dose (5 × 10⁸ organisms) killed neonatal mice in two days, presumably by direct toxic effect.

The possibility that this resistance might be due to maternal antibody was considered but no evidence of bactericidal antibody was found in adult mouse serum.

We then confirmed that this organism was pathogenic to young rats. There was a 66% death rate at three days following an intraperitoneal injection of 5 × 10⁶ viable organisms into 1-day old Sprague Dawley rats. The survivors all looked ill and it was possible to culture H. influenzae from the heart blood.

We conclude that mice have an inherent resistance to H. influenzae infection which is independent of serum antibody and that they are not likely to provide a suitable animal model for H. influenzae experiments. It is interesting that rats also seem to have a similar type of resistance but this takes some time to develop so that newborn rats are more susceptible. Rabbits and man, on the other hand, appear to have a susceptibility dependent on the absence of bactericidal antibody.

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References

Prognostic significance of serum levels of fibrin/fibrinogen degradation products and of myocardial enzymes in acute myocardial infarction

Fibrin/fibrinogen degradation increases after thromboembolism and in patients with acute myocardial infarction. It has been suggested that an increase in the level of fibrin/fibrinogen degradation products (FDP) in the first few hours after myocardial infarction may be of prognostic significance (Almer et al., 1972a and b; Baele et al., 1972 and 1973; Morris et al., 1974; Okuno and Nelson, 1974; Choudhry et al., 1975). The serum levels of some myocardial enzymes (ME), especially lactic acid dehydrogenase (LDH₃) and creatinine phosphokinase (CPK) and their isoenzymes, may also be related to the severity of the attack (Peel et al., 1962; Sobel et al., 1972; Konttinen and Sommer, 1973; Wagner et al., 1973).

Though the prognostic significance of serum FDP and ME levels in acute myocardial infarction (AMI) has been studied for each individually the significance of their levels jointly has not been investigated. We present here a preliminary report of such a study in a small number of patients.

Serum FDP, CPK, and LDH₃ levels were measured in 23 patients with AMI within 48 hours after admission to the intensive care unit. The FDP levels of 39 patients who had been in the intensive care unit were also recorded. AMI in these patients was diagnosed according to the usual criteria. FDP levels in 20 patients in the intensive care unit who were not suffering from any form of thromboembolic disease were measured as controls. FDP was measured by the method of Merskey (Merskey et al., 1969) and ME by the usual techniques.

Eleven of the 23 patients (47.8%) had FDP levels equal to or higher than 16 mg/l. Only two of the 20 patients (10%) in the control group had FDP levels above 16 mg/l. Reports of the proportion of patients with AMI who have raised serum FDP levels vary widely from 6-6% (Almer et al., 1972a), 17% (Baele et al., 1973) to 34% (Okuno and Nelson, 1974). Perhaps the high proportion (47.8%) among our patients was owing to the fact that in our area AMI patients take longer to reach the intensive care unit.

Of the 11 patients among the group of 23 who had an FDP level higher than 16 mg/l within 48 hours of admission three (27.3%) died. There was only one death among the remaining 12 patients with an FDP level lower than 16 mg/l (8.3%). These mortality percentages are similar to those reported by others for patients with high FDP levels—namely. 26% (Almer et al., 1972a), 52% (Baele et al., 1973), and 22% (Okuno and Nelson, 1974). However, when considering the maximum FDP level during the whole of a patient's stay in hospital the mortality percentages were different. Of 21 patients with a maximum FDP level higher than 16 mg/l three (13.6%) died, and of 17 patients whose FDP level was never above 16 mg/l two (11.8%) died. Thus, an increase in the FDP level seems to be of real prognostic value only when it occurs in the first 24 to 48 hours.

The results of a study of coincidental serum levels of the myocardial enzymes CPK and LDH₃, and of FDP are more interesting. Out of eight patients with raised FDP levels (> 16 mg/l) and levels of CPK > 400 U/l and of LDH₃ > 500 U/l three (37.5%) died (see table). But out of three patients with raised FDP levels and low enzyme levels none died. Out of seven patients with a high level of one or both enzymes and a low FDP level only one (16.6%) died. Finally, out of six patients with low levels of both FDP and enzymes none died.

These findings suggest that FDP and ME levels are of more prognostic value

<table>
<thead>
<tr>
<th>Serum Level</th>
<th>No. of Patients</th>
<th>No. of Patients dying</th>
<th>Mortality Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDP high</td>
<td>8</td>
<td>3</td>
<td>37.5</td>
</tr>
<tr>
<td>ME low</td>
<td>6</td>
<td>1</td>
<td>16.6</td>
</tr>
<tr>
<td>FDP high</td>
<td>6</td>
<td>1</td>
<td>16.6</td>
</tr>
<tr>
<td>ME high</td>
<td>6</td>
<td>1</td>
<td>16.6</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>4</td>
<td>17.4</td>
</tr>
</tbody>
</table>

Table: Mortality in 23 patients with acute myocardial infarction correlated with serum FDP levels in the first 48 hours and maximum serum ME (CPK and/or LDH₃) levels during the patients' stay in hospital.

<table>
<thead>
<tr>
<th>FDP high</th>
<th>ME low</th>
<th>CPK &gt; 400 U/l</th>
<th>LDH₃ &gt; 500 U/l</th>
<th>ME high</th>
<th>CPK ≤ 400 U/l</th>
<th>LDH₃ ≤ 500 U/l</th>
</tr>
</thead>
</table>

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Letters to the editor

jointly than individually. There can be a physiological basis for this. If the raised level of myocardial enzymes is the direct consequence of myocardial necrosis (Sobel et al, 1972) and the raised level of FDP indicates a fibrinolytic response to a previous thromboembolic episode (Merskey and Johnson, 1971) then the patient should be suffering from an extensive myocardial lesion and its consequential thromboembolic complications. Interestingly, none of our three patients who had a raised FDP level with low enzyme levels died. Therefore perhaps the opinion that a high FDP level is a sign of a poor prognosis in acute myocardial infarction should be revised unless it is also associated with raised myocardial enzymes.

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References

Rapid estimation of paracetamol in plasma

Many methods for the determination of paracetamol in serum and plasma have been described in recent years, and of these the method of Routh et al (1968) has gained widespread acceptance. The method uses the differential absorbance at 266 nm of an acidified and alkalinized extract in order to minimize interference by salicylate. This choice of analytical approach means that the method is relatively insensitive (< 100 µmol/l) and that both barbiturates and phenylbutazone interfere. (We encountered five cases of mixed overdose involving paracetamol and barbiturate in 1975.)

Dordoni et al (1973) described a rapid method for the determination of paracetamol to which they ascribed a lack of specificity and sensitivity. Contrary to these authors we have found that, apart from being extremely rapid, this method is more sensitive and less susceptible to interference by other commonly abused drugs than is the method of Routh (1968), but the presence of high concentrations of phenylbutazone may give misleading results (table).

The method used in our laboratory is as follows:

To 1 ml serum or plasma add 1 g NaCl (approx) and 10 ml diethyl ether (Analar). Mix gently for 30 seconds by inversion, and as it is very rare for emulsions to form the ether may be decanted directly into a quartz cuvette and the absorbance read at 250 nm against an ether blank. A serum-based standard should also be taken through the procedure.

The assay is linear to 1000 µmol/l. Precision of the method was excellent (CV = 1-8% at 750 µmol/l, N = 16). One possible objection to the method is that falsely high results might be obtained due to evaporation of the ether. This has been negligible in our experience, the absorbance of paracetamol in ether increasing by less than 0-5% per minute at 25°C and by 1% per minute at 37°C.

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References

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Interference (as µmol/l paracetamol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbitone</td>
<td>400 µmol/l</td>
<td>25</td>
</tr>
<tr>
<td>Salicylate</td>
<td>10 µmol/l</td>
<td>25</td>
</tr>
<tr>
<td>Methaqualone</td>
<td>400 µmol/l</td>
<td>50</td>
</tr>
<tr>
<td>Penylbutazone</td>
<td>300 µmol/l</td>
<td>200</td>
</tr>
<tr>
<td>Glutethimide</td>
<td>430 µmol/l</td>
<td>0</td>
</tr>
<tr>
<td>Carbromal</td>
<td>830 µmol/l</td>
<td>0</td>
</tr>
</tbody>
</table>

Table Effect of the presence of other drugs on the determination of paracetamol
Letter: prognostic significance of serum levels of fibrin/fibrinogen degradation products and of myocardial enzymes in acute myocardial infarction.

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