T CELL ACTIVATION IN TYPHOID FEVER DETECTED BY INCREASED LEVELS
OF ADENOSINE DEAMINASE

Michele Russo, Teresa Pizzella, Salvatore Nardiello, Flavio Fiorentino and Bruno Galanti
Clinic of Infectious Diseases, 1st Medical School Naples, Italy

INTRODUCTION

The demonstration of an inherited adenosine deaminase (ADA) deficiency in patients with combined immunodeficiency (Giblett et al., 1972) suggests a causal association between lymphocyte ADA levels and immune function. ADA activity is greatly increased in in vitro stimulated lymphocytes (Hovi et al., 1976) and in peripheral mononuclear cells from subjects developing an active immune response (Galanti et al., 1981). Recent data indicate that mechanisms of cell-mediated immunity play the major role in recovery from typhoid fever (Rajagopalan et al., 1982). The aim of this study is to assess the value of lymphocyte ADA assay in detecting T cell activation during typhoid fever.

MATERIALS AND METHODS

Patients and controls

We investigated 9 patients (all males, age range 14-28 years) with uncomplicated typhoid fever, diagnosed from blood culture. All patients were on therapy with chloramphenicol (2 g/die) at the time of the study. In 6 of them, samples were taken twice, the first within 7 days from the onset of fever and the second 7-10 days later. Eleven normal subjects (8 males, age range 22-36 years) from our hospital staff were controls.
Preparation of cell extracts

Peripheral mononuclear cells (PBMC) were isolated from heparinized blood by standard gradient centrifugation (Bøyum, 1968). T-enriched cell fractions were obtained by rosetting PBMC with 2-aminoethy1isothiouronium bromide-treated sheep red blood cells (Madsen and Johnsen, 1979). Cell suspensions were adjusted to a concentration of 5 x 10^6 cells/ml and sonicated at 23 kc/sec. After centrifugation at 800 g for 10 min, supernatants were immediately frozen at -20°C.

ADA assay

ADA activity was measured on supernatants by a colorimetric method (Giusti, 1974), and expressed as nmol of adenosine deaminated/min/37°C/10^7 cells.

RESULTS

ADA levels were significantly increased in T cells from typhoid fever patients (Table 1). The increase was detected already during the first week of disease: ADA values increased further in 5 of the 6 re-assayed patients.

Table 1. Levels of adenosine deaminase (ADA) activity in peripheral mononuclear cells (PBMC) and T cells from typhoid fever patients. Mean ± standard deviation is reported.

<table>
<thead>
<tr>
<th>Days of illness</th>
<th>No. of assays</th>
<th>ADA nmol/min/10^7 cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PBMC</td>
</tr>
<tr>
<td>Typhoid fever patients (9)</td>
<td>2-7</td>
<td>7</td>
</tr>
<tr>
<td>Normal controls (11)</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T cells</td>
</tr>
<tr>
<td>Typhoid fever patients (9)</td>
<td>8-20</td>
<td>8</td>
</tr>
</tbody>
</table>

°P < 0.005, °°P < 0.001 versus controls