1. **Answer (b)**


Brief summary:

This article is from a Canadian Blood Service symposium aimed at looking at blood group antigens and their emerging role in the structure and function of the red cell.

The authors presented the physiology, structure and function of the red cell as an introduction and state that ‘Many of the RBC membrane proteins are polymorphic, thereby conferring blood group activity and the capacity to be alloantigenic. As a result of antibody and RBC phenotype identification, a greater understanding of the complexity of the RBC and the function of these proteins has been obtained. These membrane proteins may act as transporters, adhesion and receptor molecules, enzymes and complement regulators. Examples of these proteins which will be discussed later in the proceedings include band 3 (carries the Diego blood group system, is an anion-exchanger, and is involved in red cell senescence), Rh complex (a possible ammonium and CO2 transporter), and Kidd (involved in urea transport).’

Dr. Petr Jarolim presented the role of band 3 in the pathogenesis of Hereditary Spherocytosis, Hereditary Stomatocytosis, and South East Asian Ovalocytosis. It is interesting to note that South East Asian Ovalocytosis results from a mutation resulting in the loss of 9 amino acids from an intracytoplasmic region of the band 3 protein which confers resistance to severe forms of malaria, although it doesn’t affect the rate of infection but results in decreased mortality from the disease.

Dr. Jean-Pierre Cartron presented the functional aspects of the Rh and the Kidd blood group systems. This presentation states that ‘Blood group gene products can be schematically divided into 5 functional categories: (i) receptors for exogenous ligands, viruses, bacteria, and parasites; (ii) adhesion molecules (iii) membrane transporters and channels (iv) enzymes (v) structural proteins. However some of these molecules may exhibit multi-functional properties, like band 3, the product of the Diego blood group gene, which is the HCO3-/Cl- exchanger, but also plays an important role as a structural protein (membrane skeleton linkage) and as receptor involved in *Plasmodium falciparum* invasion. Rh proteins belong to the functional group of transporters and have a typical membrane topology with multispanning segments (like other transporters such as the Kidd protein mediating urea transport or the Colton/aquaporin-1 protein mediating water transport). Rh proteins have also recently been recognized as another membrane attachment site of the membrane skeleton and thus play a role in the mechanical properties of the RBC membrane. The function of the Rh antigens remained elusive until recently.’ The final presentation by Dr. M.B. Kay is called ‘Red Blood Cell Senescence, Physiologic Autoantibodies, and Cellular Removal.’

2. **Answer (d)**


Brief summary:

Transfusion associated graft-versus-host disease (TAGVHD) is a rare complication of transfusion of non-irradiated blood to a susceptible recipient. Donor T cells mediate a cellular immune response against host tissue that is unresponsive to immunosuppressive therapy. The mortality rate exceeds 90%.

Most institutions provide irradiated components to:-

- Immunocompromised patients e.g. peripheral blood progenitor cell transplant recipients, immunodeficiency syndromes
- Recipients of blood from relatives or HLA matched components

The authors report the first case of TAGVHD in an apparently immunocompetent patient in the United States who was transfused during cardiac surgery. The patient developed severe leucopenia and the bone marrow biopsy showed severe hypoplasia. A skin biopsy showed Grade 11 GVHD. The patient died Postoperative Day 42.
One the RBC donors were found to be homozygous for a HLA Class 1 and Class 11 haplotype in the patient. The authors note that ‘Leucoreduction also decreases the number of T cells but has not proven to be fully effective in preventing the development of TAGVHD in immunoinactive or immunocompetent recipients’.


These authors state ‘Universal leucoreduction (UL) has been implemented in many blood centres around the world and some countries (e.g. in Europe) primarily for its documented benefit in reduction of leucocyte-associated viral transfusion-transmitted infectious diseases, for its reduction of alloimmunisation, and for its reduction of non-haemolytic transfusion reactions. UL has also been shown to lower the incidence of TAGVHD in recipients, as reported in the Serious Hazards of Transfusion (SHOT) study. Thirteen cases of TAGVHD were reported in the UK between 1996 and 2001, three of which were cardiac surgery patients (one of which received fresh blood). No reports of TAGVHD in immunocompetent patients have been reported to SHOT since 2001. As TAGVHD is a relatively rare disease in the era of irradiation, documenting an overall reduction in incidence based on UL is difficult without a large study based on a large database.’

3. Answer (b)

Reference: Lee, E et al 2007, 'Do patients with autoantibodies or clinically insignificant alloantibodies require an indirect antiglobulin test crossmatch', Transfusion, vol.47, pp.1290-1295

Brief summary:

The authors discuss the difficulties of selecting compatible red cell units in patients with warm autoimmune haemolytic anaemia or a positive DAT with free autoantibodies - similarly in patients with 'high-titre, low avidity (HTLA)-like antibodies. The safety of the immediate-spin crossmatch as an alternative to an IAHG crossmatch is discussed in patients with no underlying clinically significant alloantibodies.

The three protocols for detecting underlying alloantibodies were 1) Dilution technique 2) ZZAP autoadsorption 3) Alloadsoption with three selected papain-treated donor RBC's. The authors provide evidence that an immediate spin (or electronic) crossmatch could be used to provide compatible blood to patients shown to have autoantibodies or HTLA-like antibodies with no underlying alloantibodies.

With regard to the dilution method for detecting underlying alloantibodies the authors note that ‘it has been suggested by Leger and Garratty that dilution of the sample was not acceptable because it resulted in alloantibodies being missed. We are using a lower dilution than the 1 in 5 described by Leger and Garratty. In a study described by Knight and co-workers, the dilution method was undertaken where the clinical situation demanded that blood be provided urgently or there was too little serum available to use for adsorption studies. In 60 percent of cases, a 1-in-3 dilution was usually enough to weaken the autoantibody activity sufficiently for any underlying alloantibody to be exposed. This protocol has been adopted as an optional method by our laboratory, in the investigation of underlying alloantibodies in patients with autoantibodies. Patients with strong autoantibodies require autologous or allogeneic adsorption to prove that there are no underlying alloantibodies. Having shown this, a similar consideration can be applied when performing an IS XM.’

4. Answer (d)


Brief summary:

This article presents three cases of severe foetal anaemia in three pregnancies in the same family. Anti-M in the mother was of low titre and the baby DAT was negative in all cases. The diagnosis was confirmed by the rapid clearance of Cr51 labelled M positive red cells.

At the author's hospital 14% of red cell antibodies identified during pregnancy are anti-M however the incidence of disease in the foetus and/or newborn is reported to be extremely low. It was postulated that the mechanism of the severity of the foetal anaemia with such low titre anti-M may be similar to anti-K and anti-Ge HDFN whereby erythroid progenitor cells possess Kell and Gerbich antigens.
5. **Answer (a)**


Brief summary:

Of the 2630 adverse events reported to the Serious Hazards of Transfusion (SHOT) scheme between 1996 and 2004, 70% were attributable to the category IBCT (incorrect blood component transfused).

‘IBCT are potentially avoidable system failures throughout the transfusion chain. Process mapping of the process of prescribing, requesting, providing, and administering blood components reveals that it is a complex chain with opportunities for error at several critical points.’

Haemolytic reactions where a transfusion error is identified are reported in this category. These include 255 cases of delayed haemolytic transfusion reaction with Kidd antibodies accounting for 53% of cases and Rh antibodies 38%. Occasionally these cases are fatal.

‘In at least 6 cases of delayed haemolytic reaction, the implicated antibody, undetectable in pre-transfusion testing, had previously been identified by another laboratory, but this information was unavailable at the time of transfusion’.

‘Expert review of haemolytic reactions suggest, although there was no identifiable error, 14% might have been avoided by improved practice such as transfusion of ABO identical platelets, full investigation of patients with auto-immune haemolytic anaemia to exclude masked allo-antibodies, use of appropriate sensitive pre-transfusion testing, and a systematic approach to antibody identification and better use of reference facilities to elucidate complex mixtures of antibodies. In at least 6 cases of delayed haemolytic reaction, the implicated antibody, undetectable in pre-transfusion testing, had previously been identified by another laboratory, but this information was unavailable at the time of transfusion.’

Acute intravascular haemolysis due to major ABO incompatibility is most feared however other errors resulted from:

- Failure to provide a suitable component e.g., for neonates or women of child bearing age
- Erroneous laboratory results leading to volume overload or unnecessary exposure to blood components.

Fortunately the majority of patients receiving incorrect blood components suffer no short or long term ill effects however 20 deaths in the UK have been attributed wholly or in part to transfusion errors over the 8 year period and 92 patients suffered major morbidity.

Delayed transfusion reactions (not attributable to incorrect component selection) constituted 9.7% of the serious hazards, TRALI 6.2% and transfusion transmitted infections 1.8%.

6. **Answer (a)**


Brief summary:

LU is located on the long arm of chromosome 19, as part of the linkage group that includes the genes for the H (FUT1), secretor (FUT2) and Lewis (FUT3) glycosyltransferases, and for the LW blood group. Lu^a antibodies may be naturally occurring or immune – often IgM but may also be IgG and IgA.

Transfusion haemolytic reactions with Lutheran antibodies are usually mild and delayed in type with no reported cases of HDN requiring more than phototherapy.

There is evidence that Lu-glycoproteins appear late in erythroid production and bind to laminin (a component of the extracellular matrix) facilitating the movement of maturing erythroid cells from the erythroblastic islands to the peripheral circulation. No disease process has been found in association with the null phenotype.

The author discusses the possible association between enhanced binding of Lu-glycoproteins with contribution to the pathology of sickle cell disease and polycythaemia vera.
7. **Answer (a)**

Reference: Judd, W J, et al, 2005, ‘On a much higher than reported incidence of anti-c an R_{1}R_{1} patients with anti-E’, *Immunohaematology*, vol.21, pp.94-96

**Brief Summary:**

The authors reviewed the results of 82 R_{1}R_{1} patients with anti-E. Screening with non-ficin treated red cells by tube or gel IAT found anti-c in 32 of the 82 patients. After testing with ficin treated red cells by gel technique, 21 additional patients with anti-E were found to have anti-c. The incidence of anti-c in R_{1}R_{1} patients with anti-E was 32% with untreated RBCs and 65% with ficin treated RBCs using gel technology. The author now routinely selects c- blood for R_{1}R_{1} patients with anti-E regardless of whether or not anti-c is detected.

8. **Answer (a)**

Reference: Guidelines for Pretransfusion Laboratory Practice: 5th Edition March 2007

**Brief Summary:**

‘Once a transfusion episode has commenced, subsequent samples from the patient will have an expiry of 72 hours until a gap of three months between transfusions has occurred.’

In this question the time elapsed since the transfusion commenced is greater than 72 hours. A fresh sample would be required to exclude the presence of antibodies generated in response to the blood transfused on Monday.

9. **Answer (d)**


10. **Answer (d)**


**Brief Summary:**

This article is not directly related to this question but has been included to illustrate the importance of considering allo or autoantibodies in the patient that react at room temperature and may cause discrepant grouping reactions. The authors give an example of a group A patient with anti-P1 that reacted with A1 cells in the reverse group. Anti-P1 was subsequently identified in the patient’s plasma and the A1 cell used in the reverse group was P1 positive.