JOURNAL-BASED LEARNING EXERCISES

Each article's contents should be read, researched and understood, and you should then come to a decision on each question. The pass mark is 17 out of 20 questions answered correctly. JBL exercises may be completed at any time until the published deadline date. Please select your choice of correct answers and complete the exercises online at: **ibms.org/go/practice-development/cpd/jbl**

DEADLINE WEDNESDAY 1 NOVEMBER 2017

A and B antigen levels acquired by group O donor-derived erythrocytes following ABO-non-identical transfusion or minor ABO-incompatible haematopoietic stem cell transplantation.

Hult AK, Dykes JH, Storry JR, Olsson ML. *Transfus Med* 2017; **27** (3): 181–91. Assessment No: 080217

01	Current guidelines for transfusion support in ABO-incompatible haematopoietic stem cell transplantation (HSCT) prescribe blood components that are compatible with both the recipient and the donor ABO groups in order to avoid haemolysis of any transfused red blood cells (RBCs), the residual recipient RBCs and the engrafting donor-derived RBCs.
02	The acquisition *in vivo* of A/B antigens by group O RBCs following transfusion or HSCT has never previously been observed using standard serological techniques.
03	EDTA is a well-known chelating agent, but complex binding of the Mn^{2+} ions required for ABO transferase activity was not anticipated.
04	Time of circulation for transfused group O RBCs correlates with A antigen levels adsorbed.
05	When donor-derived group O RBCs were tested with anti-A, an increase in mean fluorescence intensity (MFI) compared to group O controls were observed in all patients but one.
06	The findings support the major role of A/B antigen adsorption from secretor plasma, but also indicate that secretor status is an absolute prerequisite for the *in vivo* conversion of group O RBCs.
07	Inactivated A_1 plasma was incubated with group O RBCs, UDP-GalNAc and $MnCl^2$, and no A antigens could be detected with anti-A.
08	The marked difference in detectable levels of adsorbed antigen between secretor individuals of different ABO blood groups reflects a variable amount of soluble antigen available in plasma.
09	Lactosylceramide is the major glycosphingolipid precursor of RBCs.
10	In a different study, levels of soluble ABO blood group substance in plasma were influenced by the homozygous expression of the *A*^{1}, *A*^{2} or *Se* alleles, respectively.
11	When incubated with the appropriate substrate, A or B antigens were not detectable in the group O RBCs after four hours.
12	Accumulating data indicate that the infusion of plasma which contains ABO antibodies may cause the rapid clearance of platelets.
13	In haematopoietic tissue, the *FUT1* (or *H*) gene encodes a 2-α-fucosyltransferase, which synthesises the H antigen mainly on type 1 oligosaccharide acceptors, linked to proteins (approximately 10%) and lipids (approximately 90%).
14	After 48 hours, group O RBCs incubated with group A_1 and B plasma expressed A and B antigens at a level almost equivalent to normal group A_2 and B RBCs.
15	When group O RBCs incubated with group A_1 RBCs were tested with anti-A, a rise in MFI was seen equivalent to the MFI seen in naturally occurring ABO subgroup A_3.
16	A greater increase in MFI was observed when group O RBCs were incubated with group A_1 secretor plasma compared to group A_1 non-secretor plasma.
17	The time course of antigen adsorption into RBCs is probably not influenced by plasma lipoproteins for lipid uptake.
18	In two secretor patients, genetically defined as *ABO*A1.01/O.02* and *ABO*A2.01/O.01.02*, respectively, it was found that there was a clear difference in A antigen levels in donor-derived group O RBCs.
19	The study provides additional support for the proposed selection of plasma components compatible with both donor and recipient ABO blood groups.
20	There may be a preference of the anti-B clone 9621A8 for type 1-based B antigen.

Evaluation of the optimal provision of formalin-fixed, paraffin-embedded material for reverse transcription-PCR in soft-tissue tumour diagnosis.

Thway K, Wren D, Lee J, Thompson L, Fisher C, Gonzalez D. *J Clin Pathol* 2017; **70** (1): 20–4 (http://jcp.bmj.com/content/70/1/20.long). Assessment No: 080717

01	Molecular genetic analysis is now a routine ancillary diagnostic modality to the histopathological diagnosis of soft tissue neoplasms.
02	When soft tissue tumours are examined by reverse transcriptase-PCR, many of the gene fusions are not identified.
03	In this paper by Thway *et al.* a comparison was made of the RNA yield from 5x10 µm scrolls, 5x5 µm scrolls and 1x10 µm scrolls.
04	The paper concluded that there was no difference in the RNA extraction and purification and the tissue sectioning strategy.
05	The authors concluded that the sole factor affecting RNA yield was the nature of the specimen type.
06	Soft tissue tumours are a homogeneous group of neoplasms.
07	Soft tissue neoplasms occur at just a limited few anatomical sites.
08	Many soft tissue neoplasms are associated with recurrent chromosomal translocations leading to characteristic gene fusions.
09	Endometrial stromal sarcomas show fusion transcripts of the *FUS-DDIT3* genes.
10	Formalin-fixed, paraffin-embedded (FFPE) samples provide the main source of patient nucleic acids for ancillary molecular investigations.
11	RT-PCR is particularly useful as it identifies specific fusion transcripts in contrast to FISH for which commercial break-apart probes are routinely used, which only provide evidence of a gene rearrangement.
12	Alveolar rhabdomyosarcoma has fusion transcripts assessed by RT-PCR on genes *PAX3-FOX01* and *PAX7-FOX01*.
13	RT-PCR has generally been less sensitive than FISH to suboptimal methods for tissue fixation and processing.
14	Monophasic synovial sarcomas can show *SS18-SSX1* fusion transcripts.
15	In tumour types that lead to technical failures by RT-PCR, myxoid neoplasms were relatively rarely represented.
16	The prominent stromal component of myxoid or fibrous stroma might lead to difficulty of RNA extraction.
17	In referred cases, tissue fixation may have been more optimally regulated than in the tertiary referral centre.
18	RNA is purified most effectively from large resections using thinner sections mounted onto glass slides.
19	Thick section scrolls could saturate the extraction and compromise the purification process.
20	Synovial sarcomas can show fusion transcripts on the *SS18-SSX1* genes.

REFLECTIVE LEARNING

01	How does this paper help to explain why transfused red cells, and the donor-derived red cells from HSCT, take on the Lewis type of the recipient?
02	How does this paper help to explain why, for example, a group O HSCT, given to a group A recipient, often fails to make an anti-A, but does make an anti-B?

01	What are soft tissue tumours? What is their incidence, pathology and outcome?
02	Describe another example where PCR is used for cellular pathology investigations.