Case reports

macher and Punnett have presented a review of 56 cases and have studied comparative mitotic behaviour of r(9) and r(13).

Ring formation of chromosome 20 with mosaicism has been previously described twice. In a 26-year-old woman with nervous symptoms and epileptic seizures the symptoms and chromosomal abnormality were presumed to be coincidental (Uchida and Lin, 1972).

Another case was a 12-year-old boy with epilepsy and behaviour disorder (Faed et al., 1972). The third case with r(20) and the only one without mosaicism was a 7-year-old boy with similar symptoms (Atkins et al., 1972).

Our patient is similar to all three in having low grade mental deficiency, behaviour problems, and epilepsy.

In all earlier patients and also in our patient r(20) seems to be relatively stable. This may be the cytogenetic explanation of the definite clinical picture. Leisti et al. (1968) suggest that the lability of the ring in r(E) patients is related to various phenotypic expressions.

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References


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Congenital discoid lupus in the newborn

The mother was in good health until 1970 when, aged 18 years, she developed an erythematous rash on her face as a result of exposure to bright sunlight. She subsequently became unwell with general malaise, headache, nausea, and vomiting. On admission to the City Hospital, Nottingham, she was found to be anaemic with a haemoglobin level of 8.2 g/dl. She had a neutropenia of 2300 white cells/mm3, and proteinuria with total serum protein of 47 g/l, and only 12 g/l albumin. She developed the nephrotic syndrome with peripheral oedema and ascites, subsequently going into renal failure and then left ventricular failure. Renal biopsy confirmed focal glomerular changes with thickening of the basement membranes and for the first time she was found to have LE cells in the peripheral blood with a positive titre of antinuclear antibody (ANA) and a reduced serum complement level at 54 mg/100 ml (Table). Treatment was started with prednisolone, her condition improved, normal renal function returned and, despite an episode of right sided pleurisy and consolidation, she was well enough for discharge 3 months after the onset of symptoms.

As an outpatient, treatment with prednisolone was continued and she was also given azathioprine; the steroid dosage varied from 15 mg t.d.s. to 5 to 10 mg alternate days and was maintained on azathioprine 25 mg b.d. until 1973. In February of that year, approximately 2½ years after the onset of her disease, she had amenorrhoea but a test for pregnancy was

<table>
<thead>
<tr>
<th>Normal adult levels</th>
<th>ANA titre</th>
<th>%DNA binding</th>
<th>C3 Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;10</td>
<td>&gt;20</td>
<td>100-250</td>
</tr>
</tbody>
</table>

**Table Serological findings in mother and infant**

Mother

<table>
<thead>
<tr>
<th></th>
<th>ANA titre</th>
<th>%DNA binding</th>
<th>C3 Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.9.70</td>
<td>400</td>
<td>-</td>
<td>54</td>
</tr>
<tr>
<td>10.11.71</td>
<td>- ve</td>
<td>16.5</td>
<td>185</td>
</tr>
<tr>
<td>1.12.72</td>
<td>20</td>
<td>NT</td>
<td>125</td>
</tr>
<tr>
<td>23.3.73</td>
<td>20</td>
<td>84-4</td>
<td>38</td>
</tr>
<tr>
<td>14.10.73</td>
<td>- ve</td>
<td>12-0</td>
<td>68</td>
</tr>
<tr>
<td>13.9.74</td>
<td>100</td>
<td>43-2</td>
<td>46</td>
</tr>
</tbody>
</table>

Infant

<table>
<thead>
<tr>
<th></th>
<th>ANA titre</th>
<th>%DNA binding</th>
<th>C3 Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.10.73</td>
<td>- ve</td>
<td>2-2</td>
<td>64</td>
</tr>
<tr>
<td>23.10.73</td>
<td>- ve</td>
<td>1-9</td>
<td>75</td>
</tr>
</tbody>
</table>

NT, not tested.
negative. The results of serological investigations from the start of her illness until this time are seen in the Table. In March 1973, an erythematous rash appeared again on her face and the back of her hands. Investigation revealed a high level of DNA binding with hypocomplementaemia and proteinuria was again present. Generally, however, she remained well, her weight increased and she made no further reference to the possibility of pregnancy. In October 1973, she became unwell with headache, abdominal pain, and visual hemianopia. She attended the Casualty Department of another hospital and was found to be in established labour. She was, therefore, transferred to the Maternity Unit at the City Hospital and delivered a female infant on 14 October 1973.

**The Infant**

The infant’s birthweight was 2.02 kg and maturity assessment suggested a gestation of 38 weeks. From the time of delivery she was noted to have scattered atrophic areas of the skin over the face, scalp, and trunk (Fig.). The limbs were spared and the general appearance of the baby otherwise was normal. The skin lesions were irregular in outline, varying from 5 to 12 mm in length. The bases of the lesions were thin and faintly bluish with small capillary vessels occasionally seen.

The infant’s subsequent progress was uneventful. Mild jaundice was noted on the third day and the serum bilirubin rose to a maximum of 9.0 mg/100 ml (153.9 μmol/l). The jaundice had disappeared by the eighth day and was presumed physiological. By the age of 1 month the skin lesions were obviously improving and the infant’s discharge was requested. The mother was advised to keep the baby out of the sun until healing was complete but with continuous improvement the baby was exposed to sunlight without ill effect. At the age of 4 months the lesions were virtually healed and by the age of 1 year minimal scarring at the site of a few of the larger lesions was the only abnormality visible. There had never been any evidence of generalized disease. LE cells were not found and both the cord blood and a specimen at 9 days of life showed a negative antinuclear antibody titre, a normal level of DNA binding, and a complement level compatible with the age of the infant.

**Discussion**

The clinical picture, immunological findings, and course of the illness confirmed the diagnosis of systemic lupus erythematosus (SLE) in this mother (Hughes, 1974). The changes in the skin of her infant are typical of those described in previous reports of discoid lupus and the benign nature of these lesions was confirmed (Jackson, 1964).

There appears to be no obvious method of correlating maternal disease and the possible outcome for the fetus. There are a number of reports confirming that the LE factor may cross the placenta and be shown in the infant’s circulation (Beck and Rowell, 1963). The infants, however, have been normal and in other cases where serious, and occasionally fatal, neonatal disease occurred LE cells and other serological changes associated with the disease have not always been found, though changes have been noted in some (Reed et al., 1967). It is difficult to explain the absence of serological changes in this infant if one presumes that the skin lesions are produced by a similar mechanism to the mother’s disease. The antinuclear antibody in the mother’s serum was shown to be complement fixing and of class IgG. This is capable of crossing the placenta but could possibly be localized fairly promptly in the skin and hence not be detectable in the serum. Immunofluorescent studies on a skin biopsy would be useful and immunoglobulins or complement deposition, if present, would help to substantiate this suggestion. Permission for skin biopsy in this infant was not obtained.

![Fig. Lesions on skin of face.](http://jmg.bmj.com/ on April 15, 2017 - Published by group.bmj.com)
If most of the anti DNA and antinuclear antibodies in the maternal circulation are already complexed with antigen, it is possible that only a fraction of these complexes would be able to cross the placenta. These may be less pathogenic and fairly rapidly eliminated from the fetal circulation; the lower complement levels seen in the newborn might also reduce their pathogenic effect. This combination of factors could possibly explain the type of lesion seen in this infant. However, it does not explain why serious, and occasional fatal, neonatal disease occurs. This could be the result of a greater quantity of complexed material crossing the placenta or it may be that this concept of the disease is incorrect and the skin and other lesions are produced by a different mechanism. The cause of SLE has not been established and there is still considerable doubt as to the significance of infection or genetic factors (Siegal and Lee, 1973). There has been an occasional report of SLE in monozygotic twins (Jokinen and Jankala, 1970) but Brunner et al. (1971) reported discordancy in identical twins and familial clustering of the disease has been observed.

Irrespective of the aetiology of the maternal and infant disease, mothers with proven systemic lupus erythematosus may rightly expect counselling and discussion of the effects of the disease on future pregnancies. McGee and Makowski (1970) in a survey of 7 patients with a total of 11 pregnancies reported 2 stillbirths and 1 spontaneous abortion; a fetal wastage rate of 27%. This confirmed a previous report by Ellis and Bereston (1952). Estes and Larson (1965) suggested that fertility rates were normal but also confirmed a high fetal wastage rate and a high rate of spontaneous abortion. Where the pregnancy survives the premature delivery rate is high. In the patients of McGee and Makowski (1970), the prematurity rate was 36%. The total number of patients reported is small but most reported series confirm these figures and there is undoubtedly a considerable risk of a failed pregnancy.

Where the infant is born at term complications may be variable. Low birthweight is common and this does not appear to have any correlation with the severity or extent of the maternal disease. Scott (1976) reviewed reports of 16 cases in which newborn infants showed clinical manifestations presumed to be associated with maternal disease. Nine had transient skin lesions of the type described in the patient in this report. In 5 of these, biopsy was reported as supporting the diagnosis. Four other patients had disseminated disease with thrombocytopenia and 1 case proved fatal. Three infants had widespread involvement with cardiac failure and heart block and all died. Antenatal diagnosis of the heart block was possible in 1 of these patients but the severity of the cardiac involvement was such as to make any treatment unlikely to be successful. Figures are not available for the number of normal infants born to mothers with systemic lupus erythematosus. These are probably not always reported.

More recently immunosuppressive drugs have been used in the treatment of autoimmune disease, including systemic lupus erythematosus. In an article on the effects on the neonate of prednisolone and azathioprine given to a mother, Cote et al. (1974) reported lymphopenia, diminished thymic shadow, and low serum concentrations of immunoglobulins M and G in the infant. The patient survived and subsequently his immune status returned to normal. The infant in this report did not show this complication, but changes in the immunological status of the newborn should be suspected when the mother is treated with immunosuppressive therapy during pregnancy.

The manifestations of systemic lupus erythematosus are protean and the disease, in the early stages particularly, may be misdiagnosed. In those cases in which a firm diagnosis has been made, and which have been reported, there have been serious implications for the survival of the pregnancy and the fetus. There is need, therefore, for caution in counselling mothers with this disease and the complications are certainly more serious than at least one standard midwifery textbook suggests (Barnes, 1974).

Our thanks are due to Dr M. S. Knapp, Consultant Physician, City Hospital, for clinical details of the mother’s illness.

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References


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Regular G21–trisomy in 3 sibs from mother with trisomy 21 mosaicism

**SUMMARY** This paper describes a family with 3 affected sibs with regular trisomy 21 Down syndrome. The condition seems to be transmitted from a phenotypically normal mother in whom G-trisomy mosaicism was identified. Giemsa banding depicted trisomy 21 mosaicism in cells from the mother. Chromosomes from the children showed a trisomy 21 in all the cells analysed.

In 1962, Smith et al. first described trisomy 21 Down syndrome associated with maternal mosaicism. Subsequently trisomy Down syndrome associated with maternal G-trisomy mosaicism has been reported in at least 12 instances. Aarskog in 1969 described a family with 2 affected sibs and made a review of cases published so far. In 1 of the families of this series the mother gave birth to 3 consecutive children with Down syndrome. Recently Kaffe et al. (1974) reported a case of trisomy 21 mosaicism in a woman with 2 children with trisomy 21 Down syndrome.

We would like to present a family in which 3 sibs show trisomy 21 Down syndrome. Chromosomes from the mother showed trisomy 21 mosaicism. Giemsa banding performed by the method of Seabright (1971), confirmed the presence of an extra G chromosome in the trisomic cells.

**Case reports**

The probands, 1 boy and 2 girls, were first seen at the genetics clinic at the ages of 13, 10, and 8, because of findings suggesting Down syndrome. They were the second, third, and fourth of 4 children (Fig. 1). The first one appeared as a normal 18-year-old youngster. Each affected child showed clinical features of Down syndrome such as brachycephaly, epicantal folds, mongoloid slant of palpebral fissures, low-placed dysplastic ears, hypotonia, and typical dermatoglyphs.

The mother was 39 years old when she was seen for the first time in 1975. She was the eldest of a sibship of 6. Her mother was 26 years old and her father 23 years old when she was born. A paternal aunt gave birth to a child with clinical features of Down syndrome at the age of 41. She had 4 uneventful pregnancies, the first one at the age of 19 and the last one when she was 29 years old, and no abortions. Her first pregnancy ended with the birth of a normal boy. Five years later, at the age of 24 years, she gave birth to a boy with typical features of Down syndrome. She became pregnant again at the ages of 27 and 29 years and gave birth to 2 more children, both of them with clinical stigmata of Down syndrome. There was no history of drug ingestion, radiation exposure, or viral infection. Each child belongs to a different father. At the time of the interview in 1975, she was 39 years old. She displayed no stigmata of Down syndrome, and her intelligence was considered normal.

![Pedigree of the family.](http://jmg.bmj.com/)

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