

LABORATORY DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE (IBD)

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Objective: To compare the results obtained by two separate reference laboratories (Prometheus Laboratories, San Diego, CA vs ARUP Laboratories, Salt Lake City, UT) for serological assays utilized in the diagnosis and differentiation of Crohn's disease (CD) and ulcerative colitis (UC), and to assess the clinical utility of the outer-membrane porin C (OmpC) IgA assay in IBD.

Methods: Sera from 197 patients suspected of having IBD were included in the study. Serological assays for anti-*Saccharomyces cerevisiae* antibodies (ASCA) IgA and IgG were performed using enzyme immunoassay (EIA) techniques by both laboratories. Atypical perinuclear neutrophil cytoplasmic antibody (pANCA) IgG was detected using indirect fluorescent antibody (IFA) techniques. Prometheus Laboratories utilized the DNase-I digest method for the detection of pANCA. ARUP Laboratories employed the standard IFA method using ethanol and formalin-fixed neutrophils for the detection of pANCA. The OmpC IgA assay is performed only by Prometheus Laboratories and is promoted as a means of detecting patients with CD who are ASCA negative. All patient samples included in this study were processed according to the University of Utah Institutional Review Board (IRB) approved protocol #13433 and meet the Health Information Portability and Accountability Act (HIPAA) patient confidentiality guidelines. No additional patient information was available for these sera.

Results: The ASCA and pANCA assays employed at ARUP Laboratories have been approved by the Food and Drug Administration (FDA) for in vitro diagnostic use and were used as the reference method for statistical comparisons. Percent agreement between the two laboratories was 93.4% for ASCA IgA, 90.9% for ASCA IgG, and 86.8% for pANCA IgG. The ASCA IgG assay performed at Prometheus showed low sensitivity (43.8%) when compared to the FDA approved assay employed at ARUP Laboratories. This finding is in agreement with the Vermeire study (Gastroenterology, 2001;120:827-833). Prometheus detected pANCA in 24 sera that were negative by the FDA approved method performed at ARUP. Further testing of these pANCA discrepant sera showed 13 (54.2%) to contain antibodies against one or more of other known neutrophil and nuclear antigens (PR3, dsDNA, RNP, Histone, Chromatin). There were 25 sera with ASCA negative/OmpC positive results reported by Prometheus testing. Three of these sera were ASCA positive (1 for IgA, 1 for IgG, 1 for both IgG and IgA) by the FDA approved assays employed at ARUP Laboratories. Fifteen of these 25 (60.0%) ASCA negative/OmpC positive sera gave positive results for pANCA IgG (9 by both laboratories, 5 by Prometheus only, and 1 by ARUP only). Note: Atypical pANCA is found primarily in IBD patients with UC (70.0%) and to a lesser extent in CD (20.0%).

Conclusion: We conclude that the ASCA and pANCA assays showed good agreement between the two laboratories, but the ASCA IgG and pANCA approved assays employed at ARUP Laboratories were more sensitive and specific (respectively) than those performed at Prometheus. The data for ASCA negative/OmpC positive sera suggest that OmpC IgA may be more prevalent and useful in patients with UC, but seems to have little diagnostic value in CD.