RADIOIMMUNOASSAY OF IMMUNOGLOBULINS IN CEREBROSPINAL FLUID

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In several neurological diseases abnormalities of immunoglobulin G in cerebrospinal fluid (CSF) are observed. These abnormalities can be qualitative (1) (restricted heterogeneity of IgG) and quantitative (2) (increased concentration of IgG in CSF). There are four other classes of immunoglobulins: IgA, IgM, IgD and IgE, some of which have particular functions. It will be of interest to obtain information on these immunoglobulins in CSF in order to arrive at a better understanding of immune-processes in neurological disease. Since the normal concentrations of IgM, IgA, IgD and IgE in CSF are much lower than that of IgG these immunoglobulins can only be measured by very sensitive assay methods, unless CSF is concentrated first.

We have developed radioimmunoassays for measuring IgA, IgM and IgD (for IgE an assay was already available) and used these to determine immunoglobulins in CSF. In this paper some aspects of the radioimmunoassays are described and some results of the measurements are shown.

Many proteins in CSF are derived from the blood. The concentration of these proteins in CSF depends on the following factors: the permeability of the blood-CSF barrier, the concentration of that protein in the blood, and the hydrodynamic radius of the protein (3). It has been shown that for IgG these parameters can be taken into account by measuring the concentration of IgG and albumin both in serum and in CSF (4); under normal conditions a linear relationship was found between the

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CSF/serum ratio of IgG (i.e. the concentration of IgG in CSF divided by that in serum) on the one hand and the CSF/serum ratio of albumin on the other hand (4). Deviations from such a relationship were found in several groups of patients with neurological diseases.

Method of Radioimmunoassay

The radioimmunoassays (RIA) were performed as shown schematically in Fig. 1. Antisera, prepared in our laboratory, were coupled to the solid phase (sepharose 4B, activated with CNBr). The following batches were used: aIgH, KH 15-19-01; aIgA, SH 14-04-04; aIgD, KH 20-06-01; aIgE, SH 25-02-08; aIgG, KH 16-103-03. The antibodies used in the second incubation step were isolated from the same sources, except for the aIgM-antibodies. These were isolated from batch KH 15-18-02. The procedure for preparing the reagents and performing the incubations were similar to those described for the RIA of IgE (5).

The lower detection limit in the RIAs used for the measurements described here was about 0.5 ng Ig; thus, when 50 µl of CSF

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Fig. 1. Procedure of the radioimmunoassays.