

Feline Blood Groups : What's new ?

Feline blood groups have significant clinical importance for transfusion medicine and reproduction within this species.

Humans and pets have several blood group systems with or without natural allo-antibodies (AB).

Blood group antigens

Since 1912, the study of feline blood groups has allowed for highlighting the existence of antigens on the surface of erythrocytes.

Decades later, the monogenic autosomal determinism of the AB system is identified with the existence of a third a^{ab} allele allowing for establishing the mode of transmission of this system's blood groups: $A > a^{ab} > b$ (TABLE 1)

Erythrocyte antigens are the glycolipids or glycoproteins that are detectable in the fetus as of the 38th day, of which the structure is a residue of sialic acid.

The structure of shingolipids is different between groups A and B, with an N-Glycolylneuraminic acid (Neu-Gc) and an N-Acetyl-Neuraminic Acid (NeuAc) respectively.

There is an enzyme, cytidine monophospho-N-acetylneuraminic acid hydroxylase (CMAH), allowing for a conversion of NeuAc to NeuGc [1].

A 2007 study shows that the conversion of NeuAc to NeuGc and of feline Group B to Group A, is the result of a mutation of the CMAH [2].

There are actually several mutations that are homozygous in cats B and heterozygous in cats A, at whom the CMAH is then active (FIGURE 1).

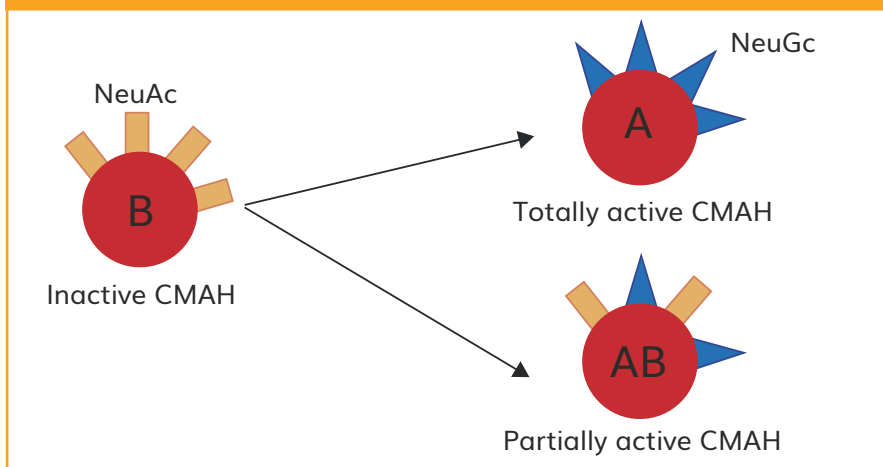
The specific mutations in Group AB cats could not be identified to date but new studies on genome analysis are underway.

The distribution of blood groups varies significantly according to geographical location and race, while type A is the most represented in the world.

TABLE 1. PHENOTYPES AND GENOTYPES IN THE FELINE AB BLOOD SYSTEM.

PHENOTYPE	A	AB	B
GENOTYPE	A/A or A/ a^{ab} ou A/b	a^{ab}/a^{ab} or a^{ab}/b	B/B

Figure 1: Action of cytidine monophospho-N-acetylneuraminic acid hydroxylase (CMAH).



In France, a 1962 study gives a prevalence of 85% of cats A and 15% of cats B.

Recent data on a broader cohort, yet unpublished, tend to adjust these values with a proportion of 85% of cats A, 13% of cats B and 2% of cats AB.

The proportion of type B can reach 25 to 50% in certain breeds such as Turkish Van, the Turkish Angora, the Cornish Rex and the Devon Rex. Conversely, certain breeds such as the Siamese and the Burmese seem not to have the b allele[3].

Natural alloantibodies

As in Humans, and unlike the Dog, the feline species possesses allo-AB without prior exposure to a blood product. These allo-AB originate from exposure to certain epitopes present in nature, whose origin remains yet unknown.

These AB belong to the immunoglobulin (Ig) family and particularly IgM, IgG, and IgE. Only 35 to 40% of the cats in group A would have a low natural anti-B type AB of low type hemagglutinins (IgM) or hemolysins (IgM and IgG).

Conversely, most of the cats in group B would possess high anti-A allo-AB titrations, for the most part of strong hemolysin and hemagglutinin type (IgM) [4].

For the AB group, studies tend to show that there is little or no hemolytic or agglutinative activity.

Recent studies have highlighted the possibility of allo-immunization in the Cat with the development of allo-AB after a whole blood transfusion [5].

Other blood systems

For several years, certain authors suspect the presence of new distinct blood antigens of the AB system.

In fact, post-transfusion hemolytic reactions or incompatible cross-match were noted between cats that were never transfused and of the same group in the AB system.

In 2007, the existence of natural allo-AB directed against a new antigen, referred to as Mik, was discovered [6].

The antigenicity and the level of Mik expression are still poorly known but this antigen is also expressed on red blood cells in Group B and A.

A recent study shows a possible allo-immunization in the Cat. In fact, certain cats transfused with compatible total blood in the AB system present incompatible cross-matches as of the second day post-transfusion [5].

A retrospective study showed that transfusion of compatible blood in the AB system increases the recipient's hematocrit if the major cross-match between the donor and the recipient is compatible [7].

The existence of erythrocyte antigens outside the AB system seems to be confirmed.

Their clinical impact and in-depth knowledge remain to be specified.



Photo 1: Quick immunochromatographic blood typing test in the AB system (©ALVEDIA). The presence of a red band at the position marked «A» or «B» indicates the expression of the corresponding antigen on the red blood cell membrane. The «C» mark indicates a control using a monoclonal anti-glycophilic antibody.

Clinical significance

Knowledge and understanding of feline blood group systems are essential in order to avoid transfusion reactions and neonatal hemolytic disease.

A transfusion reaction corresponds to a set of metabolic or immunological modifications being the cause of acute or deferred adverse effects in the recipient during transfusion of a blood product.

One milliliter of incompatible blood is enough to cause an acute transfusion reaction in a cat, that could lead to its death in nearly 30% of cases [8].

Immunological hemolytic transfusion reactions involve an antigen-AB reaction.

The neonatal hemolytic disease or neonatal isoerythrolysis is related to the ingestion of the maternal allo-AB, anti-A and, to a lesser extent, anti-B, contained in the mother's colostrum.

The transfer of immunity does not happen during the kitten's fetal life because endotheliochorial placentation in the feline species does not allow for the passage of immunoglobulins. The prevalence of this disease within the species varies from 0 to 25% depending on breed and geographical location. It has a strong economic impact on purebred cat breeding.

Grouping and compatibility tests

As the result of a significant prevalence of Group B in France and the existence of natural allo-AB against erythrocyte antigens outside of the AB system, blood grouping is essential and blood compatibility tests tend to be systematized before any blood product transfusion.

The technique providing better results in practice in on an out-patient basis is immunochromatography (Quick Test, Lab Test A+B, ALVEDIA®, PHOTO 1) [9,10].

Other feline blood group system not being well known for the time being, no grouping technique has been developed.

In veterinary medicine, several blood compatibility tests, cross-match, exist. The first methods developed in the Cat are tube methods, which include many tedious steps of red blood cell washing, incubation and centrifugation (FIGURE 2).

This method is difficult to perform, skewed by the «rouleau formation» in the Cat, the reading of the results is operator-dependent and presents a lack of standardization.

Gel techniques and immunochromatographic crossmatch have been developed by Alvedia : a quick and efficient cross-match test that can be used on an out-patient basis.

FIGURE 2: GENERAL DESCRIPTION OF THE PRINCIPLE OF THE CROSS-MATCH TEST

In fact, it allows for identifying the presence of antibodies in the recipient's serum against the donor's RBC antigens (major cross-match) or the presence of antibodies in the donor's serum against the recipient's RBC antigens (minor cross-match)

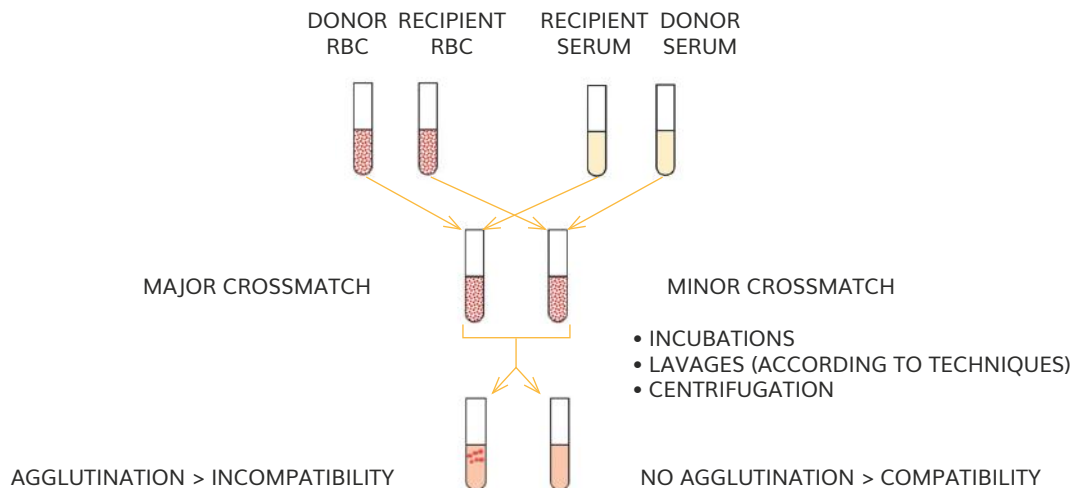
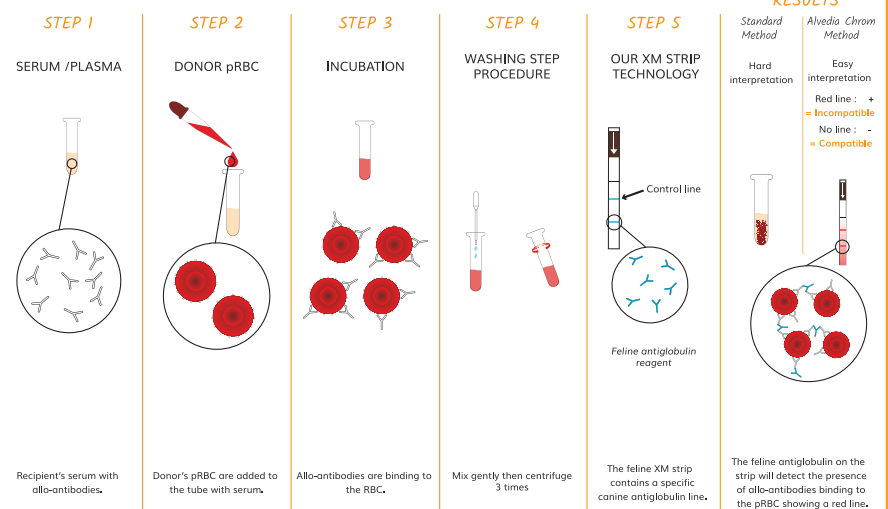


FIGURE 3 : IMMUNOCHROMATOGRAPHIC FELINE CROSSMATCH TEST



FELINE CROSSMATCH TEST

Example of positive major crossmatch result :



Conclusion

Although only a single blood system is known in the cat for the time being, there are natural allo-AB against new antigens that are, as yet, incorrectly identified.

The clinical impact of these new antigens remains to be proven, but they must be taken into account during the transfusion of a blood product or reproduction in the Cat.