Prostacyclin in systemic lupus and anticardiolipin syndrome

SIR, Antiphospholipid antibodies (the 'lupus anticoagulant', antibodies to cardiolipin, and antibodies responsible for the biological false positive test for syphilis) have been strongly associated with venous and arterial thrombosis in patients with systemic lupus erythematosus,^{1,2} according to strict diagnostic criteria proposed by the American Rheumatism Association,³ as well as in patients who do not conform to these criteria, termed 'lupus-like' or variant lupus.⁴ Clinical manifestations accompanying the presence of these antibodies have been termed the 'anticardiolipin syndrome' by Hughes⁵ and included recurrent fetal loss, thrombocytopenia, various neurological abnormalities including stroke,⁶ Guillain-Barré syndrome,⁷ myelopathy,⁸ chorea,⁹ and livedo reticularis.

The cause of the thromboses and other features is uncertain. It has been postulated that the antibodies interact with phospholipid in cell membranes of vascular tissue, impairing mobilisation of arachidonic acid and inhibiting production of prostacyclin (PGI₂).¹⁰ It was argued that since PGI₂ is a potent vasodilator and inhibitor of platelet aggregation its inhibition might cause a thrombotic state. Carreras *et al* studied a patient with recurrent arterial thromboses and intrauterine death.¹⁰ The serum IgG fraction containing the 'lupus anticoagulant' reduced the release of PGI₂ from rat aortic rings, pregnant human myometrium, and cultured endothelial cells. The inhibition was abolished by arachidonic acid. An inhibitory effect of lupus anticoagulant on PGI₂ synthesis *in vitro* has been confirmed.^{11,12} It has been found, however, that in severe atherosclerosis, where there is also reduced PGI₂ synthesis by vascular tissue *in vitro*,¹³ there is *increased* PGI₂ synthesis *in vivo*.¹⁴ The only evidence of reduced

PGI₂ synthesis *in vivo* in the lupus anticoagulant syndrome was in the case reported by Carreras *et al*,¹⁰ in whom the plasma concentration of 6-oxo-PGF_{1α}, the stable hydrolysis product of PGI₂, was fit to be reduced. It has subsequently become evident, however, that radioimmunoassay plasma 6-oxo-PGF_{1α} gives highly inaccurate values.¹⁵

We therefore used gas chromatography/negative ion electron capture mass spectrometry (the most sensitive and specific existing method) to determine plasma concentrations of 6-oxo-PGF_{1α} in eight patients (24–40 years) with anticardiolipin antibodies and a history of recurrent thrombosis, and in five patients (20–35 years) with systemic lupus erythematosus without this antibody. The anticardiolipin antibodies were measured by a modification of the original enzyme linked immunosorbent assay technique¹⁶ as described by Harris *et al*¹ and the results expressed as GPL (=IgG) or MPL (IgM) units. The results are shown in Table 1. We previously reported that in healthy non-pregnant women plasma 6-oxo-PGF_{1α} is less than 3 pg/ml.¹⁷ Two of the subjects with anticardiolipin antibodies had plasma concentrations of 6-oxo-PGE_{1α} just above this range, i.e., 3.5 and 6.8 pg/ml, but these modest increases are consistent with venous trauma during venipuncture, which was not as easy as in healthy subjects. The remaining results were all normal. It will be of great interest to determine excretion rates of metabolites of PGI₂ and thromboxane in the urine of such patients as an integrated measure of the production rate throughout the body.

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Table 1 Measurement of anticardiolipin antibodies

<i>Patient No</i>	<i>Anticardiolipin antibody titre</i>		<i>Plasma 6-oxo-PGF_{1α} (pg/ml)</i>
	<i>(GPL units)*</i>	<i>(MPL units)*</i>	
<i>Systemic lupus erythematosus with the anticardiolipin syndrome</i>			
1	247.8	—	3.5
2	7.5	—	6.8
3	8	—	<1.0
4	50	—	<1.0
5	11.8	4.2	<1.0
6	300	—	<1.0
7	50	—	<1.0
8	15.2	—	1.5
<i>Systemic lupus erythematosus without the anticardiolipin syndrome</i>			
1	—	—	1.8
2	—	—	2.1
3	—	—	2.5
4	—	—	2.8
5	—	—	1.7

*GPL units=IgG anticardiolipin antibody titre; MPL units=IgM anticardiolipin antibody titre.

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Book reviews

Clinical Rheumatology. Eds G V Ball, W J Koopman. £39.50. Pp. 356. Saunders: Eastbourne, Sussex. 1986.

This North American text sets out to present a concise and clinically comprehensive account of current rheumatology, and in this it succeeds very well. The authors virtually all come from the University of Alabama, Birmingham. Possibly because the contributors are so geographically proximate, the book is surprisingly up to date with 1985 references in a 1986 publication. The format is along conventional lines with introductory chapters on relevant basic biological sciences, clinical chapters on defined disorders, and, finally, chapters on regional symptom complexes. An amazing amount of factual information is condensed between the covers, and it is difficult to take exception to the views expressed.

It is, however, a textbook and not a reference book, and thus the chapter references are limited to less than 10. This results in a somewhat uneven feel to the book—sources of data are named in the text but do not appear in the references. It is obvious why this had to be so, as the length of the references would otherwise have exceeded the text, but possibly the authors could allow themselves more latitude in further editions. The perennial problem of the North American compared with European classification of juvenile chronic arthritis emerges. No doubt for reasons of space, little attention is given to evaluation and examination of the musculoskeletal system, and somewhat paradoxically the chapter 'On seeing patients' starts with the subheading 'use of the laboratory'. Other cultural differences emerge—the commonest cause of a persistently

raised uric acid level in patients receiving allopurinol is given as being due to extensive tophi, whereas compliance must be the commonest cause in the UK. Notwithstanding these quibbles, I thoroughly enjoyed the style and content of this book.

The major difficulty is in identifying the market for it in this country. It is too complex for undergraduates and does not contain enough detailed description of patient evaluation for MRCP candidates. Because it is not a reference book it does not replace the monoliths. It would, however, provide a sound and sensible background for any doctor embarking on a registrar or senior registrar post in rheumatology.

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IAN GRIFFITHS

Eponyms in Orthopaedics and Rheumatology. By J M H Moll. Wall chart 34½×23 inches. £5.70. Chapman and Hall: London. 1986.

'That's interesting; where did you get it?'

'That' is a wall chart designed by Dr John Moll. It contains a sketch and brief notes about 42 men who have given their names eponymously to rheumatological or orthopaedic matters, such as syndromes, signs, methods of treatment, or instruments. For each there is also an illustration of the matter to which the eponym refers. Among the portraits I am in a position to judge only one likeness (I heard the subject lecture at the Brighton Congress) and that is excellent.

This is my first success at creating brightness and interest on the walls of my office. I recommend it.

The London Hospital

H L F CURREY

Therapeutics in Rheumatology Eds. J M H Moll, H A Bird, A Rushton. Pp 539. £45.00. Chapman and Hall: London. 1986.

This book is about the drugs used in the treatment of the rheumatic disorders and to some extent relates their usage to the overall management of the patient. Its stated purpose is to inform rheumatologists generally about the plethora of antirheumatic drugs on the market and to act as a means of updating previous knowledge. It should be said at the outset that it succeeds in its main aims. One of the problems with such a book, however, is the length of time between preparation and actual publication. Inevitably, therefore, some of the information is already out of date, and for instance, one of the drugs suggested as having disease modifying properties has already been withdrawn. Few of the references are later than 1983, and this is an inherent difficulty in disseminating information in this way as a hard back volume. This delay becomes important when one of the stated aims is to act as an update facility.

The book is divided into three sections—pharmacological