ASSIUT UNIVERSITY
DRUG INFORMATION BULLETIN

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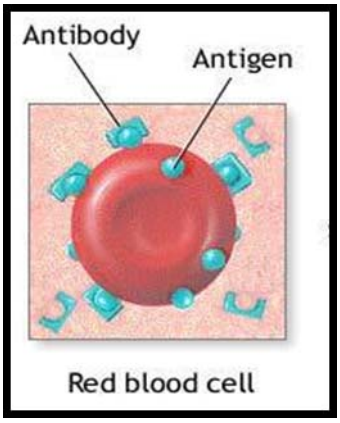
كليـــة الصيدلـــة

Hemolytic Disease of the Newborn

Hemolytic disease of the newborn, also known as **erythroblastosis fetalis**, is an alloimmune condition that develops in a fetus, when the IgG molecules (one of the five main types of antibodies) produced by the mother pass through the placenta. Among these antibodies are some which attack the red blood cells in the fetal circulation; the red cells are broken down and the fetus can develop reticulocytosis and anemia. This fetal disease ranges from mild to very severe, and fetal death from heart failure (hydrops fetalis) can occur. When the disease is moderate or severe, many erythroblasts are present in the fetal blood and so these forms of the disease can be called *erythroblastosis fetalis*.



Symptoms

Hemolysis leads to elevated bilirubin levels. After delivery bilirubin is no longer cleared (via the placenta) from the neonate's blood and the symptoms of jaundice (yellowish skin and yellow discoloration of the whites of the eyes) increase within 24 hours after birth. Like any other severe neonatal jaundice, there is the possibility of acute or chronic kernicterus. Profound anemia can cause high-output heart failure, with pallor, enlarged liver and/or spleen, generalized swelling, and respiratory distress. The prenatal manifestations are known as hydrops fetalis; in severe forms this can include petechiae and purpura.

Causes

Antibodies are produced when the body is exposed to a foreign antigen. If a mother is exposed to a foreign antigen and produces IgG (as opposed to IgM which does not cross the placenta), the IgG will target the antigen, if present in the fetus, and may affect it in utero and persist after delivery. The three most common models in which a woman becomes sensitized toward a particular antigen are:

In This Issue

1- ABO incompatibility:

The most common form of HDN is ABO incompatibility, which is usually not very severe. With an ABO incompatibility, a mother produces antibodies against her baby's blood type. These antibodies, if the mother is type O, can cross the placenta and can break down the baby's red blood cells after birth, leading to jaundice and anemia. This doesn't occur if the mother and baby have the same blood type or if the baby's blood is type O. If a mother is type A or B and the baby has a different blood type other than type O, her body can still produce antibodies against the baby's red blood cells. These antibodies are too large to cross the placenta though, and so don't usually lead to any problems.

2- Rh-induced hemolytic disease of the newborn:

Is the least common form, which can almost always be prevented. Fetal-maternal hemorrhage can occur due to trauma, abortion, childbirth, ruptures in the placenta during pregnancy, or medical procedures carried out during pregnancy that breach the uterine wall. In subsequent pregnancies, if there is a similar incompatibility in the fetus, these antibodies are then able to cross the placenta into the fetal bloodstream to attach to the red blood cells and cause hemolysis. In other words, if a mother has anti-RhD (D being the major Rhesus antigen) IgG antibodies as a result of previously carrying an RhD-positive fetus, this antibody will only affect a fetus with RhD-positive blood. Rh incompatibility can cause symptoms ranging from very mild to deadly. In its mildest form, Rh incompatibility causes the destruction of red blood cells. Full recovery is expected for mild Rh incompatibility. After birth, the infant may have:

- Yellowing of the skin and whites of the eyes (jaundice)
- Low muscle tone (hypotonia) and lethargy

Signs and tests

Before delivery, the mother may have an increased amount of amniotic fluid around her unborn baby (polyhydramnios).There may be:

- A positive direct Coombs test result
- Higher-than-normal levels of bilirubin in the baby's umbilical cord blood
- Signs of red blood cell destruction in the infant's blood

3- Anti-$Kell_1$ hemolytic disease of the newborn

Anti-$Kell_1$ is becoming relatively more important as prevention of Rh disease is also becoming more effective. Hemolytic disease of the newborn (anti-$Kell_1$) is caused by a mismatch between the $Kell_1$ antigens of the mother and fetus. About 91% of the population is $Kell_1$ negative and about 9% are $Kell_1$ positive. The disease results when maternal antibodies to $Kell_1$ are transferred to the fetus across the placental barrier.

Mothers who are negative for the $Kell_1$ antigen develop antibodies after being exposed to red blood cells that are positive for $Kell_1$. Over half of the cases of hemolytic disease of the newborn owing the anti-$Kell_1$ antibodies are caused by multiple blood transfusions, with the remainder due to a previous pregnancy with a $Kell_1$ positive baby.

Suggestions have been made that women of child bearing age or young girls should not be given a transfusion with $Kell_1$ positive blood. Donated blood is not currently screened for the Kell blood group antigens as it is not considered cost effective at this time.

Diagnosis

The diagnosis of HDN is based on history and laboratory findings:
Blood tests done on the newborn baby:

- Biochemistry tests for jaundice
- Peripheral blood morphology shows increased reticulocytes. Erythroblasts (also known as nucleated red blood cells) occur in moderate and severe disease.
- Positive direct Coombs test (might be negative after fetal interuterine blood transfusion)

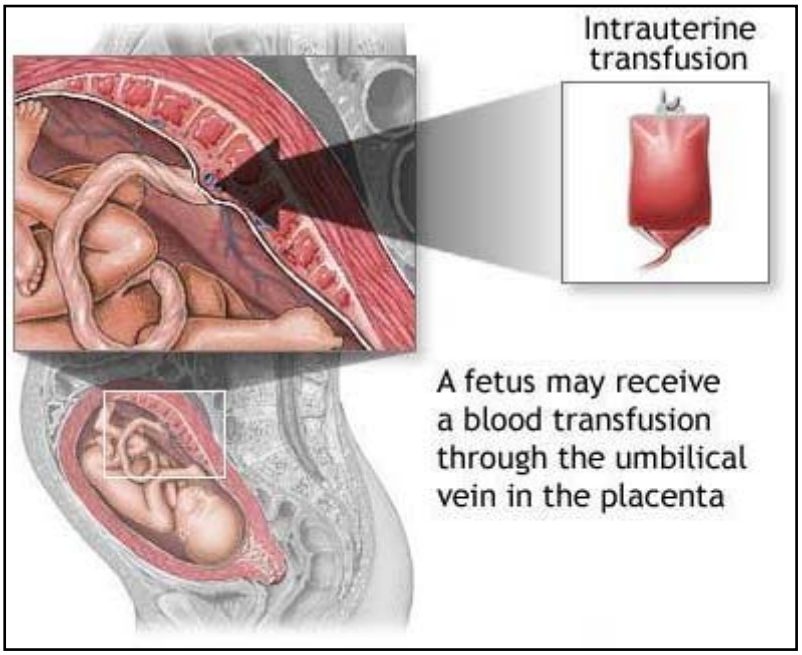
Blood tests done on the mother:

- Positive indirect Coombs test

Treatment

Before birth, options for treatment include intrauterine transfusion or early induction of labor when pulmonary maturity has been attained, fetal distress is present, or 35 to 37 weeks of gestation have passed. The mother may also undergo plasma exchange to reduce the circulating levels of antibody by as much as 75%.

After birth, treatment depends on the severity of the condition, but could include temperature stabilization and monitoring, phototherapy, transfusion with compatible packed red blood, exchange transfusion with a blood type compatible with both the infant and the mother, sodium bicarbonate for correction of acidosis and/or assisted ventilation.



Rhesus-negative mothers who have had a pregnancy with/are pregnant with a rhesus-positive infant are given Rh immune globulin (RhIG) at 28 weeks during pregnancy, at 34 weeks, and within 72 hours after delivery to prevent sensitization to the D antigen. It works by binding any fetal red cells with the D antigen before the mother is able to produce an immune response and form anti-D IgG. A drawback to pre-partum administration of RhIG is that it causes a positive antibody screen when the mother is tested, which can be difficult to distinguish from natural immunonological responses that result in antibody production.

Anti-Kell can be detected by routine antenatal antibody screening blood tests (indirect Coombs test) in a similar way to Rh disease. The treatment of hemolytic disease of the newborn (anti-K) is similar to the management of Rh disease.

References:
1) ncbi.nlm.nih.gov/pubmedhealth
2) wikipedia.org
3) pediatrics.about.com

Terminology

Kikuchi Disease

Kikuchi disease: A disorder that typically causes "swollen glands" in the neck (cervical lymphadenopathy) together with fever or flu-like symptoms. Laboratory test abnormalities include elevated erythrocyte sedimentation rate (ESR), and white blood count abnormalities (low neutrophil count and elevated lymphocyte count with atypical lymphocytes in the peripheral blood).
Kikuchi disease is fairly common in young people, predominantly young women, in Asia. Also called Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis, this condition was discovered in Japan in 1972 and since then has seen in other areas of the world.
The overall picture is suggestive of a virus infection; autoimmune factors may also play a role. However, no infectious agent has yet been identified and autoimmunity remains hypothetical.
Diagnosis is based on characteristic pathologic findings on biopsy that differentiate this disease from others such as lymphoma, systemic lupus erythematosus, and infectious lymphadenopathies.
Reference: ***medterms.com***

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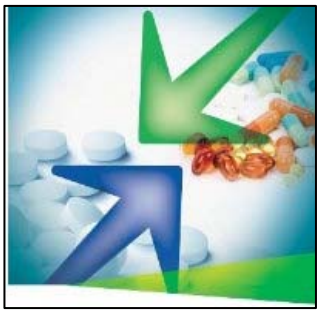
Drug- Drug Interaction



Object Drug

Digoxin (Lanoxin®)

Precipitant Drug

Itraconazole (Sporanox®)
Ketoconazole (Nizoral®)
Posaconazole (Noxafil®)

Effect

Increased digoxin concentrations and risk of digoxin toxicity

Mechanism

Inhibition of digoxin transport by P-glycoprotein resulting in reduced renal and nonrenal elimination of digoxin

Related Drugs

- Voriconazole (Vfend®) and the non-azole antifungal, terbinafine (Lamisil®), do not appear to inhibit P-glycoprotein
- Data are lacking regarding fluconazole

Options

Take Precautions

Consider Alternatives: Consider alternative antifungal agents (e.g., voriconazole or terbinafine)

Monitor: If alternatives are not appropriate, monitor patients closely for evidence of digoxin toxicity (e.g., nausea, malaise, fatigue, visual changes, headache, arrhythmias), with downward digoxin dosage adjustments as necessary. Also monitor for altered digoxin effect when itraconazole, ketoconazole, or posaconazole are changed in dosage or discontinued. If digoxin is started in the presence of one of these agents, consider conservative initial digoxin dosing.

Reference: azcert.org

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Ask the expert

Why is honey not recommended for babies?

Babies under one year of age should not be given honey because honey can carry C. botulinum spores. Babies' immune systems are not well enough developed to tolerate botulism. Although infant botulism is rarely fatal, there are many very serious possible effects, including flaccid paralysis. Babies should not be given honey in any form.

Reference: data.umms.org

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Medical news

Selenium Supplements May Harm Not Help

According to a recent study, selenium may help people who don't have enough of it, but for the people who have enough to begin with, selenium supplements may be detrimental to their health. It is shown in the study that taking the supplements may result in the development of type 2 diabetes.

The study states that selenium is a consistent, natural mineral which is present in certain foods and also in soil. High selenium intake has previously been shown to protect against certain cancers, such as lung, colorectal, bladder, and prostate cancer. It has also been known to increase male fertility and have positive effects on antiviral function.

Low selenium intake has been linked to memory and brain decline, low immune system quality, and a greater risk of death. However, studies have shown that selenium has a low therapeutic spectrum and when consumed too much may result in the development of type 2 diabetes. The authors state that worldwide, people are taking selenium supplements much more than before, because they think it lowers their chances of developing cancer and other deadly conditions, and the supplements have been sold in

large quantities with the belief that they help many health problems.

Researchers state that evidence from studies had differed greatly in whether or not selenium supplements are beneficial to health. The mix in results is due to the fact that selenium is only helpful when the levels in people taking the supplements are low. The most beneficial factor of the supplements is associated to people who have inadequate selenium blood levels. The crucial factor that needs to be emphasized is that people whose blood plasma selenium is already 122 µg/L or higher should not take selenium supplements. However, there are various health benefits, and no extra risk, for people of lower selenium status (plasma level less than 122 µg/L), who could benefit from raising their status to 130 - 150 µg/L - a level associated with low mortality.

Reference: medicalnewstoday.com

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Test Your Knowledge

1) Most home pregnancy tests assay for:

A. Estrogens
B. Follicle-stimulating hormone
C. Human chorionic gonadotropine
D. Lutenizing hormone-releasing hormone
E. progestins

2) Insulin resistance is often due to

A. excessive exercise
B. upper body obesity
C. Acute renal failure
D. B and C
E. A,B and C

3) Oral or parenteral ketorolac therapy is limited to 5 days of therapy due to an increased risk of:

A. Renal impairment
B. Gastrointestinal bleeding / perforation
C. Liver failure
D. CNS disturbances
E. A and B

4) A patient comes into your pharmacy and complains that his urine has become bright orange –red. Which of his current prescription medication may be responsible?

A. Isoniazide
B. Ethanbutol
C. Rifampin
D. Quinidine gluconate
E. Chloral hydrate

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center!

Enquiry received from Radwa Esam, Pharmacist at Assiut University Pediatrics' Hospital

Enquiry: What is the child's dose of Solumedrol® in case of acute spinal cord injury? Is it normally a large dose?

Summary of Answer:

Some evidence indicates that large IV doses of glucocorticoids (i.e.,methylprednisolone) can improve motor and sensory function in patients with acute spinal cord injury when treatment is initiated promptly following injury(within 8 hours). It's not known whether improvement in neurologic function with such therapy will routinely lead to specific improvements in disability. Solumedrol (Methylprednisolone) was given in an initial dose of 30 mg/kg IV (administerd over 15 minutes), followed after 45 minutes by a continuous IV infusion of 5-6mg/kg per hour for 23 hours.

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Interesting Medical Facts

- ✓ Your tongue has a unique print similar to your fingerprints.
- ✓ Your brain is more active at night than during the day.
- ✓ If you squeezed out all of the bacteria from your intestines, you could almost fill up a coffee mug.
- ✓ The storage capacity of human brain exceeds 4 terabytes.
- ✓ The acid in your stomach, that which helps digest your food, is strong enough to dissolve razor blades! Don't try swallowing metal objects to prove this, but hydrochloric acid (found in the stomach) can dissolve a variety of metals.
- ✓ Your stomach lining replaces itself every three to four days. If it did not do this your stomach would digest itself. If you have ever had a stomach ulcer you will know how painful this is.
- ✓ Every time you sneeze it reaches speeds of over 100mph, which is why people struggle to keep their eyes open when they sneeze.
- ✓ The attachment of the human skin to muscles is what causes dimples.
- ✓ In 1972, a group of scientists reported that you could cure the common cold by freezing the big toe.
- ✓ People who laugh a lot are much healthier than those who don't. It has been found that laughing lowers levels of stress hormones, and strengthens the immune system. Six-year-olds have it best - they laugh an average of 300 times a day. Adults only laugh 15 to 100 times a day.

- ✓ In 1815 French chemist Michael Eugene Chevreul realized the first link between diabetes and sugar metabolism when he discovered that the urine of a diabetic was identical to grape sugar.
- ✓ The first known heart medicine was discovered in an English garden. In 1799, physician John Ferriar noted the effect of dried leaves of the common plant, digitalis purpurea, on heart action. Still used in heart medications, digitalis slows the pulse and increases the force of heart contractions and the amount of blood pumped per heartbeat.
- ✓ According to the Centers for Disease Control and Prevention (CDC), 18 million courses of antibiotics are prescribed for the common cold in the United States per year. Research shows that colds are caused by viruses. 50 million unnecessary antibiotics are prescribed for viral respiratory infections.

Answers:

1-(C) Most home pregnancy tests measure levels of human chorionic gonadotropine. This agent is produced by fertilized ovum

2-(D) obesity and acute renal failure have both been associated with insulin resistance

3-(E) ketorolac inhibits platelets function, and with continued use more than 5 days may increase the risk of GI bleeding /perforation and has also been associated with changes in renal function.

4-(C) Rifampin may color sweat,tears, feces, and urine a bright orange-red.and may stain soft contact lenses.

Editorial Board

Cat's Claw

What It Is Used For

- Cat's claw has been used for centuries in South America to prevent and treat disease.
- It has been used for a variety of health conditions, including viral infections (such as herpes and HIV), Alzheimer's disease, cancer, and arthritis.
- Cat's claw has been used to support the immune system and promote kidney health, as well as to prevent and abort pregnancy.

How It Is Used

The inner bark of cat's claw is used to make liquid extracts, capsules, and teas. Preparations of cat's claw can also be applied to the skin.

Side Effects and Cautions

- Few side effects have been reported for cat's claw when it is taken at recommended dosages.
- Though rare, side effects may include headaches, dizziness, and vomiting.
- Women who are pregnant or trying to become pregnant should avoid using cat's claw because of its past use for preventing and aborting pregnancy.
- Because cat's claw may stimulate the immune system, it is unclear whether the herb is safe for people with conditions affecting the immune system.

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