

SUMMER 2007



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## President's Message-Sharon Noble MT(ASCP)

Welcome readers once again to Channels. Summer is here and I am sure all of you are busy with vacations, family and of course jobs. I hope that as summer ends you will each remember our fall meeting coming quickly on September 11 and 12. This will be at the Marriott East Hurstborne in Louisville. To make registration easier you can go to our web address [www.kabb.org](http://www.kabb.org) I hope that many of you will be able to join us there for what I'm sure will be very informative sessions. This is our joint meeting with KSCLS that we previously have had in the spring. We have a spring meeting in the works that will be held at Buckhorn Lake State Park in March 2008. We will be giving more information on that later and it is also posted on our web site. Thank you for your time and I look forward to meeting each of you in September.

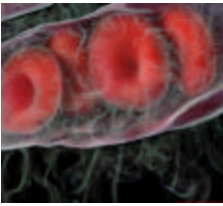


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## The MNS Blood Group System

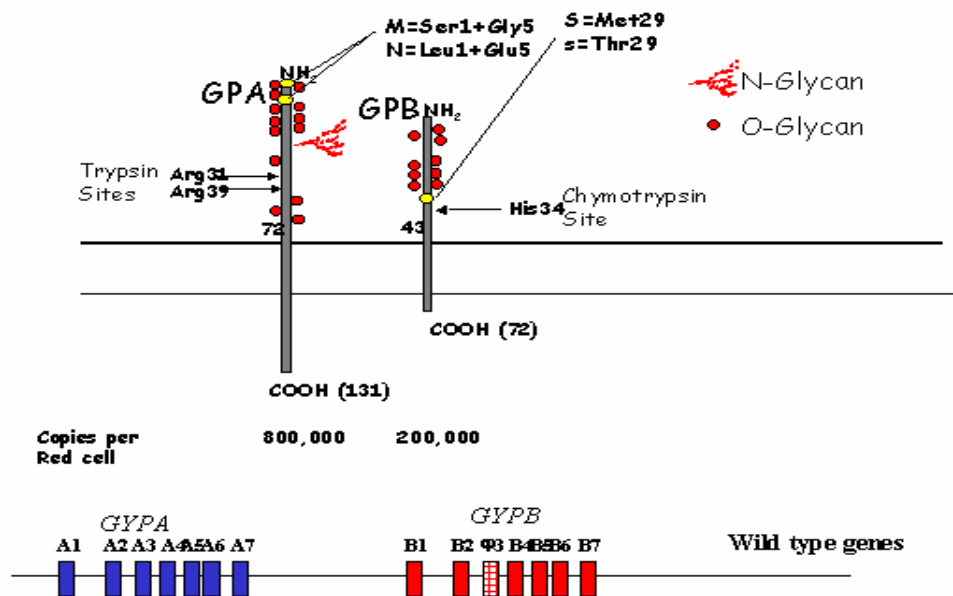
By: Mahoney E. Cobb, MD, Transfusion Medicine Fellow, PGY6, University of Louisville Department of Pathology & Laboratory Medicine, Louisville, Kentucky

William B. Lockwood, PhD, MD, Clinical Professor, University of Louisville Department of Pathology & Laboratory Medicine, Director, Transfusion Services & Tissue/Bone Bank, University of Louisville, Director, Transfusion Services, Tissue/Bone Bank & Coagulation, Norton-Kosair Children's Hospitals, Louisville, Kentucky

Landsteiner and Levine first reported the discovery of M and N antigens in 1927, making MNS the second discovered blood group system (ABO being the first in 1900). S, s and U were described some 20 years later. There are a total of 46 distinct antigens in the MNS system.<sup>1</sup> The five major antigens in the MNS system will be discussed in this article: M, N, S, s and U. The system is very complex (second only to the Rh system) and somewhat dichotomous. It has been argued that MNS is not one but rather two blood groups.<sup>2</sup> However, it seems likely that this disparate couple will stay merged and for good reason.

The MNS antigens are coded for by two closely linked loci on chromosome 4, GYPA and GYPB. GYPA codes for two codominant alleles resulting in a glycophorin A (GPA) bearing either M or N. GYPB codes for two codominant alleles giving rise to glycophorin B (GPB) with either S and U or s and U. A third rare silent allele, S<sup>u</sup>, can also occur at the GYPB locus leading to the phenotype S- s- U-. GPA/B are single pass transmembrane sialoglycoproteins.<sup>3</sup>

Figure 1: GPA/B on the RBC membrane (above) and on chromosome 4 (below)<sup>4</sup>



A third homologous gene, GYPE, is located adjacent to GYPB. Although it is not thought to encode a red blood cell (RBC) product it can contribute to the production of hybrid genes.<sup>1</sup> The MNS system antigens are found primarily on the surface of RBCs but have also been located on renal endothelium.<sup>2</sup> In terms of antigen density, GPA is the most abundant sialoglycoprotein in the red cell membrane with approximately 1 million copies. There are an estimated 0.2 million copies of GPB.<sup>1</sup> The genetic setup described above gives rise to the following phenotypic frequencies:

Phenotype	Whites	U.S. Blacks
M+ N- S+ s-	6%	2.1%
M+ N- S+ s+	14%	7%
M+ N- S- s+	8%	15.5%
M+ N- S- s-	<0.01%	0.4%
M+ N+ S+ s-	4%	2.2%
M+ N+ S+ s+	24%	13%
M+ N+ S- s+	22%	33.4%
M+ N+ S- s-	<0.01%	0.4%
M- N+ S+ s-	1%	1.6%
M- N+ S+ s+	6%	4.5%
M- N+ S- s+	15%	19.2%
M- N+ S- s-	<0.01%	0.7%

GPA and GPB, present on the surface of red RBCs, carry sugars exposing negatively charged sialic acid. This contributes to the negatively charged glycocalyx, which aids in creating the zeta potential or cell-cell repulsive forces. GPA and GPB are also thought to serve as receptors for cytokines, bacteria, and viruses. Rare GPA/B deficient phenotypes are known: MkMk lacks both glycoporphins A and B, En(a-) lacks glycoporphin A, and S-s- lacks glycoporphin B. Absence of glycoporphins does not result in disease indicating they are relatively unnecessary for normal RBC function.

Many disease states have been associated with the MNS blood group system. GPA and GPB negative/deficient RBCs are resistant to infection by *Plasmodium falciparum*.<sup>5</sup> This resistance has led to an increased incidence of certain polymorphisms in areas of malaria endemia. Studies on various populations have shown certain gametic types to be associated with allergic asthma<sup>5</sup>, Crohn's disease<sup>5</sup>, ataxia telangiectasia<sup>6</sup>, *Salmonella typhi* resistance<sup>7</sup>, essential hypertension<sup>8</sup>, and varied lipid level response to dietary intake<sup>9</sup>. GPA and GPB are also thought to be the targets of the influenzae and encephalomyocarditis viruses.<sup>2</sup> The NN genotype of GPA has been reported to be protective against bipolar disorder.<sup>10</sup> Numerous other disease links have been postulated and research in the field is ongoing.

#### ANTIBODIES OF THE MNS SYSTEM

Anti-M and anti-N are often found in persons never exposed to foreign red cells (i.e. they are 'naturally occurring'). Many times they are cold reacting, but if the reaction persists at 37°C these antibodies may be clinically significant because they can lead to hemolytic transfusions reactions (mainly of the delayed type). In order to determine the clinical significance a prewarm anti-IgG antiglobulin technique should be performed. If the result is negative, this indicates cold specificity and only a Coombs crossmatch without typing the units as M- is accepted practice. If the prewarm technique yields a positive result, an M- unit should be provided. Anti-M and anti-N display marked dosage effect, with homozygous cells reacting more strongly in vitro than heterozygous cells. This alteration in serologic reactivity is directly proportional to the number of surface antigens per red cell. Although the majority of the antibodies produced are IgM, somewhere between 50-78% contain an IgG component.<sup>4</sup> Anti-M and anti-N have both rarely been implicated in hemolytic disease of the fetus/newborn (HDFN).<sup>7</sup>

An anti-M antibody can be serologically defined in two ways:

1. An autoantibody in a M+ person
2. An alloantibody in an M- person

The case of anti-N is not as straightforward. There are three ways a person can form an anti-N.

The first, an anti-N can be formed as an autoantibody in an N+ person. This is clear-cut and rarely significant. An important phenomenon occurs serologically in the MNS system when GPB is lacking (e.g. when the S<sup>u</sup>/silent allele is present). The NH<sub>2</sub> terminal end of normal GPB is identical to GPA carrying the N antigen, therefore all people who have GPB have some N antigen, even if they are N-. In order for differentiation, this is called the 'N' antigen and as stated above is carried on GPB. As a result of this most N- individuals do not make an anti-N. Stated another way, the 'N' antigen is enough like the N antigen that when present antibody is not formed. It follows then that those who are N- and lack normal GPB are eligible to make an anti-N. The formation of this type of anti-N is important not only because of the anti-N but also primarily because these individuals are eligible to make an anti-U. This is a disaster of epic proportions because these individuals are very difficult to transfuse. Thankfully, all GPB- phenotypes are rare (U antigen frequency ~ 98.7%). In the third scenario, a person undergoing renal dialysis using a machine that has been sterilized with formaldehyde can form an antibody against the resulting modified N antigen, called Nform.<sup>2</sup>

In summary, anti-N can be formed in three ways:

1. An autoantibody in an N+ person
2. An alloantibody in an N-, 'N'- person
3. A semi-autoantibody in an N+ person exposed to formaldehyde

Most examples of anti-S and anti-s are warm reacting, mostly IgG and require exposure either via pregnancy, transfusion, etc. However, if an antibody looks like an anti-S or anti-s, but cannot be definitively identified at 37°C, looking at the immediate spin results may be helpful because these antibodies have been reported by some to react best at cooler temperatures.<sup>2</sup> These antibodies are clinically significant when they persist at 37°C. Anti-S has been implicated in both immediate and delayed transfusion reactions. Anti-s has only been reported to cause delayed reactions. Anti-S and anti-s have caused HDFN- some have been severe and at least one fatality has been reported with each. Dosage can be seen in many cases of anti-S and anti-s, but it is classically not as marked as that seen with anti-M and anti-N.

Anti-U, mentioned above, is an exposure mediated IgG antibody. It has been the cause of both immediate and delayed transfusion reactions. Anti-U is also capable of causing HDFN and one reported case was fatal. Once a patient develops an anti-U, the issue of finding a true U- unit arises. This is not a straightforward task because variants of the U antigen can also type as U-. This is not as large an issue as it may seem because most U- patients derive the needed benefit from IAT compatible U<sup>var</sup> cells. However, patients with anti-U may broaden their specificity after exposure to U<sup>var</sup> cells. Even so it is recommended to use IAT compatible RBCs typed as U- for U- patients and to not require a strict definition of U- because of the difficulty obtaining blood for these patients.<sup>3</sup>

In summary, the MNS is a highly complex blood group. This short review doesn't even scratch the surface of the molecular diversity. Thankfully, for most transfusion issues a working basic understanding of the system is adequate.

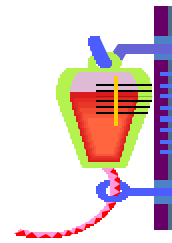
M,N antibodies	S,s,U antibodies
IgM and/or IgG	IgG
Usually insignificant	Usually significant
Most often cold reacting	Most often warm reacting
"Naturally occurring"	Require exposure
Glycophorin A	Glycophorin B
Activity reduced by trypsin	Activity stable with trypsin
Show significant dosage	Dosage less dramatic

Bits of trivia to impress your friends at dinner parties:

- Lectin for GPA borne N = *Vicia graminea* (will not agglutinate 'N' at the proper dilution)
- Lectin for M = *Iberi amara*

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# Blood Bank and Infection Control

Dee Anderson RN, MSN, CIC  
CIC is Certification in Infection Control

Throughout the processes of blood collection, processing, storage and distribution, it is essential to maintain the sterility chain to minimize blood component contamination. The general principles of infection control should also be applied in this setting for both the protection of the patient and the staff working in blood bank. Staff working in blood banks or transfusion services is at risk of exposure to pathogenic germs (organisms) in blood in a number of ways.

The most common are:

- Exposure to blood while collecting the donor specimen, during testing and when infusing the blood.
- Accidental injury with sharps (needles, scalpel blades and contaminated broken glassware), the leading cause of laboratory acquired infections.
- Splashes and sprays of blood onto mucous membranes of the mouth, nasal cavity and conjunctivae of the eyes.

The Infection control work practices of wearing a clear plastic facemask or shield, or a surgical mask and goggles, can minimize these risks. Gloves should be worn when collecting blood and performing various tests on blood. Sharps should be handled with care and disposed of immediately after use in puncture resistant sharps containers located close to the work area. In addition, decontaminate work surfaces with 0.5% chlorine solution daily or when contaminated, such as after blood spills, and place infectious waste materials in plastic bags or leak proof, covered waste containers.

If an exposure should occur, Central Baptist Hospital has a protocol in place for post exposure prophylaxis and follow up through Employee Health. The process starts with the employee, by immediately reporting the exposure to the Employee Health Nurse or the Clinical House Supervisor.

## Transfusion Reactions

Blood product transfusions sometimes cause transfusion reactions. There are several types of reactions and they vary in their severity. Some reactions may occur as soon as the transfusion is started, while some take several days or longer to develop.

Many precautions are taken before a transfusion is started to prevent a reaction from happening. The blood type of the unit is checked several times, the unit is cross matched for compatibility with the person who will receive it, and a nurse and blood bank lab technician verify both the patient and blood unit information before releasing it for use. The information is double-checked once more at the bedside before the transfusion is started.

**Allergic reaction:** This is the most common type of reaction. It occurs during the transfusion because of the body's reaction to plasma proteins in the donated blood. Usually the only symptoms are hives and itching, which can be treated with antihistamines such as diphenhydramine (Benadryl). In rare cases these reactions can be more serious.

**Febrile reaction:** Febrile transfusion reactions involve sudden fever during or within 24 hours of the transfusion. Headache, nausea, chills, or a general feeling of discomfort may accompany the fever. Acetaminophen (Tylenol) may help lessen these symptoms. These reactions are a response by the body to white blood cells in the donated blood. They occur most commonly in people who have had previous transfusions and in women who have had several pregnancies. Other types of reaction can also cause fever, and further testing may be needed to be sure that the reaction is only a febrile one. Patients who have had febrile reactions or who are at risk are usually given blood products that are **leukoreduced** (the white blood cells have been removed by filters or other means).

**Transfusion-related acute lung injury (TRALI):** This is a very serious transfusion reaction, which happens about once in every 5,000 transfusions. It often occurs within 1 to 2 hours of the transfusion, but can happen anytime up to 6 hours after a transfusion. The major symptom a patient will feel is trouble breathing; a high fever may also develop. Doctors don't know what causes this type of transfusion reaction, and medicines don't seem to help. Most of the time it goes away on its own, but experts believe that it can be fatal in 5% to 25% of cases. It is more likely to be fatal if the patient were already very ill before the transfusion. Often a patient will need oxygen and sometimes support with a breathing machine. Although any type of transfusion can cause this, it seems to happen more often when the transfusion contains a lot of plasma, such as platelet transfusions or plasma infusion. But it also occurs when red blood cells are transfused. If a patient who has had TRALI needs more blood, doctors will try to prevent future problems by "washing" the red cells in a dilute saltwater solution to remove most of the plasma while preserving the red cells.

**Acute immune hemolytic reaction:** This is the most serious type of transfusion reaction, although fortunately it is very rare. It occurs when donor and patient blood types do not match. Patient antibodies attack the transfused red blood cells, causing them to hemolyze (break open), releasing harmful substances into the bloodstream. Patients may have chills, fever, chest and lower back pain, and nausea. The kidneys may be severely damaged, and dialysis may be required. A hemolytic reaction can be life threatening if the transfusion is not stopped as soon as the reaction starts.

**Delayed hemolytic reaction:** This type of reaction occurs when the body slowly attacks antigens (other than ABO antigens) on the transfused blood cells. The blood cells break down days or weeks after transfusion. There are usually no symptoms, but the transfused red blood cells are destroyed and the patient's red blood cell count falls. In rare cases the kidneys may be affected, requiring treatment.

People don't usually have these types of reactions unless they have had several transfusions in the past. People who have this type of reaction need special blood testing before any more blood can be transfused. Units of blood that do not have the antigen that the body is attacking must be found.

**Graft-versus-host disease (GVHD):** GVHD occurs when white blood cells in transfused blood attack the tissues of a transfusion recipient who has a severely weakened immune system. It is more likely to happen if the person receiving the blood is a relative or has a similar tissue type to the donor. The recipient's immune system doesn't recognize the white blood cells in the transfused blood as foreign. This allows them to survive and attack the recipient's body tissues. Within a month of the transfusion, the patient may have fever, liver problems, rash, and diarrhea. To prevent white blood cells from causing GVHD, donated blood can be treated with radiation before transfusion. Radiation stops white blood cells from functioning but does not affect red blood cells.

## Infections

Blood transfusions can transmit infections caused by bacteria, viruses, and parasites. The chance of an infection being transmitted is very rare, but the exact risk for each type of infection varies. Testing units of blood for an infectious organism has made the blood supply extremely safe, but no test is 100% accurate.

**Bacterial contamination:** Rarely, blood becomes contaminated with tiny amounts of skin bacteria during donation. Because platelets must be stored at room temperature, these bacteria can grow rapidly. This affects about 1 in 1000-3000 units of platelets. Patients receiving these platelets may develop serious illness within minutes or hours after the transfusion is started. In 2004, blood banks started testing platelets before they are given and discarding affected units.

**Hepatitis B and C:** Viruses that attack the liver cause these forms of hepatitis. Hepatitis is the most common disease transmitted by blood transfusions. According to the American Red Cross, about one blood transfusion in 205,000 transmits a hepatitis B infection, and one blood transfusion in 1,935,000 transmits hepatitis C. In most cases there are no symptoms, but hepatitis can lead to liver failure and other problems.

Several steps are routinely taken to reduce the risk of hepatitis from blood transfusion. Potential donors are asked questions about hepatitis risk factors and symptoms of hepatitis, and donated blood is tested to find hepatitis B virus, hepatitis C virus, and liver problems that might point to other types of hepatitis.

**Human immunodeficiency virus (HIV):** HIV causes acquired immune deficiency syndrome (AIDS). Testing each unit of donated blood for HIV began in 1985, and tests for HIV are now used on all donated blood. With improved testing for HIV, the number of transfusion-related AIDS cases continues to drop. The risk of HIV transmission through transfusion is about now about one in 2,135,000. In addition to testing, the risk is reduced by asking donors questions about HIV risk factors and symptoms.

**Other infections tested for:** In addition to the tests noted above, all blood for transfusion is tested for syphilis, as well as HTLV-I and HTLV-II, viruses linked to human T-cell leukemia/lymphoma. Since 2003, donated blood has been tested for the West Nile virus as well.

**Other possible infections:** Diseases caused by certain bacteria, viruses, and parasites, such as babesiosis, Chagas disease, malaria, Lyme disease and others can also be spread by blood product transfusions. But because of screening of potential donors with questions about health status and travel, such cases are extremely rare.

## JOB OPPORTUNITY!!

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**Interesting facts about Kentucky.  
Can you answer the questions?**

1. What song was the creation of two sisters from Louisville, KY in 1893?
2. Which great horse won all of his races except for one that he lost to a horse by the name of Upset?
3. Which city leads the nation in per capita consumption of Pepsi-Cola?
4. Which county is the world's largest producer of coal?
5. What city is the only city in the U.S. build within a meteor crater?
6. Which city hosted the first American performance of a Beethoven symphony in 1817?
7. Post-It notes are manufactured in what city?
8. The first enamel bathtub was made in what city in 1856?

Answers can be found in the address box on the bottom of this page.

**SUDOKU "EASY" PUZZLE**

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Answers: 1. "Happy Birthday to you" 2. Man 'o War 3. Pikeville 4. Pike Co. 5. Middlesboro 6. Lexington 7. Cynthiana 8. Louisville