important since vasoconstriction would seem to be one of the mechanisms by which toxæmia of pregnancy may produce damage (Morris *et al.*, 1955; Dixon *et al.*, 1963). It proved easy to maintain complete blood pressure control in our patients with oral diazoxide and prolongation of pregnancy by up to 10 weeks was achieved. The diminution or abolition of albuminuria which occurred in all four patients suggests at least an amelioration of the toxæmic process and this suggestion is further supported by the normal fetal growth which took place during the period of treatment.

The successful conclusion of pregnancy in Case 1 despite the presence of considerable renal failure may well have been related to the increased renal blood flow which diazoxide is known to produce.

The only important side effect of oral diazoxide therapy that was encountered was sodium and fluid retention (Pohl *et al.*, 1972) which responded satisfactorily to frusemide. The need for twice-daily blood sugar estimations made it necessary for the patients to stay in hospital for the remainder of pregnancy. Only Case 3 developed hyperglycaemia during the last week of diazoxide treatment. Although this was easily controlled by oral tolbutamide the cessation of fetal growth at this stage suggests that treatment with insulin would have been better. The reported effect of diazoxide in diabetics is variable (Graber *et al.*, 1966; Black, 1968). In our two diabetic patients (Cases 1 and 2) the effect was minimal and only trivial increases of insulin dosage were required. In the absence of hyperglycaemia oral diazoxide therapy cannot have impaired fetal endogenous insulin production since glucose tolerance tests on the newborn babies were normal (Milner, and Chouksey, 1972).

The successful and yet fairly easy management of four cases of severe hypertension in pregnancy resistant to other therapy suggests to us that oral diazoxide deserves a trial in the management of this condition, but it is important to see and treat these patients early. We have seen other patients with much more severe hypertension, possibly antedating pregnancy, in which there has been an appreciable fetal mortality.

We wish to thank Professor D. A. K. Black for his helpful advice and discussion and Mr. T. B. Fitzgerald and Mr. R. L. Gadd for allowing us to have access to patients under their care.

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MEDICAL MEMORANDA

Isolation of Herpes Virus from Erythema Multiforme

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British Medical Journal, 1972, **2**, 570-571

Herpes virus has occasionally been isolated from lesions of erythema multiforme (Shelley, 1967; Söltz-Szöts, 1969) but the presence of the virus has never been fully explained, nor has opportunist secondary infection or contamination been excluded in some of these cases.

We report a case in which severe herpes simplex cervicitis was followed by an eruption of erythema multiforme type. Herpes virus was readily grown from the skin lesions, which were also remarkable for the intensity of their inflammatory reaction.

Case Report

A 27-year-old woman developed dyspareunia, a thick vaginal discharge, and, two weeks later, dragging lower abdominal pain and dysuria. On admission she was acutely ill with a temperature of 40°C. The lower abdomen was extremely tender and a tender,

bulky uterus was palpated per vaginam. So distressing was this manoeuvre that the cervix could not be adequately inspected. Acute salpingitis with pelvic peritonitis was diagnosed. Shortly afterwards vesicles characteristic of herpes simplex appeared on the vulva and herpes cervicitis became the presumptive diagnosis.

Soon after admission she developed an extensive and somewhat bizarre eruption involving the face, scalp, limbs, trunk, and perineal regions, consisting of discrete, fixed plaques up to 10 cm in diameter. No further lesions appeared but those present soon became covered by malodorous adherent crusts, some as thick as 2 cm, from under which serum continued to exude.

She was initially treated with ampicillin and trimethoprim-sulphamethoxazole (Septrin) (Fig. 1). Five weeks later, however, although the fever had diminished and the gynaecological condition improved the skin disorder was still causing her much distress (Fig. 2). Various topical medicaments (gentamicin, beta-methasone valerate, idoxuridine, eusol) had been of little benefit. She was then given prednisolone up to 80 mg daily. Activity of the lesions persisted for two more weeks, when suddenly and for no apparent reason the crusts became dry and began to separate. Some 15 weeks after admission to hospital the lesions had almost healed (Fig. 3). Although there was hepatic tenderness in the acute stage of the illness general physical examination throughout had elicited no other abnormalities.

INVESTIGATIONS

The haemopoietic system including bone marrow was normal apart from relative lymphopenia. The E.S.R. which was initially over 100 mm/hr, fell to normal before her discharge. Biopsy of a lesion showed tissue grossly distorted by the acuteness of the inflammatory process. Neither balloon cells nor inclusion bodies indicative of virus infection nor a perivascular infiltrate suggestive of erythema multiforme were seen.

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FIG. 1—Clinical course of illness.

FIG. 2—Facial lesions five weeks after admission.

FIG. 3—Appearance of facial lesions 15 weeks after admission.

VIRUS AND IMMUNOLOGICAL STUDIES

Herpes virus hominis (Type 2) was readily and repeatedly grown from cutaneous lesions at different sites and stages of the illness up to and including the eighth week (Fig. 4), after which growth was not obtained. Culture of blood and bone marrow showed no virus. A specimen of urine was positive for virus on a single occasion. (Staphylococci and various Gram-negative organisms isolated from the lesions were regarded as secondary invaders.)

Intradermal tuberculin (100 U) was negative. Total immunoglobulin levels, which were low in the early stages of the illness (IgG 7.2 mg/ml, IgM 0.82 mg/ml), rose to normal by the sixth week (IgG 9 mg/ml, IgA 2.6 mg/ml, IgM 14.5 mg/ml). Titres of complement-fixing virus antibodies are shown in the Table. Neutralizing antibodies against virus grown from the patient were almost absent (titre <4) on two occasions.

Complement-fixing Antibody Titre (Reciprocals) against Various Common Viruses throughout Illness

	Weeks after Admission						
	0	1	2	3	6	9	12
Herpes 1	20	80	80	80	160		40
Herpes 2	10	320	160	80	160	160	40
Mumps S	20	80	80	20	10	10	20
Mumps V	20	40	40	80	20	10	20
Cytomegalovirus	10	20	160	20	10		20
Respiratory syncytial virus	10	20	80		40		10
Para III	10	80	80		40		
Measles	10	10	160	20		40	20
Psittacosis, lymphogranuloma venereum	10		40	20			20
Zoster V	160		160	80	160	20	20
Coxiella	10	10	10	10	10		10
Mycoplasma pneumoniae	10	10	10				
Influenza A	10	10	10	20	10		10
Influenza B	10			20		10	
Sindai	10	10	10	20		20	
Adenovirus	10	10	20			10	

Lymphocyte transformation studies (performed when the patient was receiving prednisolone 80 mg per day) showed a normal phytohaemagglutinin response but some impairment of transformation in mixed lymphocyte culture (397 counts/min ^3H thymidine incorporation, control 600 counts/min.) Later when the illness had subsided and prednisolone was reduced to 10 mg on alternate days mixed lymphocyte culture had returned to almost normal (1,414 counts/min, control 102 counts/min). Plasma obtained early in the illness was anticomplementary (0.5 ml of heated serum inactivated 0.5 out of 1.8 units of guinea-pig complement in 60 minutes), indicating the presence of circulating immune complexes. This activity was not found in any subsequent specimens, in which total haemolytic complement levels were also normal. When culture of these lesions repeatedly yielded herpes virus it was feared that the patient might also have a progressive systemic herpes infection,

possibly on the basis of constitutional immune deficiency, and that this might progress to hepatitis and encephalitis. The eruption, although somewhat bizarre, however, was not composed of clusters of small vesicles characteristic of herpes simplex infection. No signs of cerebral involvement appeared and hepatic tenderness, which at first had aroused concern, disappeared rapidly.

Comment

The severe necrotizing form of herpes simplex cervicitis (due to the type 2 virus), which was first described by Wilcox (1968), has subsequently been seen with increasing frequency by venereologists and gynaecologists. In the present patient the process was so acute that she developed salpingitis and pelvic peritonitis, presumably of the same aetiology. Her skin lesions, however, were not a usual finding in this disorder. Blood and bone marrow culture yielded no virus and the one positive isolation from the urine could have been the result of contamination. Her history did not suggest an immune deficiency state and our investigations did not support such a possibility. Immunoglobulin levels, low initially, rapidly became normal. Complement-fixing antibody titres to herpes virus rose as expected and titres of antibodies against other viruses, though low at the onset, rose anamnesticly. Impairment of lymphocyte transformation could be attributed to the high corticosteroid dosage she was receiving at the time and to the effects of her severe virus infection on the lymphocytes themselves.

The presence of circulating immune complexes early in the illness suggested that her skin lesions were produced by just such a mechanism and raises the possibility that the same may be true for erythema multiforme in general (discussed but dismissed for lack of evidence by Levene and Turk, 1970).

We are greatly indebted to Dr. James Mowbray and his staff in the department of experimental pathology, St. Mary's Hospital Medical School, for undertaking both complement studies and lymphocyte transformation tests.

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