Drug was withdrawn on the twelfth day. There were no side-effects in the chloramphenicol group.

Discussion

These results show that in the treatment of severe cases of typhoid fever chloramphenicol is more effective than ampicillin as judged by the length of time taken for the temperature to subside. Further, in this series the response to chloramphenicol was uniformly good irrespective of the severity of the illness. This conclusion supports that of Patel (1964). In contrast, in six cases the treatment had to be changed to chloramphenicol because of apparent lack of response to ampicillin. It could be argued that in these cases treatment with ampicillin was not continued long enough, but in view of the worsening clinical condition of these patients it was not thought justifiable to continue.

The time taken for the temperature to subside in severe cases treated with ampicillin in this series agrees with the figures of Uwaydah and Shamma'a (1964); but those authors do not describe the severity of their cases.

Medical Memoranda

Systemic Lupus Erythematosus and Pregnancy

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This memorandum reports a case of systemic lupus erythematosus of pregnancy and reviews the literature with special reference to treatment.

Case Report

A patient, now aged 42 years, was first admitted to the medical unit in April 1957 with systemic lupus erythematosus. She gave a history of increasing breathlessness for four years which had become worse over the last month before admission. At this time she was orthopnoeic and cyanosed, with clinical evidence of atelectasis of the left base of the lung. There was inactive arthritic involvement of the hands and wrists. The diagnosis of systemic lupus erythematosus was confirmed by finding numerous lupus erythematosus cells in the blood. She was treated with steroids with considerable improvement in her effort dyspnoea. Since then she has been admitted on numerous occasions with exacerbation of her joint and muscle pains, increasing effort dyspnoea, and one episode of left-sided pleuritic chest pain. During this time her prednisolone dosage was altered according to the activity of the disease—the dosage varying between 15 to 75 mg. daily.

She attended the medical out-patients department on 28 March 1963 with a history of amenorrhoea since 1 August 1962 and complaining that her abdomen was getting bigger. The uterus was found to be enlarged to approximately 22 weeks' pregnancy. She was referred to the obstetric department. The dyspnoea became worse during the first trimester of pregnancy and improved during the middle trimester; it worsened again during the 35th to 36th week of gestation, when she was admitted to hospital. At this time there was evidence of pre-eclamptic toxemia, the blood-pressure having risen from 120/80 mm. Hg to 130/90 mm. Hg, and there was a trace of albumin in the urine. These symptoms improved with rest. Labour commenced spontaneously at the 38th week of pregnancy: the second stage was shortened by an outlet forceps delivery while the patient was in the upright position, since dyspnoea became intolerable on lying flat.

A live male infant (birth weight 5 lb. 14 oz. (2.67 kg.) ) was delivered. Nothing abnormal was found on clinical examination. Three weeks after delivery her effort dyspnoea became worse, but there was no evidence of congestive cardiac failure and the blood-pressure had returned to 120/80 mm. Hg. Prednisolone was increased to 25 mg. daily for the first two weeks post partum; the effort dyspnoea then became less and the prednisolone dosage was reduced to 15 mg. daily.

The patient has been observed in the out-patient department for 10 months after delivery and there has been no evidence of deterioration in her condition. The disease is being kept under control with prednisolone 15 mg. daily. The baby is alive and well and continues to make satisfactory progress.

The results of recent investigations are as follows: L.E. cells (occasionally present); haemoglobin, 70%; white blood count, 6,000 differential normal; E.S.R., 10; midstream urine, normal; blood urea, 40; serum protein electrophoresis: increase in gamma-globulin and slightly reduced albumin; liver function tests, S.G.P.T. 10; alkaline phosphatase, 5 K-A units; thymol turbidity, 3.1 units; zinc sulphate turbidity, 22.2 Kunkel units. The findings in respiratory function tests were consistent with hyperventilation associated with a combination of pulmonary fibrosis and ventilatory obstruction. Radiographs of the chest showed bilateral diaphragmatic elevation with partial atelectasis at both bases.

Comment

The effect of pregnancy on systemic lupus erythematosus has been excellently reviewed by Garsenstein et al. (1962), Murray (1958), and Mund et al. (1963). Friedman and Rutherford (1956) reported on the relationship of pregnancy to systemic lupus erythematosus. It appeared that fertility was not affected; the abortion rate was increased to 15.8%—approximately twice
the national average — and prematurity was increased to 15.8%, compared with the average of 7.8%. Full-term viable infants were unaffected by the disease but placental transfer of the I.E. factor has been reported (Bridge and Folley, 1954; Berlyne et al., 1957). Friedman and Rutherford’s findings and those of Murray (1958) show that benign systemic lupus erythematosus in association with pregnancy is comparatively safe and that it is not uncommon for pregnancy to have a beneficial effect on the disease. Friedman and Rutherford were of the opinion that when a flare-up appeared in pregnancy it was purely a chance occurrence. Mund et al. (1963) and Garsenstein et al. (1962) found that exacerbations occurred with particular frequency during the first eight weeks of the post-partum period. Garsenstein also found that the incidence of exacerbation was most frequent during the first 20 weeks of pregnancy, and the incidence of remission was least during this period and the first eight weeks post partum. Predominant respiratory involvement in systemic lupus erythematosus is rare, and in this case pregnancy certainly did not produce any deterioration other than that which could be attributed to diminution in vital capacity.

The treatment of systemic lupus erythematosus during pregnancy should be supervised by a physician and an obstetrician. Congenital defects, intrauterine death (Kalter and Warkany, 1959) and growth retardation of the foetus have been produced experimentally by giving cortisone to animals (Blodgett et al., 1956). There have been no reports that human foetal damage can result from cortisone therapy.

Steroid therapy does not appear to alter the course of pregnancy in systemic erythematosus and it definitely diminishes the number of exacerbations. Progression of lupus glomerulonephritis can frequently be halted by large doses of steroids. Murray (1958) has called attention to the grave prognosis when the mother has lupus glomerulonephritis, but none of his patients had been treated with large doses of prednisolone. The treatment of lupus glomerulonephritis in association with pregnancy toxemia may be difficult. Reference to this situation was made by Murray (1958). We think that in such a case the steroid dosage should be increased in the hope of producing a remission. Garsenstein et al. (1962) described four patients who had lupus glomerulonephritis out of a series of 21 pregnancies; all these patients died. We therefore feel that nothing can be lost by increasing the steroid dosage. It has been suggested by Murray (1958) that increasing albuminuria in early pregnancy should be an indication for therapeutic abortion. Garsenstein et al. (1962) did not find any relation between the histological severity of renal involvement and the foetal outcome. Ziff et al. (1958) noted albuminuria fluctuating in a manner unrelated to the evidence of disease activity. It appears that renal changes in systemic lupus erythematosus may go on for long periods without progression in many patients. We would consider, therefore, that increasing albuminuria is not necessarily evidence of a progressive renal lesion and other clinical or histological findings should be found to substantiate this.

The evidence of psychosis in patients with systemic lupus erythematosus has ranged from 0% to 24% (Jessar et al., 1953; Clark and Bailey, 1956). Ziff et al. (1958) reported an incidence of 54%, but this was because a large number of patients were taken from a medical psychiatric service. Difficulty may arise in differentiating between steroid-induced psychosis, psychosis superimposed upon a chronic illness in a patient with psychiatric predisposition, and organic psychosis in systemic erythematosus. Organic psychosis is a manifestation of severe systemic lupus erythematosus, and in pregnancy appears to arise in the third trimester or in the immediate post-partum period. Mund et al. (1963) report four cases; these patients were not receiving steroids and their symptoms subsided on prednisolone therapy. Ziff et al. (1958) found that in none of their non-pregnant cases of systemic lupus erythematosus thought to have steroid-induced psychosis did increased steroid dosage aggravate the psychosis. Some patients received electric-shock therapy concurrently. This suggested that most psychoses in patients with systemic lupus erythematosus are due to the activity of the disease rather than to the steroid therapy. It is advisable, therefore, that adequate supportive doses of steroids be administered when psychosis occurs in the presence of symptoms of active disease.

Little is known of the factors that precipitate exacerbations of the disease. The fact that the disease occurs most frequently in females between the menarche and menopause suggests that hormones may be involved (Garsenstein et al., 1962), and this is further substantiated by the exacerbation of the disease in the first 20 weeks of pregnancy. However, the decrease in the serum levels of the hydroxy corticosteroids occurs too early after pregnancy to be the only reason for the high incidence of exacerbations four to eight weeks post partum. Steroid dosage should be approximately doubled at the onset of labour and this should be supplemented by intravenous hydrocortisone 100 mg. eight-hourly up to the time of delivery. In view of the frequent exacerbation post partum we think that it would be advisable in the future to retain the steroid dosage at a high level for the first eight weeks post partum, subsequently slowly reducing the dosage to the lowest possible level that will keep the disease under control. In our case the effort dyspnoea increased approximately three weeks after delivery and the steroid dosage was maintained at the same level as during delivery — namely, 20 mg. daily of prednisolone. One week later the dosage was decreased to 15 mg. daily with no further exacerbation of the disease apart from slight aching in the small joints of the hands.

Finally one should mention that during the antenatal period false positive reactions in the routine serological tests for syphilis are not uncommon. Anaemia is common in systemic lupus erythematosus and considerable care is needed in blood transfusion, since frequent reactions occur and multiple antibodies have been reported. A too-rapid transfusion may precipitate congestive cardiac failure in an already damaged myocardium or Libman-Sacks valvulitis; it may also lead to acute renal failure in the presence of lupus glomerulonephritis.

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GILLIAN C. HANSON, M.R.C.P.
Medical Registrar, Whips Cross Hospital, London.

SOBHA GHOSH, M.R.C.O.G.
Gynaecological Registrar, Thorpe Coombe Maternity Hospital, London.

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