UNDERESTIMATION OF SERUM IgG LEVELS IN PATIENTS WITH WALDENSTROM'S MACROGLOBULINAEMIA AND A HIGH IgM BURDEN

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Background: Immunoglobulins have been measured with the Abbott Architect turbidimetric assay since June 2014 at Pathology North, Sydney, replacing the Beckman Immage nephelometric method. A discrepancy in IgG levels was observed in a small subset of patients.

Aim: To determine the characteristics of a small set of test samples that demonstrated discrepant IgG results.

Method: Patient medical histories and immunoglobulin levels were reviewed. Samples were run on alternative nephelometric and turbidimetric IgG methods and compared with protein electrophoresis. 200 consecutive samples with IgG below the Architect reference range were run in parallel with the Immage.

Results: Correlation between the methods for low level IgG was $r=0.97$. From October 2014 to October 2015, 7170 immunoglobulin levels were analysed. Of these, 183 samples had IgM concentrations above 12.0 g/L of which 36 (20%) demonstrated underestimation of IgG by the Architect. All these samples were from 10 patients with Waldenstrom's macroglobulinaemia. The measured IgG levels were unreadable or extremely low (<2.31 g/L).

Discussion: IgG levels in some patients with Waldenstrom's macroglobulinaemia and a high IgM level may be underestimated by the Architect. This may have clinical implications in diagnosing and managing coexisting immunoparesis.

COMPARISON OF TWO ENA TESTING ALGORITHMS – ALBIA VS ELISA/LINE IMMUNOASSAY

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Aims: Extractable nuclear antigen (ENA) antibody testing is often requested in patients with suspected connective tissue diseases. Most laboratories in Australia use a 2 step process involving a high sensitivity screening assay followed by a high specificity confirmation test. Multiplexing technology with Addressable Laser Bead Immunoassay (e.g., FIDIS) offers simultaneous detection of multiple antibody specificities (including dsDNA), allowing a single step screening and confirmation.

Methods: We compared our current diagnostic laboratory testing algorithm (Organtec ELISA screen, Euroimmun line immunoassay confirmation) and the FIDIS Connective Profile.

Results: 529 samples (443 consecutive + 86 known autoantibody positivity) were run through both algorithms, and 479

samples (90.5%) were concordant. 100 samples (18.9%) detected the same autoantibody profile and 379 were concordant negative samples (71.6%). The 50 discordant samples (9.5%) were subdivided into 'likely FIDIS or current method correct' or 'unresolved' based on ancillary data. 25 samples remained 'unresolved' and were sub-classified into 'potentially' vs 'potentially not' clinically significant based on the change to clinical interpretation. Only nine samples (1.7%) were deemed to be 'potentially clinically significant'.

Discussion: Overall, we found that the FIDIS Connective Profile ENA kit is non-inferior to the current ELISA screen/LIA characterisation. Reagent and capital costs may be limiting factors in using the FIDIS, but potential benefits include a single step analysis and simultaneous detection of dsDNA antibodies.

CHARACTERISATION OF PERIPHERAL B CELL PHENOTYPES IN PATIENTS WITH SARCOIDOSIS

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Background: Sarcoidosis is a chronic inflammatory disorder of unknown cause characterised by poorly defined immune deficiency.

Aim: Characterise circulating B cell phenotypes in patients diagnosed with sarcoidosis.

Methods: We undertook an audit of B cell phenotyping by flow cytometry in sarcoidosis patients performed between 2008–2015 in our diagnostic laboratory. We analysed total B cells, memory B cells (CD19+CD27+) and class-switched memory B cells (CD19+CD27+IgM–IgD–) to yield a Freiburg classification. These data were analysed according to patient immunoglobulin, ESR, CRP and ACE levels.

Results: We identified 34 patients with a diagnosis of sarcoidosis who had undergone B cell phenotyping. 44% of patients had a deficiency of class-switched memory B cells ($<0.4\%$) and were classified as Freiburg class I with 32% class Ib and 12% class Ia. Proportions of class-switched memory B cells $<0.4\%$ were associated with higher IgG levels.

Discussion: We identified a high incidence of B cell subset deficiencies in patients with sarcoidosis. Both sarcoidosis and common variable immunodeficiency are associated with granulomas, but in sarcoidosis, we observed a correlation between deficiency of switched memory B cells with increased serum IgG. This suggests that changes in B cells might reflect disease activity.

DESCRIPTIVE COHORT OF ANA NEGATIVE, ENA POSITIVE PATIENTS OVER A 7 YEAR PERIOD

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Aim: To identify and describe patients with negative ANA and positive ENA antibodies.

Methods: Information on patients who had a negative ANA and positive ENA between 1st January 2007 and 1st Jan 2014 was