Educational Discussion: Body Fluid

2015-A Body Fluid Survey (FLD)

Pleural and peritoneal fluid testing for specific analytes has been enshrined in clinical medicine for the last 40 to 60 years. Light published on the classification of pleural effusions by transudate or exudate in 1972 citing references back to the 1950's. However, from a regulatory perspective, they are no different from a uniquely developed esoteric genetic test (laboratory developed test (LDT), because few manufacturers have validated their instruments for pleural/peritoneal body fluid analysis. Nonetheless, assessment of certain parameters has been clinically validated over time and in the literature to be a standard of care for the diagnostic workup of patients with pleural/peritoneal effusions. In addition, a number of analytes have "piggybacked" into the body fluid analysis arena (even though many have not been found to be clinically useful.) Block and Algicras-Schimnich have published an excellent clinical and laboratory review/discussion on this topic. Interested participants are encouraged to review it.

In preparation for this challenge, we performed a literature review of current practices for pleural and pericardial fluids using currently published guides and recommendations in clinical medical textbooks, as well as clinical decision support resources (eg, UpToDate.com.) We also performed a free text search analysis of published references in PUBMED to determine relative importance of body fluid-analyte utility by looking at the number of references associated with each individual body fluid-analyte combination. (eg, "pleural fluid" AND Protein or "peritoneal fluid" OR ascites AND albumin.) FLD-01, FLD-02 and
FLD-03 constituents were then adjusted to match the most common clinical conditions for which there seems to be clinical validation.

FLD-01 is consistent with a normal pleural fluid. Normal is a relative term because in "normal" conditions, it would be impossible to collect pleural fluid. It is better referred to as "expected normal" or physiologic. Physiologic pleural fluid is expected to have physiologic pH and glucose concentrations accompanied by lactate dehydrogenase (LD), total protein, cholesterol and triglycerides concentrations that are in an expected proportion with their respective blood levels.

FLD-02 is consistent with a pleural effusion interpreted as “parapneumonic”. Notable for that condition is a low pH and low glucose. Elevated total protein and lactate dehydrogenase are also seen; however, these findings are diagnostic for exudate but not specific for parapneumonic. Gram stain and culture are key diagnostic criteria for this type of effusion, even though they were not evaluated in this Survey. The remainder of the reported analytes in this Survey, according to the literature and review of PUBMED citations, are not typically utilized in the workup of parapneumonic effusions.

FLD-03 is consistent with a peritoneal effusion (ascites) interpreted as “malignant.” The operative concept in malignant peritoneal effusions is that the serum serum-ascites albumin gradient (SAAG, $ALB_{serum} – ALB_{ascites}$) is less than 1.1. With serum albumin reference intervals typically 3.5 to 5.0 g/dL, we hoped that an expected fluid concentration of 4.0 g/dL would be appropriate. Total protein and LD tend to be higher with glucose being lower in these cases, but not diagnostically so. Tumor marker testing is sometimes performed; however, a) published data about their use is limited, and b) elevations can occur for reasons other than tumor. Lastly, analysis of pH has not been found to be useful with malignant cases.

The CAP provides proficiency testing for body fluid testing in recognition of the fact that measurement of these body fluid analytes is considered a clinical standard of care, with in-house analysis approaching 100%. However, the materials used for this Survey are not human serous fluids. They are artificial matrices that have been spiked and calibrated as best as possible to mimic pleural and peritoneal effusions. Consequently, they are not suitable, and do not substitute, for the internal validations required to measure and report body fluid analytes. Laboratories are required to perform such validations separately before reporting any patient results.

References

1. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr.Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med*. 1972;77:507-513.
2. Block DR, Algeciras-Schimnich A. Body fluid analysis: clinical utility and applicability of published studies to guide interpretation of today's laboratory testing in serous fluids. *Crit Rev Clin Lab Sci*. 2013 ;50:107-124.

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