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Responder Individuality in Red Blood Cell Alloimmunization

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One may define human blood groups by two fundamental characteristics: i) determinants (antigens) are located on the outer surface of human red blood cells, and ii) these antigens are capable of provoking an immune reaction. The reaction may occur 'naturally', e.g., when the ABO blood group system forms isoagglutinins, or may be observed in an allogeneic setting, e.g., during pregnancy or after transfusion of poorly matched blood, in the process of alloimmunization.

Alloimmunization may or may not occur in individuals exposed to 'non-self' blood group antigens. Many researchers have intensively studied the variables that determine the process of blood group alloimmunization. However, to date, there are only some hypotheses but no comprehensive theory as to why the immune systems of certain individuals tolerate foreign blood group antigens and others do not.

As a postulate, the panoply of known immunoregulatory systems will likely be found responsible for red blood cell alloimmunization and will therefore constitute an important area of future research [1]. This anticipation is supported by stochastic modelling, which identified a subgroup of transfusion recipients who had a dramatically increased risk of alloimmunization which appeared to be genetically determined, because it was discovered to be independent of common disease states, patient age, or the number of alloantibodies already formed, and only weakly correlated to transfusion frequency [2].

A thorough literature search has revealed something related to the topic of alloimmunization that immunohematologists would find amusing. Some researchers have investigated the immunological response of chickens following injection of sheep red blood cells. However, this research was more focused on the partitioning of nutrients between the immune system and growth pathways in order to select for optimized weight gain in different breeding lines of chicken than on addressing the potential immunological impacts of xeno-transfusions [3].

It's also amusing to find three relevant articles from European researchers in the August issue of the American Association of Blood Banks (AABB) Journal *Transfusion* [4–6], and five American groups (and only one European) reporting their findings in this December issue of TRANSFUSION MEDICINE AND HEMOTHERAPY, the official publication of the German Society for Blood Transfusion and Immunohematology (DGTI) [8–12]. May the prophets receive appropriate recognition in their own countries!

This issue of TRANSFUSION MEDICINE AND HEMOTHERAPY is an attempt to summarize and review theories, ideas, projects, and evidence in the fascinating field of 'Responder Individuality in Red Blood Cell Alloimmunization'.

Accordingly, Günther Körmöczi and Wolfgang R. Mayr present a comprehensive overview with respect to red blood cell alloimmunization [7], whereas Eric A. Gehrie and Christopher A. Tormey specifically address the influence of clinical and biological factors on transfusion-associated alloimmunization [8]. In the same context, Alex B. Ryder, James C. Zimring and Jeanne E. Hendrickson report their 'Lessons Learned from Murine Models' [9], and Sally A. Campbell-Lee and Rick A. Kittles describe specificities of red blood cell alloimmunization found in individuals with sickle cell disease patients [10]. Neil A. Hanchard, Joann M. Moulds, John W. Belmont, and Alice Chen describe their findings of genetic polymorphism and its linkage to alloimmunization in sickle cell disease patients [11]. And again, also on a predominately genetic level, Zohreh Tatari-Calderone, Naomi L.C. Luban and Stanislav Vukmanovic attempt to answer the question: 'Can Clues from Susceptibility to Autoimmunity Pave the Way?' [12], for a better understanding of 'Responder Individuality in Red Blood Cell Alloimmunization'.

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