Interferon status after measles virus infection

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Summary
Peripheral blood leucocytes from patients who had recently had measles infection were examined for their ability to produce α- or γ-interferon, their antiviral state and the level of E enzyme. These results were compared with peripheral blood leucocytes from healthy control subjects. The results show that while peripheral blood leucocytes from control patients produced α- and γ-interferon, those from the measles patients produced only α-interferon. The peripheral blood leucocytes from all the measles patients were in an antiviral state whereas those from only 20% of the controls were in this state. Since γ-interferon is mainly produced by T lymphocytes, the lack of γ-interferon production by peripheral blood leucocytes from patients with measles correlates with previously reported depressed T-cell function in patients after measles infection.

Interferons are a group of inducible proteins with antiviral, anticytotoxic and immunoregulatory properties. They are produced by various cell types and have a wide range of biological activities. 

Material and methods
Blood was taken from 8 patients who had recently had measles infection (0-14 days after infection), 1 who had recovered from the disease (>21 days after infection), and 1 with subacute sclerosing panencephalitis; the ages of the patients were between 1 and 16 years (Table I). The 11 controls were healthy laboratory personnel.

Peripheral blood leucocytes were separated by Ficoll density gradient centrifugation, and their ability to produce α-interferon and γ-interferon respectively was determined by stimulating the cells with Sendai virus (40 haemagglutination units/10^6 cells) or phytohaemagglutinin (50 μg/ml), as previously described. 

A radio-immunoassay, using a Vero cell monolayer challenged with Sindbis virus, was used to assess the amount of interferon produced by the peripheral blood leucocytes. To determine whether the peripheral blood leucocytes were in an antiviral state they were cultured with Sindbis virus and the amount of virus replication was measured by radio-immunoassay. The response to exogenous interferon was assessed by first incubating the peripheral blood leucocytes with interferon (10-100 IU/ml) for 18 hours followed by challenge with Sindbis virus; Sindbis virus replication was then determined by radio-immunoassay. Because only small quantities of blood were obtained from patients 3 and 4, only 7 of the measles patients were tested for α- and γ-interferon production.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Diagnosis</th>
<th>Stage of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>10</td>
<td>SSPE</td>
<td>Late semi-coma</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>16</td>
<td>Measles</td>
<td>24 d PI</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>1</td>
<td>Measles</td>
<td>0-7 d PI</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>6</td>
<td>Measles</td>
<td>0-7 d PI</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>8</td>
<td>Measles</td>
<td>0-7 d PI</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
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<td>0-7 d PI</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>8</td>
<td>Measles</td>
<td>7-14 d PI</td>
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<tr>
<td>8</td>
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<tr>
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<tr>
<td>10</td>
<td>F</td>
<td>6</td>
<td>Measles</td>
<td>7-14 d PI</td>
</tr>
</tbody>
</table>

The status of the measles infection was determined by clinical diagnosis. SSPE = subacute sclerosing panencephalitis; PI = post-infection.

The amount of E enzyme, one of the enzymes stimulated by interferon, was determined in peripheral blood leucocytes using the method of Schattner et al., and values are given in pmol of 2',5'-oligo-adenylic acid (2-5 A)/h/μg protein. Protein levels were determined using the Bio-Rad kit (Bio-Rad, Richmond, California, USA).

Results
The test used to determine the interferon status of the peripheral blood leucocytes from the control, measles and subacute sclerosing panencephalitis patients considers an interferon measurement of >16 IU/ml as indicative of interferon induction. All the control subjects produced α-interferon while 9 of the 10 controls produced γ-interferon. The peripheral blood leucocytes from the subacute sclerosing panencephalitis patient did not produce α- or γ-inter-
Discussion
During measles infections it has been observed that the number and proportion of circulating T lymphocytes in children decreases from 53% of the total number of lymphocytes in healthy controls to 39% in acute infections. Lucas et al. have also shown that T lymphocytes infected with measles do not undergo significant cell division following phagohagocytosis, and Smithwick and Berkovich have shown that lymphocytes from tuberculous children infected with measles virus show a diminished reaction to phagohagocytosis and to tuberculin purified protein derivative. These studies suggest that during measles infection there is a decrease in cell-mediated immunity and in T-cell function.

In the present study the interferon status of peripheral blood lymphocytes from control subjects, measles and subacute sclerosing panencephalitis patients was examined. Since the peripheral blood lymphocyte population contains both B and T lymphocytes, the production of both α-interferon and γ-interferon was examined. While the peripheral blood lymphocytes from all the control subjects and the measles patients produced α-interferon after stimulation with Sendai virus, there was no γ-interferon production by peripheral blood lymphocytes detectable from the subacute sclerosing panencephalitis patient.

However, while peripheral blood lymphocytes from 90% of the control subjects produced γ-interferon following phytohaemagglutinin stimulation, there was no production of γ-interferon by peripheral blood lymphocytes from measles and subacute sclerosing panencephalitis patients.

While peripheral blood lymphocytes from only 20% of the control subjects were in an antiviral state, those from all the measles and subacute sclerosing panencephalitis patients were in an antiviral state; this correlates with a mean E-enzyme value in the measles patients which was twice that of the control group.

From these results it can be concluded that while there is production of α-interferon in measles patients there is no detectable production of γ-interferon. In the subacute sclerosing panencephalitis patient there was no production of α- or γ-interferon, but peripheral blood lymphocytes from this patient and the measles patients were shown to be in an antiviral state by being unable to support viral replication. The inability of peripheral blood lymphocytes from the measles patients to produce γ-interferon correlates with the results of Whittle et al. and Lucas et al., which showed a decreased T-cell mediated function. It would appear that not only is there a reduction in the relative proportion of T cells after measles infection and reduced ability of T cells to divide after stimulation with phytohaemagglutinin, but γ-interferon production is abolished. This inability of peripheral blood lymphocytes (presumably T cells) to produce γ-interferon could be important in the development of complications subsequent to measles infections such as bronchopneumonia, laryngotracheobronchitis and later development of subacute sclerosing panencephalitis.

This study was supported by the National Cancer Association of South Africa, the South African Medical Research Council and the Poliomyelitis Research Foundation.

REFERENCES