follow-up in some centres. The contemporary management of haemophilia is time-consuming and if it is to be effective it demands the integrated (usually part-time) services of many medical and paramedical workers. Many haemophilia centres still lack the staff and facilities required, despite the obligation on the Health Authorities to provide these, as set out in the Department of Health and Social Security Health circular HC(76)4.

We thank the haemophilia centre directors and their staff for their kind participation in the preparation of this report. The authors are members of the working party on home therapy of the UK haemophilia centre directors.

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References

- ¹ Pool, J, Hershtold, E, and Pappenhagen, A, *Nature*, 1964, **203**, 312.
- ² Le Quesne, B, et al, *Lancet*, 1974, **2**, 507.
- ³ Jones, P, *Scandinavian Journal of Haematology*, 1977, suppl No 31, p 19.
- ⁴ Jones, P, *Proceedings of 3rd European Congress of the World Federation of Hemophilia*. London, 1976. In press.
- ⁵ Biggs, R, and Spooner, R, *British Journal of Haematology*, 1977, **35**, 487.
- ⁶ Nilsson, I M, Hedner, U, and Ahlberg, A, *Acta Paediatrica Scandinavica*, 1976, **65**, 129.
- ⁷ Kasper, C K, Dietrich, S L, and Rapaport, S I, *Archives of Internal Medicine*, 1970, **125**, 1004.
- ⁸ Ramsay, D M, and Parker, A C, *Journal of Clinical Pathology*, 1973, **25**, 243.
- ⁹ Aronstam, A, et al, *British Journal of Haematology*, 1976, **33**, 81.
- ¹⁰ Carter, F, et al, *British Medical Journal*, 1976, **2**, 465.
- ¹¹ Hansard, House of Commons, 26 February, 1975, vol 884 col 392.

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Circulating immune complexes in pre-eclampsia

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Summary and conclusions

Sixteen patients with severe pre-eclampsia had more IgG-containing and C1q-binding circulating soluble immune complexes than did 16 matched women with normal pregnancies. The clinical features of pre-eclampsia may be explained by damage due to such complexes, although raised complex levels were also present in a few women with normal pregnancies.

As immune complexes are so heterogeneous in terms of the type of antigen, class and subclass of immunoglobulin, size, and complement-binding capacity, further investigations are needed to determine their role in normal and pre-eclamptic pregnancies.

Introduction

Soluble immune complexes have been reported in the sera of women in normal pregnancy,¹ and these may arise from a physiological immunological reaction between mother and child. Immune complexes can, however, cause a wide range of diseases, depending on, for example, the amount and type of complex. Many of the features of pre-eclampsia might be explained by excess or qualitatively abnormal circulating soluble immune complexes.² We have therefore measured IgG-containing and C1q-binding complexes in the sera of women with severe pre-eclampsia and closely matched women with normal pregnancies.

Patients and methods

Sixteen pregnant women with severe pre-eclampsia were studied at gestational ages ranging from 28 to 40 weeks. The criteria for diagnosis were: (a) an increase of 30 mm Hg or more in the systolic blood

pressure and 20 mm Hg or more in the diastolic pressure above the first reading recorded in the pregnancy (always before 20 weeks); and (b) proteinuria of over 200 mg/l in three midstream uninfected urine samples or more than 1 g per 24 hour urine collection.

Sixteen women with normal pregnancies (controls) were selected who matched the patients for gestational age and parity (except for one para 3 control who was matched with a para 4 patient).

Venous blood samples were allowed to clot at room temperature, separated within three hours, and stored in aliquots in liquid nitrogen until analysis. IgG immune complexes were measured by their inhibition of IgG latex agglutination by rabbit IgM anti-human IgG³; agglutination was measured by counting unagglutinated particles on an electronic counter. C1q-binding complexes were similarly measured using purified human C1q as the agglutinating reagent.³ Samples were analysed blind in duplicate and results were expressed as percentage inhibition of agglutination. In non-pregnant people levels of inhibition are considered significant only if they are 20% or more.³

Results

All 16 patients with pre-eclampsia had detectable levels of IgG complexes, and inhibition of agglutination was greater than 20% in 11 cases. Five controls had no detectable IgG complexes and only four had more than 20% inhibition (see table). Similarly, 13 pre-eclamptic patients had raised levels of C1q-binding complexes compared with four controls. For both types of complexes mean titres were considerably higher in the patients than in the controls ($P < 0.005$; Wilcoxon's rank sum test). In the group as a whole the values of patients and controls overlapped, but most of the pre-eclamptic patients had higher values than their matched controls at each gestation studied.

Two patients who had very low levels of IgG complexes at 32 and 29 weeks' gestation (cases 2 and 3) had much higher levels of C1q-binding complexes (17.7% and 33.2% inhibition respectively).

Discussion

The cause of pre-eclampsia is unknown. It occurs predominantly in first pregnancies, and even a first trimester miscarriage is protective.⁴ This suggests that immunisation to fetal antigens may stimulate the maturation of maternal immune reactions that are necessary to prevent fetal allograft rejection. Pre-eclampsia may be caused by partial failure of these protective mechanisms.

Higher levels of circulating soluble immune complexes may not only be a marker of this relative failure but may also cause

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Levels of IgG and C1q-binding complexes ranked in order of level of IgG complexes in matched pre-eclamptic patients and normally pregnant controls

Patients with pre-eclampsia					Matched control			
Case No	Gestation (weeks)	Parity	Complexes (% inhibition)		Gestation (weeks)	Parity	Complexes (% inhibition)	
			IgG	C1q			IgG	C1q
1	40	0	3.0	3.7	40	0	32.5	27.5
2	32	0	5.5	17.7	32	0	Nil	7.8
3	29	0	6.3	33.2	29	0	9.5	11.3
4	29	1	16.0	20.5	29	1	26.5	29.9
5	31	0	19.1	21.6	31	0	16.3	24.7
6	35	0	26.1	15.2	35	0	9.0	7.5
7	28		27.5	24.0	28	0	Nil	3.4
8	33	0 + 1	27.8	35.1	33	1	23.3	14.4
9	31	4 + 1	29.7	29.7	31	3	15.2	19.2
10	29	0	32.2	37.0	29	0	0.4	1.0
11	28	0	33.5	41.6	28	0	17.5	19.0
12	34	1	33.5	34.3	34	1	Nil	5.1
13	36	0	34.5	33.9	36	0	Nil	Nil
14	34	0	41.5	30.9	34	0	8.5	10.5
15	34	0	45.3	49.3	34	0	29.8	26.3
16	35	0	50.5	46.8	35	0	Nil	13.8
Mean			27.0*	27.8†	Mean		11.8*	13.8†

*P < 0.005; †P < 0.005, Wilcoxon's rank sum test.

such clinical features of pre-eclampsia as the immunoglobulin and complement deposition in renal glomeruli,⁵ the early activation of the coagulation system,⁶ platelet consumption,⁷ and IgG depletion.* The raised levels of immune complexes in normal pregnancies that have been observed by ourselves and others¹ support the view that circulating immune complexes are not in themselves necessarily pathological in human pregnancy. Immune complexes are, however, heterogenous in terms of immunoglobulin class, subclass, size, and complement-binding capacity as well as the antigen involved, and a detailed examination of these differences has yet to be made in pregnancy. Thus, in our two patients who had low levels of circulating IgG complexes associated with much greater C1q-binding the predominant antibody might have been IgM rather than IgG. Until the properties of the immune complexes in normal and pre-eclamptic pregnancies are better characterised, the significance and function of the complexes will not be understood. This problem is to be examined in the next phase of our investigations.

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References

¹ Masson, P L, Delire, M, and Cambiaso, C L, *Nature*, 1977, **266**, 542.
² Kirkwood, E, *Lancet*, 1975, **2**, 1100.
³ Levinsky, R J, and Soothill, J F, *Clinical and Experimental Immunology*, 1977, **29**, 428.
⁴ MacGillivray, I, *Journal of Obstetrics and Gynaecology of the British Empire*, 1958, **65**, 536.
⁵ Petrucco, O M, *et al*, *British Medical Journal*, 1974, **1**, 473.
⁶ Redman, C W G, *et al*, *Lancet*, 1977, **2**, 1249.
⁷ Redman, C W G, Bonnar, J, and Beilin, L J, *British Medical Journal*, 1978, **1**, 467.
⁸ Benster, B, Wood, E J, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1970, **77**, 518.

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Comparison of the tine and Mantoux tuberculin tests

Report of the Tuberculin Subcommittee of the Research Committee of the British Thoracic Association*

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Summary and conclusions

Intracutaneous (Mantoux 5 TU) and tine tuberculin tests were performed on the opposite arms of 307 people. The

results of each test were read by two independent observers at either 48 or 72 hours. Positive readings were recorded in 59% of the Mantoux tests; induration was 10 mm or more in 34.7% of cases. Positive readings were recorded for 3.9% of the tine tests, and a further 15.5% were recorded in the doubtful category.

The tine test is unsuitable for epidemiological use because of the high proportion of negative and doubtful results in people positive on the Mantoux test. For the same reasons its usefulness in clinical practice is very limited.

Introduction

One of us (JAL), who is responsible for many routine tine tuberculin tests in a large hospital and medical student population, gained the impression that fewer positive tuberculin reactions were being recorded than might be expected, especially

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