

CORRESPONDENCE

Adenosine deaminase (ADA) isoenzymes ADA1 and ADA2 in biological fluids

To the Editor:

We read with great interest the editorial by GAKIS [1] about the extreme importance of the adenosine deaminase (ADA) isoenzymes ADA1 and ADA2 on the homeostasis of 2' deoxyadenosine and adenosine, especially when monocytes and macrophages are infected by intracellular microorganisms. Serum ADA activity is increased in various conditions such as liver disease, tuberculosis, typhoid, infective mononucleosis and certain malignancies, especially those of haematopoietic origin. The origin of serum ADA and the mechanisms by which serum activities are increased have not been fully elucidated.

Whatever the biological role of ADA1 and ADA2, it has been demonstrated that the presence (low or high) of these isoenzymes in biological fluids has diagnostic relevance. GAKIS [1] reviewed the known data on ADA activity in serum, pleural, peritoneal and pericardiac effusions, and cerebrospinal fluid (CSF) of many illnesses. To estimate the precise quantity of ADA1 and ADA2 in a specimen, one should separate the two isoenzymes. This was usually highly complicated and impractical, and some authors [1, 2] have introduced the 2'deoxyadenosine/adenosine deaminase ratio. The ratio between the rate of deamination of 2'deoxyadenosine and adenosine, performed independently in two separate test tubes, will have different values according to the relative percentages of the two isoenzymes on the specimen. Estimated data are calculated using the affinity of ADA2 for the two substrates.

However, we feel that this is not the most practical way to obtain a measurement of the relative percentage of ADA1 and ADA2 activity in the sample, especially when the readings of ADA activity can be made by an automatic analyser system with reagent kits. In our current work, we incorporated the erythro-9-(2-hydroxy-3-nonyl) adenine (EHNA), which specifically and completely inhibited only the ADA1 isoenzymes fraction [3]. Whatever the method used to measure ADA activity, an exact relationship between the isoenzymes is

readily obtained by measuring total ADA and the ADA2 which is not inhibited by 100 mmol·L⁻¹ of added EHNA. In fact, this method is being increasingly used by acquired immune deficiency syndrome (AIDS) researchers since some authors have reported a higher serum ADA activity in human immunodeficiency virus (HIV)-1 positive patients [4]. By the method we propose, some authors have found that ADA2 isoenzyme activity is of considerable prognostic value in AIDS and adult T-cell leukaemia (ATL) cases [5, 6].

References

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REPLY

From the authors:

Cordero *et al.* propose a method for measuring ADA1 and ADA2 in biological fluids as a more practical approach than that based on the substrate affinity of the two isoenzymes [1]. By using an automatic analyser system, they incorporated erythro-9-(2-hydroxy-3-nonyl) adenine (EHNA), "which specifically and completely inhibited only the ADA1 isoenzymes fraction". They

state that "whatever the method used to measure ADA activity, an exact relationship between the isoenzymes is readily obtained by measuring total ADA and the ADA2 which is not inhibited by 100 μmol·L⁻¹ of added EHNA". A few papers are quoted to support their thesis.

I regret that I could not find a detailed description of the putative new method in the letter from Cordero *et al.* or in any of the quoted papers. In particular, I did not find any information on the amount of adenosine and 2'deoxyadenosine in the mixture of enzymatic reaction.

It may be that EHNA is useful to determine ADA2 in biological fluids, but with the presented data, I cannot evaluate the method. Furthermore, I could not reproduce the method because EHNA is not commercially available.

While commenting on their references, Cordero *et al.* also say: "... ADA2 isoenzyme activity is of considerable prognostic value in AIDS and adult T-cell leukaemia (ATL) cases". ADA2 activity in HIV-positive subjects is due to the presence of HIV inside monocytes and macrophages and has no diagnostic or prognostic significance [1, 2]. One should also consider that ADA2 activity in HIV-positive subjects could be due to concomitant infections by intracellular parasites, which are exceedingly common in these patients. In patients with systematic tumours, it is ADA1 that has a clear diagnostic usefulness [1, 3, 4]. On the contrary, ADA2 increases in a few cases of lymphoproliferative diseases, but it does not allow a differential diagnosis *versus* infectious disease due to intracellular microorganisms where ADA2 is also increased [1, 2, 4].

References

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