



## Editorial

## Editorial for adult CSF total protein: Higher upper reference limits should be considered worldwide. A web-based survey



## ARTICLE INFO

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The cerebrospinal fluid total protein level is commonly used as an indicator or marker of several diseases of the peripheral - (PNS) and central nervous system (CNS). Worldwide most laboratories use the upper reference limit of 0.45 g/L for CSF protein. Based on own investigations and a global survey the authors of this paper research the worldwide upper reference limits [1]. The overarching question was, if this upper limit was a fixed level, or subject to age related changes. This investigation refers to CSF usually obtained by lumbar puncture and does not consider the ventricular CSF [2], nor children [3].

The upper value of the CSF protein is based on a historic publication in Merritt's book "the cerebrospinal fluid" [4]. This value has remained a stable reference value, which does not consider age dependent changes. As confirmed by this review this value remained unquestioned for a long time with a few exceptions.

Based on 3 studies [5–7] the authors have indicated, that the value of 0.45 g/L may not be correct and that by increasing age the upper limit of the CSF has an increased value of protein. This contrasts with the widely accepted value of upper reference value, which was used in most institutions contributing to the survey.

The acquisition of "normal" values is impossible, as for many reasons a systemic CSF study on normal persons in this age group can not be done. Even the definition of "normal" in an individual over the age of 40 or 50 years is difficult.

Therefore this assumption of an increased upper limit of CSF protein values is empirically based on the analysis of existing and accumulated data and does not follow the not the standardized study pathways.

These results are important and have implications: 1) CSF protein elevation can be the only clue for a PNS and CNS lesion and often clinicians consider this upper limit value of CSF protein very seriously. A higher age related level "normal" level would exclude false positive results.

2) The second example refers to CSF findings included in diagnostic criteria. As an example in the EFNS guidelines on the management of chronic inflammatory neuropathy [8], this value of 0.45 g/L, is listed as a supportive criterion ("level A recommendation"), which has been also critically discussed as a possible pitfall [9]. The CSF results can also be a crucial parameter for the well described dissociation cyto - albuminiquie [10] and for similar reasons produce false positive results when patients

in an age group over 50 years are investigated.

What can be learnt from this interesting report?

Neurology is based on neuroscience and practical empirical experience. Great care is taken to reach objective and precise results. The aim for the absolute "normal value" is prevalent in many investigational techniques, which also reflected in the large number of "normal values" and finally in guidelines.

Yet, over time established values can develop into dogmas, which are continued without reflection, which is exemplified by this study.

Training and education are the fundamentals of practical medicine, and neurology [11]. This is based on accumulating and updating relevant and new knowledge. Increasingly in addition to learning and adding new content, the issue of disengaging from old truth and dogmas is needed, which is termed "unlearning" [12]. It, will be necessary to change several dogmas in neurology. In summary these updated protein reference limits will improve the specificity of CSF testing.

## Conflict of interest

The author declares no conflict of interest.

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