JOURNAL-BASED LEARNING EXERCISES

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DEADLINE WEDNESDAY 3 FEBRUARY 2021

Assessment of SARS-CoV-2 serological tests for the diagnosis of COVID-19 through the evaluation of three immunoassays: Two automated immunoassays (Euroimmun and Abbott) and one rapid lateral flow immunoassay (NG Biotech).
Nicol T, Lefeuvre C, Serri O *et al. J Clin Virol* 2020; **129**: 104511 doi: 10.1016/j.jcv.2020.104511. Assessment No: 110620

01	The authors suggest that serological testing could be complementary to RT-PCR for the SARS-CoV-2 genome.	11	Samples collected from all the patients who had a positive RT-PCR result were reported to be positive in the serological assays in this study.
02	The study included serum from 293 individual patients.	12	The lateral flow assay was more sensitive than all the other tests in samples collected less than 14 days after onset of symptoms.
03	The lateral flow and CLIA assays evaluated in this study were designed to detect the presence of SARS-CoV-2 spike protein in serum.	13	The ELISA assays for IgA and IgG were the only tests which are reported to have presumed false-positive results in samples from pregnant women.
04	Seven of the samples collected in March 2019 gave a presumed false-positive result in the IgA ELISA, compared to one in the chemiluminescence immunoassay CLIA IgG.	14	The authors suggest that the technique used to collect specimens for the RT-PCR assay is not one of the factors affecting the accuracy of the result.
05	The authors reported no difficulties with interpretation of the results with the lateral flow assay.	15	In this study, the CLIA assay designed to detect IgG to the SARS-CoV-2 nucleoprotein was a quantitative method.
06	The results of this study show that detection of IgG antibody to SARS-CoV-2 spike or nucleocapsid protein indicates protection against re-infection.	16	The study included samples from two patients with COVID-19 symptoms but a negative RT-PCR result, and two with positive RT-PCR but no symptoms.
07	There was good agreement between the performance of ELISA which detected spike protein and the CLIA which detected nucleoprotein in samples collected within seven days of onset of symptoms.	17	The serological profiles of the seven individual patients included examples of seroconversion at one, two and three weeks post onset of symptoms.
08	The authors point out that when considering use of lateral flow assays as point-of-care tests, appropriate reporting of results must be considered.	18	RT-PCR for SARS-CoV-2 is the gold standard test for diagnosis of acute COVID-19 infection.
09	The CLIA which detected IgG against the SARS-CoV-2 nucleoprotein was more sensitive than the other IgG assays in samples taken up to seven days post onset of symptoms.	19	It is clearly stated that the pregnant women whose samples were included in the controls had previously been tested for SARS-CoV-2 infection.
10	Although all the reported sensitivities for all the assays evaluated were 100% in samples taken more than 14 days post onset of symptoms, the IgA assay had the highest overall specificity.	20	The controls included at least one sample containing antibodies to influenza B.

REFLECTIVE LEARNING

01	Critically review the evidence regarding the immune response to SARS-CoV-2.	02	Discuss the role of serological testing in epidemiological studies of COVID-19 transmission.

DEADLINE WEDNESDAY 3 FEBRUARY 2021

The value of BRCA-1-associated protein 1 expression and cyclin-dependent kinase inhibitor 2A deletion to distinguish peritoneal malignant mesothelioma from peritoneal location of carcinoma in effusion cytology specimens.
Wajd A, Gazzo S, Blanchet M *et al. Cytopathology* 2020; **31** (1): 5–11. doi: 10.1111/cyt.12788. Assessment No: 110820

01	The diagnosis of DMPM is difficult for several reasons including morphology overlap with other benign and malignant diseases.	**11**	In the FISH analysis, heterozygous deletion was assumed when two *CDKN2A* signals were present for one *CEN9* signal.
02	The study included 48 cases of DMPM, 71 cases of peritoneal carcinomatosis and five cases of effusion in a context of benign mesothelial proliferation.	**12**	89.5% of the DMPM cases were epithelial mesothelioma, three were biphasic and two were sarcomatoid mesothelioma.
03	Atypical reactive mesothelial cells can be seen in benign processes; for example, local infection, drug reactions, trauma and inflammation.	**13**	Calretinin staining was negative in half of the cases.
04	Epithelial membrane antigen, calretinin, cytokeratin 5/6 and WT-1 are among the immunocytochemical markers purported to be useful in the diagnosis of peritoneal mesothelioma.	**14**	60.9% of the peritoneal carcinomatosis cases were of GI tract origin, with the remaining 39.4% from a gynaecological origin.
05	There is no need for a highly specific marker for mesothelioma for application in effusion cytology specimens.	**15**	None of the peritoneal carcinomatosis cases showed loss of BAP1 expression in the tissue or the cell block samples.
06	Loss of p16 can be detected by FISH in FFPE tissues but not effusion cytology specimens.	**16**	FISH results were not interpretable due to insufficient tumour cells in 11 cases and technical failure in 22 cases.
07	p16 deletion is highly specific for malignancy but can only be demonstrated in a portion of mesotheliomas.	**17**	The study identified a loss of BAP1 expression in more than half of the peritoneal mesotheliomas, with full concordance between tissue samples and cell block samples.
08	*BAP1* mutations can increase the susceptibility to develop a variety of neoplasms including cutaneous melanoma, clear cell renal cancer, BCC or mesothelioma.	**18**	BAP1 immunostaining was confirmed to be a good biomarker to assess the diagnosis of peritoneal mesothelioma in case of malignant cells in ascites having 100% specificity in this study.
09	In this study, all the cytology specimens were prepared as cell blocks.	**19**	The study confirmed previous findings by Chiosa *et al.* and more recently Watts *et al.* and Hwang *et al.* of the usefulness of assessing 9p21 homozygous deletion in FFPE tissue by FISH to differentiate between malignant mesothelioma and reactive mesothelial proliferations.
10	Negative staining for BAP1 was defined as completely absent staining in tumour cells and positive staining as nuclear staining in >10% in the tumour cells.	**20**	*CDKN2A* deletions in gynaecological and digestive malignancies were found to be common.

REFLECTIVE LEARNING

01	Which panel of adjunctive tests is routinely used in your laboratory in the diagnosis or exclusion of mesothelioma in effusion cytology specimens? What is the rationale for these?	**02**	Review the effectiveness of this current panel and discuss the benefits and drawbacks of inclusion of additional or alternative markers such as BAP1.