Fetal infection with Aeromonas sobria and Plesiomonas shigelloides

We report a case of infection with *Aeromonas sobria* and *Plesiomonas shigelloides* that caused a fetal illness similar to cholera.

**Case report**

A 19-year-old woman with a history of bulimia nervosa was thrown into a water fountain while on holiday in Spain. No obvious infection of water occurred. Three days later she developed severe diarrhoea. The next day, because of personal problems, she took an overdose of paracetamol and eight aspirin tablets. She was admitted to hospital and given ipecacuanha and forced diuresis. Her diarrhoea continued, and three days later she returned to England and was admitted to this hospital. She was lethargic and dehydrated. Her temperature was 37-5°C, pulse 100 beats/min, and blood pressure 60/40 mm Hg. She had generalised abdominal tenderness. Investigations yielded: white blood cell count 12.7 x 10^9/L (with neutrophilia), prothrombin time 42/13 s, partial thromboplastin time 78/40 s, serum urea concentration 18.9 mmol/l (114 mg/100 ml), serum aspartate transaminase 199 U/l, serum bilirubin 7 umol/l (409 µg/100 ml), and serum alkaline phosphatase 1570 U/l. Faecal microscopy showed moderate numbers of red cells and profuse white cells. No parasites were seen.

The diarrhoea persisted and her general condition deteriorated despite treatment with intravenous fluids, erythromycin, ampicillin, gentamicin, and hydrocortisone. She developed generalised muscular tenderness. Five days later investigations showed white cell count 6.6 x 10^9/L (with neutropenia) platelet count 76 x 10^9/L, prothrombin time 124/13 s, partial thromboplastin time 134/41 s, fibrinogen concentration 2.1 g/l, serum uric acid concentration 27.5 mmol/l (165 mg/100 ml), serum creatinine 323 µmol/l (3.7 mg/100 ml), aspartate transaminase 1135 U/l, serum bilirubin 20 µmol/l (1.2 mg/100 ml), serum alkaline phosphatase 790 U/l, and creatinine kinase >30,000 U/l. She became drowsy, breathless, and hypotensive and bled from the vagina, rectum, and sites of venepuncture. She died on the ninth day of her illness despite intensive treatment.

Two days before her death stool cultures, by direct plating on deoxycholate citrate medium, yielded a mixed growth of *Aeromonas* spp and *Plesiomonas* spp. These organisms were provisionally identified on the basis of their morphology, motility, and biochemical reactions. They were later identified as *A. sobria* and *P. shigelloides* by the Public Health Laboratory Service Reference Laboratory, Porton Down. *Aeromonas* spp showed intense β haemolysis in blood agar medium, suggesting production of soluble haemolysin. *Plesiomonas* spp, however, showed only poor haemolytic activity. No other enteric pathogen was isolated.

Both organisms were sensitive to cefotaxime and chloramphenicol. Blood cultures yielded negative results.

At necropsy the colon showed mucosal oedema. Histological examination of skeletal and cardiac muscle showed multifocal fibre necrosis. The liver showed swelling, vacuolation, and separation of the hepatocytes without inflammatory infiltration. The marrow was hypoplastic, and the kidneys showed focal tubular atrophy. Fungal hyphae were seen in lung tissue.

**Comment**

*Aeromonas* sp and *P. shigelloides* are pollutants of water and soil that may produce gastrointestinal, skin, soft tissue, muscle, and bone infections, meningoitis, and endocarditis. In 1982 the Public Health Laboratory Service Centre for Microbiology and Research at Porton Down recorded 147 isolates of *aeromonas* and 24 of *plesiomonas* from patients with diarrhoea in Britain. Although early reports suggested that aeromonas are secondary pathogens, this is not always so. Two reports described patients with illnesses similar to dysentery or cholera from whom *Aeromonas* sp producing enterotoxins were

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**Correlation between results of Schick test and diphtheria antitoxin titres and side effects of diphtheria and tetanus toxoids (figures are number of subjects who provided information)**

<table>
<thead>
<tr>
<th>Schick test</th>
<th>Antitoxin titres before vaccination (IU):</th>
<th>1:0-0025</th>
<th>1:0-04</th>
<th>&gt;0:04</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunity</td>
<td></td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>No immunity</td>
<td></td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Reacts</td>
<td></td>
<td>10</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

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**Reactions to vaccine**

<table>
<thead>
<tr>
<th>Reaction type</th>
<th>Erythema (mm):</th>
<th>None</th>
<th>&lt;20</th>
<th>&gt;20-50</th>
<th>&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Body temperature (°C):</td>
<td>&lt;37.5</td>
<td>17</td>
<td>1</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.5-37.9</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;37.9</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

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There was little correlation between serological results before vaccination and the reactions to the Schick test (table). Only one of seven subjects thought to be non-immune serologically had a corresponding Schick reaction. A better correlation was seen among subjects who were serologically immune. The specificity of the Schick test was only 54% when falsely positive and negative reactions and pseudoreactions were excluded. The sensitivity was also low (69%) as 11 of the partially immune or immune subjects had pseudoreactions. Serological findings after vaccination showed that 37 of 38 subjects who were evaluated developed at least fourfold increases in antitoxin titres. The Schick test did not predict adverse reactions to the vaccine (table). The intracutaneous route caused more pronounced local reactions.

**Comment**

The prevalence of healthy adults without immunity to diphtheria found in this study supports findings in Denmark. The rapid increase in antibody titres indicated that adults aged 40 or under had been immunised previously and developed a booster response that seemed to be independent of the route of administration. Intracutaneous injections, however, caused more pronounced side effects. The Schick test, a time consuming procedure, was a poor predictor of subjects' immune state and of side effects. In contrast, a group in the United Kingdom found a high correlation between results of the Schick test and antitoxin titres. It did not however, compare the techniques in the same subjects and excluded subjects with pseudoreactions. Results more closely agreeing with ours were found by Topcu et al. A lack of correlation between immunity to diphtheria before vaccination and side effects indicates that the tetanus component of the vaccine may cause the local reactions.
isolated as the prime pathogens.1,2 About 95% of strains similar to the A sobra that we isolated are enterotoxigenic in the sucking mouse. We found no other cause for our patient’s diarrhoea.

Most serious aeromonas infections occur in immunosuppressed hosts. A fatal infection with P shigellodes was reported in a patient with sickle cell anaemia. Although our patient had a history of bulimia nervosa, she had been psychologically and physically well for over a year before presentation. The pattern of abnormalities of coagulation and liver function was not seen in patients after overdosage of paracetamol, and the liver showed only minimal necrosis.

We thank Dr P P Brown, consultant microbiologist at this hospital, and Dr J V Lee of the Public Health Laboratory Service Centre for Applied Microbiology and Research, Porton Down, for help in isolating the organisms.


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Oral contraceptives and venous thromboembolism: findings in a large prospective study

Data on venous thromboembolism occurring among participants in the Oxford-Family Planning Association contraceptive study were last reported in 1978. We summarise our latest findings here.

Subjects, methods, and results

The methods used in the study have been described.3 The investigation includes over 17000 women, who when recruited between 1968 and 1974 were married and aged 25-39; 56% were using oral contraceptives, 25% a diaphragm, and 19% an intrauterine device. During follow up data are recorded on changes in contraceptive methods, hospital referrals, and deaths. Discharge summaries are obtained after inpatient hospital stays.

The present report concerns 105 women suffering their first attack of venous thromboembolism unassociated with pregnancy or the puerperium. They were divided into two categories: those who developed disease within three months after a surgical operation (34) and those who became ill at other times (71). Each case record was assessed by one of us (DM), who as far as possible was blind to the patient’s contraceptive practice; the record was allocated to one of three diagnostic groups—namely, certain or probable deep vein thrombosis or pulmonary embolism, or both; possible deep vein thrombosis or pulmonary embolism, or both; or superficial venous thrombosis only. Account was taken of the history, physical signs, results of special investigations (chest radiography, electrocardiography, lung scanning, ultrasound scanning, phlebography, etc) and type of treatment.

Our first series of analyses concentrated on the 71 women suffering thromboembolism unassociated with surgery. In calculating woman years of exposure to risk we omitted periods of observation during pregnancy and during the three months after a delivery or operation. Variables taken into account in the calculation of adjusted incidences were age, smoking history, and history of varicose veins. Several other variables including parity and obesity index had no important influence on it. There was no significant difference in incidence between women who had never used oral contraceptives and those who had used them only in the past in any of the three diagnostic groups. Accordingly, and because of the small numbers studied, results are given only for those currently using and those not currently using oral contraceptives.

The table shows that there was a strong association between current oral contraceptive use and certain or probable venous thromboembolism (relative risk 7-2, p<0-001), a weaker association with possible thromboembolism (relative risk 3-1, p<0-02), and little or no association with superficial venous thrombosis (relative risk 1-4, NS). There was no significant association between risk and duration of use of oral contraceptives. Among current users the crude incidence of certain or probable thromboembolism/1000 woman years in those using oral contraceptives containing ≥50 μg oestrogen was 0-62 (20 cases during 32 082 woman years of observation) and in those using preparations containing <50 μg oestrogen it was 0-39 (three cases during 7606 woman years of observation). The corresponding figures for possible thromboembolism were 0-28 (nine cases) and 0-00 possible thromboembolism occurred in one woman using a progesteron only oral contraceptive.

Incidence of venous thrombosis and embolism unassociated with surgery related to use of oral contraceptives

Oral contraceptive use

<table>
<thead>
<tr>
<th>Deep vein thrombosis or pulmonary embolism certain or probable</th>
<th>Never or past</th>
<th>Current, &lt;36 months</th>
<th>Current, &gt;36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence 1000 woman years:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>6</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>0-06</td>
<td>0-63</td>
<td>0-47</td>
</tr>
<tr>
<td>No of women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence 1000 woman years:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>0-06</td>
<td>0-17</td>
<td>0-28</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>0-07</td>
<td>0-16</td>
<td>0-25</td>
</tr>
</tbody>
</table>

*Adjusted for age (four groups), smoking history (four groups), and history of varicose veins (two groups).

We also analysed the data on the 34 cases of postoperative thromboembolism, confining our attention to surgical procedures after which at least one woman suffered the disease. The incidence of postoperative thromboembolism in those using oral contraceptives during the month before surgery (12/1244, 0-96%) was almost twice as high as that in those not doing so (22/4559, 0-5%), but the difference was not significant.

Comment

Our findings agree with those of other major studies in that, firstly, the association between use of oral contraceptives and venous thromboembolism is strongest in those with a certain or probable diagnosis; secondly, the risk is limited to current users; and, thirdly, the risk is unrelated to duration of use.1 Our findings are consistent with the view that the risk is lower with pills containing <50 μg oestrogen, but the data are too few to confirm this.

We thank Mrs P Brown, Mrs D Collinge, Miss C Henry, our research assistants, and the staff of the participating clinics for their continued loyal support. We also thank the Medical Research Council for financial help.


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