Commentary

RONALD ILLINGWORTH

Children's Hospital Sheffield

It is good to be reminded of drugs that not so long ago passed away in disgrace, for someone may have failed to bury a drug or may have mistakenly resurrected it, having forgotten its dangers. Not so many years ago I missed a diagnosis of Pink disease (but was put right by my friend John Black): a chemist had found a large packet of mercury-containing teething powders.

In the 1940s and 1950s there were many articles about the dangers of boric applications to nappy rashes or burns, or of glycerine and borax for oral thrush, or for use with a pacifier—with consequent diarrhoea and vomiting, a red beefy rash, convulsions, meningism, opisthotonos, haemorrhages, circulatory collapse, and death. All my students were shown an impressive colour photograph of an infant dying with a diffuse red beefy rash due to a 'pacifier' dipped in glycerine of borax.

This case report of convulsions arising from the use of glycerine of borax is a timely reminder that when taking a history about a sick child, particularly if the diagnosis is not obvious, one should always ask what medicines or applications, prescribed or not prescribed, have been given.

Influence of pre-eclampsia on concentrations of haemostatic factors in mothers and infants

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SUMMARY The effect of pre-eclampsia on selected maternal and neonatal coagulation factors was studied by comparing plasma concentrations in 5 severely pre-eclamptic and 5 normal pregnancies. Pre-eclampsia was associated with appreciably lower maternal values of antithrombin III, plasminogen, and platelet count in late pregnancy but umbilical cord blood values showed no notable differences from normal pregnancy.

Pre-eclampsia is associated with an exaggeration of the haemostatic changes of normal pregnancy to the extent that intravascular coagulation may be shown. Only 2 studies have reported haemostatic factors in the newborn after pre-eclamptic pregnancy. Hathaway et al. found a raised umbilical cord concentration of factor VIII and the concentration of antithrombin III was half that of non-pregnant adults. Condie showed no important differences in umbilical cord blood values of fibrinogen, factor X, plasminogen, \( \alpha_2 \) macroglobulin, and \( \alpha_1 \) antitrypsin but found that fibrinolytic activity was appreciably lower in the cord blood of the pre-eclamptic group suggesting the possibility of a predisposition to intravascular coagulation in these neonates at birth. In this study of mothers in late pregnancy and their term infants, plasma concentrations of selected haemostatic factors in normal and pre-eclamptic pregnancies are compared.

Patients and methods

Five women with severe pre-eclampsia and 5 women with uncomplicated singleton pregnancies were matched for parity and mode of delivery. Maternal venous blood samples were collected before induction of labour or elective caesarean section. Umbilical cord venous blood was collected after the cord was clamped and divided but before delivery of the placenta. A free flowing venous blood sample was collected from each neonate on the 6th day of life at the time of routine screening for phenylketonuria and hypothyroidism.

Total plasma concentrations of fibrinogen, prothrombin, factor VIII, factor X, antithrombin III, plasminogen, \( \alpha_2 \) antiplasmin, \( \alpha_2 \) macroglobulin, and \( \alpha_1 \) antitrypsin were estimated by radial immunodiffusion and enzymatic assay using low molecular weight chromogenic substrates adapted for very small samples. The cord and neonatal results were corrected to a haematocrit value of 45%. The study was approved by the hospital ethical committee and informed consent was obtained from all the mothers.
Table  Total plasma concentrations of haemostatic factors after normal and pre-eclamptic (PET) pregnancies, expressed as non-pregnant adult concentrations (mean (SD) %)

<table>
<thead>
<tr>
<th></th>
<th>Non-pregnant pooled adult reference</th>
<th>Late pregnancy</th>
<th>Umbilical vein</th>
<th>Sixth day neonatal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>PET</td>
<td>Normal</td>
<td>PET</td>
</tr>
<tr>
<td>Uric Acid (mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>100 (24)</td>
<td>269 (69)</td>
<td>440 (25)*</td>
<td></td>
</tr>
<tr>
<td>Prothrombin</td>
<td>100 (18)</td>
<td>117 (22)</td>
<td>126 (15)</td>
<td>63 (14)</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>100</td>
<td>319 (152)</td>
<td>425 (113)</td>
<td>175 (71)</td>
</tr>
<tr>
<td>Factor X</td>
<td>100 (20)</td>
<td>116 (56)</td>
<td>162 (30)</td>
<td>66 (29)</td>
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<tr>
<td>Antithrombin III</td>
<td>100 (14)</td>
<td>98 (9)</td>
<td>68 (23)†</td>
<td>51 (17)</td>
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<tr>
<td>Plasminogen</td>
<td>100 (23)</td>
<td>113 (16)</td>
<td>68 (38)†</td>
<td>27 (16)</td>
</tr>
<tr>
<td>α1 antiplasmin</td>
<td>100 (11)</td>
<td>116 (22)</td>
<td>116 (20)</td>
<td>118 (25)</td>
</tr>
<tr>
<td>α2 antitrypsin</td>
<td>100 (23)</td>
<td>124 (28)</td>
<td>119 (14)</td>
<td>135 (40)</td>
</tr>
<tr>
<td>α1 antitrypsin</td>
<td>100 (17)</td>
<td>209 (83)</td>
<td>270 (107)</td>
<td>327 (40)</td>
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<tr>
<td>Platelets × 10⁹/l</td>
<td>150 (400)</td>
<td>247 (81)</td>
<td>186 (33)†</td>
<td>259 (88)</td>
</tr>
</tbody>
</table>

* P < 0.01, † P < 0.05 between normal and pre-eclamptic pregnancies (Mann-Whitney U test) [‡ Standard deviation not available from collaborating laboratory].

Conversion: SI to traditional units—uric acid 1 mmol/l ≈ 16.8 mg%; platelets 1 × 10⁹/l ≈ 1000/μl.

Results

The results are shown in the Table. The late pregnancy samples showed appreciably lower concentrations of antithrombin III, plasminogen, and platelet count associated with pre-eclampsia. There were no important differences in values of haemostatic factors in the umbilical cord blood of infants of mothers with pre-eclampsia compared with infants of mothers with normal pregnancy, but by the 6th day the factor X value, the fibrinogen concentration, and the platelet count were considerably higher in the infants of mothers with normal pregnancies.

Discussion

Our findings in maternal blood agree with the established view that intravascular coagulation occurs in pre-eclampsia.1 Concentrations of prothrombin and α2 antiplasmin in pre-eclampsia (not previously reported) were not appreciably different from those in normal pregnancy. In agreement with Condie,8 umbilical cord blood values of haemostatic factors were not remarkably different after pre-eclamptic pregnancies compared with normal pregnancies. Low concentrations of fibrinogen, prothrombin, factor X, antithrombin III, and plasminogen; normal (non-pregnant adult) values of α1 antiplasmin and platelets; and raised values of α2 macroglobulin and α1 antitrypsin agree with published reports.5 6

The discrepancy between concentrations of plasminogen and the fibrinolytic inhibitors α2 antiplasmin and α2 macroglobulin in the newborn5 raises the possibility of a haemostatic balance between increased inhibition of fibrinolysis and decreased production of fibrin from low concentrations of clotting factors. The raised value of factor VIII antigen in cord blood after normal pregnancy has been explained as a reaction to the stress of birth7 and is not altered by pre-eclampsia. In both groups of infants the factor VIII concentrations were greater after the reported non-pregnant values2 and this study shows that they return to normal by 6 days. By the 6th day the concentrations of fibrinogen, factor X, and platelet count were considerably lower, in the infants of mothers with pre-eclampsia but these differences may well be caused by influences other than the maternal condition.

Lower fibrinolytic activity in the cord blood of infants of mothers with pre-eclampsia has been reported3 and may reflect the greater depression of fibrinolysis in the maternal system associated with pre-eclampsia. An alternative explanation may be that in pre-eclampsia the placenta exerts a greater than normal influence on both maternal and fetal circulations.

Our results show no remarkable differences in the concentrations of haemostatic factors in cord blood after pre-eclampsia compared with normal pregnancy. Further investigations of the effect of pre-eclampsia on neonatal coagulation should be directed towards differences in clotting and fibrinolytic activities rather than the absolute values of haemostatic factors.

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References

Expiration induced femoral flow in neonatal coarctation of aorta

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SUMMARY In a 3 day old infant with coarctation of the aorta a loud Doppler signal synchronous with expiration was present for some hours in the femoral vessels, with only barely audible signals synchronous with cardiac systole. It is suggested that in the presence of severe aortic constriction and temporary ductal closure, blood was pumped through the infradiaphragmatic arteries by increased intrathoracic expiratory pressure.

We believe that the following phenomenon may not have been reported before.

Case report

A baby girl aged 72 hours was transferred from another hospital because of pallor and pyrexia. Her birth had been normal, at term, and she weighed 3.82 kg. At 12.15 am the infant was slightly cyanosed, there was forceful grunting expiration at a rate of 56/min, her cardiac rate was 150/min, and her liver edge was palpable 4 cm below the costal margin in the right nipple line. Precordial and epigastric pulsation were prominent but femoral pulsation was not detected. The blood pressure in both arms was 150 mm Hg systolic (Doppler ultrasound, 3.5 cm cuff). When the Doppler probe was placed sequentially over the femoral arteries a loud signal synchronous with expiration was heard over each artery and very faint signals synchronous with cardiac systole were audible on increasing the volume of the ultrasound. The expiration induced signal was heard at a lower intensity in the right popliteal fossa and was abolished by 20 mm Hg pressure in a 5 cm cuff on the thigh.

Digoxin, frusemide, and oxygen were given and arrangements were made for transfer to hospital in Dublin later that morning. About 8 hours later blood pressure in the right arm was 120 mm Hg and the expiration induced signal had been replaced in the groins by one synchronous with systole. The femoral systolic artery pressure was 70 mm Hg. As she was being transferred cardiac arrest occurred.

At necropsy the essential findings were a hypoplastic aortic arch with a tight infantile coarctation immediately distal to the left subclavian artery. There was a patent but narrow ductus. The other relevant findings were right ventricular dilation and hypertrophy, anatomically patent but functionally closed foramen ovale, and normal thoraco-abdominal aorta. The aortic valve was tricuspid and no endocardial fibroelastosis was seen.

Discussion

During the initial observations blood flow in the femoral arteries coincided with expiration and virtually no flow synchronous with cardiac systole was detectable. We presume that at that time ductal closure occurred which added to the severe aortic constriction and severely restricted flow into the descending aorta. We suggest that the flow detected in the femoral arteries was induced by the pumping action of a high intrathoracic expiratory pressure on the descending aorta, sufficient to produce a pressure of at least 20 mm Hg. Since an expiratory intrathoracic pressure of 92 cm H$_2$O (67.6 mg Hg) has been recorded in a neonate and pressure of about 240 cm H$_2$O (176.5 mm Hg) in an adult male undergoing physical stress, it seems reasonable that with retrograde flow largely prevented by aortic and ductal constriction, high intrathoracic pressure could pump blood in the descending aorta downwards. This would imply that sufficient blood was...