JOURNAL-BASED LEARNING EXERCISES

Please select your choice of correct answers and complete the exercises online at: **www.ibms.org/cpd/jbl**

DEADLINE WEDNESDAY 2 OCTOBER 2019

Flow cytometry-based diagnosis of primary immunodeficiency diseases.

Kanegane H, Hoshino A, Okano T *et al. Allergol Int* 2018; **67** (1): 43–54.
www.sciencedirect.com/science/article/pii/S1323893017300679
Assessment No: 070519

01	IRAK4 is a kinase that plays a crucial role in Toll-like receptor (TLR) and IL-2 receptor signalling.
02	Lymphocytes from patients with X-linked SCID (X-SCID) show deficient CD132 expression.
03	A large number of PIDs can be diagnosed by analysing expression of specific intracellular proteins.
04	Lymphocytes from patients with XLP1 lack expression of X-linked inhibitor of apoptosis (XIAP) protein.
05	Most patients with CVID or hyper IgM syndromes have decreased switched memory B cells.
06	Laboratory diagnosis of CGD is performed by the measurement of superoxide production, and is evaluated by flow cytometry using DHR123 oxidation.
07	Patients with IL-10 receptor deficiency demonstrate reduced STAT3 phosphorylation when stimulated with IL-2.
08	CTLA4 is a co-stimulatory molecule expressed by activated T cells.
09	XLA is characterised by the absence of circulating B cells and severe reduction of all serum immunoglobulins due to mutations in the *BTK* gene.
10	CD40L (CD145) expression by activated CD4+ T cells is absent or reduced when assessed by anti-CD40L-specific mAbs in most but not all patients with X-linked HIGM.
11	CD40 deficiency, one of several autosomal recessive HIGM syndromes, is a phenocopy of CD40L deficiency that can be identified by assessing CD40 expression on B cells, monocytes or dendritic cells.
12	CMCD is characterised by persistent or recurrent *Candida albicans* infections of skin, nail and mucosal membranes.
13	A small subset of CVID is caused by mutations in ICOS, CD19 and BAFFR (TNFRSF13C).
14	CD19 forms complexes with CD21, CD81 and CD225 which collaborate with the B-cell receptor upon antigen recognition.
15	WAS is a rare X-linked disorder characterised by persistent microthrombocytopenia, eczema, cellular and humoral immunodeficiency, and an increased risk of autoimmune disease and haematologic malignancy.
16	XLP is classified into type 1 (XLP1) caused by mutations in the *SH2D1A* gene encoding XIAP, and type 2 (XLP2) caused by mutations in the *XIAP* or *BIRC4* gene encoding SAP.
17	While patients with XLP1 have elevated numbers of iNKT cells, patients with XLP2 have variable low numbers of iNKT cells.
18	Genetic defects affecting granule-mediated cytotoxicity are associated with FHL, including perforin (FHL2), Munc13-4 (FHL3), syntaxin 11 (FHL4) and Munc 18-2 (FHL5) deficiencies.
19	Most patients with ALPS have mutations in genes which regulate the extrinsic Fas-mediated programmed cell death pathway.
20	IPEX syndrome, a rare X-linked autoimmune disorder caused by mutations in the *FOXP3* gene, is characterised by severe enteropathy, endocrinopathies (diabetes and/or thyroiditis) and eczematous dermatitis.

Vitamin D supplementation and total cancer incidence and mortality: a meta-analysis of randomized controlled trials.

Keum N, Lee DH, Greenwood DC, Manson JE, Giovannucci E. *Ann Oncol* 2019; **30** (5): 733–43. Assessment No: 070319

01	Mendelian randomisation studies have found that genetic variation in 25(OH)D levels is associated with the incidence of most cancers.
02	Vitamin D toxicity may cause hypercalcaemia and kidney stones.
03	Results from this paper show that vitamin D supplementation affects cancer incidence.
04	Vitamin D supplementation has an inverse effect on overall mortality.
05	Randomised control trials of one year or less were included in this meta-analysis.
06	Vitamin D supplementation has an immediate effect on cancer mortality.
07	Vitamin D plays a role in cell differentiation and apoptosis, inhibition of cancer cell proliferation and angiogenesis, and has anti-inflammatory and immunomodulatory properties.
08	This paper hypothesises that supplement dose and/or attained serum 25(OH)D levels may affect the anti-cancer effectiveness of vitamin D.
09	Earlier studies show that vitamin D has an equal effect on cancer incidence and mortality.
10	Serum levels of less than 125 nmol/L are considered insufficient.
11	There is evidence that the geographical association between solar UV exposure and cancer is stronger for mortality than incidence.
12	Epidemiological evidence suggests a potential benefit (of vitamin D supplementation) only for the incidence of lung and breast cancers.
13	It may take up to six months for serum 25(OH)D levels to reach equilibrium after supplements are started.
14	A limitation of this study is that most of the RCT study populations were ethnically diverse.
15	Results from this paper show that daily vitamin D supplementation and less-frequent bolus doses are equally effective in affecting cancer mortality.
16	Results from this paper show that vitamin D supplementation affects cancer mortality.
17	Results from previous meta-analyses of randomised controlled trials of vitamin D supplementation and cancer incidence & mortality were consistent.
18	A strength of this study is that the influence of vitamin D supplementation could be assessed over a period of three to 10 years.
19	The VITAL study shows increasing benefits over time of vitamin D supplementation.
20	Vitamin D supplementation of at least 1500–2000 IU/day is required to raise serum 25(OH)D levels above 75 nmol/L.

REFLECTIVE LEARNING

01	Critically appraise the use of flow cytometry and genetics in the diagnosis of primary immunodeficiency.
02	Discuss the limitations of using patient and disease controls in flow cytometry.
	Outline the principles of Mendelian randomisation studies.
	Does this paper, and other similar studies, provide evidence that would convince you to take vitamin D supplements?