Correspondence

TO THE EDITOR, British Journal of Venereal Diseases

Penicillinase-producing Neisseria gonorrhoea in Jakarta, Indonesia

Sir,

Between 30 April 1981 and 30 April 1982, 156 cases of gonorrhoea were confirmed by culture in the department of microbiology of the Medical Faculty, University of Indonesia. Of these cases, 39 were due to infection with penicillinase-producing Neisseria gonorrhoeae (PPNG). No PPNG strains had been detected in this department before April 1981. All 156 cases occurred in Indonesian patients, both male and female. The first impression was that men seemed to be more affected by PPNG infections than women (table I). Statistically the difference was not significant at the 1% level ($\chi^2 = 0.42$, $P<0.5$). Does this imply that men and women run a similar risk of developing PPNG infections?

Isolation and identification of PPNG and non-PPNG strains were carried out according to standard methods. The minimum inhibitory concentration of penicillin was measured by a plate dilution method. All PPNG strains showed resistance to 128 $\mu$g/ml penicillin G. Further testing of higher concentrations of penicillin could not be performed since these 39 PPNG strains did not remain viable. Several PPNG strains collected later (after April 1982) were tested at higher concentrations of penicillin (table II); none of the 14 PPNG strains showed any inhibition of growth on 10-unit penicillin discs.

Yours faithfully,

S Josodiwondo

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<table>
<thead>
<tr>
<th>Patients' sex</th>
<th>PPNG strains</th>
<th>Non-PPNG strains</th>
<th>Total No of cases</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>37</td>
<td>105</td>
<td>142</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>117</td>
<td>156</td>
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<table>
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<th>Minimum inhibitory concentrations (MICs) of penicillin for 14 PPNG strains</th>
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<tbody>
<tr>
<td>MIC of penicillin ($\mu$g/ml):</td>
</tr>
<tr>
<td>128</td>
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<tr>
<td>PPNG Strains</td>
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</table>
including myalgia, arthralgia, anorexia, and nausea. In cases 3 and 4 the patients had less severe reactions with rises in temperature to 38.9°C and 38°C respectively and an increase in pulse rate to 100/minute. Both patients showed a slight rash potentiation and felt nauseated and unwell for short periods. In cases 5 and 6 and the control subject 7 no reactions either objective or subjective occurred. When they did occur reactions began three to four hours after initiation of treatment.

A fall in intravascular kininogen occurred in several patients. This fall was most pronounced in the patients in cases 1 and 2 who had severe JHRS (figure). In case 1 the patient had a fall in intravascular kininogen of 60% (from 5.2 to 2.1 μmol equivalents of bradykinin/litre of plasma), the maximum occurring between the 1½- and three-hour intervals; in case 2 the patient had a fall of 96% (from 2.85 to 0.18 μmol equivalents of bradykinin/litre of plasma), the maximum occurring between the one- and three-hour intervals. In both patients values returned to normal by the six-hour interval. In cases 3 and 4 the patients had a less pronounced fall in kininogen of 16% and 23% respectively, which was shorter in duration. No fall in intravascular kininogen occurred in cases 5 and 6 or in the control subject 7. The intravascular concentrations of IgG, IgM, and IgA rose slightly over the first four hours in cases 1 and 2; in cases 3 and 4 and the control subject 7 no overall changes occurred during the period of observation.

The JHR in the patients studied was associated with an early reduction in intravascular kininogen values, reflecting pronounced kinin formation. The degree of this change in individual patients paralleled the severity of the reaction and we propose that kinin may play a part in the pathogenesis of the JHR. It is unlikely that falls in kininogen values are due to non-specific extravasation of plasma proteins or transient haemodilution, since during this time the concentrations of three major classes of immunoglobulins tended to rise or remain steady.

Depletion of prekallikrein, an intermediate enzyme precursor in the plasma kinin forming system, and other protein mediators in *Borrelia recurrentis* infection has been shown during the JHR two hours after treatment; these values returned to normal in the convalescent period. Other workers failed to show plasma kinin formation during the JHR in secondary syphilis but they omitted to take blood samples before the three-hour interval.

The scheme proposed by Loveday and others suggested several possible sites of kinin formation during the JHR: via immune complexes, Hageman factor, early complement components, and lysozymal enzymes. Kinins so formed would have biological properties to mediate, at least in part, the subsequent reaction. In addition they proposed that the main site of the JHR in syphilis was extravascular. This may explain why only the patients having severe reactions (and pronounced activation of kininogen) showed significant changes in kininogen in the intravascular compartment. The rapid return to normal values after 3-4 hours may not reflect cessation of activation but merely an increase in overall synthesis.

Further work is in progress to clarify the role of plasma enzyme systems in the pathogenesis of the JHR.

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**References**