The 2017 McDonald criteria recommend that intrathecal IgG synthesis (ie, oligoclonal bands, OCB, Figure A) be considered in the diagnosis of multiple sclerosis [1]. However, the practical implications of this recommendation relate to analytical accuracy of the test for OCB and the clinical interpretation of the test results.

The analytical accuracy has now become excellent [2,3]. This positive development relies on improvements in sample acquisition, handling, storage, and use of standardised protocols. However, the laboratory interpretation of the OCB patterns can be challenging. In a nutshell, only the presence of ≥2 bands in the CSF, but not in the serum, represents a positive test result (Figure A) [3]. There are other less specific and confusing patterns (Figure B&C). In the UK, the External National Quality Assessment (UK NEQAS) data for detecting OCB in reference samples from people with multiple sclerosis and other inflammatory and non-inflammatory neurological disorders give an analytical sensitivity of 92.8% (8,205 tests) and specificity of 94.1% (personal communication Dr Egner and Dr Patel).

The clinical interpretation of OCBs for a diagnosis of multiple sclerosis has changed from substitution for radiological dissemination in space (DIS, before 2010) to ‘no substitution’ (2010-2017) followed by substitution for dissemination in time (DIT, since 2017). Why? Radiological DIS is the main contributor to diagnostic specificity in multiple sclerosis [4], but OCB are not specific for multiple sclerosis and can be found in at least 30 diseases [2]. Therefore the clinical diagnostic specificity of OCB for multiple sclerosis drops from 94% (11,136 patients) for comparison to healthy controls and people with non-inflammatory neurological diseases to 61% (2,331 patients) for comparison with people with inflammatory aetiologies [2]. A comprehensive CSF examination (in addition to OCB) will be helpful to exclude other inflammatory aetiologies and increase the analytical specificity.[5].

The practical implications of changing from the 2010 to the 2017 revision of the McDonald criteria are illustrated by the following patient. A 39 year old woman reported symptoms suggestive of demyelination. The MRI showed five non-enhancing lesions in three different regions typically affected in multiple sclerosis (Figure D-G). Therefore radiological DIS (infratentorial, juxtacortical, spinal) but not DIT was met according to the 2010 criteria (references in [1]). Clinically she only ever had one attack. In this patient a diagnosis of multiple sclerosis could not be made in 2010. There was evidence for intrathecally produced IgG (OCB) in the CSF. Therefore, with radiological evidence for DIS, the CSF result can substitute for DIT and a diagnosis of multiple sclerosis could have been made with the revised 2017 criteria [1]. Consequently, she would be eligible for approved disease-modifying therapies for multiple sclerosis under the 2017 criteria, despite not being eligible under the 2010 criteria .

In conclusion, the paradigm shift to permit a positive CSF result to substitute for DIT rather than to substitute for DIS is a logical one, but it reinforces the responsibility of clinical neurologists to request state of the art CSF analyses [5] and to encourage their laboratories to participate in schemes designed to ensure high analytical standards [2].

Figure: (A) OCB in CSF only in a patient with MS, (B) OCB in CSF and serum in a patient with a neuro-inflammatory disorder, (C) artefact due to poor sample handling/storage [2]. Brain and spinal cord MRI of a 39 year old woman demonstrating non-contrast enhancing lesions indicated by red arrows: (D) one infratentorial, (E) one juxtacortical, (F) one cervical spinal and (G) two thoracic. The MRI fulfils the 2017 radiological criteria for DIS, but not DIT [1].