distribution in these peoples is still unknown, although casual observation suggests that there may be significant differences between Africans and Caucasians, and possibly even between different populations within the African group.

In the present study two epidemiological surveys were carried out, one in a rural, semitribal African population and the other in a fully urbanized African community in Johannesburg. The diagnosis of rheumatoid arthritis was based on the Rome criteria using the three parameters of clinical polyarthritis, radiological evidence of erosive arthritis, and positive serological tests for rheumatoid factor.

In the rural African population the prevalence of 'definite' rheumatoid arthritis was 0.12%; and of 'definite' and 'probable' rheumatoid arthritis combined, 0.87% of those over 15 years. Such clinical and radiological changes as occurred were invariably mild and no one in the entire survey had features characteristically associated with established rheumatoid arthritis.

In marked contrast, the prevalence of inflammatory polyarthritis in the urban Africans was similar to that in Caucasian populations: 'definite' rheumatoid arthritis occurred in 0.9% and 'definite' and 'probable' rheumatoid arthritis combined in 3.3% of those over 15 years. The difference between the two African populations was statistically highly significant ($P=0.01$). Moreover, the form and severity of the clinical and radiological features in the urban community closely resembled those seen in Caucasians; 24 respondents (4.4%) had clinical polyarthritis, 2 with the classical changes of long-standing rheumatoid arthritis, and 25 (4.5%) had radiological signs of erosive arthritis. In both African groups a positive latex fixation test was recorded in over 10% of the population tested. No obvious cause for this was found.

The marked intraracial differences in disease pattern shown point to the importance of sociological and environmental factors in the pathogenesis of rheumatoid arthritis.

Rheumatoid Synovitis and Joint Disease. The Relationship Between Arthroscopic and Histological Changes. D. B. Yates and J. T. Scott (*Charing Cross Hospital, London W6*). Published in full in the *Annals*, 1975, **34**, 1.

Raised Plasma Kininogen Levels in Rheumatoid Arthritis. Response to Indomethacin and Relationship to Clinical Indices. J. N. Sharma, I. J. Zeitlin, P. M. Brooks, and W. C. Dick (*Department of Physiology and Pharmacology, University of Strathclyde, Glasgow; and Centre for Rheumatic Diseases and University Department of Medicine, Royal Infirmary, Glasgow*)

All previous work suggests that plasma kininogen concentrations in patients with inflammatory seropositive rheumatoid arthritis fall within the normal range (Jasani, Katori, and Lewis, 1969). These results were obtained from patients who were receiving anti-inflammatory drugs.

Plasma kininogen levels were measured by the method of Brocklehurst and Zeitlen (1967) in 7 patients with classical rheumatoid arthritis after withdrawal of all therapy for 48 hours, and again after one week of indomethacin therapy. The levels for plasma kininogen ob-

tained after withdrawal of therapy were markedly raised and fell after a week of indomethacin therapy but were still above the levels observed in normal subjects ($n=7$) and in patients convalescing in an orthopaedic ward with fractures (Table I). The reduction in plasma kininogen values was mirrored by a rise in indomethacin levels and a fall in the articular index of joint tenderness, pain index, and grip strength in these same patients (Table II).

Table I

	Plasma kininogen level (Bradykinin equivalents/ml) (mean $\pm$ SD)
Rheumatoid arthritis ($n=7$)	
Pre-indomethacin	12.9 $\pm$ 1.2
Post-indomethacin	7.2 $\pm$ 1.0
Fracture patients ($n=5$)	4.9 $\pm$ 1.2
Normals ($n=3$)	
Pre-indomethacin	5.0 $\pm$ 1.2
Post-indomethacin	5.0 $\pm$ 1.2

Table II

	Pre-indomethacin	Post-indomethacin
Articular index (mean $\pm$ SEM)	16.6 $\pm$ 9.3	11.9 $\pm$ 4.2
Pain index (mean $\pm$ SEM)	3.3 $\pm$ 0.7	1.9 $\pm$ 0.4

Time course studies in a further 3 patients with rheumatoid arthritis in whom all drugs were withheld for 48 hours and indomethacin (150 mg/d) was administered for 7 days confirm these findings and show that the fall in plasma kininogen occurs within 4 hours of drug administration. Indomethacin will not produce a fall in kininogen values in normal subjects nor in fracture patients and does not directly affect the bioassay. We have shown that the plasma kininogen concentration in patients with untreated rheumatoid arthritis is raised and falls with the use of indomethacin. The interaction and inter-relationships between anti-inflammatory drugs and prostaglandin and kinin, chemical mediators of inflammation, requires reconsideration. Whereas it is recognized that indomethacin will inhibit the prostaglandin synthetase enzymes, this is the first report which documents an effect upon the kinin system.

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Aortic Valve Incompetence and Replacement in Rheumatoid Arthritis. J. M. I. Iveson, U. Thadani, M. Ionescu, and V. Wright (*Department of Rheumatology, Cardiology and Cardiothoracic Surgery, General Infirmary at Leeds*). Published in full in the *Annals*, 1975, **34**, 312.

Thin Sclerae. A Clinical Illusion. P. J. Rooney, D. D. M. McGavin, G. R. Sutherland, and R. Railton (*The Centre for Rheumatic Diseases and University Department of Medicine, Glasgow Royal Infirmary; Departments of Ophthalmology and Radiology, Southern General Hospital, Glasgow, and Regional Department of Physics and Bio-engineering, Glasgow*)

Scleritis occurs in a significant proportion of patients with rheumatoid arthritis. It is often followed by patches of blue discoloration of the sclera. This discoloration is due to choroid pigment becoming visible beneath areas of sclera rendered translucent as a result of the inflammatory process. Such areas of discoloration are often referred to as areas of 'scleral thinning' and may be associated with clinical anxieties regarding rupture of the globe. Enucleation for imminent rupture is not infrequent, yet the true incidence and extent of thinning in such areas is unknown as no method of *in vivo* measurement of scleral thickness is yet available. Preliminary studies using B-scan ultrasonography to delineate scleral thickness in this group of patients are reported.

A standard ultrasonic machine for general application has been used (Nuclear Enterprises Disonograph 4102). A 5 MHz focused transducer was used and coupling was obtained through a direct water bath (Sutherland, 1974). Horizontal scans were made transversely through areas of scleral translucency in 8 patients with quiescent scleritis. The scans were made with the gaze averted to obtain maximal exposure of the abnormal areas of sclera. 8 comparable normal subjects were studied as controls. Measurement of scleral thickness was made on the polaroid print of the B-scan using a measuring microscope and the true scleral thickness calculated on the basis of a sound velocity in the sclera of 1620 m/s. The mean scleral thickness within 1 cm of the limbus in the normal group was $0.62 \text{ mm} \pm 0.13 \text{ mm}$ (SD) which compares well with

the anatomical observations reported. The standard error of paired observations using this technique is very small. In the abnormal eyes the mean was $0.56 \text{ mm} \pm 0.14 \text{ mm}$ (SD) but it was significant that only 3 of the 8 subjects showed local areas of thinning. 2 of these subjects showed a distinct step from the 'normal' to the thinned areas, a feature also visible clinically.

This limited study is important in showing a new technique which is atraumatic and safe and which offers a way of determining the natural history and prognosis of scleral translucency and scleral thinning following scleritis. This study shows conclusively that scleral translucency is not synonymous with scleral thinning and it may rationalize the indications for enucleation and scleral grafting in this problematical clinical situation.

Ups and Downs of Indomethacin Bioavailability. P. M. Brooks, M. A. Bell, J. J. Walker, A. C. Kennedy, R. D. Sturrock, and W. C. Dick (*The Centre for Rheumatic Diseases and University Department of Medicine, Royal Infirmary, Glasgow*)

This paper reports results obtained during the preliminary part of a combined clinical and laboratory programme of investigation into the drug indomethacin. Indomethacin plasma concentrations were measured by the method of Hucker and others (1966). Indomethacin 'profiles' were constructed by determining plasma levels at regular intervals after oral administration of a standard dose of drug. Duplicate estimates of plasma concentration gave a standard error of the difference of 0.05 mg/ml. Day-to-day reproducibilities of indomethacin profiles have been determined.

The indomethacin profile was reflected in the expected changes in clinical indices of disease activity (Lee and others, 1973).

Table of results

Normal controls			Scleritis group		
No.	Actual measurement on Polaroid film (mm) 5 mm from limbus	Calculated scleral thickness (mm)	No.	Actual measurement on Polaroid film (mm) 5 mm from limbus	Calculated scleral thickness (mm)
1	0.80	0.46	1	0.80	0.46
2	0.78	0.45	2	0.82	0.47
3	1.18	0.67	3	1.00	0.57
4	0.95	0.54	4	0.76	0.43
5	0.78	0.45	5	0.92	0.53
6	1.28	0.73	6	0.96	0.55
7	0.70	0.40	7	1.16	0.66
8	1.14	0.65	8	0.64*	0.37
Mean		0.54	Mean		0.50
SD		0.12	SD		0.09
SEM		0.04	SEM		0.03
1 cm from limbus			1 cm from limbus		
1	1.36	0.78	1	1.08	0.62
2	1.30	0.75	2	0.62*	0.35
3	1.08	0.62	3	1.24	0.71
4	0.80	0.46	4	0.96	0.55
5	1.24	0.71	5	0.80	0.46
6	0.96	0.55	6	0.82	0.47
7	0.82	0.47	7	1.40	0.80
8	—	—	8	1.00	0.57
Mean		0.62	Mean		0.57
SD		0.13	SD		0.14
SEM		0.05	SEM		0.05

* Limit of resolution of Disonograph 4102 calculated scleral thickness derived from estimated speed of ultrasound in scleral tissues and known magnification of polaroid film.