

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 4 OCTOBER 2017

Toxicology in clinical laboratories: challenging times. Brown NW. <i>Br J Biomed Sci</i> 2017 (Epub ahead of print). Assessment No: 070317		Chronic mucocutaneous candidiasis disease associated with inborn errors of IL-17 immunity. Okada S, Puel A, Casanova JL, Kobayashi M. <i>Clin Transl Immunology</i> 2016; 5 (12): e114. doi:10.1038/cti.2016.71 Assessment No: 070517	
01	The EMCDDA reports the most widely abused drug to be cocaine.	01	The Janus kinase inhibitor, ruxolitinib, has been trialled in two patients with GOF- <i>STAT1</i> mutations, leading to improvement of chronic mucocutaneous candidiasis (CMC) and autoimmune syndrome, but with significant adverse effects.
02	Synthetic cannabinoids are the most numerous NPS in Europe.	02	The IL-17 receptor family consists of four members (IL-17RA, IL-17RB, IL-17RC and IL-17).
03	Legal high (NPS) use is not associated with significant adverse effects.	03	In 2009, a primary immunodeficiency, which associates with a genetic defect of <i>CARD9</i> , was identified in the patients who suffer from CMC and invasive fungal infections.
04	Cannabis strength has remained constant over the last few years.	04	Chronic mucocutaneous candidiasis is characterised by recurrent or persistent infections affecting the nails, skin, and oral and genital mucosae, caused by <i>Candida</i> spp., often <i>C. albicans</i> .
05	Synthetic cannabinoid use can be detected using cannabis drug screening methods.	05	Most patients with CMC disease (CMCD) are treated with topical and/or systemic antifungal agents.
06	Phenazepam is primarily detected in the urine as its demethylated metabolite.	06	Hyper IgE syndrome (HIES) has either a dominant or recessive pattern of autosomal inheritance, with the rare autosomal-recessive (AR) HIES largely shown to be caused by mutations in <i>DOCK8</i> .
07	Euphoria is a known side effect of pregabalin.	07	There are several reports describing increased frequency of circulating IL-17-producing cells in <i>CARD9</i> -deficient patients, probably explaining the clinical phenotype of CMC.
08	The number of admissions for alcohol-related disease has almost doubled in 10 years.	08	Neutrophils from <i>CARD9</i> -deficient patients show a selective <i>C. albicans</i> -killing defect that is CR3- and <i>CARD9</i> -independent, but NADPH oxidase-dependent.
09	CDT can be used to detect binge drinking.	09	Patients with APECED produce neutralising autoantibodies against IL-17A, IL-17F and/or IL-22, leading to development of CMC.
10	It is impossible to adulterate an oral fluid sample.	10	Hyper IgE syndrome is a primary immunodeficiency disease, is characterised by elevated serum IgE levels, recurrent staphylococcal skin abscesses, eczema and pulmonary infections.
11	Clinical cut offs are clearly defined.	11	Peripheral blood mononuclear cells from autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) patients with CMC show decreased IL-17F and IL-22 secretion <i>in vitro</i> .
12	Immunoassay drug screening methods can be used to detect NPS.	12	ROR γ T is a master transcription factor of Th17 cells.
13	Buprenorphine is always present in the urine of persons regularly taking the drug.	13	Patients with AR-complete IL-12p40 or IL-12R β 1 deficiencies show decreased frequencies of circulating IL-17-producing cells, albeit a less severe reduction than observed in patients with autosomal-dominant (AD) HIES.
14	Nefopam is known to give false-positive opiate screen results.	14	There is some controversy regarding the frequency of circulating IL-17-producing cells in <i>CARD9</i> -deficient patients.
15	GC cannot be used to screen for thermally labile drugs.	15	<i>STAT3</i> -deficient patients frequently develop CMC associated with other infectious and clinical manifestations.
16	In-source fragmentation when using LC-MS/MS is not a significant problem in toxicology.	16	The <i>STAT3</i> mutations identified in AD HIES patients are gain-of-function (GOF) and exert a dominant positive effect on wild-type <i>STAT3</i> -mediated signalling.
17	Deuterium loss from internal standards may be a serious issue.	17	The first patient reported with AR IL-17RA deficiency was born to consanguineous Argentinian parents.
18	LC-high resolution MS requires careful use when identifying drugs and metabolites.	18	The first case of AR-complete IL-12p40 deficiency was identified in 1998 in a patient born to consanguineous parents who developed disseminated infection with BCG and <i>S. enteritidis</i> .
19	ISO 15189 is acceptable for forensic toxicology.	19	APECED, also called APS-1 syndrome, is an autosomal-dominant inherited disorder caused by bi-allelic mutations in <i>AIRE</i> .
20	Amphetamine half-life in the body is decreased with acidic urine.	20	ACT1 also has an inhibitory role in B-cell survival by upregulating CD40 and B-cell-activating factor receptor through interaction with TRAF3.

REFLECTIVE LEARNING

01	You are required to re-establish your laboratory's toxicology service following the retirement of the previous postholder. Given that the analytical workload is 1200 samples a month, what techniques will you use to perform the analyses, and why?	01	Review the pathways of inborn errors of IL-17 immunity and outline the mutations which give rise to a compromised immune system.
02	Discuss ion suppression, in-source fragmentation and isobaric interference in MS-based assays.	02	Discuss the role of IL-17 in mucocutaneous immunity to <i>Candida</i> in humans.