TABLE IV—RELATION BETWEEN 3-YEAR SURVIVAL IN 43 MASTECTOMISED PATIENTS WHO HAD ⩾4 POSITIVE NODES AND SEX OF FIRST CHILD

Sex of 1st child	No. of patients	No. alive at 3 yr	Statistical significance
M	21	19 (90%)	$\chi^2=5{\cdot}55$
F	22	13 (59%)	$0{\cdot}01<P<0{\cdot}02$

number of patients in each group with a specified number of positive nodes.

The M/F sex ratio of the entire study population (1·08) is not statistically different from that of the overall French population (1·05) suggesting that the sex of the first child does not influence the risk of breast cancer.

DISCUSSION

We cannot exclude the possibility that our findings are due to chance or bias since the differences barely reach statistical significance in tables I and II, but the fact that statistical significance is reached, especially that achieved in table III, makes chance or bias unlikely.

Our study considers the sex of only the first child since the first birth appears to be an important determinant for breast cancer history. MacMahon et al. have shown that the earlier the age at which a woman first gave birth, the lower the risk of breast cancer.[1] On the other hand we found the prognosis to be more unfavourable for those women with breast cancer who gave birth before the age of 23 than for those women who did so between 23 and 30.[2,3] It has also been shown that the earlier the first birth, the earlier the onset of mammary cancer.[4] But these findings do not entitle us to believe that the other pregnancies have no influence.

The influence of the sex of the first child on the prognosis of breast cancer may be due to a difference in fetal gonadal secretions between males and females; human fetal testes (in contrast to ovaries and to adrenals) produce a significant amount of testosterone between the 8th and 15th weeks of pregnancy.[5,6] Late miscarriage should also be considered, since the male embryo may have secreted hormones before the abortion.

In order to find out whether the sex of the first child retains its prognostic significance in patients with equal degrees of lymph-node involvement, we studied the 3-year survival of the 43 patients operated on during 1964–1974 who had at least 4 positive nodes. We found that the sex of the first child retains its prognostic significance in patients with the same degree of lymph-node involvement (table IV), but studies on larger populations are needed. It may also be interesting to know whether the sex of the first child influences other female malignancies.

We thank Mme J. Macé for help with statistics.

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References continued at foot of next column

PLASMAPHERESIS IN RAYNAUD'S DISEASE

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Summary Understanding of the pathogenesis, clinical course, and treatment of Raynaud's disease is confused and unsatisfactory, and no success in treatment can be promised. Five patients with severe Raynaud's disease, who had not responded to other forms of treatment, were treated by plasmapheresis, which produced a striking improvement. Ultrasonic velocimetry showed that segments of digital arteries which had been thought to be permanently occluded became patent and remained patent after plasmapheresis.

INTRODUCTION

THE symptoms of Raynaud's disease range from slight susceptibility of the digital circulation to cold to severe crippling by pain, ulceration, and even gangrene. The search continues for an underlying cause of Raynaud's disease and for methods for monitoring the course of the disease. Its variable presentation makes classification difficult and unsatisfactory. Furthermore, terminology is often contradictory[1,2] and the result of conventional treatments are unpredictable.

Plasmapheresis was carried out on five patients in an attempt to modify the effects of increased blood-viscosity, circulating immune complexes, or vasoactive substances.

PATIENTS AND METHODS

Four women and one man, aged 24 to 52 years, were diagnosed clinically as having Raynaud's disease. Four patients had severe digital ulceration at the time of treatment. Six upper dorsal sympathectomies had been performed in four patients. The patients' digital arteries were scanned by continuous-wave directional Doppler velocimeter under resting conditions and again after exposure to cold. Two patients underwent digital arteriography before and after treatment.

The patients were then treated by plasmapheresis of 2–2·5 l of plasma weekly for a total of five treatments. The plasma exchange was carried out with exhausted plasma or a combination of fresh-frozen plasma and purified protein fraction with an 'Aminco Celltrifuge' (Travenol Laboratories Co. Mayo, Ireland). After treatment the patients underwent careful physical examination and ultrasonic velocimetry.

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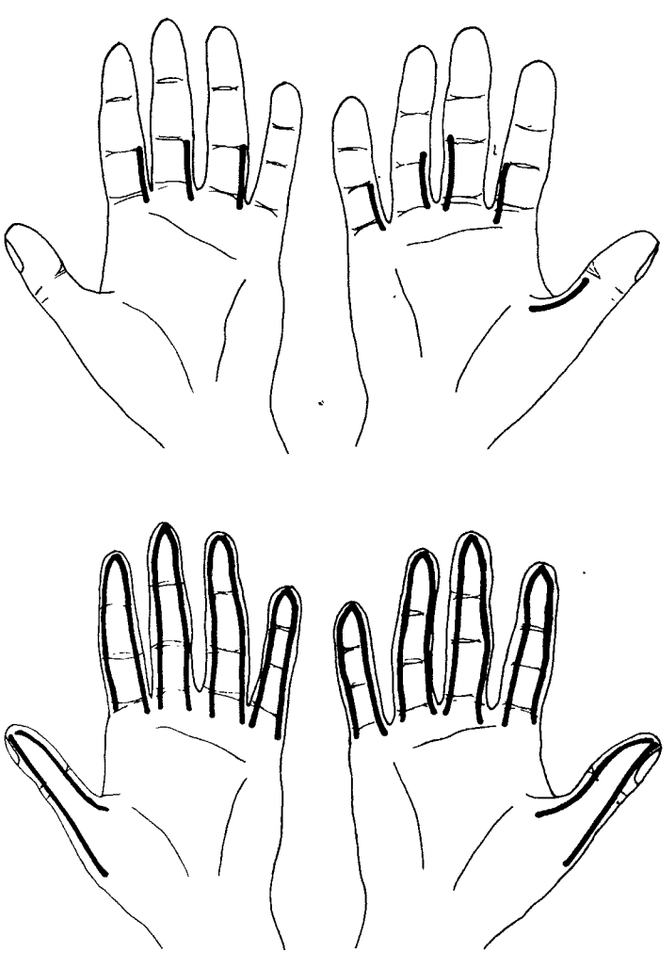
RESULTS

Ultrasonic scanning of the arteries before treatment revealed a variable pattern of arterial segment occlusion. In the worst cases no patent digital arteries could be demonstrated. In two patients digital angiography confirmed the pattern of blockage detected by ultrasound.

All patients tolerated plasmapheresis well. In two patients who were studied during treatment, examination of the digital arteries revealed the segment of patent artery extending slowly towards the fingertips. In all patients the pattern improved on the day after treatment, but there was usually some regression during the succeeding weeks to the pretreatment pattern (see accompanying fig.). Despite this regression definite improvement persisted for at least 6 months. Moreover, all ulcers but one healed during treatment and all patients state that their attacks of Raynaud's symptoms have been reduced in frequency and in intensity. Blood-viscosity was measured in three patients and a marked reduction was found after plasmapheresis, particularly at low shear-rates.

DISCUSSION

Plasmapheresis has, in this group of patients, produced a far better remission of Raynaud's disease than any other form of treatment. Ultrasonic velocimetry has proved to be a simple and objective method with which to assess this disease.



Topographical plan of ultrasonically detected digital arteries. Upper figure shows the vessels which were patent before treatment; lower figure shows increased patency after treatment.

One suggestion as to the cause of Raynaud's disease proposes that there might be changes in blood-viscosity, especially at low temperatures, which might impair digital blood-flow. Other factors that may influence blood-viscosity include platelet aggregation, erythrocyte aggregation, and deformability of red cells. Although we have not examined these factors in detail nor other possible mechanisms for changes in viscosity, our finding of a reduction in viscosity with increased digital artery flow after plasmapheresis is in keeping with reports associating blood-viscosity with Raynaud's disease.[3] We propose plasmapheresis as a form of therapy in patients with severe Raynaud's symptoms refractory to other forms of treatment. A randomised, prospective trial is in progress to assess the value of plasmapheresis in Raynaud's disease and other small-vessel diseases.

We thank the staff of both our departments, of the department of radiology at King's College Hospital, and of the departments of surgery and hæmatology, St. George's Hospital, London

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Hypothesis

DISEQUILIBRIUM IN CONTROL OF PROTEOLYSIS AS A CAUSE OF PRE-ECLAMPSIA

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Summary The interrelated systems which control proteolysis may go into disequilibrium during pregnancy so that a renin-like enzyme in the plasma produces effects such as the early clinical manifestations of pre-eclampsia; the overactivity of the renin-like enzyme may in turn lead to undue activity of other physiological systems including those of the coagulation and complement systems.

INTRODUCTION

PRE-ECLAMPSIA may be ascribed to disequilibrium of the proteolytic control system. The clinical presentation of loss of control of proteolysis during pregnancy differs in form and tempo from that in the non-pregnant (a) because of the links[1] between the different systems controlling proteolysis and (b) because during pregnancy there is an alteration in the availability of some of the enzymes taking part in the several reaction cascades, each a controlled proteolytic process. However, the final stage of loss of control of proteolysis—i.e., coagulation—is the same in both groups.

In this paper the interrelation between systems con-