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Altered lysosomal proteins in neural-derived plasma exosomes in preclinical Alzheimer disease

It is necessary to identify biomarkers to detect patients at risk for Alzheimer disease well before neurological signs and symptoms are observed. The goal is to provide early treatment to limit or reverse neuronal damage, which may prevent development of the disease. Recent reports have shown significantly higher levels of the pathogenic proteins P-T181-tau, P-S396-tau, and β-amyloid 1–42 in Alzheimer disease (AD) patients compared with case controls. These exosomal proteins correctly classified more than 96 percent of patients with AD. The authors conducted a study to examine neurally derived plasma exosomes from patients with AD, patients with frontotemporal dementia, and cognitively normal matched controls for differences in quantities and types of lysosome-associated proteins. They retrospectively identified patients with amnestic mild cognitive impairment or mild to moderate dementia from AD who donated blood for a study. Patients with a behavioral variant of frontotemporal dementia were also identified. Results showed that mean exosomal levels of cathepsin D, lysosome-associated membrane protein 1 (LAMP-1), and ubiquitinylated proteins were significantly higher (unlike levels of heat shock protein 70, which were significantly lower) for AD patients compared with controls. Levels of cathepsin D, LAMP-1, and ubiquitinylated protein were also significantly higher for patients with AD than patients with frontotemporal dementia. These proteins were also significantly different from those of matched controls in 20 patients one to 10 years before and at diagnosis of AD. The authors concluded that levels of autolysosomal proteins in neurally derived blood exosomes distinguished patients with AD from case controls and may predict preclinical AD up to 10 years before onset. These results confirm, in patients with AD, the early appearance of neuronal lysosomal dysfunction and suggest that autolysosomal proteins may be useful biomarkers in large prospective studies.

Goetzl EJ, Boxer A, Schwartz JB, et al. Altered lysosomal proteins in neural-derived plasma exosomes in preclinical Alzheimer disease. *Neurology.* 2015;85(1):40–47.

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Clinical laboratory quality practices when hemolysis occurs

Even with advances in clinical laboratory testing, hemolyzed specimens continue to cause interference, resulting in a delay in result reporting, additional test ordering, complications in interpreting results, and increases in health care costs. Since most laboratory tests in chemistry involve measuring the light that passes through a specimen, hemolysis may interfere with the absorption of light. This is especially true for spectrophotometric assays. Hemolysis also may interfere with test results by releasing analytes normally found in red blood cells into patients' serum or plasma. Examples of elevated analytes as a result of specimen hemolysis are potassium and lactate dehydrogenase. The authors used the College of American Pathologists' Surveys program to query CAP Chemistry Survey participants about their hemolysis practices. They received responses from 24 percent (846 of 3,495) of the participants. Many had written hemolysis policies for potassium (85 percent), lactate dehydrogenase (69 percent), and glucose (55 percent), but fewer had standardized hemolysis reports between their primary and secondary chemistry analyzers for these three analytes. Forty-nine percent of participants took corrective action to reduce hemolysis during the past year and used, on average, 2.4 different approaches. These corrective actions included

collecting and distributing data to administration, troubleshooting outliers, retraining phlebotomists, and establishing quality improvement teams. When asked to comment about progress with corrective actions, 70 percent noted slow to no progress and two percent reported giving up on improvement. In summary, hemolysis continues to be a barrier for laboratory testing, and many of the issues point to concerns with techniques during collection of blood samples. Practices for measuring, reporting, and reducing hemolysis rates need to be improved.

Howanitz PJ, Lehman CM, Jones BA, et al. Clinical laboratory practices when hemolysis occurs. *Arch Pathol Lab Med.* 2015;139:901–906.

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