cord, or head. While this may be distressing for mom to watch, it is easier on the baby.

Note: Iso jaundice is not the same as breastfeeding jaundice. Breastfeeding will not make your iso baby's jaundice worse.

Conversely, if the baby is breastfeeding well and appears healthy and vigorous, this can be reassuring. The mother may have breastfed previous babies who also developed significant jaundice. If so, she may be one of the approximately 20-40% of women who have above-average levels of beta-glucuronidase in their breast milk, which potentiates and prolongs hyperbilirubinemia in their breastfed babies.37

In the presence of Rh isoimmunization, a cord bilirubin level of more than 5 mg/dL or a rate of rise in serum bilirubin of more than 0.5-1 mg/dL/h is predictive of the ultimate need for exchange transfusion.37

Parenteral administration of immunoglobulin G (IVIG) has been shown in controlled clinical trials to reduce the need for exchange transfusion in both Rh and ABO immune-mediated hemolytic disease. Its mechanism of action is not entirely clear. Administration in hyperbilirubinemia resulting from isoimmune hemolytic disease that is unresponsive to phototherapy and/or is approaching exchange level has been recommended by the AAP in its 2004 revised clinical practice guideline.
Note: If IVIG was used, it can affect vaccines. No live virus vaccines for at least 7-12 months after last infusion. My dr said Ivig blocks antibodies from attaching to the cells, so any made by the body in response to the vaccine wouldn't stay, and the shots would need to be started over again. See the section on IVIG for more information.

What is the best outcome?
With proper care and treatment, baby will remove the destroyed blood cells from their system and the bilirubin levels will drop. Treated properly, there are usually no long term problems from bilirubin.

What is the worst outcome?
Untreated jaundice can cause brain damage, Kernicterus, Cerebral Palsy, BIND, and more. It can ultimately lead to death.

**Bronze Baby Syndrome**

What is it?
Bilirubin in the blood is found in two forms: conjugated (direct) and unconjugated (indirect). Conjugated bilirubin has already been bound and is ready to be excreted by the body. In bronze baby syndrome, there is a build up of conjugated bilirubin that can’t get out of the body fast enough. This causes the baby to turn green, gray, bronze, or black.

How is it found?
A visual check of the baby and a blood test showing the conjugated bilirubin will confirm bronze baby syndrome.

Bilirubin tends to peak around days 4-6 with ISO babies. One thing to watch out for, is rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended.

What is the treatment?
Treatment options include exchange transfusion, and IVIG. In some cases the removal of lights will help. Lights are there to help bind the bilirubin and get it ready to move out of the body. In bronze baby syndrome, the bilirubin is already bound, it just can’t get out of the body fast enough. Removing lights MUST be weighed carefully against baby’s trend and rate of rise, whether or not bili has peaked, and if there’s been significant rebound with light withdrawal. The presence of conjugated bilirubin and bronze baby syndrome does not mean that you should not continue phototherapy, especially if baby is still near the exchange threshold.

Bilirubin tends to peak around days 4-6 with ISO babies. One thing to watch out for, is rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended.
What is the best outcome?
Bronze baby syndrome is not harmful and will gradually resolve over a few weeks.

What is the worst outcome?
While bronze baby syndrome itself is not harmful, it can be a sign of other bilirubin issues such as kernicterus and bilirubin needs to be monitored closely.

Kernicterus
What is it?
Kernicterus is bilirubin staining on the baby's brain. It can cause several neurological problems.

Immune hemolytic disease, most often Rh isoimmunization (erythroblastosis fetalis), is the prototype etiology for kernicterus\(^37\).

How is it found?
Hematologic laboratory evaluation is the cornerstone of evaluation of the baby with hyperbilirubinemia. Although jaundice can be appreciated clinically, observation alone is not a reliable method to assess the severity or estimate risk factors for the infant.\(^37\) Your baby must be blood tested.

When assessing possible kernicterus, remember that a history of risk for hemolytic disease can be an important clue to a neonate's increased risk of pathologic hyperbilirubinemia, particularly Rh antigen incompatibility between mother and baby\(^37\).

Note: Male infants have consistently higher levels of serum bilirubin than do female infants. Among infants reported in the US kernicterus registry, 67% of the patients were male\(^37\).

Theoretically, most cases of kernicterus may be completely prevented by initiation of phototherapy in every baby shortly after birth. Therefore, this devastating neurologic disease could be prevented most of the time. As such, a significant component of medicolegal liability is introduced into the management of hyperbilirubinemia. Clinical reports of kernicterus in the absence of profound hyperbilirubinemia, coupled with the lack of definitive standards of care for the initiation of phototherapy, further complicate this exposure. As with all medical care, conformity with published clinical guidelines, rationale for departure from accepted clinical norms, and good documentation are the best defenses.

Many hospitals have developed clear documents that outline the standard for evaluation and treatment of hyperbilirubinemia, and some of these risk-management approaches have appeared in the medical literature. That being said, learned minds the world over acknowledge the lack of evidence directing best practice for neonatal hyperbilirubinemia and the complexities that will always demand individualized treatment approaches.[18, 19]

What is the treatment?
The definitive method of removing bilirubin from the blood is via exchange transfusion. This is currently the indicated approach in the presence of clinical bilirubin-induced neurologic dysfunction (BIND) when the bilirubin level has reached dangerous levels despite preventive
efforts. Phototherapy is the most common method aimed at prevention of bilirubin toxicity. In the presence of Rh isoimmunization, a cord bilirubin level of more than 5 mg/dL or a rate of rise in serum bilirubin of more than 0.5-1 mg/dL/h is predictive of the ultimate need for exchange transfusion.

Parenteral administration of immunoglobulin G (IgG) has been shown in controlled clinical trials to reduce the need for exchange transfusion in both Rh and ABO immune-mediated hemolytic disease. Its mechanism of action is not entirely clear. Administration in hyperbilirubinemia resulting from isoimmune hemolytic disease that is unresponsive to phototherapy and/or is approaching exchange level has been recommended by the AAP in its 2004 revised clinical practice guideline.

To help ensure that infants may reach their maximum neurodevelopmental potential, referring babies with bilirubin-induced neurologic dysfunction (BIND) to a neurodevelopmental pediatrician skilled in caring for these patients is important. Early identification of and intervention for neurodevelopmental deficits has been shown to positively impact an infant's long-term neurodevelopmental prognosis.

What is the best outcome?
The outcome with Kernicterus varies greatly. Please refer to a Kernicterus source for more information, such as: http://www.kernicterus.org or http://www.pic-k.org or http://emedicine.medscape.com/article/975276-overview

What is the worst outcome?
Kernicterus can kill.

**BIND**

What is it?
Bilirubin-induced neurologic dysfunction (BIND) is the term applied to the spectrum of neurologic abnormalities associated with hyperbilirubinemia. It can be further divided into characteristic signs and symptoms that appear in the early stages (acute) and those that evolve over a prolonged period (chronic).

Please refer to another source for more information, such as: http://www.kernicterus.org or http://www.pic-k.org, or http://emedicine.medscape.com/article/975276-overview

**Neutropenia**

What is it?
Neutropenia is an abnormally low number of white blood cells. These cells, which are called neutrophils, help the body fight infection.

How is it found?
Neutropenia is found through a CBC and differential blood test.

What is the treatment?
In many cases, neutropenia goes away on its own as the bone marrow recovers and begins to produce enough white blood cells. In rare cases when the neutrophil count is low enough to be life threatening, the following treatments may be recommended: Medicines to stimulate white blood cell production, Antibodies from donated blood samples (intravenous immune globulin)\(^{40}\)

In severe cases, the granulocyte colony-stimulating factor (G-CSF) has been successfully used to increase the neutrophil counts although resistance to G-CSF has occurred due to anti-HNA-2 isoantibodies. On the one hand G-CSF resistance can be the result of reduced neutrophil production in the bone marrow as HNA-2 expression begins very early in myelopoiesis, on the other hand, G-CSF causes increased HNA-2 expression on the neutrophil surface promoting antibody binding and phagocytosis by macrophages. In these cases high doses of intravenous immunoglobulin (IVIG) might be an alternative although ineffective IVIG treatment of NIN has been repeatedly reported. \(^{39}\)

What is the best outcome?
The baby's outlook depends on the cause of the neutropenia. Isoimmune neutropenia will also get better once the mother's antibodies are out of the baby's bloodstream. \(^{40}\)

What is the worst outcome?
If neutropenia is not caught, even an infection from a small cut can be deadly. However, most infections usually do not cause long-term side effects after the neutropenia goes away or is treated. \(^{40}\)

Additional Information
If your baby is neutropenic, ask your doctor about waiting to do the rotavirus vaccine.

**Thrombocytopenia**

What is it?
Thrombocytopenia is an abnormally low number of platelets \(^{45}\). It is especially common after IUTs.

How is it found?
Thrombocytopenia is found through a CBC and differential blood test.

What is the treatment?
In many cases, thrombocytopenia goes away on its own, or an infusion of platelets may be necessary.

What is the best outcome?
The baby's outlook depends on the cause of the thrombocytopenia. Isoimmune thrombocytopenia will also get better once the mother's antibodies are out of the baby's bloodstream. \(^{40}\)

What is the worst outcome?
If thrombocytopenia is not caught, severe bleeding can occur. Bleeding can even occur in the brain or intestinal tract. \(^{45}\)
Part 8: After Birth Interventions

It is important to talk with your hospital before you give birth to make sure that they can treat your baby accordingly. Not all hospitals are able to do exchange transfusions, or IVIG. Make sure that the hospital you will be delivering at is ready and able to do these on your baby.

Risk disclaimer
All interventions carry risk, not intervening also carries risk. Talk with your doctor about all of your options. If you feel your baby's needs aren't being met, ask to speak with a supervisor, NICU doctor, pediatric hematologist, patient advocate, or start calling other hospitals. You've got a baby with Hemolytic Disease of the Newborn if you've got a positive coomb's test, and they need to get appropriate care. Wait and see, not checking labs until x hours after birth, and ignoring the aap guidelines for phototherapy and exchange transfusions are not indicators of appropriate care.

Bili Light

Bilirubin tends to peak around days 4-6 with ISO babies. You need to watch out for rebounding jaundice. ISO babies tend to have a decrease in bilirubin when on lights, but rapidly increase when the lights are removed. This can occur up to 3-4 days after removal from lights, so keep checking the bilirubin levels even after treatment has ended. Below is the AAP's recommendation for phototherapy graph. By having an iso baby, you will need to be looking at the medium or high risk lines depending on how many weeks you were when you gave birth. If your baby falls on or above the lines, you'll want to get him on a bilirubin light.

These lights emit a certain wavelength of light that helps remove the bilirubin from the baby's system. Their risk is minimal. The two main complications are dehydration and if the light isn't done correctly, sunburn like burns. You can still touch your baby when he's under lights, and you can still breastfeed. This can be done by pointing the lights at you, using a bili blanket, or only removing baby for 10-15 minutes to feed, and then putting right back under lights. You want the baby under the lights with as much exposed skin as possible, so expect him to be naked except for a diaper and goggles unless you're using a hospital biliblanket. Home biliblankets should not be used because they're not effective enough with iso.

Lights are most effective when left on for a period of time. What you do not want is baby on lights for 12 hours, off overnight, and then back on in the morning. You want to keep the lights on until the bilirubin is at a safe level and declining regularly. Remove them 1 light at a time, and test for rebounds. If baby rebounds, expect to go back under lights. Once baby isn't rebounding, and bilirubin is decreasing on it's own, you're usually good to go.
Blood Transfusions
There are a few kinds of blood transfusions. You can have a platelet transfusion, a red blood cell transfusion (sometimes called a top up), or an exchange transfusion. Some transfusions may affect your baby receiving non live vaccinations for up to 4 months afterwards. Make sure you talk with a pediatric hematologist, not a regular doctor, about what vaccines are safe for your child when. Blood products, such as platelets, exchange transfusions, and IVIG, contain significant amounts of antibodies to infectious agents. These products are made from other people's blood, and therefore contain their antibodies in adult amounts. These antibodies are present because of natural or vaccine induced immunity. Because there's so many antibodies in the blood products, it can interfere with the baby's immune response to vaccines. The baby's body won't make enough antibodies because it already sees all the adult antibodies.51

Platelet transfusions are useful for thrombocytopenia. They're just the packed platelets, nothing else.

Red blood cell transfusions are useful for anemia. These are generally done later with iso babies, at a few weeks old. This kind of transfusion will not remove the antibodies, but will put new blood that is antigen negative into the baby. For example, if you've got anti-Kell, your baby needs Kell negative blood. The risks of a RBC transfusion are lower than with an exchange transfusion, and are generally done later, once the bilirubin is taken care of. Think of it as topping off the baby so that they've got enough blood.
Exchange transfusions carry more risk. In this transfusion, they remove all of the baby's blood and replace it with donor blood. This is usually done twice, in what's called a double volume exchange. It is very helpful when treating HDN, but it does carry risk.

This is the transfusion graph. First determine your risk. If you are having a sensitized pregnancy, you are either medium or high risk. Then determine your baby's age and plot their numbers. The exception to this graph is with the cord blood. If at birth your cord bili levels are already over 4.5\(^5\), an exchange transfusion should be considered. At the very least, IVIG should be administered while prepping blood for baby.

The following are indications for exchange transfusion:
- Severe anemia (Hb < 10 g/dL)
- Cord bilirubin > 4 mg/dL.
- Rate of bilirubin rises more than 0.5 mg/dL despite intensive phototherapy
- Severe hyperbilirubinemia\(^5\)
- Serum bilirubin-to-albumin ratio exceeding levels that are considered safe\(^5\)

IVIG has been shown to reduce the need for an exchange transfusion.
IVIG
IVIG stands for intravenous immunoglobulin. It is a product made from human blood plasma. The AAP recommends IVIG if the total bilirubin is rising despite intensive phototherapy or if the level is within 2-3 mg/dL of the exchange level. If necessary, this dose can be repeated in 12 hours. IVIG has been shown to reduce the need for exchange transfusions in hemolytic disease of the newborn.

One of the problems with IVIG is that it can affect vaccines. You need to wait 11 months for live vaccines after IVIG. If your child has had a live virus vaccine within 14 days before receiving IVIG, the dose will need to be repeated after the wait period is up. Most doctors will not know this. That is why it's important to talk with a pediatric hematologist, and do your research.

The routinely used live vaccines are:

1. MMR (measles, mumps and rubella)
2. Varicella (chicken pox)
3. Flumist Live Attenuated Influenza Vaccine (LAIV) which is the influenza vaccine given as a intranasal spray. You can ask for a non-live version that is a shot.
4. Rotavirus
5. Oral polio vaccine (OPV). This vaccine is no longer used in the U.S.
6. Shingles (Herpes Zoster)
7. BCG (Vaccine against TB-Tuberculosis) This is no longer a routinely used vaccine in the US, but is used under many circumstances. It is still used, especially in countries where TB is prevalent.

Live vaccines that are used in special circumstances such as during travel to a foreign country or during an epidemic are: Oral Typhoid Vaccine and the Yellow Fever Vaccine.

Blood products, such as platelets, exchange transfusions, and IVIG, contain significant amounts of antibodies to infectious agents. These products are made from other people’s blood, and therefore contain their antibodies in adult amounts. These antibodies are present because of natural or vaccine induced immunity. Because there's so many antibodies in the blood products, it can interfere with the baby's immune response to vaccines. The baby’s body won't make enough antibodies because it already sees all the adult antibodies.

Note: Some babies have an allergic reaction to the IVIG. If this is the case, talk with your doctor about trying a different brand.

Erythropoietin
Erythropoietin is a hormone produced by the kidneys. It promotes the formation of red blood cells by the bone marrow. It is used as a treatment for anemia. Erythropoietin is done to help prevent late onset anemia. Especially in IUT babies, the bone marrow is suppressed, causing low levels of erythropoietin, and red blood cells are not being made. Erythropoietin is given to decrease the need for a transfusion. If your baby has a low retic and continues to have dropping hemoglobin, talk with your doctor about trying erythropoietin.
Part 9: Things to Think About

**Postpartum Depression**

Depression can happen at any time during or after pregnancy. I want to share with you my experience. Pregnancy can be overwhelming on it's own, even a “normal” pregnancy, but when you add in all of the what ifs and things that could possibly happen in an iso pregnancy, it can be downright terrifying. I did ok during pregnancy, but I tried my best not to get attached to my third born (2nd sensitized), just in case something went wrong and we lost her. This was a horrible idea. Every baby, no matter how long they're here for, deserves to be loved. I waited until 36 weeks to set up the nursery. Talk about last minute. I didn't want any reminders around if something did go wrong. Thankfully, we were lucky, and nothing went horribly wrong.

After birth, we had to fight for testing and treatment for our baby. It was hard, let alone trying to recover from the triathlon of giving birth. When we left the hospital, I didn't feel bonded to my baby at all. I knew she was mine, and I knew I'd fight like hell to get her the care she needed, but I didn't feel the “awww” that comes with having a baby. I loved her (because that's what you're supposed to do), but I didn't feel it, or enjoy her. I spent most of my days just not interested in anything. I felt empty inside. Everything was boring, there was both nothing to do, and I felt trapped by a sense of there's so much to do. I would get irritated easily, and just was a bear to be around. I never wanted to hurt myself or others, and I always passed those screenings they give at your postpartum visits, so I lied and told myself (and everyone else), that everything was fine. It wasn't. My insomnia came back, and I'd fluctuate between not falling asleep for hours, and sleeping 12-16 hours a day.

I should have sought help, but didn't. I want to encourage you not to struggle through it like I did, and seek out help.

Another thing to consider, buy yourself a good prenatal vitamin. I found that when I switched from my free/cheap store brand vitamins to a good quality whole foods vitamin, things started getting easier. I had more energy, and I felt better. Turns out the kind I get has got extra goodies in them to help with mood, energy, and nausea. I buy My Kind Organics prenatal vitamins or RAW Garden of Life Prenatals (p.s. they're cheaper off eBay).

There's a wealth of information at:

**Postpartum Anxiety**

Another thing to keep an eye out for is anxiety. I know, telling you not to worry about things in a pregnancy this complicated is ridiculous. I'm not saying don't worry, and I'm definitely NOT saying don't advocate for your baby, but don't let it get out of hand. I found myself having anxiety attacks at 6 months pregnant, and ironically enough, it wasn't about the pregnancy! It was about the other “stuff”, anything else in life. I could be relaxing and reading a book when I'd have an anxiety attack out of nowhere. Apparently there is this thing called postpartum anxiety, that can actually happen during pregnancy. If you're struggling, try to get help. Talk
with your doctor and see if you can get a referral for help, or find someone to talk to. Pregnancy is no fun if you can't enjoy it. I really wish I'd gotten to enjoy my last pregnancy more.

**PTSD**
Post-traumatic stress disorder happens with pregnancy too. It can be devastating. Please check with your provider. Unfortunately, many doctors just think of postpartum depression or baby blues (which is not the same as PPD), and do not consider postpartum post-traumatic stress disorder. This seems more likely to occur if you've had a previous stillbirth, or end up having an emergency in labor.

Signs of PTSD include weepiness, anxiety, and depression (similar to PPD), but PTSD also includes insomnia, irritability and angry outbursts, panic attacks, nightmares about the birth, a desire to avoid the baby or avoid anything relating to the birth, feeling detached from loved ones, and a sense that some other disaster is imminent.  

The best course of action is to avoid PTSD if at all possible. Interview your provider, hospital staff, NICU, and pediatrician. Make sure you're comfortable with them and their care plan. Ask about all of your options, but know that you can't plan what to do in all scenarios. Get the help you need as you recover from birth, or have your partner get you help.

Some additional resources include:
http://www.postpartum.net/learn-more/postpartum-post-traumatic-stress-disorder/
http://www.postpartumprogress.com/postpartum-ptsd-risk-factors-symptoms
https://www.midwiferytoday.com/articles/healing_trauma.asp
http://www.solaceformothers.org/PTSD_info.html

**Having More Children**
Children are a wonderful blessing. If you want more children, I'd like to encourage you to talk with your partner, and if you're comfortable with it, go for it. Many iso mothers are given a 0% chance of having a live baby. With all of the new technologies out there (plasmapheresis, IVIG, MCAs, IUTs, and more), chances are better than ever if you can find the right doctor for your care.

**In-Vitro Fertilization**
Aside from natural conception methods, one option some women choose is In-Vitro Fertilization (IVF) with Preimplantation Genetic Diagnosis (PGD). This allows you to choose to implant only the antigen negative embryos. What you do with the antigen positive embryos is up to you. Some insurances will cover this process because it is cheaper than having to pay for an iso pregnancy and NICU care afterwards.

**Having an Iso baby**
Having a baby is a great thing. Having an iso baby (or babies), means you should be prepared for a little more work. You'll have more doctors visits, more lab work and blood tests, more specialist appointments, more to keep track of, and more stress. The cost of having an iso baby is higher than a normal pregnancy depending on your insurance. The biggest thing
to consider is that an iso baby takes more time, and iso babies can arrive at any time. They're totally worth it though, but consider how more doctors visits will affect your job, spouse, and other children. With a little extra prep work such as freezer meals, on-call babysitters, explaining to your boss, and knowledge of the Family Medical Leave Act (FMLA), it's totally doable.

**How an Iso pregnancy will affect your family**

You'll want to consider how an iso pregnancy will affect your spouse, children, and possibly extended family members. Consider how multiple doctors appointments will affect your children's school or summer schedules, and try to find a simple way to explain things to them. We just said, “Mommy has to go to the doctor to check on the baby.” It was simple enough for our little ones (2.5, and 1 years old), but older children may want more information. The pregnancy can cause stress for them too, so keep checking in with them to see how they're doing and how they're handling everything.

It can be difficult to find a way to explain things to others, and you may get some negative responses. Discuss it as a couple, and decide ahead of time how you will respond to negativity. This can be especially difficult if you've had a loss, or complications previously.

**Mourning the Lost**

It's absolutely devastating to lose your baby. Words cannot fully express how you feel. Please seek care for yourself and your family from a qualified professional. The hospital where you give birth will have a social worker who will be able to help with emotional support, and things like planning ceremonies. Try to find a way to remember your baby. Some women choose hand prints, photos, jewelry, or other things that have special meaning. Give yourselves time to grieve and heal.

Please consult additional resources such as:

http://americanpregnancy.org/pregnancy-loss/stillborn-surviving-emotionally/

http://www.firstcandle.org/grieving-families/
Commonly Used Iso Abbreviations

A
AAP: American Academy of Pediatrics
ABO: A, B or O blood type
Amnio: Amniocentesis
ANC: Absolute Neutrophil Count
Anti-: Antibody

B
Bili: Bilirubin
BIND: Bilirubin-induced Neurological Dysfunction
BPP: Biophysical Profile

C
C-Section: Cesarean Section
CBC: Complete Blood Count

D
DAT: Direct Antiglobulin Test (aka Direct Coombs)

F
FDA: Food and Drug Administration (United States)
FMH: Fetal Maternal Hemorrhage

H
Hct: Hematocrit
HDN: Hemolytic Disease of the Newborn
Hg or Hgb: Hemoglobin

I
IAT: Indirect Antiglobulin Test (aka Indirect Coombs)
IGR: Intrauterine Growth Retardation
Iso: Isoimmunization
IUT: Intrauterine Transfusion
IVIG: Intravenous Immunoglobulin

K
KB: Kleihauer-Betke (test)

M
MCA: Middle Cerebral Artery (scan)
MFM: Maternal Fetal Medicine
MoM: Multiple of the Median

N
NICU: Neonatal Intensive Care Unit
NST: Non Stress Test

P
PSV: Peak Systolic Velocity
PUBS: Percutaneous Umbilical Cord Blood Sampling

R
RBCs: Red Blood Cells
Retic: Reticulocyte count
Rh: Rhesus Factor
### Prenatal Testing

**Mom's Blood Type:** _________________  **Dad's Blood Type:** _________________

**Antibody Screen:** _________________  **Dad's Genotype:** _________________

#### General Testing

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<tr>
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#### Titers, PSV, MoM

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<tr>
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<th>MoM</th>
<th>Titer</th>
<th>Titer</th>
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#### MCA Chart

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<th>Gestational Age</th>
<th>Median (1.0)</th>
<th>1.5 MoM</th>
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<td>35.2</td>
<td>52.8</td>
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MCA Scans

PSV and MoM - Your technician will probably get several different numbers during the scan. Record the highest and lowest PSV numbers, but also make sure to record the best, cleanest number. It’s not uncommon to have some really out there numbers because of baby’s position or activity, so make sure to record the range.

<table>
<thead>
<tr>
<th>Date</th>
<th>PSV best</th>
<th>MoM best</th>
<th>PSV low</th>
<th>PSV high</th>
<th>MoM low</th>
<th>MoM high</th>
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IUTs

Here is a place to record data when you have IUTs. After the transfusion, ask what the starting number is (some doctors will use hct or hgb) and the ending number. This will show you how much the IUT was needed. You can also record the volume of blood added. Your doctor will use a formula to calculate how long the transfusion will last based on these numbers and give you a date for your next IUT. Usually this is 2-3 weeks after the first one, but may be sooner if baby is really low on blood.

<table>
<thead>
<tr>
<th>Date</th>
<th>Starting hct or hgb</th>
<th>Ending hct or hgb</th>
<th>Volume added</th>
<th>Next IUT</th>
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</table>
### Baby Is Here

- **Birth Date:** __________
- **Time:** ______________ 
- **Gestational Age:** __________
- **Weight:** ____________
- **Blood Type:** __________ 
- **Direct Coomb's:** ____________

#### Laboratory Test Results

<table>
<thead>
<tr>
<th>Date</th>
<th>Hemoglobin</th>
<th>Hematocrit</th>
<th>Retic</th>
<th>Bilirubin (total)</th>
<th>Neutrophils</th>
<th>Platelets</th>
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#### Notes:

- **Date:** 
- **Bilirubin:** 60

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Notes:
Iso Affects You (Even If You're Not Pregnant)! Get a Medical Alert Card - Here's why.

Since it seems to come up a lot, I'm covering the medical alert card and its importance again. Our antibodies don't just affect our babies, they affect us too. The same antibodies that destroy baby's blood cells because they've got the antigen, will also destroy donor blood cells. If you get injured, end up unconscious, or have some other emergency situation and need blood, it's important for the doctors to know about your antibodies so they can find compatible blood. Once you have antibodies, you will have them for life. Your body will always remember how to make them quickly if it ever finds incompatible blood. Even if your antibodies are too low to titer or undetectable, the medical personnel need to know about them. If they don't a hemolytic transfusion reaction occurs (more info about that below). About 20 people die in the USA each year because of them. 5 minutes to fill out a free medical alert card, or order a bracelet can literally save your life.

Below is a free medical alert card. Fill in the info, print it, fold it in half and put it in your wallet. Make sure the top line, “Emergency Medical Alert”, is visible. Bonus if you can laminate it. Put “Transfusion Alert: Anti-E antibodies” or whatever your antibody is right where it says “Transfusion Alert”.

<table>
<thead>
<tr>
<th>EMERGENCY MEDICAL ALERT</th>
<th>EMERGENCY MEDICAL ALERT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Blood Type:</td>
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<tr>
<td>Address:</td>
<td>Transfusion Alert:</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Phone:</td>
<td>Existing Conditions:</td>
</tr>
<tr>
<td>Birthdate:</td>
<td></td>
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<tr>
<td>Contact 1:</td>
<td>Allergies:</td>
</tr>
<tr>
<td>Phone:</td>
<td></td>
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<tr>
<td>Contact 2:</td>
<td>Doctor:</td>
</tr>
<tr>
<td>Phone:</td>
<td>Phone:</td>
</tr>
</tbody>
</table>
Additional Information About Transfusion Reactions

"Acute hemolytic transfusion reactions may be either immune-mediated or nonimmune-mediated. Immune-mediated hemolytic transfusion reactions caused by immunoglobulin M (IgM) anti-A, anti-B, or anti-A,B typically result in severe, potentially fatal complement-mediated intravascular hemolysis. Immune-mediated hemolytic reactions caused by IgG, Rh, Kell, Duffy, or other non-ABO antibodies typically result in extravascular sequestration, shortened survival of transfused red cells, and relatively mild clinical reactions. Acute hemolytic transfusion reactions due to immune hemolysis may occur in patients who have no antibodies detectable by routine laboratory procedures."53

Easier to understand transfusion reaction info: https://medlineplus.gov/ency/article/001303.htm

Hemolytic Transfusion Reactions In 2011, the number of reported fatal hemolytic transfusion reactions increased from 7 (18%) in 2010 to 9 (30%) of confirmed transfusion related fatalities. There were increases in both ABO hemolytic reactions and non-ABO hemolytic reactions. Despite these recently observed increases, a downward trend in the total number of reported fatalities due to hemolytic transfusion reactions has continued since 2001. In 2011, there were six reports of non-ABO fatal hemolytic transfusion reactions: Two of the six cases were attributed to errors in the lab:

- In one case, an anti-K was correctly identified; however, an error in pulling segments for K typing and compatibility testing resulted in the transfusion of an incompatible, K positive unit.
- In a second case, a positive antibody screen misread as negative resulted in transfusion of an incompatible Fya positive unit. The immediate spin compatibility test did not detect the incompatibility.54
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34 Erythropoietin in human fetuses with immune hemolytic anemia and hydrops fetalis. 


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Isoimmunization (also called alloimmunization), occurs when a woman’s immune system is sensitized to foreign blood cell antigens. This causes the woman to make antibodies that cross the placenta and destroy baby's blood cells. During pregnancy, some of the mother's antibodies cross the placenta and enter the fetal circulation. In cases of iso, the antibodies destroy the baby's blood cells and cause Hemolytic Disease of the Newborn.

Antibody? Antigen? What's my body doing again?
Antigen – foreign protein on red blood cells of dad or baby
Antibody – made by mom to defend her body from the antigen
Antigens are foreign. Antibodies defend the body.

How it works
Dad makes the E antigen and passes it to baby. When baby's blood and mom's blood mix, mom's blood finds the foreign antigen and makes antibodies to defend her body. This is called sensitization. The antibodies then find the foreign cells and destroy them in a process called hemolysis (hemo = cell, lysis = death). The next time mom's sensitized body finds the E antigen, her antibodies are primed and ready to attack the foreign cells. So when mom has baby #2, who has dad's E antigen, her antibodies cross the placenta and attack the baby's blood.

This book is a primer for some of what you can expect during an iso pregnancy. It covers tests, interventions, newborn care, and more, in an easy to understand format. Great for all moms with newly discovered antibodies. An excellent reference to help make your pregnancy and newborn care easier.