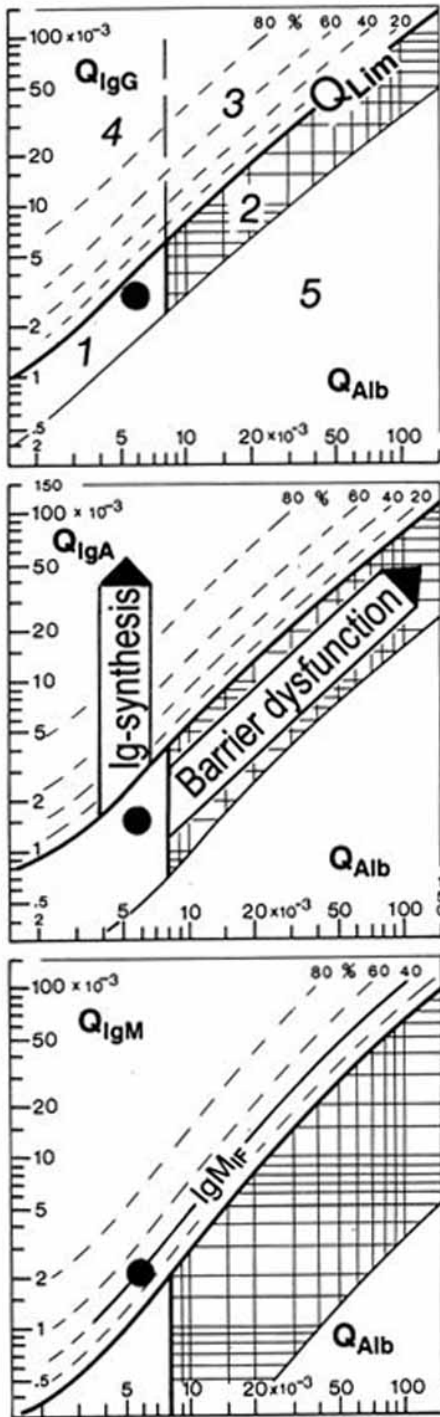# CSF/serum quotient diagrams for IgG, IgA, IgM with hyperbolic graphs according to Reiber (1994).

The reference ranges of blood-derived IgG, A, M fractions in CSF (range 1 and 2) include between upper (QLim) and lower hyperbolic discrimination lines 99% (+/-3 SD) of the 4300 patients investigated. The upper hyperbolic curves (thick lines) of the reference range represent the discrimination lines QLim (Lim from limit) between brain-derived and blood-derived immunoglobulin fractions in CSF. Values above QLim represent intrathecal fractions (IF) in percent of total CSF concentration as IgGIF, IgAIF, or IgMIF.

These intrathecal fractions can be conveniently and directly read from the quotient diagrams with lines for 20, 40, 60 and 80% intrathecal synthesis with reference to the upper discrimination line (QLim) as 0% synthesis. The example shows IgMIF = 40%. The limit of the reference range for QAlb between normal and increased CSF protein concentration (blood-CSF barrier dysfunction) is age-dependent with a general for the age groups above 5 years: $QAlb = (4 + age(y.)/15) \times 10^{-3}$ ( e.g. vertical line at $QAlb = 8 \times 10^{-3}$ for patients up to 60 years).

The diagrams depict five ranges: 1 = normal; 2 = pure blood-CSF barrier dysfunction (i.e., reduced CSF turnover); 3 = intrathecal Ig synthesis with a reduced CSF turnover and 4 = intrathecal Ig synthesis without change in CSF turnover. Values below the lower hyperbolic line, in range 5, indicate a methodological fault. The characterization of the hyperbolic functions has taken into account the analytical imprecision with coefficients of variation between 3 - 8% for the quotients of albumin, IgG, IgA and IgM. Due to larger variations between laboratories, intrathecal Ig synthesis should be considered elevated if the intrathecal fraction IgIF is larger than 10%.

The diagrams for IgG, IgA amnd IgM should be arranged above each other referring to the common albumin quotient to facilitate the recognition of the disease-related immunoglobulin patterns. The data in the diagram are from a patient with a facial nerve palsy. An intrathecal IgM fraction of IgMIF = 40% and oligoclonal IgG (with IgGIF = 0) led to further analysis of Borrelia-specific Antibody Index. The Borrelia (IgG) AI = 4.3 and Borrelia (IgM) AI = 3.2 indicates Borrelia as the cause of the disease.