Relationship of cerebrospinal fluid protein concentration determined by dye-binding and urinary dipstick methodologies

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A routine cerebrospinal fluid (CSF) examination includes determination of the protein concentration and erythrocyte, nucleated, and differential cell counts. For many central nervous system (CNS) diseases, the nucleated cell count and protein concentration increase together. However, an increased protein concentration suggests CNS disease even if the nucleated and differential cell counts are normal. Therefore, determination of CSF protein concentration is important in the diagnosis, prognosis, and treatment of CNS disease.

Since quantitative methods for determination of CSF protein concentrations are not always readily available, alternative screening or semiquantitative methods are used. The Pandy test, which involves mixing CSF with phenol, is one such test. The sensitivity and correlation of the Pandy test with other analytical tests are quite good (1), but the Pandy test may not detect small increases in protein concentration with accuracy and precision. Recently, the urinary dipstick has been used to estimate CSF protein concentration (2). These data, comparing protein concentrations determined using urinary dipsticks and a quantitative dye-binding technique, showed a trace reaction in normal dogs (protein concentration < 0.25 g/L), and 1+, 2+, and 3+ reactions corresponding to CSF protein concentrations between 0.28 and 0.75, 1.15 and 2.40, and 4.70 and 5.90 g/L, respectively (2). Most veterinary hospitals have urinary dipsticks; therefore, the dipstick technique would be a convenient procedure for estimating CSF protein concentration. Since CSF protein concentration determination is an important test in the characterization of CNS disease, and the preliminary study used only a small sample size, we examined a larger number of samples of canine CSF, comparing dye-binding and dipstick methodologies.

One hundred samples of canine CSF were obtained from two referral practices (Veterinary Teaching Hospital, University of Guelph; Veterinary Referral Clinic of Mississauga) over a six-month period. The protein concentrations in fresh samples were determined by the trichloroacetic acid(TCA)-Ponceau S dye-binding method (3) using human albumin standards (American Dade, Aguada, Puerto Rico) and by urinary dipstick (Multistix, Ames Division, Miles Laboratories Ltd., Etobicoke, Ontario). The negative, trace, 1+, 2+, 3+, and 4+ readings on the urinary dipsticks correspond to 0, <0.3, 0.3-1.0, 1.0-3.0, 3.0-20.0, and >20 g protein/L, respectively. Tests were done by four laboratory technologists with at least eight years of experience each.

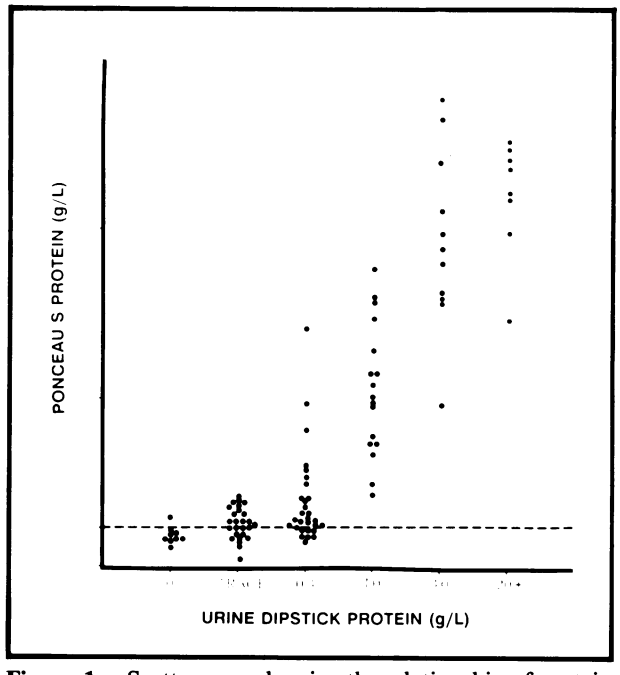

Figure 1. Scattergram showing the relationship of protein concentrations in 100 normal and abnormal canine cerebrospinal fluid samples determined by quantitative dye-binding (Ponceau S) and semi-quantitative methods (urine dipstick). The dashed line at 0.25 g protein/L represents the upper reference limit of normal canine cerebrospinal fluid.

The data, presented as a scattergram (Figure 1), were not linearly related. Since the CSF of normal dogs has less than 0.25 g protein/L (4), normal dogs should have a negative or trace CSF dipstick readings. The CSF from one of nine dogs with negative dipstick readings and one-half (13 of 26) of the dogs with trace dipstick readings had mild increases in CSF protein concentration when measured by the quantitative dye-binding method. Therefore, if a dipstick CSF protein concentration is negative, or trace, there is an 11%, or 50%, probability of the quantitative protein concentration being above the upper reference limit, respectively. Eight of 29 dogs (28%) with a 1+ reading had normal quantitative CSF protein concentrations. Conversely, 72% of dogs with a 1+ dipstick reading can be expected to have a mild or moderate increase in CSF protein concentration. All dogs with a 2+ or greater dipstick reading had increased CSF protein concentra-

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tions. There was a wide degree of overlap of CSF protein concentrations determined by the TCA-Ponceau S method between groups rated negative to 1+ and those rated as 2+ or greater.

Clinical decisions based on a 2+ or greater dipstick reading are highly reliable. The urinary dipstick is valuable only as an initial screening test for estimating CSF protein concentrations, with the understanding that false positive and false negative test results occur

Using the urinary dipstick to estimate the CSF protein concentration appears practical, although the data presented here are not as optimistic as first reported (2). It is clear that a dog could have an increased CSF protein concentration, yet have a trace (50% probability), or more rarely a negative (11% probability), dipstick reading. A false negative estimate of a mildly increased CSF protein concentration may not alter the diagnosis, prognosis, and treatment offered at initial evaluation, but in some circumstances, such as CNS neoplasia, the results could misguide the clinician. In contrast, 28% of dogs having normal CSF protein concentrations will be wrongly identified as having 1+ (0.3 g/L) CSF protein concentrations using the dipstick technique and these dogs may be treated unnecessarily. Clinical decisions based on a 2+ or greater dipstick reading, however, are highly reliable.

The urinary dipstick is valuable only as an initial screening test for estimating CSF protein concentrations, with the understanding that false positive and false negative test results occur, particularly when the protein concentration is near the upper reference limit. Therefore, to ensure appropriate diagnosis and treatment, an aliquot of CSF should be submitted for quantitative analysis to confirm the dipstick test result. Only quantitative methods should be used for sequential monitoring of CSF protein concentrations.

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