

RHEUMATOID ARTHRITIS IN THE WESTERN CAPE

- A CLINICAL STUDY

BY

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THIS WORK IS DEDICATED TO

MY WIFE INDOO AND SONS

KALPESH, PRIYESH AND YASHIN

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TABLE OF CONTENTS

	<u>PAGE</u>
DEDICATION	i
ACKNOWLEDGEMENTS	ii - iv
TABLE OF CONTENTS	1 - 4
ABBREVIATIONS	5 - 6
ABSTRACT	7 - 10
CHAPTER 1            INTRODUCTION	11 - 18
CHAPTER 2            METHODOLOGY	19 - 48
Selection of patients	19 - 22
Demographic data and history	22 - 27
Functional assessment	27 - 28
Nutritional assessment	29 - 30
Musculoskeletal assessment	30 - 34
Keratoconjunctivitis sicca	34 - 36
Cardiac assessment	36 - 37
Pulmonary assessment	37 - 39
Neurological assessment	39 - 41

	<u>PAGE</u>
Radiographic assessment	41 - 44
Laboratory investigations	44 - 46
Statistical methods	47 - 48
CHAPTER 3	DEMOGRAPHIC DATA
	49 - 64
CHAPTER 4	ASSESSMENT OF THE NUTRITIONAL STATUS
	65 - 76
CHAPTER 5	FUNCTIONAL ASSESSMENT
	77 - 85
CHAPTER 6	GENERAL FEATURES, ASSOCIATIONS AND COMPLICATIONS
	86 - 96
CHAPTER 7	CERVICAL SPINE
	97 - 107
CHAPTER 8	SHOULDERS
	108 - 114
CHAPTER 9	HANDS
	115 - 152
9.1	Resorptive arthropathy
	116 - 123
9.2	Clinical assessment of the hands
	124 - 141
9.3	Handedness and the prevalence of deformities, severity of radiographic changes and function of the hand
	142 - 152

		<u>PAGE</u>
CHAPTER 10	FEET	153 - 164
CHAPTER 11	OTHER JOINTS AND RADIOGRAPHIC FINDINGS	165 - 182
	11.1 Wrists	166 - 169
	11.2 Elbows	170 - 172
	11.3 Hips	173 - 176
	11.4 Assessment of radiographic involvement	177 - 182
CHAPTER 12	FRACTURES	183 - 189
CHAPTER 13	UPPER GASTROINTESTINAL SYMPTOMS AND PEPTIC ULCERS	190 - 196
CHAPTER 14	LABORATORY FINDINGS	197 - 227
	14.1 Biochemical abnormalities	198 - 208
	14.2 Immunological abnormalities	209 - 217
	14.3 Iron status and anaemia	218 - 227
CHAPTER 15	THERAPEUTIC REQUIREMENTS	228 - 242
CHAPTER 16	SURGICAL REQUIREMENTS	243 - 256

		<u>PAGE</u>
CHAPTER 17	EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS IN COLOUREDS	257 - 324
	17.1 Introduction	258 - 262
	17.2 Cardiac involvement - clinical and echocardiographic study	263 - 278
	17.3 Keratoconjunctivitis sicca	279 - 288
	17.4 Peripheral neuropathy - clinical and electrophysiological study	289 - 298
	17.5 Pulmonary involvement - clinical and lung function tests	299 - 308
	17.6 Prevalence of extra-articular manifestations - summary	309 - 324
CHAPTER 18	SUMMARY AND CONCLUSION	325 - 344
APPENDICES	1-4 Functional disability	345 - 347
	5 Classification of rheumatoid thumb deformities	347
	6 Radiographic evaluation of rheumatoid arthritis by standard reference films (Larsen et al 1977)	348
	7 Reference range for laboratory tests	349
REFERENCES		350 - 399

ABBREVIATIONS

AAI	atlanto-axial impaction
AAS	atlanto-axial subluxation
ADI	atlanto-dentate interval
ALT	alanine aminotransferase
ANF	antinuclear factor
ARA	American Rheumatism Association
AST	aspartate aminotransferase
BD	boutonniere deformity
BMI	body mass index
B.U.T.	break up time
CRP	C-reactive protein
CTS	carpal tunnel syndrome
DIP	distal interphalangeal
DL	distal latency
DS DNA	double-stranded DNA
DU	duodenal ulcer
ECG	electrocardiograph
ESR	erythrocyte sedimentation rate
FEV <sub>1</sub>	forced expiratory volume in one second
FRC	functional residual capacity
FTS	flexor tenosynovitis
FVC	forced vital capacity
GGT	gamma glutamyl-transpeptidase
GU	gastric ulcer
HOCUM	hypertrophic obstructive cardiomyopathy
IBW	ideal body weight
Ig	immunoglobulin

IP	interphalangeal
KCO	transfer coefficient
KCS	keratoconjunctivitis sicca
LDH	lactate dehydrogenase
LVID	left ventricular internal dimension
MAC	mitral annular calcification
MCH	mean corpuscular haemoglobin
MCP	metacarpophalangeal
MCV	mean corpuscular volume
MEP	maximum expiratory pressure
MIP	maximum inspiratory pressure
MTP	metatarsophalangeal
MTPJs	metatarsophalangeal joints
MUAC	mid upper arm circumference
NSAIDs	non steroidal anti-inflammatory drugs
PCV	peroneal conduction velocity
PIP	proximal interphalangeal
RA	rheumatoid arthritis
RF	rheumatoid factor
RV	residual volume
SCAT	sheep cell agglutination test
SND	swan-neck deformity
T <sub>4</sub>	thyroxine
TB	tuberculosis
TIBC	total iron binding capacity
TLC	total lung capacity
T <sub>L</sub> CO	transfer factor for carbon monoxide
TSF	triceps skin fold
UAMC	upper arm muscle circumference

## RHEUMATOID ARTHRITIS IN THE WESTERN CAPE

### - A CLINICAL STUDY

#### ABSTRACT

This survey was conducted to determine the spectrum of rheumatoid arthritis (RA) in patients seen in the Rheumatology Unit at Groote Schuur and Princess Alice Orthopaedic Hospitals in Cape Town. A group of 256 patients (104 Coloureds, 100 Caucasians and 52 Africans) were studied and the findings in the different races were compared. The prevalence of the extra-articular manifestations of RA were studied in the Coloured patients by clinical assessment, laboratory tests and specialised investigations such as echocardiography, pulmonary function tests and nerve conduction studies.

The mean age of onset of RA was 40,5 years, the mean duration was 12,3 years and the female : male ratio was 2,8 : 1. Two hundred patients (78,1%) belonged to the milder American Rheumatism Association (ARA) functional classes 1 and 2. Malnutrition was present in 23,2%, it was commoner in men and was associated with a higher mean erythrocyte sedimentation rate and more severe functional disability. Obesity was noted in 10,5%. The prevalence of fractures was 7% and the majority of these patients were elderly females who developed a fracture after a fall. Upper gastrointestinal symptoms such as dyspepsia and epigastric pain were noted in 47,7% and 13,3% had peptic ulcers. The complications which were noted in patients with peptic ulcers were gastrointestinal haemorrhage or perforation in 26,5% and iron deficiency anaemia in 11,8%.

The prevalence of resorptive arthropathy was 5,1%. Flexor tenosynovitis was noted in 56,6% of the patients. The commonest deformities in the hands were swan-neck deformity (28,9%), boutonniere deformity (23,8%) and ulnar deviation (17,2%). Although there was no significant difference in the prevalence of flexor tenosynovitis and deformities of the fingers in the dominant and non-dominant hand, radiographic changes and functional impairment were more severe in the dominant hand. Atlanto-axial subluxation and/or impaction were detected in 115 patients (46,4%) but only 4 patients (1,6%) developed a myelopathy. There was a poor correlation between the severity of radiographic changes and the presence of hyperreflexia. Radiographic changes were noted in the shoulders in 41,9% and the hips in 25,8% of the patients. Radiographic changes were noted in the feet in 90,2% of the patients. Deformities of the feet were detected in 47,6% but only 28,2% had some modification of their footwear.

A rise in the alkaline phosphatase was noted in 42,3% and only 6,5% had a raised gamma glutamyl-transpeptidase. A mild elevation of the blood urea was present in 28,1% but only 6,6% had a urea of >10 mmol/l. Only seventeen patients (6,6%) had a raised creatinine while 43,4% had a reduced level. A positive rheumatoid factor was noted in 78,9% and 36% had a positive anti-nuclear factor. Anaemia was present in 37,8% at the time of assessment and 8,3% had iron deficiency (serum ferritin <15ng/l).

The therapeutic requirements for RA included referral to physiotherapy (67,6%), occupational therapy (50%), slow acting anti-rheumatic drugs (63,7%), oral NSAIDs (100%), NSAID suppository (45,4%),

corticosteroids (32,8%), antidepressants (24,2%), tranquilisers (31,3%) and surgery (49,2%). The most frequent sites of surgery were the hands, wrists, metatarsophalangeal joints and hips. Forty patients (15,6%) had a replacement arthroplasty of one or more of the four major weight bearing joints.

The extra-articular manifestations of RA were noted in 92 patients (88,5%). The commonest manifestations were anaemia (54,8%), subcutaneous nodules (29,8%), lymphadenopathy (23,1%) and keratoconjunctivitis sicca (21,2%). Although echocardiographic abnormalities were detected in 31 patients (37%), the only findings which were considered to be related to RA were the presence of pericardial effusion in 5 patients (6%) and minor abnormalities of the E-F slope in 4 patients. Abnormal nerve conduction studies were noted in 26,2%, and 25,9% of these patients had abnormalities of more than one nerve. The abnormalities which were considered to be related to RA were carpal tunnel syndrome (14,9%), reduced lateral popliteal conduction velocity (10,5%) and sural nerve involvement (6,9%). There was a poor correlation between the clinical findings and electrophysiological tests. The abnormalities of pulmonary function tests which were considered to be related to RA were interstitial lung disease (4,8%), pleural involvement (9,6%), impaired diffusion capacity (5,8%), pulmonary nodule (1%) and airways obstruction (1%). There was a significant increase in the prevalence of a positive rheumatoid factor in patients with nodules. There was also a significant association between nodules and lymphadenopathy, and between a positive rheumatoid factor and abnormal lateral popliteal or sural nerve conduction studies. However, none of the other

extra-articular manifestations of RA were related to the presence of nodules or seropositivity.

There were marked similarities in the majority of the features of RA among the races. However, in Africans, the mean age of onset was nearly a decade earlier, the mean values for the total serum globulins and immunoglobulin G were significantly higher, the prevalence of peptic ulcers and femoral neck fractures was lower, wrist involvement was more severe and surgery to the forefoot, carpal tunnel release and flexor tenosynovectomy were performed less often.

Unlike previous studies, many different aspects of RA were studied in the same group of patients in this survey and detailed clinical information was obtained on the spectrum of RA. Despite the widely differing socio-economic, genetic and cultural backgrounds, most of the features of RA were similar in the different race groups. This survey has also shown that greater attention should be given to the problem of anaemia, peptic ulcers, the use of modified footwear, malnutrition and the benefits of physiotherapy and occupational therapy. The relatively favourable outcome of RA is demonstrated by the finding that with the use of surgery, drug therapy, physiotherapy and occupational therapy, the majority of patients (78,1%) belonged to the milder ARA functional classes. Extra-articular manifestations are very common in RA. Although the specialised tests are invaluable in studying the frequency and severity of extra-articular manifestations in RA, they are of little clinical value in the routine management of patients with RA. Therefore, they only need to be considered when there are clinical indications for their use.

## CHAPTER 1

### INTRODUCTION

Rheumatoid arthritis (RA) was first recognised as a distinct clinical entity by Landre Beauvais in 1800 (Short 1974). He noted that the clinical characteristics of RA were different from those of classical gout. In 1853, Charcot published a report on a series of 41 cases of rheumatoid arthritis together with illustrations of the deformities of the hands (Fraser 1982). Charcot was also the first to draw attention to Sydenham's (1624-1689) work which appeared to describe RA (Fraser 1982). The term rheumatoid arthritis was introduced into the medical literature by Sir Alfred Baring Garrod in 1859 (Short 1974).

Studies in human paleopathology have provided convincing evidence of the presence of ankylosing spondylitis in ancient remains. There is however, no evidence of RA before the 19th century (Short 1974). Sturrock and co-workers have reported that ancient Indian medical writings strongly suggest that RA may have existed as a distinct entity at least 2000 years ago and a more detailed study of ancient Indian and Chinese literature may support the contention that RA is an ancient disease (Sturrock et al 1977). Five paintings of the Flemish School depicted appearances resembling those of RA (Dequecker 1977) and paintings attributed to Peter Paul Ruben (1577-1640) have also shown evidence of progressive RA (Appelboom et al 1981).

The diagnosis of RA is easily made in patients with severe disease and typical clinical findings, but it may be difficult in patients with early disease and atypical manifestations. The need to compare the prevalence, incidence, manifestations, course and treatment of RA in different studies led to the proposed American Rheumatism Association (ARA) diagnostic criteria for RA in 1956 and these were revised 2 years later (Ropes et al 1956, Ropes et al 1958). Subsequent revisions were made in Rome in 1961 (Kellgren 1962) and in New York in 1966 (Bennett and Burch 1967) for use in population studies.

The prevalence of definite or probable RA varied from 2,7% to 5,1% in different surveys (Cobb et al 1957, Lawrence 1961, Wolfe 1968a). Wolfe reviewed the epidemiological studies in RA, and reported that published data showed that the prevalence of RA was remarkably uniform all over the world regardless of geographic or climatic differences between populations (Wolfe 1968b). Hochberg found that even though the prevalence of RA varied in different surveys, the prevalence of definite RA in Caucasians was estimated at 1% (Hochberg 1981).

Epidemiological studies in South Africa have shown that the prevalence of definite RA, based on a modification of the Rome criteria (Kellgren 1962), was 0,12% and 0,68% in the rural Tswana and Xhosa populations respectively (Beighton et al 1975, Meyers et al 1977) and 0,90% in an urban African population (Solomon et al 1975). The prevalence of definite and/or probable RA was 3,3% in the urban population compared with 0,87% in the rural Tswana population and the difference was highly significant ( $p < 0,01$ ; Beighton et al 1975, Solomon et al 1975).

The prevalence of definite or probable RA was 0,68% in a rural Coloured population in Namaqualand (Meyers 1982).

The medical and social aspects of the treatment of RA, the age of onset, sex ratio, duration of disease, functional capacity, clinical findings, biochemical abnormalities and radiographic findings have been reported in large studies (Duthie et al 1955, Sharp et al 1964, Ragan 1949, Short and Bauer 1948). Although the articular manifestations of RA have been extensively studied in other parts of the world, most of the surveys have usually reported a detailed analysis of a single anatomical site such as the shoulder, neck, hands, feet etc, and these have usually been performed in different communities in different hospitals. There is a lack of clinical surveys which involve an analysis of the clinical and radiological assessment of several joints in the same group of patients. Furthermore, studies of extra-articular manifestations of RA have also usually involved a single aspect of the disease such as cardiac or pulmonary involvement.

Apart from the studies discussed below, the only other reports of RA in South Africa have been confined to case reports or evaluation of drug therapy. The first clinical study of RA in South Africa was reported by Anderson in 1970; he studied 23 African patients with probable or definite RA who were admitted to hospital over a 3 month period (Anderson 1970). He noted that in comparison to Caucasians, the disease was milder, tended to be remitting in character and systemic involvement and gross deformities were rare. In addition,

the radiological changes were not severe and there was a good response to anti-inflammatory medication. These findings differ from the series reported in the Transkei and Ciskei (Percy-Lancaster 1974). They had 65 patients, 19 of whom had definite RA (3 of these patients were under 16 years and were probably patients with juvenile chronic arthritis). The severity of the disease in this study was graded as mild in 8 patients, moderate in 4 patients and 7 had severe disease. The occurrence of severe disease in Africans has also been noted in other studies (Chalmers and McNeill 1976, Mody and Naidoo 1982, Kalla et al 1982). A survey on the social and rehabilitational aspects in 100 Caucasians with RA in Pretoria has been reported (Brighton and Louw 1981). There was a lack of understanding of the role of physiotherapy and occupational therapy and therefore these services were underutilized. An echocardiographic study showed that pericardial effusion and/or pericardial thickening and abnormalities of mitral valve motion are common in RA (Schorn et al 1976).

Information about the age of onset, sex ratio, severity, functional disability, therapeutic requirements, the need for surgery, clinical features, articular and extra-articular manifestations and serological findings is not available for the different communities with RA in South Africa. The need for a better understanding of the clinical spectrum and manifestations of RA in the different communities prompted this study. Rheumatology is still in its infancy in South Africa in comparison to other Western countries. The consequences of infection and malnutrition constitute a major health problem which affects the majority of the population. Political reforms and the

subsequent socioeconomic upliftment of the underprivileged communities will lead to increasing urbanisation of the population. If environmental factors are important in the genesis of RA, and the increased prevalence of RA which has been noted in epidemiological studies in urban Africans suggest that this is likely, then the number of patients with RA can be expected to increase in future. There will be a greater demand on the limited health care resources for the management of patients with RA. It is therefore essential to have information on the spectrum of RA, and in particular, the therapeutic requirements.

This study would also provide information on the articular manifestations, prevalence of upper gastrointestinal symptoms and the frequency of peptic ulcers, prevalence of fractures, assessment of the nutritional status, biochemical and immunological abnormalities and therapeutic requirements, including the need for surgical treatment, in the same group of patients. An intergroup analysis could be undertaken to determine whether there were any differences among the different racial groups. In addition, information on the spectrum of RA in a large population of patients from three major communities in South Africa would be obtained. The results may also have therapeutic implications and may influence clinical decision making. The functional classification of a random sample from the arthritis clinic population would also provide information on the outcome of management policies adopted in the arthritis unit. The referral pattern of patients to physiotherapy and occupational therapy may highlight the need for increasing awareness of the possible benefits of these modes

of therapy. If a high prevalence of deformity of the feet is found, then greater attention to footwear may be necessary. In view of the high prevalence of atlanto-axial subluxation in RA, the correlation of abnormal radiological findings with symptoms and clinical abnormalities could provide guidelines for the further management of these patients.

If malnutrition is found to be common in RA, then corrective measures may be necessary to prevent their contribution to the morbidity associated with RA. A high prevalence of upper gastrointestinal symptoms and peptic ulcers in patients with RA, would emphasize the need to determine whether active ulcers are present in patients with anaemia or gastrointestinal symptoms such as epigastric pain or dyspepsia. The frequency and the nature of surgery performed in RA would provide important information on the resources required to adequately manage patients in other parts of the country and would therefore influence the provision of health care facilities. If there is a high prevalence of extra-articular manifestations using specialised investigations, then it may be possible to recommend guidelines for the use of these tests.

The Rheumatology Unit of the University of Cape Town is the oldest and largest in South Africa and serves patients of all population groups; there are a large number of Coloureds and Caucasians and a smaller number of Africans. In addition, the health services in the Western Cape are among the best in South Africa; a transport service is provided by the Cape Provincial Administration which enables disabled

people who may be confined to a wheelchair or to bed, to be brought to hospital for regular visits to outpatient clinics, and physiotherapy and occupational therapy departments. Furthermore, the facilities for rehabilitation and the orthopaedic surgical expertise available for rheumatology patients in the Unit are comparable to the services available in many Western communities. Therefore, this provided an excellent opportunity to undertake an indepth survey on the spectrum of RA in patients from different communities since all were managed by the same staff under similar conditions and intergroup comparisons could be made. The Groote Schuur Hospital, which is a teaching hospital attached to the University of Cape Town, has the resources and expertise required to undertake a survey on the prevalence of the different extra-articular manifestations of RA.

The Coloured population of South Africa represents a group with a genetic admixture (Negro-Caucasoid) and they constituted about half of the patients who attended the Rheumatology Unit. They were selected for the study of the extra-articular manifestations of RA as they represent a group who have not been studied previously elsewhere. The spectrum of medical disorders in Coloureds is variable and there is a high incidence of tuberculosis and rheumatic fever which are also common in Africans. However, the prevalence of systemic lupus erythematosus is higher in Coloured females in comparison with the other communities (Jessop and Meyers 1973). The prevalence of hypertension and ischaemic heart disease have been noted to intermediate between Caucasians and Africans but a recent survey has shown that the prevalence of hypertension and the risk factors for

ischaemic heart disease are higher in Coloureds than in Caucasians and Africans (Bronte-Stewart et al 1955, Vogelpoel and Schrire 1955, Steyn et al 1985).

## CHAPTER 2

### METHODOLOGY

#### 1. SELECTION OF PATIENTS

The Rheumatic Diseases Unit of the Department of Medicine, University of Cape Town, has an arthritis clinic at the Groote Schuur Hospital and the Princess Alice Orthopaedic Hospital. The Groote Schuur Hospital is the major teaching hospital of the University of Cape Town. The Groote Schuur Hospital has 1,353 beds and a very busy general outpatient department. The average number of outpatient visits per year over the past 5 years was 904,105 and the average number of hospital admissions per year over the past 5 years was 48,021 admissions (Groote Schuur Hospital Annual Reports: 1981 to 1985). Patients with rheumatic diseases are referred to the arthritis clinic from the general outpatient department, the medical wards or directly from general practitioners and other hospitals. The Princess Alice Orthopaedic Hospital is a specialist orthopaedic and rheumatology hospital; patients are referred here directly by general practitioners or other hospitals.

The hospital records of all the patients who attended the arthritis clinic at Groote Schuur or Princess Alice Orthopaedic hospitals on one or more occasion, over a 16 month period from

January 1982 to April 1983, were reviewed. All the patients who were assessed as having classical or definite RA were considered eligible for participation in the study. There were 330 Coloureds, 203 Caucasians and 55 Africans. There were only 15 Indians, and therefore it was decided to exclude them from the survey. All the African patients with RA who were attending the arthritis clinic were approached to take part in the study; 52 of the 55 patients agreed and were included in the study. Random tables were used to select the Coloured and Caucasian patients for inclusion in the study. Of the group of 131 Coloureds and 124 Caucasians who were approached to participate in the study, 104 Coloureds and 100 Caucasians entered the study. The reasons for excluding the remaining patients are summarised in Table 2.1.

Nineteen patients refused to participate in the study, mainly because of inability to get time off from work.

Initially all the patients were either contacted by telephone or interviewed during a follow up visit to the arthritis clinic. If there was no response by telephone or if the patients did not have a telephone, a letter and subsequently a telegram were sent to them. If there was still no response, a district nursing sister tried to contact the patients at their previous known address. A determined effort was made to contact patients who were selected for inclusion in the study because if we selected only those patients who were currently attending the clinic, then there may have been a bias towards including patients with more severe disease.

TABLE 2.1

	<u>COLOUREDS</u>	<u>CAUCASIANS</u>
1) Number of patients selected	131	124
2) Number of patients excluded	27	24
Reasons for exclusion from study:		
(i) refused	9	10
(ii) could not be contacted	12	3
(iii) did not satisfy criteria for RA	5	6
(iv) died	1	5
3) Number of patients studied	104	100

The aim of this survey was to study the clinical and radiological manifestations of RA which included a functional assessment of the various joints and an overall assessment of functional disability. Therefore, a predominantly outpatient population of patients with RA were studied. If the survey had been undertaken in patients who were admitted to hospital, it would have been difficult to evaluate the clinical and functional assessment during an active flare or post operative rehabilitation of patients after major surgery.

A study of patients with RA who attended a specialist arthritis clinic clearly introduces a bias towards more severe disease in the study population than a similar survey in the community. However, most of the clinical studies which have been conducted in

RA have been undertaken in hospital based populations. Therefore, it would still be possible to compare the findings in this survey with other published data.

All the patients were aware of the nature of the study and agreed to participate in the study.

## 2. DEMOGRAPHIC DATA

All the patients were interviewed and the following information was recorded:

- A) The age, sex, race, marital status and area of residence.
- B) The hospital or clinics which the patients were regularly attending for the management of their RA.
- C) The status of the patient at the time of assessment i.e. whether they were outpatients or inpatients. The reason for admission to hospital was noted in the case of the hospitalized patients.
- D) The total number of hospital admissions to Groote Schuur or Princess Alice Orthopaedic Hospitals for the investigation or management of illnesses related to their RA. The number of admissions for surgery was also noted.
- E) A history of handedness.

## 3. FAMILY HISTORY

A family history of RA was recorded. If there was a family history

of arthritis but the nature of the arthritis was uncertain, then this was recorded separately. This information was obtained by history only and was not verified by a study of the family members.

#### 4. OCCUPATIONAL HISTORY

The following information was documented:

- A) Whether a patient was working at the time of assessment (full-time, part-time or casual).
- B) Whether a patient had to stop work or change their occupation because of their arthritis.
- C) Whether a patient received a disability grant or a pension from the state or some other source.
- D) Occupational exposure to dust.

#### 5. ALCOHOL AND SMOKING

The following information was noted:

- A) A history of alcohol intake in the past or present, and also the duration and pattern (Gillis et al 1973).
- B) A history of smoking in the past or at present; if a history of smoking was obtained, then the duration and number of cigarettes per day was noted.

## 6. PAST MEDICAL HISTORY

### A) UPPER GASTROINTESTINAL SYMPTOMS AND PEPTIC ULCERS

A history of peptic ulcers, the presence of symptoms such as dyspepsia or epigastric pain, gastrointestinal bleeding, surgery for peptic ulcers and therapy for peptic ulcers and dyspepsia were recorded. The clinical records of all the patients who had symptoms were reviewed. The results of the barium meal and endoscopic studies were noted in patients who had these tests. Patients who had dyspepsia or epigastric pain but in whom a definite diagnosis of peptic ulcers was not established, were recorded separately.

### B) ASSOCIATED DISEASES

A history of diseases such as diabetes, hypertension, ischaemic heart disease, tuberculosis (TB), asthma, rheumatic fever or rheumatic heart disease was obtained for each patient.

### C) FRACTURES

All the patients were asked about a history of fractures and the following was noted:

- i) A history of any trauma, such as a fall or other injury prior to the development of the fracture.
- ii) The age and duration of RA at the time of the fracture
- iii) A history of previous steroid therapy
- iv) The presence and site of the fracture were determined

from a review of the clinical records and radiographs.

D) THERAPY

The following aspects of therapy were recorded in all patients:

- i) Physiotherapy: A history of referral to physiotherapy and the modalities of therapy used in the past or present.
- ii) Occupational Therapy: A history of referral to occupational therapy and the recommended management in the past or present; a history of the use of arch supports, metatarsal bars or other modification of the footwear.
- iii) Drug Therapy:
  - (a) A history of ingestion of analgesics, antidepressants, tranquilisers, non steroidal anti-inflammatory drugs (NSAIDs), haematinics, antacids, diuretics and hypotensive drug therapy; the number of different NSAIDs taken over the past year; the use of suppositories. This information was verified by a review of the hospital records.
  - (b) A history of past or present treatment with injectable gold (Sodium aurothiomalate: 'Myocrisin'), oral gold (Auranofin: 'Ridaura'), penicillamine, chloroquine, sulphasalazine, cyclophosphamide, azathioprine and dapsone and the mean duration of treatment.

(c) Patients who were on corticosteroids were asked about the duration of therapy and the present daily dose.

(d) A history of local corticosteroid injections and the number of injections; a specific note was made of whether a patient received injections of steroid and local anaesthetic in or around the shoulder.

E) SURGERY

A history of any surgery for RA and the nature of the surgical procedure was recorded and confirmed by a review of the clinical records.

Flexor tenosynovectomy or repair of ruptured extensor tendons in one hand was recorded as one procedure irrespective of the number of operations or the number of digits involved. Rerouting of the extensor tendons over the wrist was invariably combined with excision arthroplasty of the ulnar head, and this was considered as one procedure. Soft tissue operations such as olecranon bursectomy or excision of subcutaneous nodules were noted separately as soft tissue procedures.

7. ARTICULAR HISTORY

The following information was recorded:

A) The age of onset and the duration of RA; the duration of

hospital follow up at Groote Schuur and Princess Alice Orthopaedic Hospitals as these records were available for review.

- B) The duration of morning stiffness at the time of assessment and the presence of morning stiffness of more than one hour at any stage.
- C) A history of pain in the hips, knees, ankles, midfoot, forefoot, shoulders, elbows, wrists, hands and temporomandibular joints.
- D) A history of swelling of any of the joints was recorded.
- E) A history of pain in the neck and its relationship to movement of the neck.

## 8. FUNCTIONAL ASSESSMENT

All the patients in the survey were interviewed and their functional status was graded according to the ARA functional classification (Steinbrocker et al 1949; Appendix 1), the Joint Committee classification (Joint Committee: UK, 1954; Appendix 2), the Swezey functional disability classification (Swezey 1978; Appendix 3) and the Lee functional index (Lee et al 1973; Appendix 4).

According to the Lee functional index a score is allocated as follows: 0 if a patient can perform a task without difficulty, 1 if a task can be performed with difficulty, eg, pain or weakness, and 2 if a patient cannot perform a particular task. The

questions related to walking were "can you walk" (question 11) and "can you walk without" a) someone's help, b) crutches and c) a walking stick (question 12). It was noted that in the majority of the patients a similar score was obtained for question 11 and the three sections under question 12. The only time a different score was obtained was when a patient needed assistance in walking. This represented only a small number of patients and it was therefore decided to omit question 12. Thus a modification of the Lee functional index was used in this survey.

#### 9. SYSTEMATIC ENQUIRY

A detailed systematic history was obtained and symptoms which were specifically recorded were as follows:

- A) Symptoms of Sjogren's syndrome such as dryness, burning, itching, grittiness of the eye, dry mouth or salivary gland enlargement.
- B) Gastrointestinal - nausea, dyspepsia, epigastric pain, haematemesis or melaena.
- C) Neurological - a history of headaches, weakness, paraesthesiae, numbness and sphincter control was recorded.
- D) Cardiopulmonary - chest pain, cough (if productive, the nature and the amount of sputum), the presence and severity of dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea and oedema. A history of occupational or environmental exposure to dust or pets such as birds was noted.

## 10. NUTRITIONAL ASSESSMENT

The nutritional status was assessed in all the patients. Those patients who were unable to stand or in whom measurements could not be made due to deformities of joints, were excluded from further analysis.

The assessment of the nutritional status was based on standardized anthropometric techniques (Jelliffe 1966, Blackburn and Thornton 1979, Grant et al 1981). The anthropometric measurements which were recorded were the height, weight, midupper arm circumference (MUAC) and the triceps skin fold thickness (TSF). The TSF was measured with the Harpenden calipers. All the measurements were made by the same observer (GMB). The upper arm muscle circumference (UAMC), the body mass index (BMI) and percentage of ideal body weight (% IBW) were calculated from the anthropometric measurements. The international standards for height and weight, upper arm muscle circumference and triceps skin fold thickness were used to determine the BMI and the UAMC, TSF and IBW as a percentage of the normal values (Jelliffe 1966).

A reduction in the body weight was determined by calculation of the % IBW, the fat stores were assessed from the TSF thickness, skeletal muscle from the UAMC and the visceral protein status was determined from the serum albumen concentration. A reduction in the weight to less than 80% of the ideal body weight, UAMC less than 80% and TSF less than 60% were considered to indicate a

significant reduction or depletion.

## 11. PHYSICAL EXAMINATION

### A) General Examination

A general medical examination was performed in all the patients. The presence of oedema, clubbing, cyanosis, skin rashes, cutaneous vasculitis, lymphadenopathy, leg ulcers and the presence and site of rheumatoid nodules were recorded.

### B) Systemic Examination

The eyes were examined for the presence of episcleritis, scleritis or any other abnormality. The presence of an enlarged liver and spleen were recorded. The chest and cardiovascular system were examined to detect any abnormality. A neurological examination was conducted in all the patients to detect any abnormality; particular attention was paid to the presence of a neuropathy (peripheral or entrapment) or a myelopathy. The tone, power, reflexes, sensation and the presence of muscle wasting were noted. Tinel's sign and Phalen's test were performed to clinically detect the presence of median nerve compression. The tendon reflexes were recorded as absent, reduced, normal, brisk or very brisk.

### C) Musculoskeletal Examination

A Ritchie articular index score (Ritchie et al 1968) and the

joint hypermobility score (Beighton et al 1973) were recorded in all the patients.

i) Shoulders

The presence of tenderness of the acromioclavicular and shoulder joints was noted. The shoulders were examined for the presence of swelling, rotator cuff tendinitis, bicipital tendinitis and adhesive capsulitis. The movements which were recorded were passive abduction, and passive internal and external rotation with the shoulder in abduction.

ii) Hands

The hands were examined and the presence of the following was noted:

- a) Resorptive arthropathy of the fingers; resorptive arthropathy is considered to be present if there is shortening of the digits, redundant skin folds and resorption of the articular surfaces.
- b) Tenderness of the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints.
- c) The presence of swelling of MCP, PIP and distal interphalangeal (DIP) joints and the carpometacarpal and interphalangeal (IP) joints of the thumb; swelling of these joints was graded as mild, moderate or severe.
- d) A swan - neck deformity (SND) or boutonniere

deformity (BD) involving the fingers; if a deformity was present, the patient was asked to flex the finger fully to determine whether the deformity was mobile, partially fixed or fixed.

- e) Deformities of the thumbs as described by Nalebuff (Flatt 1983; Appendix 5).
- f) Subluxation of the MCP joints; if volar subluxation of the MCP joints was present, they were examined to determine whether it was reducible or irreducible (dislocated).
- g) The presence of extensor tendon rupture, extensor tendon dislocation at rest or extensor tendon dislocation on motion was noted; the extensor tendons were examined on the dorsal surface of the hand and over the MCP joints.
- h) Uncorrectible ulnar deviation (UD), which was considered to be present if the deformity could not be actively corrected by the patient.
- i) The presence of flexor tenosynovitis (FTS); flexor tenosynovitis was considered to be present if the patient had two or more of the following criteria: pain, tenderness or swelling localised to the flexor tendon or tendon sheath, crepitations, snapping, locking and limitation of digital flexion or extension (Gray and Gottlieb 1977).
- j) The function of the thumb was assessed by determining the apposition score; the apposition of

the tip of the thumb to the base of the little finger (score 5 = maximum), to the tip of the little finger (score 4), to the tip of the ring finger (score 3), the middle finger (score 2), the index finger (score 1) and a score of 0 was given if the latter was not possible.

- k) The assessment of the function of the other four fingers was determined by asking the patient to make a fist and the distance from the tip of the finger to the proximal palmar crease was measured for each finger.

iii) Feet

Tenderness of the ankles, subtalar, midtarsal and metatarsophalangeal joints (MTPJs) and the presence of swelling of the ankles were noted. The range of movement of the subtalar and midtarsal joints was recorded as 1 - normal, 2 - reduced or 3 - ankylosed. The forefoot was examined to detect the presence of clawing and overriding of the toes and callosities under the metatarsal heads. The presence of any deformity of the hind foot and midfoot was noted with the patient standing barefoot.

iv) Wrists

The presence of tenderness, swelling, inferior radioulnar crepitus and inferior radioulnar subluxation

(piano key sign) were recorded. The wrists were examined for the presence of subluxation or dislocation and if present, it was recorded as being either subluxed but reducible or subluxed and irreducible.

v) Elbows

The elbows were assessed to determine the presence of synovial swelling, medial epicondylitis, lateral epicondylitis and crepitus of the superior radioulnar joint. The range of movement (active flexion and extension) was recorded with a goniometer and was expressed as a percentage of the normal value (American Academy of Orthopaedic Surgeons 1965). The extension of the elbow to the neutral position was recorded as a zero value, hyperextension as a positive value and a flexion deformity as a negative value.

## 12. EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

The Coloured patients in the study were selected for specialized tests to determine the prevalence of extra-articular manifestations of RA. The following aspects of RA were studied:

A) KERATOCONJUNCTIVITIS SICCA

All the patients who had a history of symptoms of keratoconjunctivitis sicca (KCS) were referred to an Ophthalmologist (JCH) for a detailed assessment to detect the

presence of KCS.

A history of symptoms such as burning, itching, dryness, grittiness, soreness, foreign body sensation, photophobia, diminished vision and tearing were recorded and graded as 0 - nil, 1 - mild, 2 - moderate and 3 - severe. The marginal tear film was assessed by slit lamp examination. The tear film thickness at the margin of the upper and lower lids should be at least 1 mm in width and have a good convex surface. The tear film was assessed as being normal or reduced and the presence of any debris within it was noted. A drop of fluorescein 1% was then instilled into each eye followed by a microdrop of 1% Rose Bengal applied to the superior bulbar conjunctiva with a sterile wooden applicator stick. The presence of staining of the cornea and/or conjunctiva was noted on slit lamp examination and was graded as 0 - nil, 1 - mild, 2 - moderate and 3 - severe.

The break up time (B.U.T.) is a useful test for detecting an unstable tear film which is found in mucin deficient dry eyes and in some patients with KCS. The interval between the last complete blink and the development of the first randomly distributed dry spot in the pre-corneal tear film is defined as B.U.T. The test is repeated 3 times and the average figure is recorded. The normal values range between 15 and 45 seconds and values less than 10 seconds are highly suggestive of an unstable tear film. The test was performed

without any topical anaesthesia and without holding the lids open as this causes mechanical stretching of the tear film and produces a shorter B.U.T. The Cobalt blue filter of the slit lamp was used while scanning the corneal surface and the patient was asked not to blink. The fluorescein in the tear film fluoresces and dry spots are seen as dark spaces developing in the tear film.

The standard Schirmer test was performed. A 35 mm piece of Whatman No 41 filter paper was used and the folded portion was placed between the lid and the bulbar conjunctival surfaces of the lateral part of the lower lid. The amount of wetting of the filter paper after 5 minutes was measured.

B) CARDIAC INVOLVEMENT

Clinical examination of the cardiovascular and respiratory systems was performed by 2 observers, one of whom was a cardiologist (JES). All the patients had a 12 channel electrocardiograph (ECG) which was analysed by the cardiologist.

An echocardiogram was performed on each patient using an Aloka SSD Phased Array Sector Scanner with a 2,3 Megahertz transducer. Patients were positioned in a 30°-60° left oblique position with the shoulder slightly elevated. Two dimensional (2-D) sector scans were performed in the long axis and short axis parasternal position and also from the

apex and subcostal positions. The M-mode echocardiograms were measured in the standard way from the long axis parasternal view. The left ventricular internal dimension (LVID) was measured just below the tips of the mitral valve at the end of systole and diastole, and hence fractional shortening was calculated (LVID diastole - LVID systole / LVID diastole x 100). The mitral valve recordings were taken wherever possible to include the posterior leaflet and the conventional E-F slopes were calculated. The aortic dimension and left atrial dimension were measured at end diastole and end systole respectively. The pericardial echo was inspected from as many views as possible and the presence or absence of pericardial effusion or thickening was noted.

D) PULMONARY FUNCTION TESTS

Spirometry was assessed by means of the flow volume loop which was performed with a wedge spirometer and XY recorder (Med-Science 570). The best of three satisfactorily performed manoeuvres was used. The response to a bronchodilator was assessed by repeating the flow volume loop five minutes after the inhalation of 4 puffs of a beta-2 agonist aerosol. All 104 patients were able to perform the spirometry satisfactorily. Functional residual capacity (FRC) was measured by the helium dilution method (expirograph: Godart) and the total lung capacity (TLC) and residual volume (RV) were obtained during this test. The transfer factor for carbon monoxide ( $T_LCO$ ) and transfer

coefficient (KCO) were obtained by the single breath method (Carbon monoxide transfer test: P.K. Morgan). Two tests were performed with an interval of 5 minutes, and if they were performed satisfactorily, the mean value was used as the result. Three patients were unable to sustain the required ten second breath hold and thus satisfactory results were obtained in 101 patients. The maximum inspiratory and expiratory mouth pressures (MIP and MEP) were performed at RV and TLC respectively (Black and Hyatt 1969). In this test, the patient is required to sustain maximal effort for at least one second and the best of three such measurements was taken as the result. All the measurements taken were compared with the predicted values based on each subject's age, sex, height and weight. In the case of flow volume variables, the values for Caucasians were used since local experience shows that the pulmonary function values for Coloureds are more closely related to the values for Caucasians than for Africans. For the purposes of grouping and statistics, the measured values were expressed as a percentage of the predicted values in all patients. Interpretation of the pulmonary function test results was performed by a respiratory physician (SCM) without reference to the clinical and radiological data. In the case of  $T_LCO$ , KCO, MIP and MEP, the severity of the abnormality was assessed individually for each test. The presence and severity of airflow obstruction, a restrictive abnormality or a combination of both of them was determined by jointly

examining the flow volume loop and full volume data for each subject. Upper airway obstruction was identified by the appearance of the flow volume loop as well as the extent of the abnormality of the peak inspiratory and expiratory flow rates.

The criteria employed in interpreting the pulmonary function tests were as follows:  $T_LCO$ , KCO, MIP and MEP were considered to be abnormal if the values were below 80% of the predicted values; a restrictive defect was present if either the forced vital capacity (FVC) or TLC were more than 2 standard deviations below the predicted values; airways obstruction was present if either the forced expiratory volume in one second ( $FEV_1$ ) or  $FEV_1/FVC$  ratio were more than 2 standard deviations below the predicted values.

#### E) NEUROLOGICAL ASSESSMENT AND ELECTROPHYSIOLOGICAL TESTS

The history and findings on neurological examination were noted in all the patients. Electrophysiological tests to determine the conduction velocities on the median (motor and sensory), lateral popliteal (motor) and sural (sensory) nerves were performed using the Medelec Ms 6 Electromyograph apparatus. Patients were examined in a warm, screened room, and the investigation was not performed unless the skin was adequately warm to touch. Surface electrodes were used for the recording of stimulation. At the sites of stimulation, the cathode was positioned nearest the active, recording electrode, and a supramaximal stimulus was used. The stimulus

was a square-wave signal of 0,1 msec. duration. The motor latencies were measured to the onset of the initial negative deflection from the baseline, whereas sensory studies were measured to the peak of the negative deflection.

#### MOTOR STUDIES

- i) Median nerve - The active electrode was placed on the mid-belly of the abductor pollicis brevis and the reference electrode was on the distal tendon. The distal latency was estimated by stimulating 8 cm proximal to the active electrode. The trunk velocity was estimated from a stimulation in the antecubital fossa.
- ii) Lateral popliteal nerve - The active electrode was placed on the extensor hallucis brevis and the reference electrode was 2,5 cm distally. Distal latency was estimated by stimulating 8 cm proximally to the active electrode, and trunk velocity was estimated from stimulation at the fibula head.

#### SENSORY STUDIES

- i) Median nerve - A ring electrode was used on the index finger, with the active recording electrode positioned 14 cm proximally. Electronic averaging was used to obtain a signal from 32 stimulations at 1 Hz.
- ii) Sural nerve - The active, recording electrode was placed immediately below the lateral malleolus, and the reference electrode was 2,5 cm distally. Stimulation was performed 14 cm proximally and averaging of 32

stimuli at 1 Hz was used.

### 13. RADIOGRAPHIC ASSESSMENT

Radiographs of the chest (postero-anterior and lateral), hands and wrists (postero-anterior), cervical spine (postero-anterior, lateral, flexion and extension), shoulders (postero-anterior) and feet (postero-anterior) were performed in all patients. In order to reduce costs, radiographs of the ankles (postero-anterior) and pelvis (postero-anterior) were performed in only the Coloureds and Africans. The Africans were chosen because ankle involvement was reported to be commoner in Africans (Anderson 1970), and the Coloureds were studied because they represent a group who have not been studied elsewhere.

The radiographs of the hands, wrists, shoulders, ankles, feet and hips were graded by 2 observers (GMM and OLM) according to the Larsen standard radiographs (Larsen et al 1977; Appendix 6). An interobserver analysis was performed after the radiographs of all the Coloured patients had been graded by the 2 observers. The radiographs of the patients who had surgery or severe deformity, where grading was not possible, were excluded from the interobserver comparison. The assessment of the two observers is considered to be in agreement or satisfactory if both observers recorded the same grade or if there was a difference of one grade (Larsen et al 1977). In their earlier report, Larsen et al noted that there was about 90 percent agreement between 2 observers for

seropositive rheumatoid arthritis (Larsen et al 1977). In a later study, an agreement of 92% and 98% was noted when two pairs of observers were compared (Larsen et al 1979). In other studies (Grindulis et al 1983, Scott et al 1985) the correlation coefficient has been determined and a very good correlation has been observed among different observers. The statistical methods which were used to report the correlation of the radiographic findings between different observers have been the subject of criticism from statisticians (Kirwan 1984, Lewis 1985). The results of the findings between the two observers for the various joints and the percentage agreement is shown in Table 2,2. An agreement of more than 94% was found for all the joints. An intraobserver analysis of the radiographic gradings of the hands and wrists showed that there was a 94% agreement when reported by the same observer (GMM).

If patients had surgery to a joint or severe deformity where grading was not possible, then they were excluded from the inter-racial comparison. The severity of radiographic involvement among the races was assessed by comparing the Larsen score as follows (Larsen et al 1977, Scott et al 1985):

- a) Hands:             Sum of MCP joints + PIP joints + IP joints of the thumb
- b) Wrists:            Combined score for both wrists
- c) Feet:              Sum of 2nd to 5th MTPJs + IP joints of the big toes
- d) Total score:      Hands + (wrists x 5) + feet

The range of the score was 0-100 for the hands, 0-10 for the wrists, 0-50 for the feet and 0-200 for the total score.

The radiographs of the cervical spine were assessed by an orthopaedic surgeon (AF) without any knowledge of the patients clinical data. A randomly selected group of 40 radiographs were reported by a senior orthopaedic surgeon (IL) and a good correlation was noted between the two observers. Atlantoaxial subluxation (AAS) and instability were assessed by measuring the atlanto-dentate interval (ADI) in each of the three views. An ADI of more than 3 mm was considered abnormal. Atlanto-axial impaction (AAI) or cranial settling was estimated using McGregors line which extends from the posterior tip of the hard palate to the most caudal point of the occiput (McGregor 1948). Cranial projection of the odontoid process above this line is measured and values of more than 7 mm were abnormal. This method has distinct deficiencies but it was chosen as the most appropriate single measurement available (Hinck et al 1961). The presence of subaxial subluxation was also recorded.

The radiographs of the chest were read independently by a respiratory physician (SCM), a radiologist (BM) and a cardiologist (JES). Inter-reader differences were few and of minor extent. These were resolved by reference to a second senior respiratory physician (SRB) who had access to the patients clinical data.

TABLE 2.2

INTEROBSERVER COMPARISON OF RADIOGRAPHIC GRADINGS ACCORDING  
TO THE LARSEN SCORE

<u>JOINTS</u>	<u>NUMBER OF JOINTS</u>	<u>IDENTICAL SCORE</u>	<u>1 GRADE DIFFERENCE</u>	<u>2 OR MORE GRADE DIFFERENCE</u>	<u>% AGREEMENT</u>
Wrists	138	88	45	5	96,4
MCP	690	477	185	28	95,9
PIP	690	433	220	37	94,6
MTP	680	402	245	33	95,1
Shoulders	124	80	38	6	96,2
Ankles	132	83	42	7	94,7
Hips	138	97	39	2	98,6

#### 14. LABORATORY INVESTIGATIONS

The following tests were performed in all the patients:

- A) The full blood count was performed with the Coulter S-plus automated counter.
- B) The presence of blood, glucose and protein in the urine was tested with the Ames dipstix.
- C) The blood urea, electrolytes, serum creatinine, calcium, phosphorus, albumen, globulins, gamma glutamyl-transpeptidase (GGT), aspartate aminotransferase (AST), alanine

aminotransferase (ALT), lactate dehydrogenase (LDH) and alkaline phosphatase were measured with the Technicon SMAC 12 Autoanalyser.

- D) The serum iron and total iron binding capacity were measured by the Ferrizine method (Hyland Diagnostics) and the percentage saturation was calculated.
- E) The serum ferritin level was determined with a ferritin radioimmunoassay kit (Amersham).
- F) The serum protein electrophoresis was performed using the Beckman Microzone system.
- G) The level of immunoglobulin G, A and M were measured with the Behring Laser Nephelometer.
- H) The erythrocyte sedimentation rate (ESR) at 1 hour was measured by the Westergren method.
- I) The C-reactive protein (CRP) was assayed using the rocket immunoelectrophoresis method (antibody from Hoechst).
- J) The level of the circulating immune complexes was measured by using the modified  $I^{125}$  Ciq binding test (Zubler et al 1976).
- K) The presence and the titre of rheumatoid factor (RF) was determined by the Latex test (slide agglutination technique: Ortho diagnostics) and the sheep cell agglutination test (SCAT; slide agglutination technique: Rheumaton supplied by Wampole laboratories). A latex titre of 1/80 or higher and/or a SCAT of 1/16 or higher were considered to be seropositive.
- L) The antinuclear factor (ANF), smooth muscle antibody and

antimitochondrial antibody were assayed by the indirect immunofluorescence technique (Johnson and Holborow 1973).

- M) The level of the double stranded anti-DNA antibody (DS DNA) was measured by the millipore filtration technique (Ginsburg and Keiser 1973).
- N) The thyroid antibodies (microsomal and thyroglobulin) were tested by the haemagglutination in microtitre well system using thymune M and thymune T kits supplied by Wellcome laboratories.
- O) The free serum thyroxine (T4) level was assayed by radioimmunoassay (Amersham).

Tests A to C and H to M were performed at the time of clinical assessment. A sample of blood was collected, the serum was stored and the remaining tests were performed at a later date. There was inadequate serum available for some patients and therefore it was not possible to do all the tests in every patient. The reference range for the laboratory tests is included in Appendix 7.

#### 15. REVIEW OF THE HOSPITAL RECORDS

The hospital records of all the patients were reviewed and the following information was recorded:

- A) Duration of hospital follow up.
- B) The presence of diagnostic criteria for the diagnosis of classical or definite RA.

- C) The presence of subcutaneous nodules to determine whether there were patients who had nodules in the past and which were not present at the time of study.
- D) The highest titre of rheumatoid factor and the lowest haemoglobin value.
- E) The occurrence of any of the extra-articular manifestations or complications of RA eg. cutaneous vasculitis, cutaneous ulcers, episcleritis, entrapment or peripheral neuropathy, fractures, ruptured Baker's cyst, septic arthritis or any other abnormalities apart from the manifestations directly related to the joints.
- F) The dates of commencement and stopping remittive agent therapy, the presence and sequelae of adverse effects and the physicians assessment of response to therapy.
- G) Current drug therapy and the number of different non steroidal anti-inflammatory drugs (NSAIDs) used during the preceding year.
- H) The surgical procedures which were performed.

## 16. STATISTICAL METHODS USED IN THE STUDY

1. If both variables were categorised, a chi-square test was used in a 2 x r table and if significant, pairwise comparisons were done. The Fisher's exact test was used to calculate the p-value in the 2 x 2 tables if the numbers were small.
2. If one variable was categorical and the other was

continuous, a one-way analysis of variance was done. If the F-test was significant, a pairwise t-test was performed and the level for significance was adapted according to Bonferroni to provide for multiple testing procedures (Neter and Wasserman 1974).

3. If two variables had categorical data and one was a continuous variable, then a two-way analysis of variance was done. If there was no interaction, the main effects were tested to detect any significance (t-test).
4. If the data were paired, then the McNemar's test of symmetry was used for categorical data and the paired t-test was applied for continuous variables.
5. If a relationship was studied between continuous variables, then Pearson's correlation coefficient was used.
6. For multivariate analysis, if one wanted to determine which variables were the most important to discriminate between races and to differentiate between two groups, a discriminant analysis was used.
7. According to Bonferroni, if multiple testing is done (eg, pairwise), the level of significance for the individual tests must be adapted for the number of tests performed on the data. Since this was a probing survey, we wished to detect all possible differences and / or relationships. Thus the Bonferroni recommendation was ignored (unless otherwise stated) and all values significant at the 5% level were reported together with the actual p-values.

## CHAPTER 3

### DEMOGRAPHIC DATA

#### 1. RACE, AGE, SEX AND DURATION OF RHEUMATOID ARTHRITIS

All 256 patients who were studied fulfilled the American Rheumatism Association (ARA) criteria for the diagnosis of classical or definite RA (Ropes et al 1958); 84% had classical RA and 16% had definite RA. There were 104 Coloureds (40,6%), 100 Caucasians (39,1%) and 52 Africans (20,4%).

The age of onset and the age at the time of assessment in the three racial groups are shown in Figure 3.1 and Figure 3.2. The duration of RA is shown in Figure 3.3. The mean age at onset of RA, mean age at the time of assessment, mean duration of RA and the sex ratio for the Coloureds, Caucasians and Africans and the total study population are shown in Table 3.1. There were 189 females (73,8%) and 67 males (26,2%) with a female to male ratio of 2,8 : 1.

There was no significant difference in the ratio of females to males in the 3 racial groups ( $p=0,36$ ). There was no interaction between race and sex with respect to age at onset, age at the time of assessment and duration of RA. There was a relationship between race and the age at onset, age at the time of assessment

and duration of RA. Therefore, the races were compared further for each of these 3 variables.

The age of onset of RA in Caucasians was significantly different from that of the Coloureds ( $p=0,0012$ ) and Africans ( $p=0,0002$ ). The mean age at assessment was significantly higher in Caucasians compared to Coloureds ( $p < 0,0001$ ) and Africans ( $p < 0,0001$ ), and also in Coloureds compared to Africans ( $p < 0,0011$ ). There was no significant difference in the duration of RA in Caucasians in comparison with the Coloureds ( $p=0,1054$ ) but the mean duration of RA in Africans was significantly less than Coloureds ( $p=0,0074$ ) and Caucasians ( $p=0,0001$ ).

## 2. AREA OF RESIDENCE

The area of residence of the patients is shown in Table 3.2. Eighty four percent of the patients were living within the municipality of Cape Town or within the Cape Town Divisional Council and a further 7,0% were resident in other municipalities in the Peninsula. Only 9,0% of the patients were living outside the Cape Peninsula.

## 3. ATTENDANCE AT HOSPITALS AND ADMISSION DATA

There were 124 patients (48,4%) who were attending a follow up clinic at the Princess Alice Orthopaedic Hospital, 120 patients (46,9%) attended the arthritis clinic at Groote Schuur Hospital

and 12 patients (4,7%) attended other hospitals or clinics. One hundred and forty six patients (57,0%) had been admitted to these hospitals during the course of their disease. The total number of hospital admissions was 373 and therefore, the mean number of admissions for those who were hospitalised was 2,6 per patient. One hundred patients had 227 hospital admissions for surgery and therefore, in this group, there were 2,27 admissions per patient for surgery. The rest of the admissions were for medical reasons, usually the control of an acute flare, rehabilitation or other problems related to RA.

#### 4. STATUS AT THE TIME OF ASSESSMENT

The majority of the patients i.e. 235 patients (91,8%) were out-patients at the time of assessment. Fifteen patients (5,9%) were in hospital for medical management; they were assessed prior to discharge from hospital. Three patients (1,2%) were admitted for surgery and were assessed prior to surgery, while a further 3 patients (1,2%) who had surgery, were seen prior to discharge from hospital.

#### 5. MARITAL STATUS

The marital status of the patients is shown in Table 3.3. The majority of the patients listed under the category 'other', were people who were separated from their spouses but were not legally divorced.

#### 6. DOMINANT SIDE

A correlation of handedness and the prevalence of deformities and the severity of radiologic changes in the hand was to be undertaken in the survey of hand involvement in RA. Therefore, handedness was recorded and the results are shown in Table 3.4.

#### 7. OCCUPATIONAL HISTORY

The details of the occupational history are summarised in Table 3.5. Only 31,3% were employed at the time of assessment. One hundred and twenty four patients (48,4%) had to modify or stop work because of their arthritis. The mean duration of unemployment in those who had to stop work was 9,9 years. Fifty four patients (21,1%) were receiving a disability grant for a mean duration of 6,7 years, while a further 24 patients (9,4%) were receiving a government pension (old age pension).

#### 8. ALCOHOL INTAKE

The data on alcohol intake is shown in Table 3.6. Twenty six patients (10,2%) had a past history of alcohol intake and 35,6% of them were heavy drinkers while 65,4% were light or social drinkers. A history of alcohol intake at the time of the study was obtained in 101 patients (39,5%); only 5 patients (5%) were heavy drinkers while the remaining 96 patients (95%) were light or social drinkers.

## 9. SMOKING

A past history of smoking was obtained in 47 patients (18,4%) and 93 patients (36,3%) were currently smoking (Table 3.7). The mean duration of smoking in those who stopped smoking was 13,8 years, with one-third of the patients having smoked for less than 5 years. The number of cigarettes smoked per day (past or present) was recorded in 116 patients and is shown in Table 3.7.

## 10. FAMILY HISTORY

A family history of RA in first degree relatives was obtained in 48 patients (18,8%) with a high frequency of 30% being noted in Caucasians (Table 3.8). The history of RA was based on a history of polyarthrititis which included involvement of the hands and the patients knowledge of the diagnosis having been made by doctors in their family members. This information was not verified by a study of the family members.

## 11. ASSOCIATED DISEASE

A history of other diseases which were present in the patients is summarised in Table 3.9. The prevalence of hypertension in the study population was 21,5%, 9,4% had asthma, 8,2% had tuberculosis and 6,3% had a history of ischaemic heart disease.

## DISCUSSION

The ratio of female to males of 2,8 : 1 in this study was similar to the 2,7 : 1 noted by Duthie et al in their study of 282 patients in Edinburgh (Duthie et al 1955) and there were no significant differences among the races (Table 3.10). The mean age of onset in Caucasians was similar to the Edinburgh study (Duthie et al 1955), but was significantly greater than that of the Coloureds and Africans. The patients seen in this survey had their disease for a much longer period.

The younger mean age of onset of RA in Africans may be due to several factors. Firstly, the African population in the Cape Peninsula was less than the Caucasians and Coloureds (Coloureds 53,2%, Caucasians 33,1%, Africans 12,6%, Indians 1,2%; National Population Census 1980). In addition, in South Africa there are twice as many Caucasians over the age of 45 than Coloureds and Africans. Therefore, there would be fewer Africans with onset of RA at an older age and the mean age of onset would consequently be lower. Secondly, some patients travel from areas as far as the Transkei to Cape Town in order to have access to proper medical care which is not available in their own areas. It is mainly the younger people who would travel to Cape Town and therefore this factor may also lower the mean age of onset. Although the above factors may contribute to the lower mean age of onset of RA, it is also possible that there is a true difference among the races and that RA begins at a younger age in Africans.

The majority of the patients (91%) were resident in the Cape Peninsula and 95,3% were regularly attending the outpatient clinics at Groote Schuur and Princess Alice Orthopaedic Hospitals. There were 100 patients (39,1%) who had been admitted to the Rheumatic Disease Unit for surgery and a further 26 patients (10,2%) had surgery at other hospitals. Therefore, nearly half of our patients had been hospitalised for surgery. Laine and Vainio found that one third of their RA patients had surgery (Laine and Vainio 1964).

Rheumatoid arthritis affected the occupation of many patients, as 124 patients (48,4%) had to either modify their work or stop working because of their arthritis. About thirty percent of the patients were dependent on the state for financial support with 21,1% receiving a disability grant while a further 9,4% were pensioners. In South Africa there is an abundance of unskilled and semi-skilled workers and it is often difficult for young healthy adults, especially Coloureds and Africans, to obtain permanent employment. Therefore, it is not surprising that disabled patients have greater difficulty in obtaining full time employment and 38,5% of the Coloureds, 19,2% of the Africans and 4% of the Caucasians were receiving a disability grant.

Community surveys in South Africa have shown that 8,2% of the Caucasians and 18,2% of the Cape Coloureds were either misusers of alcohol (excess drinkers) or alcoholics (Gillis et al 1973). There were 14 patients (5,5%) who had a history of heavy alcohol intake (past or present). Excess alcohol intake is more common in males than females and the lower prevalence in our RA patients may be related to

the predominance of females in the study.

A history of smoking was obtained in 54,7% of our patients and one third of these patients had smoked in the past while two thirds were current smokers. In community studies, 58,0% of Coloured men and 40,8% of Coloured women had smoked in comparison to 47,3% of Caucasian males and 17,3% of Caucasian females (Rossouw et al 1983, Steyn et al 1985).

The prevalence of hypertension in this study was 21,5%. In community surveys the prevalence of hypertension, when adjusted for age against the Caucasians, is for females, Coloureds 33,6%, Caucasians 17,8% and Zulus 34,1% and in the case of males, Coloureds 28,21%, Caucasians 24,3% and Zulus 26,9% (Steyn et al 1985).

FIGURE 3.1

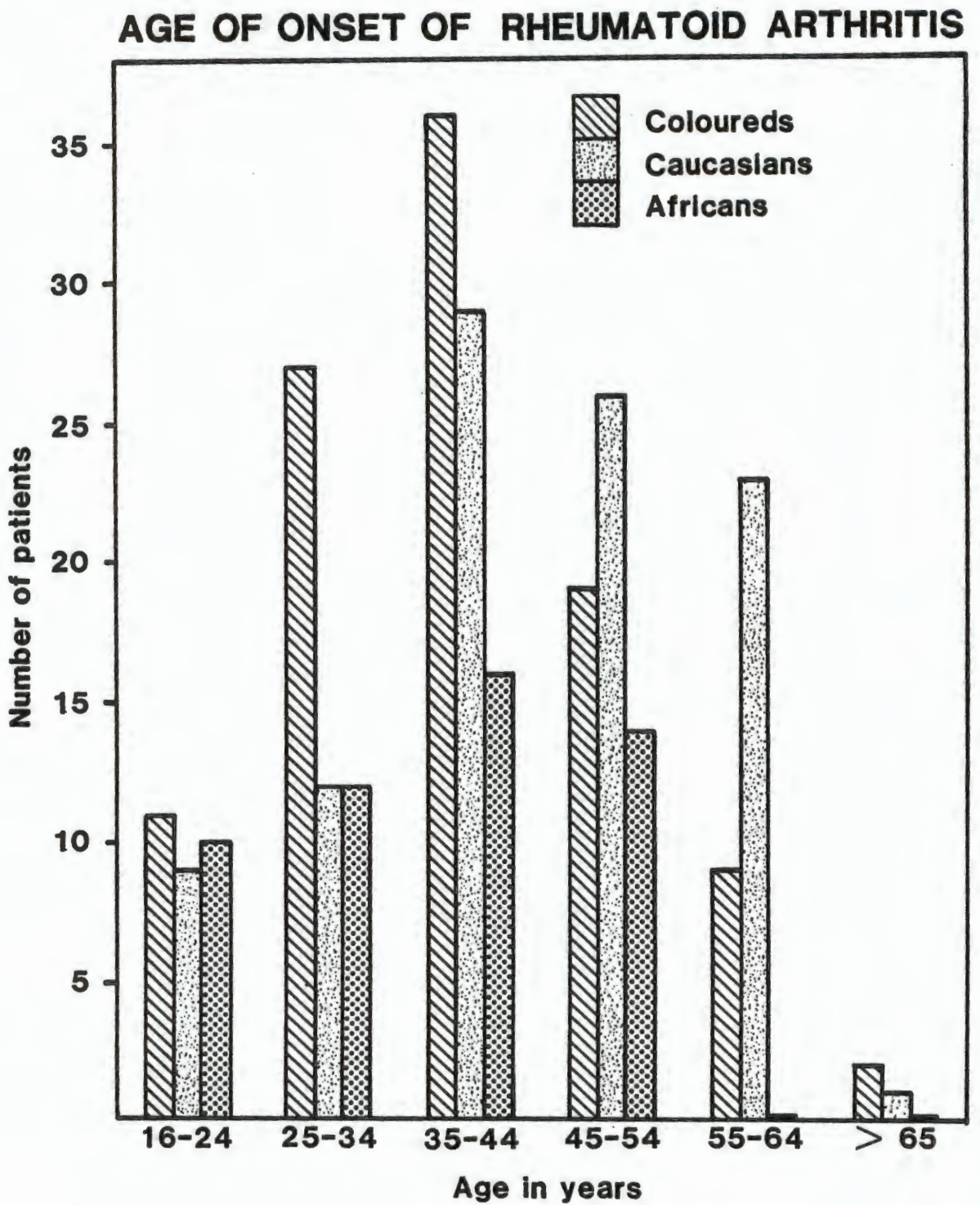


FIGURE 3.2

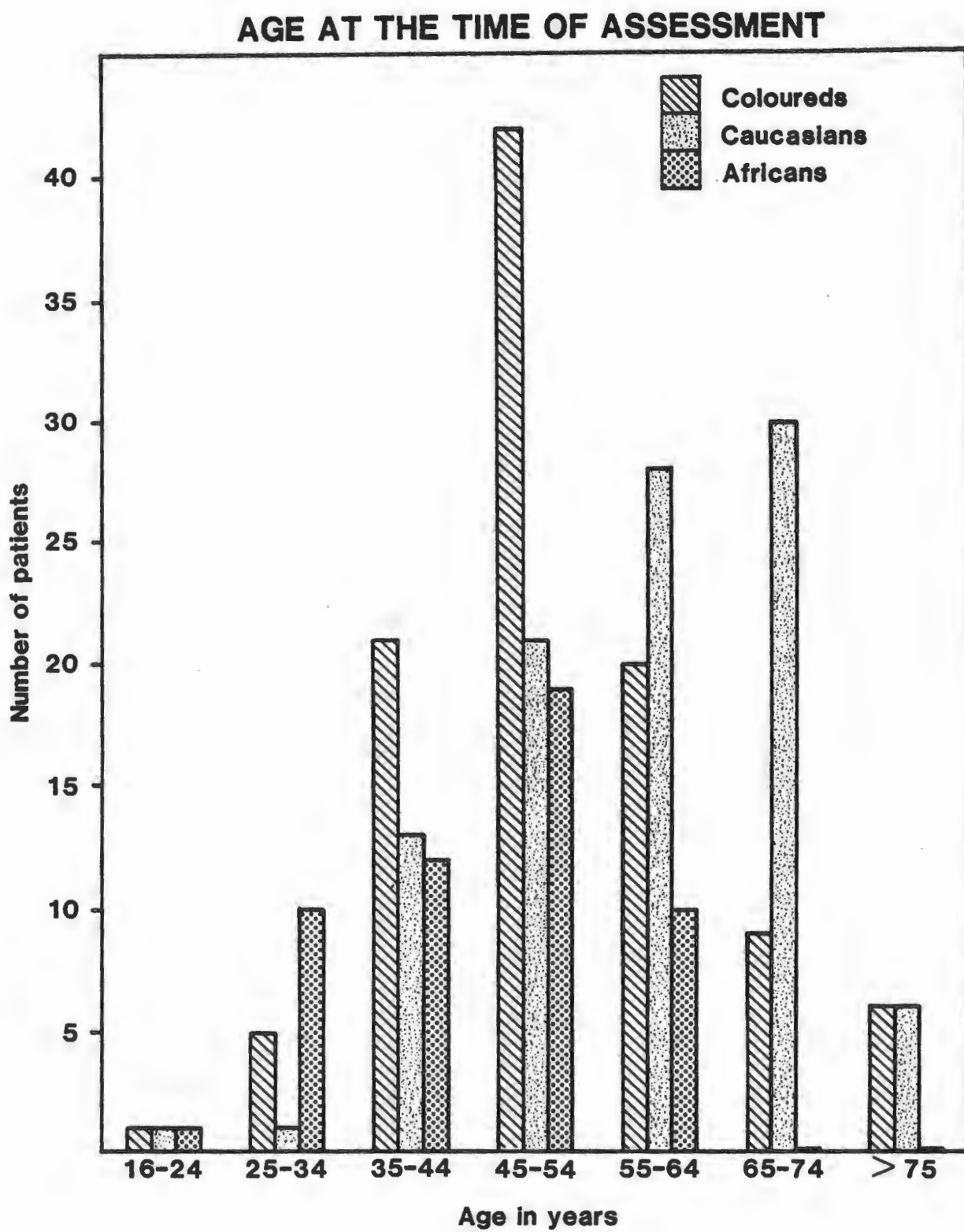


FIGURE 3.3

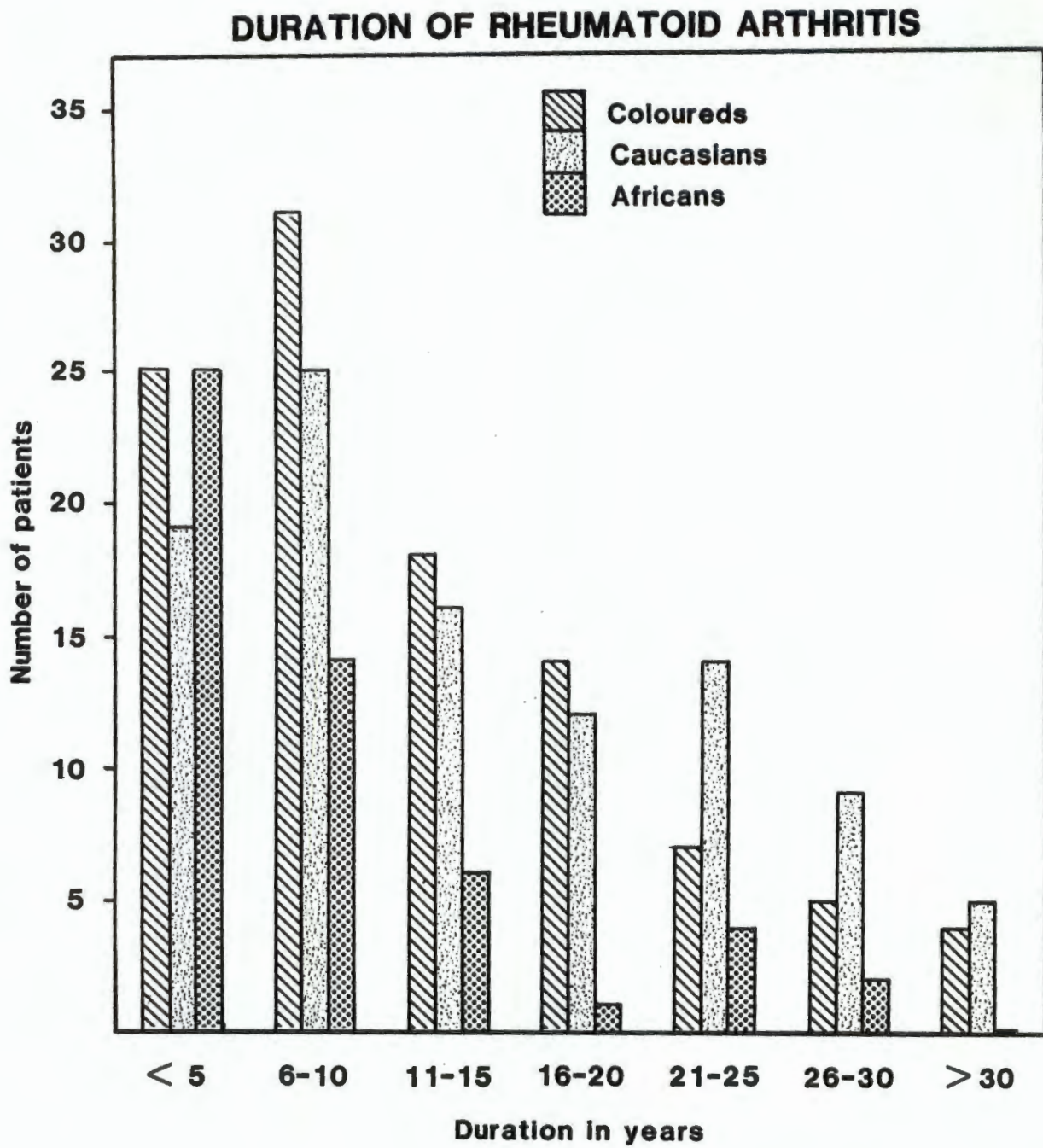


TABLE 3.1

THE MEAN AGE, SEX RATIO AND DURATION OF RA  
IN THE THREE RACIAL GROUPS

	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL
Number of patients	104	100	52	256
Number of patients as a percentage	40,6	39,1	20,4	100
Age at assessment (years)	51,1	58,9	44,6	52,8
Range	21-80	24-81	22-60	21-81
Age at onset (years)	38,9	44,2	36,6	40,5
Range	16-70	17-68	17-54	16-70
Duration of RA (months)	148,2	173,0	98,3	147,8
Duration of RA (years)	12,4	14,4	8,2	12,3
Range (years)	1,1-50	0,9-43	0,5-27	0,5-50
Females : Males Ratio	72:32 2,3:1	76:24 3,2:1	41:11 3,7:1	189:67 2,8:1

TABLE 3.2

PLACE OF RESIDENCE

PLACE OF RESIDENCE	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL % (n=100)
1	88	72	44	204	79,7
2	6	5	0	11	4,3
3	0	17	1	18	7,0
4	7	6	7	20	7,8
5	3	6	0	3	1,2

- \* 1 = Cape Town City Council  
 2 = Divisional Council  
 3 = Peninsula  
 4 = Outlying Municipalities  
 5 = Outlying Divisional Councils

TABLE 3.3

	<u>MARITAL STATUS</u>				TOTAL %
	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	
1. Unmarried	14	14	10	38	14,8%
2. Married	54	58	30	142	55,5%
3. Divorced	9	3	3	15	5,9%
4. Widowed	24	23	4	51	19,9%
5. Other	3	2	5	10	3,9%

TABLE 3.4

	<u>DOMINANT SIDE</u>				TOTAL %
	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	
RIGHT	97	90	46	233	91,0
LEFT	6	8	2	16	6,3
RIGHT / LEFT	1	2	4	7	2,7

TABLE 3.5

OCCUPATIONAL HISTORY

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
No. who were employed:					
Part time	28	36	16	80	31,3
Full time	4	14	5	23	9,0
Casual, other	23	20	10	53	20,7
	1	2	1	4	1,6
No. who changed/ stopped work because of arthritis	62	37	25	124	48,4
No. receiving disability grant	40	4	10	54	21,1
No. receiving pension					
Government	11	12	1	24	9,4
Work, other	4	20	1	25	9,8

TABLE 3.6

ALCOHOL INTAKE

ALCOHOL INTAKE	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
Past	15	8	3	26	10,2
Present	32	63	6	101	39,5
TOTAL	47	71	9	127	49,7

TABLE 3.7

	<u>SMOKING</u>				TOTAL %
	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	
Smoking					
Past	18	24	5	47	18,4
Present	51	34	8	93	36,3
TOTAL	69	58	13	140	54,7
No. of cigarettes per day					
< 10	34	11	7	52	20,3
11-20	23	15	2	40	15,6
21-30	4	13	0	17	6,6
31-40	0	5	0	5	2,0
> 40	1	1	0	2	0,7
Duration of smoking - Mean (in years)	24,5	30,1	26,1		
Duration of stopping smoking - Mean (in years)	10,4	17,2	6,8		

TABLE 3.8

	<u>FAMILY HISTORY OF RA</u>				TOTAL %
	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	
First degree relative with RA	14	30	4	48	18,8
Other family Members	4	18	3	25	9,8
Osteoarthritis	3	18	1	22	8,6
Other joint disease e.g. gout	5	15	0	20	7,8
Arthritis - nature unknown	35	34	11	80	31,3

TABLE 3.9

ASSOCIATED DISEASES

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
Diabetes	4	4	0	8	3,1
Hypertension	23	22	10	55	21,5
Ischaemic Heart Disease	3	12	1	16	6,3
Tuberculosis	11	4	6	21	8,2
Asthma	11	10	3	24	9,4
Rheumatic Fever	7	6	1	14	5,5
Rheumatic Heart Disease	0	0	0	0	0,0

TABLE 3.10

COMPARISON OF DEMOGRAPHIC DATA WITH THE FINDINGSBY DUTHIE et al (1955)

	PRESENT STUDY				DUTHIE et al (1955)
	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL	
Mean age of onset (years)					
Females	37,7	44,3	35,2	39,8	43,5
Males	41,5	44,2	41,6	40,5	44,6
Mean age at time of assessment (years)					
Females	50,9	58,4	44,0	52,4	50,5
Males	51,7	60,8	46,7	54,2	50,6
Duration of arthritis (years)					
Females	13,3	13,8	10,3	12,6	7,3
Males	10,3	16,2	4,5	11,4	6,0
Sex ratio					
Females : Males	2,3 : 1	3,2 : 1	3,7 : 1	2,8 : 1	2,7 : 1

## CHAPTER 4

### ASSESSMENT OF THE NUTRITIONAL STATUS

#### INTRODUCTION

Assessment of the nutritional status of medical and surgical patients in hospitals in Westernized communities has shown that significant depletion of the body stores of protein and energy occurs in 40% to 60% (Bistrian et al 1974, Bistrian et al 1976, Young and Hill 1978). Nutritional support plays an important role in total patient care in a variety of medical and surgical conditions such as cancer, inflammatory bowel disease, liver failure and chronic pancreatitis.

Muscle wasting and weight loss are important consequences of active polyarticular disease in RA. A reduction in the serum albumen has also been noted in RA and it was attributed to an increase in albumen breakdown due to a hypercatabolic state (Wilkinson et al 1965). Helliwell et al recently assessed the nutritional status of 50 RA patients using a combination of anthropometric and biochemical measurements and found evidence of malnutrition in 26% (Helliwell et al 1984).

The aim of this survey was to determine

- i) the prevalence of malnutrition, including obesity, in a large group of RA patients from 3 different communities.
- ii) whether there were any differences in the malnourished and

obese patients in comparison with the remainder of the patients.

## RESULTS

There were 164 females and 56 males with a female to male ratio of 2,9:1. The mean age of the patients was 52,6 years (range 21-81 years) and the mean duration of RA was 12,3 years (range 0,5-43 years). The demographic data and the ARA functional classification in the 3 communities studied is shown in Table 4.1. The mean values for the anthropometric measurements and the serum albumen are summarised in Table 4.2.

A reduction in the serum albumen to less than 35g/l was noted in only 15 patients (6,8%) and IBW values of less than 80% were also detected in 15 patients (6,8%). A reduction in the UAMC was noted in 32 patients (14,5%) and TSF values of less than 60% were detected in 26 patients (11,8%).

A reduction of one or more of the anthropometric measurements was noted in 45 patients (20,5%), of whom 26 were females and 19 were males. There were 25 patients (11,4%) who had a reduction of only one measurement, 12 (5,5%) had a reduction of two and 8 (3,6%) had a reduction of all three measurements. When the serum albumen and anthropometric measurements were considered together; 51 patients (23,2%) had a reduction of one or more parameters, of whom 32 were females and 19 were males. Twenty seven patients (12,3%) had a reduction in one parameter, 13 (5,9%) had a reduction of two, 9

patients (4,1%) had a reduction of three and 2 patients (1,0%) had a reduction of all four parameters. There was no statistically significant difference in the prevalence of one or more abnormalities of anthropometric measurements and serum albumen in the 3 different communities ( $p = 0,7144$ ).

The data on the 51 patients who were malnourished was compared with the rest of the patients in the study (Table 4.3). In the malnourished group, there was a significant increase in the proportion of males ( $p=0,0424$ ) and they had more severe functional disability ( $p=0,0235$ ) and a higher mean ESR ( $p=0,0003$ ). There were no other significant differences in the 2 groups.

There were 23 patients (10,5%) who were obese with a BMI of  $>30$ . This group included 11,2% of the Coloureds (10 patients), 4,5% of the Caucasians (4 patients) and 20,9% of the Africans (9 patients). Pairwise comparisons among the races showed that obesity was significantly more common in African females in comparison with Caucasians ( $p=0,0095$ ). When the obese patients were compared with the rest of the patients in the study, no significant differences were detected in the 2 groups (Table 4.4). There was also no association between obesity and steroid therapy.

An increase in the fat stores with the TSF thickness of  $>120\%$  of the international standards was noted in 104 patients (47,3%); this group included 51,7% of the Coloureds, 34,1% of the Caucasians and 65,1% of the Africans.

Apart from the 220 patients who had complete data, there were an additional 17 patients in ARA functional class 4 in whom the TSF, UAMC and serum albumen results were available. Six of these patients (35,3%) had one or more abnormalities. Three patients had a mild reduction of only the serum albumen (mean value 34 g/l), two patients had a reduction in all 3 parameters and one patient had a reduction in the UAMC only.

### DISCUSSION

There is no single anthropometric measurement or biochemical test for the assessment of nutritional status. Nutritional status has been assessed by using a combination of anthropometric measurements, biochemical tests and measurements of immune competence (Blackburn and Thornton 1979, Grant et al 1981, James 1982, Jelliffe 1966). Baker et al have shown that the clinical evaluation of nutritional status correlated well with objective evaluation in patients seen prior to surgery (Baker et al 1982).

There have been variations in the use of anthropometric measurements among different workers. The ideal body weight has been calculated as a percentage of normal based on the various frame sizes. There is no clear definition for frame size and 50% of the population is arbitrarily assigned to medium frame, 25% to small and 25% to large frame (Grant et al 1981). The body mass index, which is based on the weight and height, has been reported to have the best correlation with body fat (Bray 1981, James 1982). The fat stores have been assessed

from measurement of the triceps skin fold thickness and the triceps skinfold was found to be the most predictive among a number of body sites tested in a study involving 22,000 people (Pett and Ogilvie 1956). James has suggested that four skinfold measurements should be made because of individual and racial differences in the distribution of body fat (James 1982). The protein stores are determined from the arm muscle circumference and this measurement has also been criticised because it assumes that the midarm muscle compartment is circular and that bone is relatively consistent in size (Blackburn and Thornton 1979). The visceral protein status can be assessed by measurement of serum albumen, transferrin or total iron binding capacity, thyroxine binding prealbumen and retinol binding protein (Grant et al 1981). The assessment of the nutritional status in this study was undertaken using the international standards for height, weight, triceps skin fold thickness and upper arm muscle circumference (Jelliffe 1966). Although the assessment of the nutritional status in a particular group of patients with RA may be more accurate if compared with controls from the same community, the use of international standards allows intergroup comparison based on the same normal values. Furthermore, many of the surveys on nutritional status have been based on the international standards (Bistrian et al 1974, Bistrian et al 1976, Young and Hill 1978, O'Keefe et al 1983).

The assessment of nutritional status in RA is associated with additional problems. The determination of the height of patients may be difficult in patients with fixed deformities of the joints and therefore these patients were excluded from the present study. Anaemia

is common in RA and therefore calculation of the transferrin levels from the total iron binding capacity will produce inaccurate results unless iron deficiency has been excluded. The serum creatinine concentration varies with the muscle mass and the mean serum creatinine values have been shown to be significantly lower in patients with rheumatic diseases (Nived et al 1983). Skin tests have been used as a measure of immune competence and these are of limited value as patients with RA may have impaired delayed cutaneous hypersensitivity (Helliwell et al 1984).

Helliwell et al studied 50 outpatients with classical or definite RA and found evidence of malnutrition in 13 patients (26%; Helliwell et al 1984). Their patients were considered to be malnourished if they had a reduction of at least one anthropometric measurement in conjunction with two or more biochemical abnormalities. In the present study, a reduction of one or more anthropometric measurement was noted in 45 patients (20,5%) and a further 6 patients had a reduction in the serum albumen ( $<35\text{g}/\ell$ ) without any abnormality of the anthropometric measurements. There was no significant difference in the prevalence of malnutrition in the 3 different communities. This is surprising because a nutritional survey among hospitalised medical and surgical patients from the same communities showed that malnutrition was commoner in Coloureds and Africans (O'Keefe et al 1986).

Obesity was significantly more common in Africans than in Caucasians but there were no significant differences in the age, sex ratio,

functional classification, indices of active disease and the use of steroids in the obese patients in comparison with the rest of the patients. Malnutrition was present more often in males, and patients who were malnourished had a significantly higher ESR and a more severe functional disability. It is likely that the prevalence of malnutrition may have been underestimated as accurate results could not be obtained in patients with more severe functional disability. However, the prevalence of abnormalities of the anthropometric measurements which were available in 17 patients in functional class 4, were similar to the remainder of the patients.

In a survey of 803 hospitalized urban Africans, depletion of fat stores was noted in 82% of males and 55% of females and a reduction in serum albumen was noted in 61% of females and 68% in males (O'Keefe et al 1983). However, they found that obesity and an increase in fat stores were common in a female control population and the mean values as a percentage of the international standards were 126% for weight and 134% for TSF in female factory workers and 145% for weight and 188% for TSF in female hospital domestic staff.

Although a high prevalence of malnutrition has been noted in medical and surgical patients in different communities, malnutrition was detected less often in outpatients with a chronic disease like RA. It is probable that malnutrition would be detected more often if hospitalised RA patients are studied as they are more likely to have active disease which may be associated with weight loss and severe constitutional manifestations.

In conclusion, malnutrition was detected in 51 patients (23,2%) and obesity was present in 23 patients (10,5%). There was no relationship between obesity and the duration of disease, severity of functional disability and steroid therapy. Malnourished patients had a higher ESR, more severe functional disability and males were more frequently affected. Nearly half of the malnourished patients had abnormalities of two or more parameters used for the diagnosis of malnutrition. Therefore, it is important to recognise that malnutrition may also contribute to morbidity in RA. It may be necessary to correct the malnutrition, especially in patients who require multiple surgical procedures.

TABLE 4.1

DEMOGRAPHIC DATA IN THE 3 COMMUNITIES STUDIED

	<u>Coloureds</u> (n=89)	<u>Caucasians</u> (n=88)	<u>Africans</u> (n=43)	<u>Total%</u> (n=220)
Female to male ratio	2,3:1	3,2:1	4,4:1	2,9:1
Mean age (in years $\pm$ SD)				
Females	49,8 $\pm$ 12,3	57,7 $\pm$ 12,3	44,8 $\pm$ 10,0	52,0 $\pm$ 12,8
Males	51,0 $\pm$ 9,7	61,9 $\pm$ 11,7	47,0 $\pm$ 8,7	54,5 $\pm$ 11,8
TOTAL	50,2 $\pm$ 11,5	58,7 $\pm$ 12,2	45,2 $\pm$ 9,7	52,6 $\pm$ 12,6
Mean duration of RA (years)	11,7 $\pm$ 8,6	14,5 $\pm$ 9,9	8,8 $\pm$ 7,8	12,3 $\pm$ 9,2
Functional classification (ARA)				
Class 1	26	24	11	61
Class 2	49	55	22	126
Class 3	14	9	10	33
TOTAL	89	88	43	220

TABLE 4.2

## A COMPARISON OF THE AGE, ANTHROPOMETRIC MEASUREMENTS AND SERUM ALBUMEN AMONG MALES AND FEMALES

	AGE (Years)	HEIGHT (Metres)	WEIGHT (Kg)	TRICEPS SKINFOLD THICKNESS (mm)	MID ARM CIRCUM- FERENCE (cm)	SERUM ALBUMEN	BODY MASS INDEX	ARM MUSCLE CIRCUM- FERENCE
COLOUREDS								
Females (n=62)	49,8 ± 12,3	1,55 ± 0,06	59,3 ± 11,3	22,3 ± 7,5	28,3 ± 4,1	40,2 ± 4,3	24,7 ± 4,7	21,3 ± 2,7
Males (n=27)	51,0 ± 9,7	1,63 ± 0,06	60,7 ± 11,7	10,2 ± 4,8	26,7 ± 4,0	40,3 ± 4,1	22,8 ± 4,3	23,5 ± 3,4
CAUCASIANS								
Females (n=67)	57,7 ± 12,3	1,59 ± 0,7	59,1 ± 11,4	17,9 ± 6,4	26,7 ± 4,2	40,9 ± 4,3	23,2 ± 3,5	21,1 ± 3,0
Males (n=21)	61,9 ± 11,6	1,72 ± 15,8	63,3 ± 15,8	11,6 ± 3,5	26,0 ± 5,6	38,1 ± 4,7	21,4 ± 4,9	22,3 ± 5,2
AFRICANS								
Females (n=35)	44,8 ± 10,0	1,57 ± 0,7	67,0 ± 13,2	25,0 ± 8,6	30,2 ± 4,4	38,4 ± 3,2	27,1 ± 4,5	22,4 ± 2,4
Males (n=8)	47,0 ± 8,7	1,64 ± 0,5	61,9 ± 10,9	10,5 ± 3,5	26,5 ± 3,4	39,4 ± 3,8	23,1 ± 4,0	23,2 ± 2,8
TOTAL	52,6 ± 12,6	1,60 ± 0,8	61,1 ± 12,3	18,4 ± 8,4	27,6 ± 4,5	39,9 ± 4,2	24,0 ± 4,5	21,8 ± 3,2

TABLE 4.3

COMPARISON OF THE FINDINGS IN THE MALNOURISHED PATIENTS  
AND THE REST OF THE PATIENTS  
 (Percentages within each group in parentheses)

	<u>MALNOURISHED</u> n=51	<u>REMAINDER</u> n=169	<u>p VALUE</u>
Age (mean)	51,20 ± 13,20	53,05 ± 12,42	0,3594
Sex Female:Male	32 : 19	132 : 37	0,0424
Duration of RA (mean - months)	155,35 ± 108,07	144,43 ± 111,33	0,5369
Rheumatoid Factor			
Postive	44 (86,3)	126 (74,6)	
Negative	7 (13,7)	43 (25,4)	0,0887
Articular Index Score	6,00 ± 5,93	5,80 ± 5,02	0,8105
ESR	92,86 ± 47,72	65,54 ± 45,59	0,0003
CRP	29,82 ± 27,37	21,82 ± 19,37	0,0209
Functional Class			0,0235
1	16 (31,4)	45 (26,6)	
2	22 (43,2)	104 (61,5)	
3	13 (25,5)	20 (11,8)	

TABLE 4.4

COMPARISON OF THE FINDINGS IN OBESE PATIENTS AND  
THE REST OF THE PATIENTS

(Percentages within each group in parentheses)

	<u>OBESE</u> n=23	<u>REMAINDER</u> n=197	<u>p VALUE</u>
AGE (mean)	52,81 $\pm$ 12,69	51,04 $\pm$ 12,00	0,5265
SEX Female:Male	20 : 3	144 : 53	0,2067
Duration of RA (Mean - months)	150,28 $\pm$ 109,91	118,48 $\pm$ 113,28	0,1919
Rheumatoid Factor			
Positive	16 (69,6)	154 (78,2)	
Negative	7 (30,4)	43 (21,8)	0,4290
Articular index Score	5,68 $\pm$ 5,12	7,30 $\pm$ 6,06	0,1581
ESR	72,20 $\pm$ 47,50	69,18 $\pm$ 47,65	0,7779
CRP	24,04 $\pm$ 22,00	20,78 $\pm$ 19,34	0,4972
Functional Class			0,6100
1	6 (26,1)	55 (27,9)	
2	15 (65,2)	111 (56,3)	
3	2 (8,7)	31 (15,7)	

## CHAPTER 5

### FUNCTIONAL CLASSIFICATION

#### INTRODUCTION

The therapeutic goals in the management of RA include relief of pain, preservation of function and prevention of joint destruction. It is essential to evaluate function or the degree of loss of function. Taylor considered the evaluation of function in four categories viz slight, moderate, severe and extreme degrees of impairment of function (Taylor 1937). Steinbrocker et al defined the 4 groups more clearly and proposed the American Rheumatism Association (ARA) Functional Classes 1 to 4 (Steinbrocker et al 1949). In 1954, the joint committee of the Medical Research Council and the Nuffield Foundation (Joint Committee: UK - 1954) used a five point scale (grade 1 to grade 5) which was similar to the ARA functional classification.

Swezey stated that a functional evaluation for arthritis should be concise, reproducible, inexpensive, quick to administer and preferably objective (Swezey 1978). It should distinguish upper and lower extremity dysfunction and also consider the head, neck and trunk. He proposed an abbreviated functional assessment (Swezey functional disability classification) which distinguishes upper extremity (self care) from lower extremity (mobility) as an alternative to the ARA functional classification. In 1973, Lee et al proposed a functional

index (Lee functional index) based on a 17 point questionnaire and this has been shown to take approximately 2 minutes and the inter- and intra- observer errors are low (Lee et al 1973).

The aim of this survey was to:

1. determine the functional classification of all the patients in the study based on the ARA, Joint Committee (UK), Swezey functional disability classification and the Lee functional index.
2. determine whether there was a correlation of the ARA and the Joint Committee (UK) classification with each other and with the total score and the separate upper and lower limb scores for the Swezey classification and Lee functional index.

## RESULTS

The functional classification of patients according to the ARA classification is shown in Table 5.1, and the classification in the different races is shown in Figure 5.1. The majority of the patients belonged to the milder functional class 1 (25,8%) and 2 (52,3%). There were 37 patients (14,5%) in class 3 and 19 patients (7,4%) in class 4. The results of the Joint Committee classification (UK) is shown in Table 5.2. The Swezey functional disability classification for the upper and lower limbs is shown in Table 5.3 and the distribution of the combined upper and lower limb score is shown in Table 5.4. The distribution of the score for the modified Lee functional index is shown in Table 5.5 (minimum value 0 to a maximum of 32).

The correlation of the ARA functional class, Joint Committee, Swezey functional disability classification and the Lee functional index score with each other is shown in Table 5.6. There was a highly significant correlation in all instances ( $p < 0,001$ ) and the value of the correlation coefficient,  $r$ , ranged from 0,81 to 0,94. The value for  $r^2$ , the coefficient or index of determination, which gives the proportion of the variation of one variable which is explained by the other, ranged from 0,65 to 0,88.

The correlation of the ARA and Joint Committee (UK) classification with the separate upper and lower limb scores of the Swezey classification and the Lee functional index is shown in Table 5.7. There was a highly significant correlation ( $p < 0,001$ ) in the scores for the upper and lower limbs using the four different classifications or scores. In the upper limb, the  $r$  value ranged from 0,68 to 0,93 and the value of  $r^2$  from 0,46 to 0,86. In the lower limb, the  $r$  value ranged from 0,82 to 0,93 and  $r^2$  from 0,67 to 0,86.

## DISCUSSION

The value of assessing the functional status of patients with RA has been reviewed (Swezey 1978). The traditional assessment of the activities of daily living and the use of comprehensive protocols and questionnaires (Lowman 1958, Helewa et al 1982, Granger and Greer 1976 Robinson and Bashall 1973) are usually carried out by occupational therapists or in departments of physical medicine and rehabilitation. They are valuable in following the course of the disease and in

planning a rehabilitation programme for patients with varying disability.

The ARA functional classification has been used most widely by rheumatologists because it is brief and concise and provides an overall assessment of the functional status of the patient. The Joint Committee (UK) classification is very similar to the ARA classification except that patients who are completely bedridden are grouped separately in grade 5 and some of the patients who may belong to the ARA functional classes 2 and 3 would be scored a grade higher in the Joint Committee classification. One of the limitations of the ARA and Joint Committee classifications is that it does not distinguish between problems in the upper and lower limbs. The advantage of the Swezey classification is that it is possible to determine whether the disability is in the upper and/or lower limbs and improvement or deterioration in function in either could be noted. The Lee functional index includes questions referring to different joints, making it possible to determine the anatomical site of the disability such as the neck, shoulder or hands.

Lee et al found that there was generally an increase in their functional index score with increasing ARA functional class although there was a considerable overlap (Lee et al 1973). They also found a highly significant ( $p < 0,001$ ) correlation between the total functional index score and the time to walk 50 feet, grip strength and the Ritchie articular index score. The upper limb score also correlated with the grip strength and the lower limb score with the time to walk

50 feet.

In the present study there was a very good correlation when the ARA functional classification, Joint Committee (UK), Swezey functional disability classification and a modified Lee index score were compared with each other. There was also a highly significant correlation when the ARA and Joint Committee (UK) classification were compared with either the upper or lower limb grade obtained with the Swezey functional disability classification and the modified Lee functional index score.

In conclusion, the present study shows that the ARA functional classification, which has been used in many studies since 1949, correlates very well with the information derived from the Joint Committee (UK), Swezey functional disability classification and a modification of the Lee functional index score. The Swezey functional disability classification and the Lee index score provide useful additional information in individual patients. However, in large clinical studies on RA, the ARA functional class adequately describes the functional status of the patients.

FIGURE 5.1

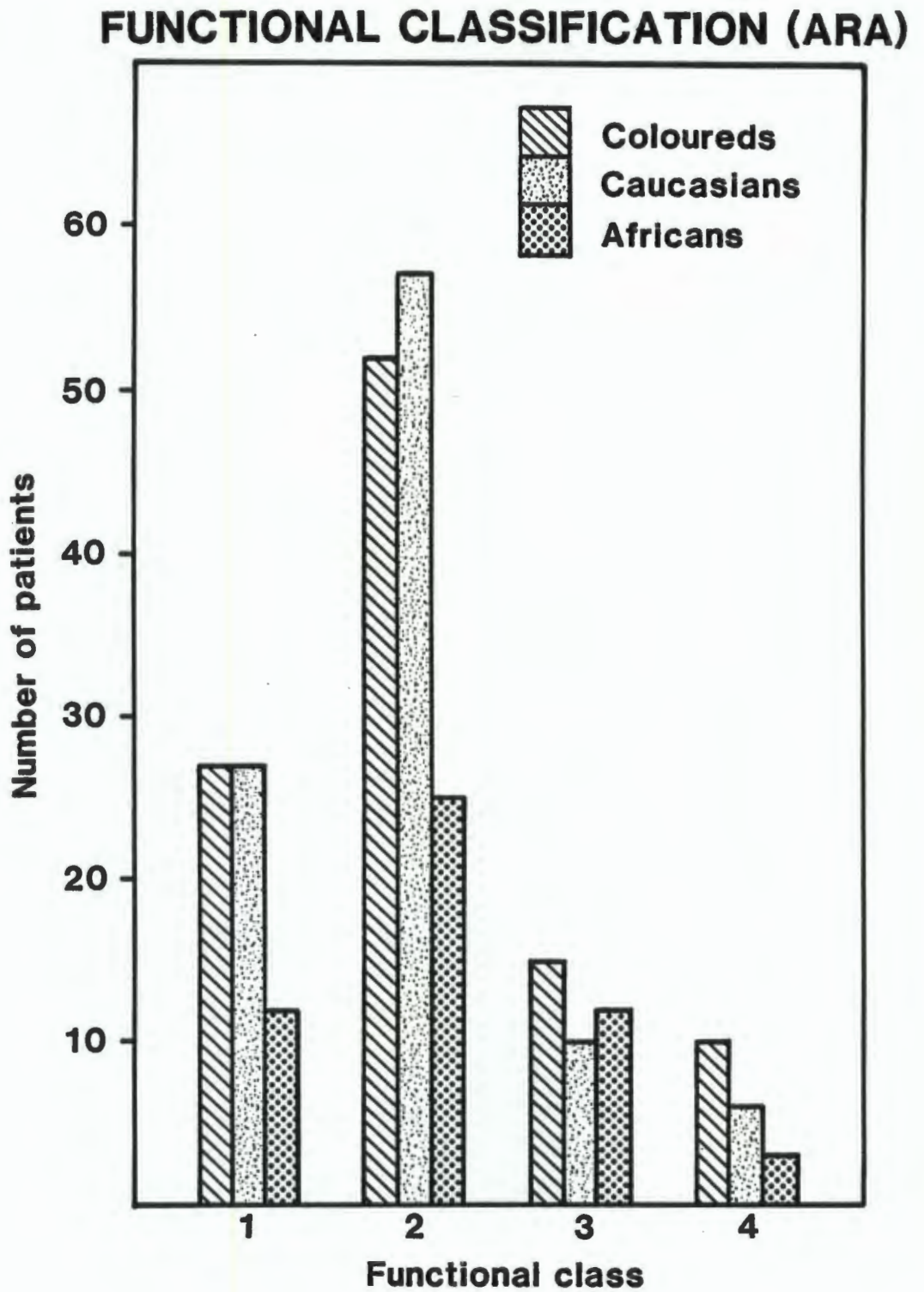


TABLE 5.1ARA FUNCTIONAL CLASS

FUNCTIONAL CLASS	NUMBER (n=256)	PERCENT
1	66	25,8
2	134	52,3
3	37	14,5
4	19	7,4

TABLE 5.2JOINT COMMITTEE (Great Britain)

FUNCTIONAL CLASS	NUMBER (n=256)	PERCENT
1	66	25,8
2	110	43,0
3	52	20,3
4	19	7,4
5	9	3,5

TABLE 5.3SWEZEY FUNCTIONAL DISABILITY CLASSIFICATION

GRADE	UPPER LIMB		LOWER LIMB	
	NUMBER	PERCENT	NUMBER	PERCENT
1	74	28,9	78	30,5
2	117	45,7	81	30,6
3	37	14,5	71	27,7
4	15	5,9	11	4,3
5	13	5,1	15	5,9

TABLE 5.4

SWEZEY FUNCTIONAL DISABILITY CLASSIFICATION - COMBINED UPPER AND LOWER  
EXTREMITY SCORE

SCORE	NUMBER (n=256)	PERCENT
2	64	25,0
3	21	8,2
4	70	27,3
5	40	15,6
6	29	11,3
7	11	4,3
8	5	2,0
9	6	2,3
10	10	3,9

TABLE 5.5

DISTRIBUTION OF THE TOTAL SCORE FOR THE LEE FUNCTIONAL INDEX

SCORE	NUMBER	PERCENT
0	34	13,0
1-5	77	30,1
6-10	62	24,2
11-15	38	14,8
16-20	19	7,4
21-25	15	5,9
> 25	11	4,3

TABLE 5.6

CORRELATION OF ARA FUNCTIONAL CLASS (1), JOINT COMMITTEE  
(UK) (2), SWEZEY FUNCTIONAL DISABILITY CLASSIFICATION (3),  
AND LEE FUNCTIONAL INDEX SCORE (4)

	1	2	3	4
1	1,0000	0,9387	0,9312	0,8256
2		1,0000	0,9342	0,8129
3			1,0000	0,8587
4				1,0000

TABLE 5.7

CORRELATION OF ARA (1), AND THE JOINT COMMITTEE FUNCTIONAL  
CLASS (2) WITH THE SEPARATE UPPER AND LOWER  
LIMB SCORES OF THE SWEZEY FUNCTIONAL DISABILITY CLASSIFICATION  
(3) AND LEE FUNCTIONAL INDEX SCORE (4)

UPPER LIMB	1	2	3	4
1	1,0000	0,9387	0,8917	0,6963
2		1,0000	0,8847	0,6779
3			1,0000	0,7513
4				1,0000
LOWER LIMB	1	2	3	4
1	1,0000	0,9387	0,8862	0,8221
2		1,0000	0,8984	0,8236
3.			1,0000	0,8485
4.				1,0000

## CHAPTER 6

### GENERAL FEATURES, ASSOCIATIONS AND COMPLICATIONS

#### INTRODUCTION

Prior to the presentation of the findings in the various joints, information about the prevalence of pain in the various joints, the Ritchie articular index score and the frequency of the various ARA diagnostic criteria which were recorded are presented in this chapter. The presence or absence of hepatosplenomegaly and lymphadenopathy were also noted in all the patients. Other observations such as the frequency of septic arthritis or bursitis, the prevalence of a ruptured Baker's cyst and the hypermobility score are also included in this chapter.

#### 1. JOINT PAIN

The prevalence of pain in the various joints (past or present) is shown in Table 6.1. The most frequent sites for pain were the hands (98,4%), wrist (98%), knees (93,8%) and the shoulders (93,4%). Pain in the hips was noted in only 35,2% and 52,7% had pain in the temporomandibular joints. There was no correlation between the number of painful sites and the duration of RA.

## 2. RITCHIE ARTICULAR INDEX SCORE

The Ritchie articular index score at the time of assessment was recorded in all the patients and the distribution of the score is shown in Table 6.2. A score of 0 was recorded in 44 patients (17,2%) and 131 patients (51,2%) had a score of 5 or less. A score of more than 10 was recorded in 55 patients (21,5%).

## 3. ARA DIAGNOSTIC CRITERIA

The frequency of the various ARA diagnostic criteria (Ropes et al 1958) in the study population is shown in Table 6.3. There were 41 patients (16%) who had definite RA while the remaining 215 patients (84%) has classical RA. The number of criteria which were present in the different communities is shown in Table 6.4. All the patients satisfied the clinical criteria, except the presence of subcutaneous nodules. The occurrence of morning stiffness and joint pain were based on history and the presence of joint swelling was determined at the time of assessment or from a review of the clinical records. There were only 3 patients who did not have any radiographic changes.

## 4. HEPATOSPLENOMEGALY

The liver was enlarged in 83 patients (32,4%) on palpation or percussion. The edge of the liver was measured below the subcostal margin in the mid-clavicular line and the liver edge

was 1 cm in 15 patients (5,9%), 2 cm in 40 patients (15,6%), 3 cm in 23 patients (9,0%) and 4 cm or more in 5 patients (2,0%). The spleen was palpable in 9 patients (3,5%).

#### 5. LYMPHADENOPATHY

Lymphadenopathy was detected in 56 patients (21,9%) with 48 patients having localized enlargement and 8 patients had involvement of more than one site. The most frequent site was the axilla in 43 patients (16,8%).

#### 6. HYPERMOBILITY SCORE

A comparison of the hypermobility score in the 3 racial groups is shown in Table 6.5. The frequency of the various findings is shown in Table 6.6. None of the patients satisfied the criteria for the diagnosis of the benign hypermobility syndrome but a score of 3 was recorded in 3 patients.

#### 7. RUPTURED BAKER'S CYST

A ruptured Baker's cyst occurred in 10 patients (3,9%) and was bilateral in 2 patients. The diagnosis was confirmed on arthrography in 8 patients and was made on clinical assessment alone in 2 patients. Two patients required surgical excision, one of whom developed a rupture into the thigh and the other had a calf cyst.

## 8. SEPTIC ARTHRITIS AND BURSITIS

Two patients developed a septic arthritis of the knees which was due to staphylococcus aureus in one patient and beta haemolytic streptococcus in the other patient. One patient developed a septic calf cyst and beta haemolytic streptococci were isolated on culture of the fluid aspirated from the calf. One patient developed a septic olecranon bursitis due to staphylococcus aureus. One patient developed acute aortic incompetence and even though no organism was isolated on blood culture, aortic root abscesses were noted at surgery and therefore aortic valve replacement was performed.

## DISCUSSION

The importance of infection in RA and its role as a cause of death has been recognised since 1953 (Cobb et al 1953). Kellgren et al drew attention to the problems of suppurative arthritis, bone infection and skin abscesses in 12 patients with severe RA (Kellgren et al 1958). Their patients had an increase in joint pain and swelling but fever and leucocytosis did not always occur. Staphylococcus aureus is the most common organism and was detected in 9 of 17 cases of septic arthritis in RA reported by Russell and Ansell (Russell and Ansell 1972). Huskisson and Hart reported the occurrence of 24 infections in 12 patients with RA (Huskisson and Hart 1972). Two patients in the present study developed infections due to staphylococcus aureus, one of whom had a septic arthritis and the other patient had a septic

olecranon bursitis. An infected calf cyst due to corynebacterium has been reported previously (Good and Rapp 1979); in this survey one patient developed a similar complication due to beta-haemolytic streptococcus.

The prevalence of lymphadenopathy varies from 19% to 96% in different series (Short et al 1957). Robertson et al studied 100 patients with RA and noted that lymphadenopathy was present in 82% of the patients and 52% of controls, splenomegaly was noted in 1 patient and another had splenectomy for Felty's syndrome (Robertson et al 1968). In the present survey, the presence of small, shotty lymph nodes was not recorded and significant lymphadenopathy was detected in 56 patients (21,9%). Hepatomegaly has been noted in 10% to 20% of patients from as early as 1 year after the onset of the disease (McKenna and Wright 1985). An enlarged liver was noted in 56 patients (32,4%) in this study.

A ruptured Baker's cyst was present in 3,9% in this survey. Jayson and Dixon have demonstrated that fluid from the anterior compartment of the knee may enter the popliteal portion but not readily return (Jayson and Dixon 1970). The one way valve may produce very high pressure and the popliteal cysts may lead to the formation of calf cysts or they may rupture into the calf or rarely into the posterior thigh (Hall and Scott 1966, Jayson and Dixon 1970).

Rheumatoid nodules occur in 20%-35% of patients with RA (Harris 1981) and were detected in 28,1% in this survey. A positive latex test for

rheumatoid factor is detectable in 70% or more of RA patients (Carson 1981) and was detected in 78,9% of our patients during the course of their disease.

In conclusion, the most frequent sites for joint pain were the hands, wrists, knees and shoulders. A positive rheumatoid factor had been detected in 78,9% and 28,1% had subcutaneous nodules. Lymphadenopathy was present in 21,9%, hepatomegaly was noted in 32,4% and 3,5% had splenomegaly. The prevalence of a ruptured Baker's cyst was 3,9% and 2 patients (0,8%) developed septic arthritis. The benign hypermobility syndrome was not detected in any of the patients.

TABLE 6.1

JOINT PAIN

JOINT	NO	PAST	PRESENT	TOTAL PAST OR PRESENT	TOTAL %
Cervical Spine	156	116	85	201	78,5
Temporomandibular	21	93	42	135	52,7
Shoulders	17	108	131	239	93,4
Elbows	41	117	98	215	84,0
Wrists	5	113	138	251	98,0
Hands	4	138	114	252	98,4
Hips	166	53	37	90	35,2
Knees	16	112	128	240	93,8
Hindfoot	43	115	98	213	83,2
Midfoot	109	81	66	147	57,4
Forefoot	61	91	104	195	76,1

TABLE 6.2

DISTRIBUTION OF THE RITCHIE ARTICULAR INDEX SCORE

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
0	17	21	6	44	17,2
1	14	6	3	23	9,0
2	7	9	4	20	7,8
3	6	9	1	16	6,3
4	6	4	2	12	4,7
5	4	10	2	16	6,3
6-10	25	27	18	70	27,3
11-15	18	10	8	36	14,1
16-20	5	2	5	12	4,7
>21	2	2	3	7	2,7

TABLE 6.3

THE FREQUENCY OF THE VARIOUS ARA DIAGNOSTIC CRITERIA FOR RA

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
Morning stiffness	104	100	52	256	100
Pain in joint	104	100	52	256	100
Swelling of joint	104	100	52	256	100
Swelling of another joint	104	100	52	256	100
Symmetrical joint swelling	104	100	52	256	100
Subcutaneous nodules	31	28	13	72	28,1
Radiographic changes	101	100	52	253	98,9
Rheumatoid factor	80	78	44	202	78,9
Synovial fluid	5	15	4	24	9,4
Nodule histology	4	3	0	7	2,7
Synovial histology	4	15	5	24	9,4

TABLE 6.4

THE NUMBER OF ARA DIAGNOSTIC CRITERIA PRESENT IN THE  
THREE RACES AND TOTAL GROUP

NUMBER OF CRITERIA	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
5	1	0	0	1	0,4
6	16	16	8	40	15,6
7	57	40	26	123	48,0
8	24	34	16	74	28,9
9	5	9	2	16	6,3
10	1	1	0	2	0,8

TABLE 6.5

HYPERMOBILITY SCORE IN RHEUMATOID ARTHRITIS

TOTAL SCORE	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)
0	96	99	50	245
1	5	0	1	6
2	1	0	1	2
3	2	1	0	3

TABLE 6.6

ASSESSMENT OF HYPERMOBILITY IN RHEUMATOID ARTHRITIS

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)
Extension of little finger beyond 90°	1	0	0	1
Apposition of thumb to forearm				
Right	3	0	1	4
Left	0	0	0	0
Hyperextension of elbow beyond 10°				
Right	1	1	0	2
Left	3	1	0	4
Hyperextension of knees beyond 10°				
Right	4	1	1	6
Left	1	0	1	2
Spinal flexion - palm to floor	0	0	0	0

## CHAPTER 7

### CERVICAL SPINE

#### INTRODUCTION

Radiological evidence of cervical spine involvement is found in 17% to 86% of patients with RA; this wide range is due to the difficulty in grading the various radiographic changes, the inter- and intra-observer errors and patient selection (Komusi et al 1985). Garrod, who first introduced the term rheumatoid arthritis, found that 36% of his 500 patients had cervical spine involvement (Komusi et al 1985). Patients with cervical spine involvement may be asymptomatic, complain of local pain, have reduced cervical mobility or develop neurological complications such as vertebral basilar ischaemia, myelopathy and sudden death. Atlanto-axial subluxation (AAS) is the most common radiographic finding in RA and was detected in 25% of 353 patients studied by Conlon et al (Conlon et al 1966). A poor correlation between clinical and radiographic findings has been noted in several studies (Nakano 1975, Stevens et al 1971, Mathews 1969, Cabot and Becker 1978 and Smith et al 1972). Ball and Sharp have noted that early diagnosis of cervical spine involvement depends on an increased awareness and suggested that it should be considered in every RA patient who develops any form of neurological disturbance (Ball and Sharp 1971).

The surgical treatment consists of upper cervical bony fusion which

may be associated with a high failure rate (Conaty and Mongan 1981, Ferlic et al 1975, Ranawat et al 1979) and also increased morbidity and mortality (Cregan 1966, Crellin et al 1970, Koota et al 1977, Meijers et al 1974, Meijers et al 1984). The indications for surgery are not well defined but most workers agree that intractable pain and significant or progressive neurological impairment are indications for surgery (Bryan et al 1982, Pellici et al 1981, Ranawat et al 1979).

A classification of the neurological abnormalities into 3 stages has been proposed but this grading has not been widely accepted (Ranawat et al 1979). However, in most clinical surveys, patients were not immediately subjected to surgery when neurological involvement was noted (Smith et al 1972, Mathews 1974, Stevens et al 1971).

The aim of this survey was to determine the prevalence of cervical instability in RA and to determine whether there was any correlation between the clinical and radiographic findings.

## RESULTS

There were 4 patients who had pyramidal tract or posterior column involvement. One patient developed cranial settling and bilateral pyramidal tract signs 2 years before the survey and had occipitocervical fusion; the second patient had AAS of 14mm with bilateral pyramidal tract signs and also had cervical fusion; the third patient had previous bilateral total hip and knee replacement and had mild hypertonia with bilateral extensor plantar response due

to multiple subaxial sUBLuxation and cranial settling and she was managed conservatively as she did not have any significant disability; the fourth patient had AAS of 8 mm and was found to have very brisk reflexes, Lhermitte's sign on flexion of the neck and posterior column involvement of both upper limbs, and was managed conservatively with a cervical collar as she refused surgery. There was one other patient who had AAS with very brisk reflexes and intractable neck pain for which she had cervical fusion. Therefore, there were 3 patients who had occipitocervical fusion, two of whom had bilateral pyramidal tract signs and the third patient had AAS with marked hyperreflexia and severe neck pain.

Abnormal neurological findings were detected in several other patients in the study. One patient had spastic paraparesis of both lower limbs which was attributed to meningo-vascular syphilis which had been diagnosed 15 years earlier and he did not have any abnormalities of the cervical spine. One patient had a right femoral neuropathy which was considered to be a mononeuritis on the basis of rheumatoid arteritis. There were 10 patients who had distal sensory neuropathy with predominant lower limb involvement. Four patients with a sensory neuropathy had a history of very heavy alcohol intake and alcohol was considered to be the cause of the neuropathy in these patients. None of the remaining patients with a neuropathy had diabetes or other cause for the neuropathy which was thought to be related to RA. One of the patients with a sensory neuropathy and a history of very heavy alcohol intake, had an old left hemiplegia with pyramidal tract signs on the left and x-rays showed evidence of AAI. Of the remaining 9

patients with sensory neuropathy, 2 had AAS (8mm and 7mm), one had AAI and the other 6 had no radiographic abnormalities. There were three other patients with hemiparesis and one with verteobasilar insufficiency who had normal cervical spine radiographs. These four patients were considered to have cerebrovascular disease.

Adequate radiographs were available in 248 of the 256 patients who were studied. Atlanto-axial subluxation was present in 90 patients (36,3%) and 34 patients (13,7%) had cranial settling or atlanto-axial impaction; these groups included 9 patients who had both AAS and AAI. Therefore, a total of 115 patients (46,4%) had evidence of AAS and/or AAI and the neurological findings in these patients are shown in Table 7.1. Ten of the 115 patients (8,7%) had very brisk reflexes, 34 patients (29,6%) had brisk reflexes and in the remaining 71 patients (61,7%) the reflexes were normal. Therefore, the majority of the patients with AAS or AAI had no abnormal neurological findings. A sub group of patients with a more severe radiological deformity were arbitrarily selected to determine if neurological abnormalities were more common in this group. All the patients who had an atlanto-dentate interval of more than 8mm and/or if McGregors line was breached by more than 10 mm were considered separately; there were 27 patients (Table 7.1) and 15 of these patients had no significant neurological changes while the remaining 12 patients (44,4%) had hyper-reflexia, which was very brisk in only one patient.

The radiographs of the 90 patients with AAS showed that 50 patients (55,6%) had a relatively constant displacement while the remaining 40

demonstrated a mobility of more than 5 mm on flexion and extension views. There was no difference in the prevalence of neurological abnormalities in the patients with mobile or constant AAS. There was no correlation between the prevalence of neck pain and headache and AAS.

Twenty patients (8,1%) had subaxial subluxation but this did not exceed 2mm in any patient and therefore these findings were not considered as contributory factors to neurological pathology.

The patients who were found to have brisk or very brisk reflexes were considered separately to determine whether there was a correlation between the prevalence of reflex changes and cervical spinal pathology. The results are summarised in Table 7.2; there were 85 patients in this group and nearly half (48%) had normal cervical spine radiographs. The presence of AAS, AAI or both was noted in 44 patients (52%) with hyperreflexia but these signs were not of any predictive value for cord compression as they were also often detected in patients without cervical spine involvement. If the patients who had very brisk reflexes were considered separately, then 10 of the 25 patients (40%) had AAI and/or AAS while the remaining 15 patients (60%) had no abnormality.

## DISCUSSION

The neurological assessment of a patient with RA is associated with many problems. Patients may have weakness and wasting related to the

arthritis rather than due to a neurological deficit. A reduction in the mobility of joints and the associated fixed deformities may result in difficulty in assessing the power and reflexes. Abnormalities of gait are more likely to be due to arthritis of the lower limb joints than sensory ataxia. Nevertheless, a careful neurological assessment is essential as patients with RA may develop neurological complications as a result of cervical spine involvement or due to a peripheral neuropathy which may take several different forms (Nakano 1975).

About 30% - 40% of all patients with chronic RA and severe peripheral joint disease who are admitted to hospital have radiological evidence of cervical spine subluxation (Nakano 1975). The major complications resulting from cervical subluxation are quadriplegia and sudden death (Davis and Markley 1951, Mikulowski et al 1975). Surgical management of the different forms of cervical subluxation is associated with significant morbidity and mortality. Therefore, in view of the frequent occurrence of cervical subluxation in RA and a benign course in the majority of patients, it is unacceptable to subject all these patients to potentially high risk surgery (Mathews 1974, Rasker and Cosh 1978, Smith et al 1972, Uddin et al 1970, Winfield et al 1981). However, the risks are higher after the onset of neurological complications and therefore it is essential to have clinical guidelines which help to select a high risk group who would benefit from surgery.

Weissman et al reviewed the data of 194 patients with RA who developed either AAS or AAI and found that upper spinal cord compression

developed more often in men, with the presence of AAI and when AAS was greater than 9mm (Weissman et al 1982). In the present study there were 4 patients who developed pyramidal tract or posterior column signs and 2 of them had AAI and 2 had severe AAS (8mm and 14mm).

The presence of AAS and/or AAI was noted in 115 patients (46,4%) and the majority (61,7%) of these patients had no neurological abnormalities. There was a poor correlation between the presence of AAS or AAI and the presence of hyperreflexia. The occurrence of subtle quadriparesis, hyperreflexia and early proprioceptive loss in the hands may be signs of early spinal cord compression (Nakano 1975). Stevens et al found AAS in 36% of 100 patients with RA (Stevens et al 1971). Twenty four (67%) of their 36 patients with AAS had hyperreflexia and were considered to have a myelopathy while a further 10 patients without subluxation also had hyperreflexia.

Marks and Sharp reported that sensory symptoms were the presenting manifestation in 23 of their 31 patients with a rheumatoid cervical myelopathy and that 19 of these patients were initially diagnosed as having an entrapment or peripheral neuropathy (Marks and Sharp 1981). A cervical myelopathy associated with cervical spondylosis has also been reported to present initially as a peripheral neuropathy (Clarke 1958). The commonest types of peripheral neuropathy in rheumatoid arthritis are the entrapment neuropathies and a mild distal sensory neuropathy which usually has a good prognosis (Pallis and Scott 1965). Ten of our patients (4%) had a distal sensory neuropathy but there was no progression of the neurological lesion in any of the patients. Four

of the patients with a sensory neuropathy had significant abnormalities of the cervical spine, 2 of them had AAI and the other 2 had AAS (8mm and 7mm)

When the neurological findings were compared with the radiographic findings, there were 85 patients (34,3%) who had hyperreflexia and 41 of these 85 patients (48,2%) had normal radiographic findings. Therefore, there was a poor correlation between the presence of hyperreflexia and the presence of spinal radiographic abnormalities.

Winfield et al noted that cervical subluxation is an early feature of RA and in over 80% of patients who have subluxation, it developed within 2 years of the onset of RA (Winfield et al 1981). In a follow up study they reported that 34 of their 100 patients with RA, who were seen for a mean period of 9,5 years, developed atlanto-axial or subaxial subluxation (Winfield et al 1983). There was progression of the subluxation in only 9 patients (9%) after the first two years and they were considered to be at risk of developing a cervical myelopathy. However, only one of their 100 patients developed a cervical myelopathy and 2 other patients had upper cervical fusion for severe occipital pain. Similar findings were noted in the present survey where the mean duration of RA was 12,3 years, four patients developed a myelopathy and one patient had fusion for severe neck pain.

The present study shows that AAS and AAI are common in RA and were noted in 115 patients (46,4%). However, only 5 of these patients

developed significant neurological complications or required surgery. All the patients who developed a myelopathy had AAI and/or significant AAS and therefore this survey supports the findings of Weissman et al (1982) that severe AAS (atlanto dentate interval of more than 9mm) and the presence of AAI are definite risk factors and indicate very close clinical monitoring but are not in themselves indications for surgery. The presence of hyperreflexia showed a poor correlation with the presence of subluxation in the cervical spine and should not be considered as a sign of myelopathy in the absence of other abnormalities.

TABLE 7.1

NEUROLOGICAL FINDINGS IN PATIENTS WITH RADIOGRAPHIC ABNORMALITIES(Percentage in Parentheses).

RADIOLOGICAL FINDINGS	TOTAL	NEUROLOGICAL FINDINGS		
		NORMAL	ABNORMAL	ABNORMALITY
(A)				
AAS	81 (32,6)	52	29	Bilateral pyramidal tract signs (1 patient) Bilateral posterior column signs (1 patient) Hyperreflexia - all patients
AAI	25 (10,1)	13	12	Bilateral pyramidal tract signs (2 patients) Hyperreflexia
AAS + AAI	9 (3,6)	6		Hyperreflexia
Total	115 (46,4)	71	44	
(B)				
Severe AAS*	13 (5,2)	9	4	Hyperreflexia (includes one patient with pyramidal tract signs)
Severe AAI**	14 (5,6)	6	9	Hyperreflexia (includes one patient with pyramidal tract signs)

\* AAS of more than 8 mm

\*\* McGregor's line breached by more than 10 mm

TABLE 7.2

RADIOLOGICAL FINDINGS IN PATIENTS WITH NEUROLOGICAL ABNORMALITIES(Percentage in Parentheses)

CLINICAL FINDINGS	RADIOLOGICAL FINDINGS				
	Normal	AAI	AAS	AAI + AAS	TOTAL
(A)					
Increased tendon reflexes	26	11	21	2	60 (24,2)
Markedly increased tendon reflexes	15	1	8	1	25 (10,1)
Total	41	12	29	3	85 (24,3)
(B)					
Pyramidal tract signs	-	2	1	0	3
Posterior column signs	-	0	1	0	1
Peripheral neuropathy	6	2	2	0	10

## CHAPTER 8

### SHOULDER

#### INTRODUCTION

Golding referred to the shoulder as 'the forgotten joint' in rheumatoid arthritis as there was a relative lack of radiological literature on the shoulder even though it was an important source of pain and disability (Golding 1962). Cruess noted that standard textbooks of rheumatology made only passing reference to the problem of shoulder involvement in RA and that no large article in the medical literature covered the subject in detail (Cruess 1980). McNair et al studied the clinical and radiological aspects of the shoulder in 50 patients with RA who were seropositive and had evidence of erosive joint disease on skeletal survey (McNair et al 1969). In one of the largest studies which has been performed so far, Ennevaara carried out a clinical, radiological and arthrographic study in 200 patients who had symptoms referable to the shoulder (Ennevaara 1967). Laine et al found evidence of involvement of the scapulohumeral joint in 47,1% of 155 patients who had symptoms referable to the shoulder (Laine et al 1954).

The aim of this study was to determine the prevalence of clinical and radiological involvement of the shoulder in a randomly selected group of patients with RA as most of the previous surveys studied patients

who had symptoms referable to the shoulder.

## RESULTS

### 1) Clinical Findings

A history of past or present pain in the shoulder was obtained in 239 patients (93,4%) and 201 patients (78,5%) had pain in the neck. Pain in the shoulder at the time of assessment was present in 131 patients (51,2%) and neck pain was present in 85 patients (33,2%). Tenderness of the shoulder at the time of assessment was present in 77 patients (30%) with the tenderness being bilateral in 36 patients (14%). Acromioclavicular joint tenderness was present in 47 patients (18,4%). Swelling of the shoulder was noted in 3 patients (1,2%), pain on passive movement in 62 patients (24,2%), clinical involvement of the rotator cuff in 37 patients (14,5%) and bicipital tendinitis in 11 patients (4,3%). A history of injection of steroids and local anaesthetic in and around the shoulder joint was obtained in 114 patients (44,5%).

### 2) Radiological Findings

Nine patients had surgery to the shoulder and their radiographs were excluded from further analysis. Of the remaining 247 patients, the radiographs of 241 patients (482 joints) were available for analysis. They were graded according to the Larsen

et al standard radiographs and the results are summarised in Table 8.1 (Larsen et al 1977). There was a good correlation of the findings by the two observers and agreement was recorded in 95,2% of the shoulders.

### 3) Surgery

Nine patients (3,5%) had a Benjamin double osteotomy of the shoulder with one patient having surgery to both shoulders. One of these patients also had an acromioplasty.

## DISCUSSION

Fleming et al described the features which were noted at the onset of RA in 102 patients and they found that the right shoulder was involved in 37%, the left in 42% and that bilateral involvement was present in 30% (Fleming et al 1976). Jacoby et al found that the shoulder joint was ultimately involved in 47% of the patients who were followed for 11 years (Jacoby et al 1973). Ennevaara reported a clinical, radiological and arthrographic study of the shoulder in 200 patients with RA who had pain on movement of the glenohumeral joint (Ennevaara 1967). The pain was referred from the neck in 20% of his patients and 10,5% had other syndromes or disorders which may cause pain in the shoulder. A history of past or present pain in the shoulder was obtained in 239 (93,4%) of our patients and it is likely that some of these patients had pain which was referred from the neck or other sites. Atlanto-axial subluxation and/or atlanto-axial impaction was

detected in 115 patients (46,4%) in this study and it is likely that some of these patients had pain which was referred to the shoulders. Shoulder pain was present in 131 patients (51,2%) at the time of assessment and tenderness of the shoulders was noted in 77 patients (30%). Ennevaara found clinical involvement of the acromioclavicular joint in 55,5% and noted that tenderness on palpation was the commonest and diagnostically most important sign (Ennevaara 1967). Tenderness of the acromioclavicular joint was present in 47 (18,4%) of our patients. Laine et al studied 277 unselected and hospitalized patients with RA and found that 27% had evidence of scapulohumeral involvement (Laine et al 1954).

Ennevaara has reported on the difficulty in making a definite clinical diagnosis of rotator cuff tendinitis (with or without rupture), bicipital tenosynovitis and retractile capsulitis in patients with RA who may also have glenohumeral arthritis (Ennevaara 1967). Neer has also commented on the possible coexistence of subacromial bursitis, supraspinatus tendinitis with or without tears of the supraspinatus tendon and/or bicipital tenosynovitis in patients who did not have RA (Neer 1972). He also found calcium deposits in the tendons at surgery in a few patients even though they were not visible radiologically. Rathburn and Macnab studied the microvascular pattern of the rotator cuff and documented the presence of avascular zones in the supraspinatus, infraspinatus and biceps tendons (Rathburn and Macnab 1970). They noted that degenerative changes occurred first and were always more extensive in the areas of avascularity. Therefore, it is possible that degenerative changes may occur at more than one site

simultaneously.

Ennevaara found clinical involvement of the rotator cuff in 167 patients (83,5%) of whom 90 patients had cuff rupture demonstrated on arthrography (Ennevaara 1967). The remaining 77 patients were considered to have rotator cuff tendinitis. Laine et al found that 4,7% of their 277 patients had rotator cuff tendinitis and 3,2% had bicipital tendinitis (Laine et al 1954). Clinical involvement of the rotator cuff was noted in 37 patients (14,5%) at the time of assessment and 11 (4,3%) had bicipital tendinitis. A history of injection of steroids and local anaesthetic in and around the shoulder was obtained in 114 patients (44,5%), the majority of which were for tendinitis or bursitis. Pain on passive movement of the shoulders was present in 62 patients (24,2%). This was considered to be due to glenohumeral arthritis in the majority of the patients, but the possibility that severe limitation of movement with pain was due to adhesive capsulitis or rotator cuff rupture, could not be excluded on clinical assessment alone.

In the present study, the presence of erosions and joint space narrowing or more severe destructive changes (grades 2 to 5) were noted in 174 joints (36%). A grade 2 or more severe change in at least one of the joints was noted in 101 patients (41,9%). The radiographic abnormalities described by McNair et al were the presence of either erosions, subarticular sclerosis or remodelling of the humeral head or any combination of these abnormalities in 42% of their patients (McNair et al 1969). Ennevaara found radiographic

involvement of the glenohumeral joint in 67,5% of his 200 patients (Ennevaara 1967). The abnormalities which he noted were osteoporosis (27%), joint space narrowing (16,5%), pseudocysts (18,5%), erosions (46%) and osteosclerosis (10,5%). The Larsen standard radiographs of the shoulder were used to grade the severity of changes in this study so that the frequency and severity of radiographic involvement could be compared with other studies in future (Larsen et al 1977). Larsen's grading system was used to grade 18,628 joints by De Carvalho and this survey included an analysis of 685 shoulder joints (De Carvalho 1981).

Arthroplasty of the shoulder was not being performed in our unit at the time of the study. Therefore, only 9 patients (3,5%) had surgery (Benjamin double osteotomy) to the shoulder. It is likely that many of the patients with destructive arthritis of the shoulder would benefit from shoulder arthroplasty and surgery would have been undertaken more frequently if arthroplasty was available.

Shoulder pain is common in RA and was noted in 93,4% of the patients. There were 114 patients (44,5%) who had received articular or peri-articular injections of corticosteroids and local anaesthetic. Rotator cuff tendinitis was noted in 14,5% and 4,3% had bicipital tendinitis. A Larsen grade 2 or more severe change in at least one of the shoulders was noted in 41,9% of the patients. Only 9 patients (3,5%) had surgery to the shoulder joint.

TABLE 8.1RADIOGRAPHIC GRADING OF THE SHOULDER\*

<u>Grade*</u>	No of Joints (n=482)	No of Joints % (n=100)
0	75	15,6
1	236	49,0
2	84	17,4
3	30	6,2
4	28	5,0
5	29	6,0

\* Radiographic grade according to Larsen et al (1977) standard radiographs.

## CHAPTER 9

### HANDS

- 9.1 Resorptive arthropathy
- 9.2 Clinical assessment of the hands
- 9.3 Handedness and the prevalence of deformities, severity of radiographic changes and function of the hands.

## CHAPTER 9.1

### RESORPTIVE ARTHROPATHY

#### INTRODUCTION

Resorptive arthropathy is defined as an articular disorder which is characterised by severe resorption of bone commencing at the articular surface or its margins and spreading proximally and distally (Swezey et al 1972). It predominantly affects the hands and feet and may produce redundant overlying skin as a consequence of the loss of underlying bone.

The first recorded description of a case of resorptive arthropathy was by Bourdillon in his doctoral thesis in 1888 (Swezey et al 1972). The term 'La Main en Lorgnette' (opera glass hand) was used initially by Marie and Leri in 1913 to report a patient with polyarthritits whose fingers were shortened with excessive skin folds and gave the impression that the phalanges were retracted into one another like an opera glass (Solomon and Stecher 1950). In 1972, Swezey et al reviewed the problem of resorptive arthropathy and noted that the majority of the 51 cases who had been reported were associated with RA or psoriasis (Swezey et al 1972). Resorptive arthropathy or arthritis mutilans is one of the clinical patterns of psoriatic arthritis and occurs in about 5% of patients with psoriatic arthritis (Wright and Moll 1976). An Institute of Medical Literature search of the English

Literature over the past 20 years revealed only 3 reports on RA and resorptive arthropathy (Swezey et al 1972, Swezey et al 1973, Nalebuff and Garrett 1976). Many of the patients reported with RA and resorptive arthropathy were documented prior to the use of diagnostic criteria for RA and the availability of tests for rheumatoid factor.

The aim of this survey was to determine the prevalence of resorptive arthropathy in RA and to determine whether these patients have any characteristic clinical or serological features.

## RESULTS

There were 13 patients who had a resorptive arthropathy based on the clinical finding of shortening of the digits with redundant skin folds, and radiographic evidence of resorption of the articular surfaces. The overall prevalence of resorptive arthropathy was 5,1%. The prevalence in Coloureds was 5,8%, in Caucasians 4% and in Africans 5,8%.

The clinical findings in these 13 patients were analysed further and compared with the total study population. The age, sex ratio and the duration of RA was compared with a previously reported group of 13 patients (Nalebuff and Garrett 1976) and with the results of the total study population (Table 9.1.1). A comparison of the functional classification, presence of nodules, rheumatoid factor and anti-nuclear factor is shown in Table 9.1.2.

The radiographs of all the patients were graded according to the Larsen et al standard radiographs and the mean values for the wrists, hands and feet are summarised in Table 9.1.3 (Larsen et al 1977). Five of the 13 patients with resorptive arthropathy had total hip replacement which was bilateral in 3 patients. The mean radiographic score for the shoulder was 3,6 (maximum possible score 5). The radiographs of the cervical spine showed evidence of AAS in 4 patients and 2 patients had evidence of AAI. There were 4 patients in whom cranial settling could not be adequately assessed on the available plain radiographs.

The resorptive changes were most frequently noted in the MCP and PIP joints, ulnar styloid and MTP joints in the feet, as shown in Figure 9.1.1. The severity of the changes varied in different individuals. Some patients may have early resorptive changes such as the tongue in groove deformity (Nalebuff and Garrett 1976) while others have the characteristic egg cup deformity or marked whittling of the ends of the phalanges (Figure 9.1.1). Radiographic changes in the carpal bones in the wrists ranged from severe resorptive changes to ankylosis. Severe resorptive changes were also detected in the elbows, shoulders and hips.

## DISCUSSION

The pathological features which were noted in the first RA patient described by Marie and Lerii (Solomon and Stecher 1950) were fatty replacement of articular structures, granulation tissue between bony

structures and sparing of tendons, nerves and blood vessels except for mild endarterial thickening. The occurrence of severe destructive and resorptive changes in resorptive arthropathy associated with RA and psoriatic arthritis has a strong resemblance to the resorptive changes seen in Charcot's joints. However, nerve conduction studies and electromyographic studies have not demonstrated any evidence of a neurologic disorder in patients with resorptive arthropathy (Swezey et al 1973). The prevalence of resorptive arthropathy in this study was 5,1%, which is similar to the prevalence of about 5% which has been noted in psoriasis (Wright and Moll 1976). The mean age of 49,2 years and mean duration of RA of 19,8 years was similar to the previously recorded findings (Nalebuff and Garrett 1976). There was only one male in the 13 patients reported by Nalebuff and Garrett, while in the present study the female to male ratio was 2,3 : 1, which is similar to the overall population of RA patients (Nalebuff and Garrett 1976). The patients with resorptive arthropathy had their disease for a mean duration of 19,8 years in comparison with 12,3 years for the total study population.

The clinical and laboratory features of a relatively large group of patients with resorptive arthropathy have been infrequently reported (Nalebuff and Garrett 1976, Solomon and Stecher 1950). There was no difference in the prevalence of subcutaneous nodules in the patients with resorptive arthropathy and the total study group. Although 69,2% of the patients with resorptive arthropathy had a positive rheumatoid factor at some stage of their disease, only 38,5% had a positive rheumatoid factor at the time of assessment. Therefore, it is likely

that because many of the patients had burnt out disease, they may have become seronegative. A more severe functional disability was noted in the resorptive arthropathy patients as 38,5% belonged to class 3 and 4.

There was a marked increase in the severity of the radiographic changes, based on the Larsen score, in the resorptive arthropathy patients in the hands, feet and wrists. Severe involvement was also present in the hips as 5 of the 13 patients (38,5%) had hip arthroplasty compared to 16 (6,6%) of the remaining 243 patients in the study.

In conclusion, the prevalence of resorptive arthropathy in RA was 5,1%. Patients with resorptive arthropathy tended to have disease of longer duration and a lower prevalence of seropositivity but the mean age and sex ratio were similar to other patients. There was no significant difference in the prevalence of subcutaneous nodules in the two groups but radiographic changes were much more severe in patients with resorptive arthropathy. Hip arthroplasty was also performed more frequently in these patients.

TABLE 9.1.1DEMOGRAPHIC DATA

	Resorptive Arthropathy Group (n=13)	Nalebuff and Garrett (1976) (n=13)	Total Study Group (n=256)
Age (in years)			
Mean	49,2	49	52,8
Range	36-63	33-72	21-81
Duration (in years)			
Mean	19,8	22	12,3
Range	3,3-34	8-47	0,5-50
Female : Male Ratio	2,3:1	12:1	2,8:1

TABLE 9.1.2CLINICAL AND LABORATORY DATA

	Number (n=13)	Percent	Total Study Group - Percent
Nodules	4	30,8	28,1
Seropositive			
Past or present	9	69,2	78,9
Present	5	38,5	61,5
Positive ANF	3	23,1	36,0
Functional Class (ARA)			
1	0	0	25,8
2	8	61,5	52,3
3	3	23,1	14,5
4	2	15,4	7,4

TABLE 9.1.3

MEAN RADIOGRAPHIC SCORE BASED ON THE LARSEN et al (1977)  
STANDARD RADIOGRAPHS

Joints (Right & Left)	Maximum possible Score	Resorptive Arthropathy Group	Total Study Population*
MCP 1 - 5 IP thumb + (2 - 5 PIP)	100	79,6	35,7
Wrists	10	9,6	5,7
IP Big Toe + (2 - 5 MTP)	50	37,8	19,4

\* Patients who had joint surgery or severe deformity where grading was not possible were excluded and the mean scores of 188 patients were recorded.





FIGURE 9.1.1. (A) Resorption of the ulnar styloid, collapse of the carpal bones with ankylosis of the wrist, 'pencil-in-cup' deformities of the MCP joints and earlier resorptive changes in the PIP joints. (B) Resorption of the ulnar styloid with ankylosis of the radio-carpal, inter-carpal and carpometacarpal joints. (C) The PIP joints show the 'tongue-in-groove' configuration. (D) Resorption of the 1st metatarsal head with subluxation and resorption of the proximal phalanx. There is also resorption of the heads of the 2nd to 5th metatarsals. (E) Marked osteoporosis with severe resorption of the 1st to 3rd metatarsal heads.

## CHAPTER 9.2

### CLINICAL ASSESSMENT OF THE HAND

#### INTRODUCTION

RA has a predilection for the small joints of the hands and may affect the function of the hand in many different ways. RA is a systemic disease and factors which may contribute to impaired hand function are joint synovitis, tendon synovitis, muscle lesions, nerve lesions and vasculitis. A combination of factors contribute to the development of deformities characteristic of RA such as the swan neck deformity, boutonniere deformity, ulnar deviation and volar subluxation of the metacarpophalangeal joint and various types of deformities of the thumb. Over the past two decades there have been major advances in the surgical management and in the understanding of factors which contribute to impaired function of the hand. The subject of hand involvement in the rheumatic diseases has been reported in detail in two recent excellent books (Wyn Parry 1984, Flatt 1983).

The aim of this study was to undertake a clinical assessment of the hand to determine the prevalence, distribution and severity of hand involvement in RA.

## RESULTS

### 1. GENERAL

A history of present or past pain in the hands was obtained in 252 patients (98,4%). Tenderness of the MCP joints at time of assessment was noted in both hands in 73 patients (28,5%) and in one hand in 61 patients (23,8%). Tenderness of the PIP joints was present in both hands in 17,2% and in one hand in 37 patients (14,5%).

### 2. THUMB

#### a) DEFORMITIES

The commonest deformity noted in the thumb was the Z shaped deformity or Nalebuff type 1 deformity which was present in 62 hands (12,2%). The type 2 deformity was noted in 9 hands (1,8%) while the type 3 and type 4 deformity were each noted in only one hand (0,2%). Arthritis mutilans of the thumb was noted in 16 thumbs (3,1%) in 9 patients (3,5%).

#### b) SWELLING

Swelling of the carpometacarpal joint was noted in 20 hands (3,9%); it was mild in 12 (2,3%) and moderate in 8 hands (1,6%). Swelling of MCP joints was present in 183 hands (35,7%); it was mild in 99 joints (19,3%), moderate in 59 (11,5%) and severe in 25 (4,9%). The interphalangeal joint was swollen in 93 hands (18,2%); the swelling was mild in

72 joints (14,1%), moderate in 16 (3,1%) and severe in 5 (1%).

c) APPOSITION SCORE

The apposition score for the hands was recorded in 500 hands (250 patients) and the results are summarised in Table 9.2.1. Full apposition of the thumb to the base of the little finger was possible in 65,4% of the hands, a score of 4 was recorded in 23,8% and a more severe disability (score 0 to 3) was noted in 54 hands (19,8%). The combined apposition score for the right and left thumbs is shown in Table 9.2.2.

3. SWAN-NECK DEFORMITY

A swan-neck deformity (SND) of one or more fingers was noted in 74 patients (28,9%); the mean number of fingers involved was 3,5 per patient; a deformity was noted in 122 fingers (11,9%) in the right hand and 140 fingers (13,7%) in the left hand (Table 9.2.3); the deformities were mobile in 110 fingers (42,0%) partially fixed in 136 (51,9%) and fixed in 16 (6,1%). The number of fingers with a SND is shown in Table 9.2.4. A SND was present in 15,6% of the middle fingers (ie, 80 fingers in the right and left hand), 13,5% of the ring, 11,7% of the index and 10,4% of the little fingers.

#### 4. BOUTONNIERE DEFORMITY

There were 61 patients (23,8%) who had a boutonniere deformity of one or more fingers of the right or left hand; a mean of 2,1 fingers were affected per patient; it was noted in 67 fingers (6,5%) in the right hand and in 64 fingers (6,3%) in the left hand (Table 9.2.5); the deformities were mobile in 87 fingers (66,4%), partially fixed in 43 (32,8%) and fixed in only one finger (0,8%). The number of fingers which were affected is shown in Table 9.2.4. The deformity was noted in the ring fingers in 9,6% (ie, 49 ring fingers of the right and left hand), in 9,2% of the middle, 5,5% of the little and 1,4% of the index fingers.

#### 5. EXTENSOR TENDON DISLOCATION OR RUPTURE

There was abnormality of the extensor tendon in 137 fingers (13,3%) in the right hand and in 120 fingers (11,7%) in the left hand; tendon dislocation on motion was noted in 69 fingers (26,8%), tendon dislocation at rest in 186 fingers (72,4%) and tendon rupture in 2 fingers (0,8%) as shown in Table 9.2.6.

#### 6. METACARPOPHALANGEAL JOINT SUBLUXATION OR DISLOCATION

Subluxation of the MCP joints was noted in 199 fingers (19,4%) in the right hand and 164 fingers (16,0%) in the left hand; the subluxation was reducible in 100 fingers (27,6%) and irreducible

in 263 fingers (72,4%) as shown in Table 9.2.7. Irreducible subluxation or dislocation of the fingers was noted in 14,5% of the index fingers, 15,8% of the middle, 11,1% of the ring and 10,0% of the little fingers of the right and left hand.

#### 7. ULNAR DEVIATION

Ulnar deviation involving one or more fingers of the right and/or left hand was noted in 44 patients (17,2%); there was involvement of 95 fingers (9,3%) in the right hand and 97 fingers (9,5%) in the left hand. When the fingers of both hands were considered together, ulnar deviation was present in 46 index fingers (9,0%), 49 middle (9,6%), 48 ring (9,4%) and 49 little fingers (9,6%). The number of fingers which showed ulnar deviation is shown in Table 9.2.4.

#### 8. FLEXOR TENOSYNOVITIS

Flexor tenosynovitis was present in 221 (17,3%) fingers in the right hand and in 193 fingers (15,1%) in the left hand (Table 9.2.8); there were 145 patients (56,6%) who had flexor tenosynovitis of one or more fingers of the right or left hand and a mean of 2,9 fingers were involved per patient. The fingers which were most frequently involved were the index in 139 patients (27,1%) and the middle in 121 patients (23,6%). The ring (12,9%) and the little fingers (10,0%) were less frequently involved and the thumb was involved in only 37 patients (7,2%).

9. ASSESSMENT OF FUNCTION OF THE HAND

The distance from the tips of the fingers to the proximal palmar crease was measured in millimetres (mm) and the mean values for each of the fingers in the right and left hand and the overall means for both hands are shown in Table 9.2.9. The impairment of function was most severe in the index finger followed by the middle, ring and little fingers respectively for both the right and left hands. The distribution of the scores for each of the fingers is shown in Table 9.2.10.

10. COMPARISON OF THE PREVALENCE OF FTS, DEFORMITIES AND HAND FUNCTION IN THE 3 RACES

The number of people who had FTS, SND, BD and UD in the different races is shown in Table 9.2.11. There was no significant difference in the prevalence of SND and FTS. Boutonniere deformity was more common in Africans in comparison with Caucasians (Fisher's exact test  $p=0,0076$ ) and UD was commoner in Caucasians when compared to Africans (Fisher's exact test:  $p=0,0064$ ).

The mean number of fingers with FTS, SND, BD and UD is shown in Table 9.2.12; there was no significant difference among the races in the prevalence of FTS; SND was commoner in Coloureds in comparison with Africans ( $p=0,0045$ ); BD was commoner in Africans ( $p=0,0017$ ) and Coloureds ( $p=0,0157$ ) in comparison with Caucasians

and UD was commoner in Caucasians than Africans ( $p=0,0105$ ).

The mean values for the total distance from the tip of the fingers to the palmar crease for all the fingers of the right and left hand is shown in Table 9.2.13. The values for Africans were significantly lower than the Coloureds ( $p=0,0002$ ) and the Caucasians ( $p=0,0002$ ).

## DISCUSSION

The involvement of the thumb in RA results in the disturbance of the normal biomechanics; activities such as buttoning of clothing or manipulation of small objects may be difficult due to lack of control or instability of the thumb (Nalebuff 1984). Initially four types of thumb deformities were reported (Nalebuff 1984). The commonest type of deformity in the thumb is the Nalebuff type 1 or Z shaped deformity which was noted in 62 hands (12,2%).

The clinical and histological pattern of tendon lesions in RA were reported by Kellgren and Ball (Kellgren and Ball 1950). The prevalence of flexor tenosynovitis ranged from 5% - 38% in different clinical studies reviewed by Gray and Gottlieb; they noted FTS in 55% of their 100 patients and a mean of 3,1 tendons were involved per patient (Gray and Gottlieb 1977). There were 145 patients (56,6%) who had FTS in the present survey and the mean number of tendons involved per patient was 2,9. The tendons which were most frequently involved were the index and middle fingers followed by the ring,

little finger and thumb, in decreasing order of frequency; these findings are similar to the observations by Gray and Gottlieb (Gray and Gottlieb 1977).

A SND of the fingers was detected in 28,9% of the patients and the mean number of fingers involved was 3,5 per patient in comparison with a BD which was detected in 23,8% and the mean number of fingers involved was 2,1 per patient. The prevalence of SND in the different fingers ranges from 15,6% for the middle fingers to 10,4% for the little fingers. A BD was most commonly noted in the middle and ring fingers and was present in only 1,4% of the index fingers (ie, 7 index fingers in the right and left hands). A BD is due to rupture of the central extensor tendon and its transverse fibres, usually as a result of synovitis of the PIP joint (Tubiana and Toth 1984). Since synovitis is frequently noted in the index finger, the reason for the rarity of a BD in the index finger is unclear.

Various mechanisms have been proposed for the development of ulnar drift and they include articular, tendinous, muscular, the metacarpal descent and the physiological action of the thumb (Tubiana and Toth 1984). Ulnar deviation of the fingers was detected in 17,2% of our patients in comparison with 27% of 300 patients and 21,2% of 292 patients in other studies (Brewerton 1957, Vainio and Oka 1953). There was nearly equal involvement of all the fingers in our study but Brewerton noted that the medial fingers were more frequently involved (Brewerton 1957).

The assessment of the function of the hand is essential to assess

disability, plan rehabilitation and surgery, and then to assess the response to the different forms of therapy. A detailed functional assessment is usually conducted by an occupational therapist and various schemes have been recommended in the assessment of hand function (Clawson et al 1971, Swanson et al 1983, Treuhaft et al 1971, Evans and Lawton 1984). In the present survey the function of the thumb was assessed by determining the apposition score which depended to a variable extent on abduction, apposition and flexion. Although the apposition score is also dependant on flexion of the fingers, it was used as it provided a simple index of thumb function. There was some impairment of full apposition in one third of the hands but this was not severe in most of the patients.

The ability of the patient to flex the finger fully may be reduced if there is impaired flexion of either the MCP, PIP, and DIP joints and also with the presence of FTS and stiffness of the intrinsic muscles. The carpometacarpal joints of the ring and little fingers also make a small but important contribution to full flexion of these fingers (Brewerton 1957). The flexion of the fingers was most severely limited in the index fingers with less severe involvement of the middle, ring and little fingers respectively. Interracial comparison showed that the finger tip to palmar crease distance was significantly lower in Africans in comparison with the Coloureds and Caucasians. Therefore, overall hand function was significantly better in Africans.

Involvement of the hands is common in RA. There were 74 patients (28,9%) who had a swan neck deformity, 61 patients (23,8%) had a

boutonniere deformity, 44 patients (17,2%) had ulnar deviation and 56,6% had flexor tenosynovitis of one or more fingers. There was more severe impairment of hand function in Caucasians in comparison with Africans.

TABLE 9.2.1

APPOSITION SCORE

SCORE	COLOUREDS (n=204)	CAUCASIANS (n=196)	AFRICANS (n=100)	TOTAL (n=500)	TOTAL %
0	3	2	0	5	1,0
1	8	11	2	22	4,4
2	4	4	0	8	1,6
3	7	11	1	19	3,8
4	49	54	16	119	23,8
5	133	114	81	328	65,4

TABLE 9.2.2

APPOSITION SCORE (COMBINED FOR BOTH HANDS)

TOTAL SCORE (0-10)	COLOUREDS (n=102)	CAUCASIANS (n=98)	AFRICANS (n=50)	TOTAL (n=250)	TOTAL %
1	2	1	0	3	1,2
2	2	2	1	5	2,0
3	1	2	0	3	1,2
4	0	2	0	2	0,8
5	2	3	0	5	2,0
6	4	3	0	7	2,8
7	5	6	0	11	4,4
8	16	20	8	44	17,6
9	8	10	2	20	8,0
10	62	49	39	150	60,0

TABLE 9.2.3

PREVALENCE OF SWAN NECK DEFORMITIES

	INDEX (n=256)	MIDDLE (n=256)	RING (n=256)	LITTLE (n=256)	TOTAL (n=1024)	TOTAL %
Right Hand	28	36	34	24	122	11,9
Left Hand	32	44	35	29	140	13,7
TOTAL	60	80	69	53	262	12,8
Mobile	22	33	34	21	110	42,0
Partially Fixed	36	45	30	25	136	51,9
Fixed	2	2	5	7	16	6,1

TABLE 9.2.4

THE NUMBER OF FINGERS WHICH HAD A SWAN NECK DEFORMITY (SND),  
BOUTONNIERE DEFORMITY (BD), FLEXOR TENOSYNOVITIS (FTS)  
AND ULNAR DEVIATION. (n=256)

NUMBER OF FINGERS	SND	BD	FTS	ULNAR DEVIATION
0	182	195	115	212
1	19	25	43	6
2	12	18	32	8
3	13	10	27	2
4	7	5	19	13
5	6	0	10	0
6	4	1	7	2
7	6	2	3	4
8	7	0	0	9

TABLE 9.2.5

PREVALENCE OF BOUTONNIERE DEFORMITIES

	INDEX	MIDDLE	RING	LITTLE	TOTAL	TOTAL %
Right Hand (n=256)	3	26	28	10	67	6,5
Left Hand (n=256)	4	21	21	18	64	6,3
TOTAL (n=512)	7	47	49	28	131	6,4
Mobile	6	32	30	19	87	66,4
Partially Fixed	1	15	18	9	43	32,8
Fixed	0	0	1	0	1	0,8

TABLE 9.2.6

EXTENSOR TENDON DISLOCATION OR RUPTURE

	INDEX	MIDDLE	RING	LITTLE	TOTAL	TOTAL %
Right hand (n=256)	24	35	36	42	137	13,4
Left Hand (n=256)	20	26	28	46	120	11,7
TOTAL (n=512)	44	61	64	88	257	12,5
Tendon Dislocation						
a) on motion	18	11	11	29	69	26,8
b) at rest	26	49	53	58	186	72,4
Tendon Rupture	0	1	0	1	2	0,8

TABLE 9.2.7

METACARPOPHALANGEAL SUBLUXATION OR DISLOCATION

	INDEX	MIDDLE	RING	LITTLE	TOTAL	TOTAL %
Right Hand (n=256)	51	59	45	44	199	19,4
Left hand (n=256)	48	45	38	33	164	16,0
TOTAL (n=512)	99	104	83	77	363	17,7
<b>Reducible</b>						
Subluxation	25	23	26	26	100	27,6
<b>Irreducible</b>						
Subluxation	74	81	57	51	263	72,4

TABLE 9.2.8

PREVALENCE OF FLEXOR TENOSYNOVITIS

FINGER	RIGHT HAND (n=256)	LEFT HAND (n=256)	TOTAL (n=512)	TOTAL %
Thumb	13	24	37	7,2
Index	81	58	139	27,1
Middle	71	50	121	23,6
Ring	33	33	66	12,9
Little	23	28	51	10,0
TOTAL	221	193	414	

TABLE 9.2.9MEAN DISTANCE FROM FINGER TIPS TO PROXIMAL PALMAR CREASE

FINGER	RIGHT HAND	LEFT HAND	OVERALL MEAN
Index	26,0	24,2	25,1
Middle	22,7	21,6	22,2
Ring	19,8	17,9	18,9
Little	13,2	12,2	12,7
TOTAL	80,7	75,9	

TABLE 9.2.10

DISTRIBUTION OF FUNCTIONAL SCORES FOR EACH FINGER

DISTANCE IN MM	RIGHT HAND				LEFT HAND			
	2 (n=251)	3 (n=252)	4 (n=253)	5 (n=253)	2 (n=252)	3 (n=253)	4 (n=251)	5 (n=251)
0-5	17	67	98	142	38	82	112	143
6-10	22	20	20	11	20	17	13	16
11-20	70	40	28	28	57	38	31	25
21-30	56	42	33	26	56	36	32	30
31-40	38	31	29	18	38	32	20	10
41-50	23	21	17	7	20	20	17	12
51-60	13	17	10	14	14	12	11	10
60	12	14	18	7	9	16	15	5

TABLE 9.2.11

THE PREVALENCE OF DEFORMITIES OF THE HANDS IN THE DIFFERENT RACES

(percentages in parentheses)

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	p VALUE
FTS	54 (51,9)	64 (64,0)	27 (51,9)	145 (56,6)	0,1637
SND	36 (34,6)	29 (29,0)	9 (17,3)	74 (28,9)	0,0799
BD	26 (25,0)	16 (16,0)	19 (36,5)	61 (23,8)	0,0176
UD	17 (16,3)	24 (24,0)	3 ( 5,8)	44 (17,2)	0,0176

TABLE 9.2.12

THE MEAN NUMBER OF FINGERS WITH DEFORMITIES IN THE DIFFERENT RACES

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)
FTS	1,413+1,924	1,960+2,093	1,365+1,738	1,617+1,969
SND	1,356+2,417	0,951+1,882	0,500+1,291	1,029+2,043
BD	0,567+1,275	0,230+0,584	0,942+1,501	0,512+1,144
UD	0,615+1,603	1,120+2,388	0,308+1,462	0,750+1,944

TABLE 9.2.13

COMPARISON OF THE MEAN FINGERTIP TO PALMAR CREASE DISTANCE  
IN THE 3 RACES

	MEAN OF TOTAL SCORE	MEAN PER FINGER
COLOURED	174,495 + 152,742	21,812 + 19,093
CAUCASIANS	169,030 + 127,642	21,336 + 16,265
AFRICANS	96,860 + 96,460	12,309 + 12,241
TOTAL	156,992 + 136,211	19,746 + 17,156

### CHAPTER 9.3

## HANDEDNESS AND THE PREVALENCE OF DEFORMITIES, SEVERITY OF RADIOGRAPHIC CHANGES AND FUNCTION OF THE HAND

### INTRODUCTION

When patients with hemiplegia or poliomyelitis develop rheumatoid arthritis (RA), the paralysed muscles are either spared or less severely involved (Thompson and Bywaters 1962, Glick 1967). The most likely explanation for the asymmetrical involvement is the relative lack of use of the paralysed limb (Thompson and Bywaters 1962). Physical rest or immobilization is a beneficial form of therapy and has been shown to have a potent anti-inflammatory effect (Lee et al 1974, Partridge and Duthie 1963). Bone cysts or geodes have been reported more frequently in patients with RA who do heavy manual work because the inflamed synovium may be forced into the porous cancellous bone (Castilo et al 1965, Gaunt and Rinker 1970, Jayson et al 1970).

The factors which contribute to the development of deformities of the hands are the structural changes of RA together with the forces involved in the use of the hands (Kemble 1977, Smith et al 1966, Elison et al 1971). Hakstian and Tubiana emphasized the importance of tissue destruction in the production of deformity and stated that external forces of hand use only have a secondary effect (Hakstian and Tubiana 1967). Hasselkus et al studied the relationship between

handedness and clinical involvement of the hand in RA, and did not find any evidence of significantly greater joint destruction in the dominant hand (Hasselkus et al 1981). However, increased severity of radiographic changes has been reported in the dominant hand (Mattingly et al 1979, Owsianik et al 1980).

The aim of this survey was to determine

- a) Whether there was a relationship between handedness and
  - i) the prevalence of SND, BD, FTS and ulnar deviation
  - ii) the severity of radiographic changes in the hands
  - iii) the function of the hand based on the assessment of the finger tip to palmar crease distance for all the fingers.
- b) Whether there were any differences in the distribution of the deformities, the severity of radiographic changes and function in the different fingers.
- c) The factors which contributed to impaired flexion of the fingers.

## RESULTS

### 1. DEFORMITIES OF THE FINGERS

The prevalence of FTS, SND, BD and ulnar deviation in the different fingers of the right and left hand is shown in Table 9.3.1. There was no significant difference in the proportion of patients who had SND, BD, FTS and uncorrectible UD in the right hand in comparison with the left hand.

The prevalence of FTS or deformity in a finger was compared with other fingers of the same hand and the results which were significantly different were as follows (the test level of significance was adapted according to Bonferroni):-

A. SWAN NECK DEFORMITY

- i) Right hand - the middle and ring fingers were more than the little finger
- ii) Left hand - the middle finger was more than the little finger

B. BOUTONNIERRE DEFORMITY

- i) Right hand - the middle and ring finger were more than the index and little fingers
- ii) Left hand - the middle, ring and little finger were more than the index finger

C. FLEXOR TENOSYNOVITIS

- i) Right hand - the index and middle fingers were more than the thumb, ring and little fingers; and the ring finger was more than the thumb
- ii) Left hand - the index finger was more than the thumb, ring and little fingers; and the middle finger was more than the thumb and little fingers

D. ULNAR DEVIATION

There were no significant differences in the prevalence of

ulnar deviation in the different fingers.

## 2. RADIOGRAPHIC FINDINGS

The mean Larsen scores for all the individual joints and groups of joints are shown in Table 9.3.2. The mean Larsen score for all the MCP and the PIP joints (including the IP joints of the thumb) was significantly higher for the right hand than the left hand ( $p < 0,001$ ). When the MCP + PIP joints were compared separately, the mean values for the right hand were also significantly higher than the left hand. The combined score for each finger (MCP and PIP) was compared with the corresponding finger in the the opposite hand and the values for all the fingers were significantly greater in the right hand (Table 9.3.3). The comparison of the mean radiographic score for each finger with the other fingers of the same hand is shown in Table 9.3.4.

## 3. ASSESSMENT OF HAND FUNCTION

The mean distance from the tip of the finger to the proximal palmar crease for each finger is shown in Table 9.3.5. The overall mean distance for the right hand was greater than the left hand ( $p=0,0174$ ). The mean values were highest for the index fingers followed by the middle, ring and little fingers. The mean distance for each finger was compared with the other fingers of the same hand; the values for all the fingers in the left hand

were significantly different from each other while in the right hand all the fingers were significantly different from each other except the middle and ring fingers.

4. RELATIONSHIP BETWEEN FLEXION SCORE AND THE RADIOGRAPHIC SCORE, THE PRESENCE OF FTS OR DEFORMITIES OF THE FINGERS

The clinical data on the hands was studied further to determine whether there was a relationship between the flexion score for each finger, and the severity of the radiographic score for the same finger (combined Larsen score for the MCP and PIP joints of a finger) or the presence of FTS, SND, BD and ulnar deviation in the same finger. A linear relationship was found between the flexion score and the radiographic score for each finger ( $p < 0,001$  for all the fingers of the right and left hand) and also the presence of SND ( $p < 0,05$  for all the fingers of the right hand and the left index, middle and ring fingers). When stepwise multiple linear regression was applied, it was found that either the radiographic score alone or both of these variables (radiographic score and the presence of SND) contributed significantly to explaining the variation in the flexion score as follows: the radiographic score alone for the right ring and little fingers and the left middle, ring and little fingers; and both the radiographic score and presence of SND for the right index and middle fingers and the left index fingers.

## DISCUSSION

The presence of significantly greater damage in the dominant hand on radiological assessment has been reported by Mattingly et al in a study of 30 patients and Owsianik et al who studied 20 patients with RA (Mattingly et al 1979, Owsianik et al 1980). In the present study of 210 patients, these findings were confirmed and there was significantly greater involvement of the dominant hand ( $p < 0,0001$ ).

Dickson et al measured the flexion and pinch force of the fingers and found that the index and middle fingers were significantly stronger than the ring and little fingers (Dickson et al 1972). The earliest erosions in the MCP joints were found to occur in the index and middle fingers (Martel et al 1965). Mattingly et al also found that the MCP joints of the index and middle fingers were more severely damaged than the other MCP joints and these findings were confirmed in this survey (Mattingly et al 1979). The combined MCP and PIP score for each finger was highest for the index and middle fingers in the right and left hands except for the right index and right little fingers (Table 4). It is likely that the severe changes in the index and middle fingers occur because of the greater use of these fingers. The combined score for the thumb (MCP and IP) was significantly less than the combined score (MCP and PIP) for each of the other fingers in the right and left hands. Mattingly et al also found that the joint damage was least severe in the thumb (Mattingly et al 1979).

The prevalence of ulnar deviation and handedness has been studied

previously and conflicting results have been noted (Kemble 1977, Fearnley 1951, Treuhaft et al 1971, Lush 1952). There were no significant differences in the prevalence of ulnar deviation, SND, BD and FTS in the dominant and non-dominant hand in this study. An analysis of the factors which may contribute to impaired function of a finger (flexion score), showed that the most important factors were the severity of radiographic changes and the presence of SND.

In conclusion, there was significantly greater radiographic involvement of the dominant hand and the index and middle fingers were most severely involved. The function of the hand was also more severely impaired in the dominant hand. The severity of radiographic changes and the presence of SND were the most important factors which contributed to impaired function of the fingers. There was no significant difference in the prevalence of FTS, SND, BD and ulnar deviation in the dominant and non-dominant hand.

TABLE 9.3.1

PREVALENCE OF SND, BD, UD AND FTS IN THE DIFFERENT FINGERS  
(n=210)

DEFORMITY		F I N G E R				
		THUMB	INDEX	MIDDLE	RING	LITTLE
SND	(R)		25	33	31	31
	(L)		30	41	32	25
BD	(R)		3	24	25	10
	(L)		4	19	20	18
FTS	(R)	11	74	63	30	21
	(L)	23	54	46	30	25
UD	(R)		20	23	24	26
	(L)		24	25	22	21

TABLE 9.3.2

COMPARISON OF THE LARSEN SCORE FOR THE PIP AND MCP JOINTS  
OF THE RIGHT AND LEFT HANDS

JOINT	RIGHT (Mean $\pm$ SD)	LEFT (Mean $\pm$ SD)	NUMBER	p VALUE*
IP THUMB	1,443 $\pm$ 1,102	1,405 $\pm$ 1,027	210	0,4940
PIP INDEX	1,699 $\pm$ 1,173	1,512 $\pm$ 1,097	210	0,0019
PIP MIDDLE	1,967 $\pm$ 1,321	1,719 $\pm$ 1,254	210	0,0030
PIP RING	1,900 $\pm$ 1,422	1,771 $\pm$ 1,270	210	0,1112
PIP LITTLE	1,838 $\pm$ 1,370	1,686 $\pm$ 1,216	210	0,0478
MEAN OF ALL PIP + IP THUMB	8,838 $\pm$ 5,238	8,086 $\pm$ 4,721	210	0,0004
MCP THUMB	1,867 $\pm$ 1,276	1,695 $\pm$ 1,121	210	0,0336
MCP INDEX	2,462 $\pm$ 1,593	2,409 $\pm$ 1,575	210	0,5301
MCP MIDDLE	2,252 $\pm$ 1,502	2,176 $\pm$ 1,513	210	0,3882
MCP RING	1,924 $\pm$ 1,432	1,790 $\pm$ 1,395	210	0,0848
MCP LITTLE	2,114 $\pm$ 1,517	1,833 $\pm$ 1,385	210	0,0005
MEAN OF ALL MCP	10,619 $\pm$ 6,125	9,905 $\pm$ 5,819	210	0,0024
MEAN OF ALL PIP + MCP	1,947 $\pm$ 0,072	1,799 $\pm$ 0,065	210	<0,0001

\* paired t-test

TABLE 9.3.3  
COMPARISON OF LARSEN SCORE FOR EACH FINGER (MCP + PIP) WITH  
THE CORRESPONDING FINGER IN THE OPPOSITE HAND

MEAN SCORE	RIGHT	LEFT	NUMBER	p VALUE*
THUMB	3,309+ <u>1,991</u>	3,100+ <u>1,729</u>	210	0,0311
INDEX	4,167+ <u>2,361</u>	3,933+ <u>2,203</u>	210	0,0049
MIDDLE	4,219+ <u>2,339</u>	3,895+ <u>2,277</u>	210	0,0030
RING	3,824+ <u>2,409</u>	3,562+ <u>2,294</u>	210	0,0164
LITTLE	3,952+ <u>2,480</u>	3,519+ <u>2,141</u>	210	0,0002

\* paired t-test

TABLE 9.3.4  
PAIRWISE COMPARISON OF THE MEANS OF THE TOTAL SCORE (PIP + MCP)  
FOR EACH FINGER WITH OTHER FINGERS OF THE SAME HAND\*

	FINGER				
RIGHT	3	2	5	4	1
	<u>4,219+2,339</u>	<u>4,167+2,361</u>	<u>3,952+2,480</u>	<u>3,824+2,409</u>	<u>3,309+1,991</u>
LEFT	2	3	4	5	1
	<u>3,933+2,203</u>	<u>3,895+2,277</u>	<u>3,562+2,294</u>	<u>3,519+2,141</u>	<u>3,100+1,729</u>

\*NB: 1) Two means not underlined by the same continuous line differ significantly

2) Comparison by means of the paired t-test with test level of significance adapted according to Bonferroni

TABLE 9.3.5

PAIRWISE COMPARISON OF THE MEAN VALUES OF THE FINGER TIP TO PALMAR  
CREASE DISTANCE FOR THE RIGHT AND LEFT HANDS (n = 224)

	RIGHT HAND (Mean + SD)	LEFT HAND (Mean + SD)	p VALUE *
2	26,013+16,782	24,017+18,385	0,0329
3	22,629+20,830	21,106+21,442	0,1220
4	19,865+21,594	17,914+21,122	0,2442
5.	12,960+18,708	11,978+17,229	0,2442
TOTAL (R)	20,366+17,996	18,754+17,763	0,0174

\* paired t-test

## CHAPTER 10

### FEET

#### INTRODUCTION

Although involvement of the foot has been recognised as an important source of pain and disability in rheumatoid arthritis (RA), the feet have been relatively neglected by physicians and rheumatologists (Dixon 1981).

Rheumatoid involvement of the feet was noted in 91,3% of 618 females and 84,9% of 337 males in Finland (Vaino 1969). Ismein and Fournier noted clinical involvement of the feet in 85% and radiological involvement in 77% (Ismein and Fournier 1967). Radiological changes in the feet were noted in 90% of 105 patients with classical RA whereas changes in the hands were noted in 75% (Thould and Simon 1966).

The radiographic evaluation of RA by the use of standard reference films has been reported (Larsen et al 1977). The reference films for the hands and wrists have been shown to have a high reproducibility in many studies (Larsen et al 1979, Grindulis et al 1983, Scott et al 1985). However, the standard radiographs of the other joints have not been studied frequently.

The aim of this study was:

- (i) to determine the frequency of clinical involvement of the ankle, subtalar joint, midtarsal joints and the forefoot in RA.
- (ii) to study the frequency and severity of radiological involvement of the ankles and forefoot based on the Larsen et al standard radiographs in a large group of patients (Larsen et al 1977).

## RESULTS

### (1) ANKLES

A history of pain in the hindfoot (past or present) was obtained in 213 patients (83,2%). This pain was interpreted as ankle joint pain but may have arisen from the subtalar joint or periarticular structures in some of the patients. Tenderness of the ankles was noted at the time of assessment in 69 patients (27%). Swelling of the ankles was noted in 45 joints (8,8%) or 33 patients (12,9%) at the time of assessment while a past history of swelling of the ankles was obtained in a further 281 joints (55,1%) or 146 patients (57,3%.)

The severity of the radiographic changes is shown in Table 10.1. The radiographs of the ankles were available in 152 of the 155 Coloured and African patients (i.e. 304 joints). Four patients had surgery to 6 ankle joints and the remaining 298 joints were

graded according to the Larsen standard radiographs (Larsen et al 1977). There was agreement in the radiographic gradings between the two observers in 94,7% of the ankles.

## (2) SUBTALAR AND MIDTARSAL JOINTS

A history of pain in the midfoot (past or present) was obtained in 147 patients (57,4%). Tenderness was present at the time of assessment in the subtalar joints in 13 patients (5,1%) and the midtarsal joints in 63 patients (24,6%). The range of movement of the subtalar joints was normal in 312 joints (61,2%), reduced in 140 joints (27,4%) and 58 joints (11,4%) were ankylosed. The range of movement of the midtarsal joints was normal in 292 joints (57,3%), reduced in 190 joints (37,3%) and 28 joints (5,5%) were ankylosed.

## (3) FOREFOOT

A history of pain in the forefoot (past or present) was obtained in 195 patients (76,1%). Tenderness of the metatarsophalangeal joints (MTPJs) was noted at the time of assessment in 91 patients (35,5%).

Subluxation of one or more MTPJs was present in 347 feet (68,0%) in 182 patients (71%); crowding or overriding of the toes in 137 feet (26,9%) in 85 patients (33,2%) and callosities under the metatarsal heads were noted in 159 feet (31,2%) in 95 patients

(37,1%).

The results of the radiographic findings for the IP joints of the big toe and the MTPJs of the other toes of both feet are shown in Table 10.2. The radiographs of the patients who had surgery or severe deformity were excluded and the remaining 229 patients were analysed further. The mean radiographic grade for each toe in the right and left foot and the total score for both feet is shown in Table 10.3.

The mean radiographic grade was highest for the 5th MTPJ with a decreasing grade for the 4th, 3rd and 2nd MTPJs and the 1st IP joints respectively for both feet (Table 10.3). However, there was a statistically significant increase in the severity of the radiographic grade for the right 5th MTPJ when compared to the other toes in this foot; in the left foot, the 3rd, 4th and 5th MTPJ were significantly more severely involved than the 2nd MTPJ and 1st IP joint ( $p < 0,05$ ).

There was no difference in the mean radiographic score for the right foot in comparison with the left foot. The total radiographic score for the right and left feet together ranged from 0 (minimum) to 50 (maximum possible score) and the frequency of the various scores is shown in Table 10.4. The score ranged from 0-10 in only 37 patients (16,2%), from 11-20 in 103 patients (45,9%), from 21-30 in 54 patients (23,6%) and 35 patients (15,3%) had a score of greater than 30.

#### (4) GENERAL

The presence of deformity of the hindfoot and midfoot was assessed in 232 patients (464 feet). Fourteen patients were unable to stand; this information was not recorded in a further 10 patients. The appearance of the foot was normal in 245 feet (52,4%). A planus deformity was noted in 67 feet (14,3%), planovalgus in 137 (29,3%), varus in 11 (2,4%) and an equinus deformity in 4 feet (0,9%).

A total of 72 patients (28,2%) had some form of modification of their footwear. An arch support was used by 35 patients (13,7%), metatarsal bars by 32 patients (12,5%), surgical shoes by 34 patients (13,3%) and 9 patients (3,5%) had other modification to the shoes.

The frequency of the various surgical procedures to the hindfoot, midfoot and forefoot in the total group of 255 patients will be discussed in the chapter on surgical requirements in RA.

#### DISCUSSION

The commonest site of involvement of the foot is the MTPJ (Dixon 1970). Swelling around the MTPJ broadens the foot as the joints are forced apart by swelling (Dixon 1970). As the disease progresses, the intermetatarsal joint ligaments stretch and splaying of the forefoot occurs. The fibro-fatty cushion on the plantar surface migrates

anteriorly, the toes sublux dorsally, the extensor tendons shorten and the metatarsal heads sublux to a subcutaneous site on the plantar surface (Dixon 1970, Calabro 1962).

Symptoms and signs of forefoot involvement were noted in 85% of 50 hospitalized patients with RA (Minaker and Little 1973). In the present study a history of past or present pain in the forefoot was obtained in 76,1% of patients and 71% had subluxation of the MTPJ. The metatarsal heads were subluxed in 78,5% of 200 consecutive admissions with classical or definite RA (Vidigal et al 1975). Crowding or overriding of the toes was present in 33,2% and callosities under the metatarsal heads were noted in 37,1% of the 255 patients in this study. Vidigal et al found callosities under the MTPJs in over 30% of the feet and pressure lesions on the dorsum of the toes were noted in 30% of the fibular 4 toes (Vidigal et al 1975).

Clinical involvement of the midtarsal joint was noted in 28% and the subtalar joint in 21,5% of 200 patients (Vidigal et al 1975). However radiological changes were noted in 62% and 32% of the midtarsal and subtalar joints respectively. In the present study, a history of past or present pain in the midfoot was obtained in 57,4%. Tenderness was noted in 5,1% of the subtalar joints and 24,6% of the midtarsal joints. The range of movement of the subtalar joints was reduced in 27,5% of the feet and another 11,4% were ankylosed. The movement of the midtarsal joint was reduced in 37,3% of the feet and 5,5% were ankylosed. Vainio has found that the frequency of radiographic changes of the midtarsal joints increases with the duration of RA and

that complete stiffness of the midfoot was noted in more than 10% of the cases of RA (Vainio 1956).

In the present survey radiographic changes from grade 2 to 5 were noted in 26,2% of the ankles. Clinical involvement of the ankles has been noted in 16% to 48,5% (Vidigal et al 1975, Minaker and Little 1973) and radiographic changes have been noted in 26% to 40% (Vidigal et al 1975, Jakubowski 1969). Vainio noted that radiographic changes appeared late and complete stiffness of the ankles rarely occurred (Vainio 1956).

Radiological changes in the MTPJs were present in 88% of 200 patients (Vidigal et al 1975). The presence of grade 2 or more severe changes in at least one of the toes was noted in 230 patients (90,2%) in this study. There was no significant difference in the mean scores of the right and left foot. The mean radiographic score was highest in the 5th MTPJ, followed by the 4th, 3rd and 2nd MTPJs and then the IP joint of the big toe. The 1st MTPJ is not included in Larsen's grading system as it is often involved with osteoarthritis (Larsen et al 1977). Vainio found that the MTPJ of the big toes are most frequently involved, followed by the MTPJs of the 5th toe and IP joint of the big toe (Vainio 1956).

Sixty percent of the patients studied by Vidigal et al required modified shoes but only a third had received them and found them preferable to normal shoes (Vidigal et al 1975). In the present study, 72 patients (28,2%) had used arch supports, metatarsal bars,

surgical shoes or had some other modification to their shoes. However, since deformity of the feet was noted in 47,6% of the patients, a greater attention needs to be paid to footwear in these patients.

Minaker and Little found forefoot spread in 86% of their patients, 52% had a flexible flat foot and 16% had a rigid flat foot (Minaker and Little 1973). Deformity of the foot on standing was noted in 47,6% of the feet in this study and the commonest abnormalities were planovalgus deformity (29,3%) and planus deformity (14,3%). In a study of 1000 patients with RA, Vaino found that the most frequent deformity in the foot was the hallux valgus in 58,8%, hammer toes in 53,2%, splay foot in 33,2% and hallux rigidus in 10,4% (Vainio 1956).

Anderson reported a clinical study of 23 Africans with RA and noted that ankle involvement was a prominent feature and that a history of ankle pain and/or swelling was recorded in 19 (82,6%) of the 23 patients (Anderson 1970). In the present survey a history of pain in the hind foot was obtained in 213 patients (83,2%) and 179 patients (70,2%) had a history of swelling of the ankles. There was no difference in the prevalence of pain in the hindfoot or swelling of the ankles in the three racial groups. Therefore, the findings of this survey do not support the observation by Anderson that ankle involvement was commoner in Africans (Anderson 1970).

The foot is an important source of disability in RA. A history of pain in the forefoot was obtained in 76,1% and a Larsen grade 2 or more severe change in one or more toes was noted in 90,2%. Subluxation

of the metatarsophalangeal joints was present in 71%, callosities under the metatarsal heads in 37,1% and overriding of the toes in 33,2%. Although deformities of the feet were noted in 47,6%, only 72 patients (28,2%) had some modification of their footwear and therefore greater attention to footwear is necessary.

TABLE 10.1RADIOGRAPHIC GRADING IN THE ANKLES (Larsen et al 1977)

<u>GRADE*</u>	<u>NO. OF JOINTS</u> (n=298)	<u>NO. OF JOINTS</u> (percent)
0	79	26,5
1	141	47,3
2	45	15,1
3	20	6,7
4	5	1,7
5	8	2,7

TABLE 10.2

RADIOLOGICAL FINDINGS IN THE FEET

<u>GRADE</u>	<u>IP</u>					<u>TOTAL</u>	<u>IP</u>					<u>TOTAL</u>	<u>TOTAL</u> (R+L)	<u>TOTAL%</u> (R+L)
	<u>1</u>	<u>2</u>	<u>3</u>	<u>MTPJ</u> <u>4</u>	<u>5</u>		<u>1</u>	<u>2</u>	<u>3</u>	<u>MTPJ</u> <u>4</u>	<u>5</u>			
0	12	14	14	13	11	64	11	13	11	10	8	53	117	4,6
1	119	130	115	117	86	567	122	135	112	110	90	569	1136	44,5
2	72	33	28	26	39	198	84	34	26	30	45	219	417	16,3
3	31	28	35	33	43	170	23	21	42	36	36	158	328	12,9
4	9	8	18	22	30	87	6	9	19	23	32	89	176	6,9
5	9	24	26	26	30	115	8	23	24	26	25	106	221	8,7
SURGERY	0	15	15	14	13	57		16	16	15	13	60	117	4,6
DEFORMITY	3	3	4	4	3	17	1	4	5	5	6	21	38	1,5

TABLE 10.3

MEAN RADIOGRAPHIC GRADE FOR THE INTERPHALANGEAL JOINT OF BIG TOE AND  
MTPJs OF THE OTHER TOES

	<u>RIGHT</u>	<u>LEFT</u>	<u>TOTAL (R + L)</u>
IP big toe	1,705	1,639	3,344
2nd MTP	1,784	1,722	3,507
3rd MTP	2,000	2,031	4,031
4th MTP	2,026	2,097	4,123
5th MTP	2,330	2,242	4,573

TABLE 10.4

DISTRIBUTION OF THE TOTAL RADIOGRAPHIC SCORE FOR THE FEET

<u>SCORE</u>	<u>NUMBER OF PATIENTS</u> (n=229)	<u>PERCENT</u>
0 - 5	11	4,8
6 -10	26	11,4
11-15	66	28,8
16-20	37	16,2
21-25	33	14,4
26-30	21	9,2
31-31	15	6,6
36-40	7	3,1
41-45	10	4,4
46-50	3	1,3

## CHAPTER 11

### OTHER JOINTS AND RADIOGRAPHIC FINDINGS

- 11.1 Wrists
- 11.2 Elbows
- 11.3 Hips
- 11.4 Assessment of radiographic involvement

## CHAPTER 11.1

### WRISTS

Involvement of the wrist is a common and often early manifestation of RA. The aim of this survey was to determine the frequency of symptoms related to the wrist, the findings on clinical examination and the frequency and severity of radiographic changes.

### RESULTS

A history of past or present pain in the wrists was obtained in 251 patients (98,4%); 138 patients (53,9%) had pain at the time of assessment. Tenderness of one or both wrists was present in 127 patients (49,6%). The findings on clinical examination of the wrist were swelling in 109 patients (42,6%), inferior radioulnar crepitus in 101 patients (39,5%) and inferior radioulnar subluxation (piano key sign) in 74 patients (28,9%). The presence of subluxation or dislocation of the wrists was noted in 102 joints (19,9%) in 66 patients (25,8%); 24 joints (4,7%) were subluxed but reducible and the remaining 78 joints (15,2%) were subluxed and irreducible.

The radiographs of 255 patients (510 joints) were available for analysis. Thirty four patients had surgery to the wrists; they were excluded and the radiographs of the remaining 221 patients (442 joints) were graded according to the Larsen et al standard radiographs

by 2 observers (Larsen et al 1977). There was agreement in the radiographic gradings in 96,4% of the wrists. The frequency of the different radiographic grades is summarised in Table 11.1.1. A grade 2 or more severe change was noted in 81,7% of the wrists; 40% of the wrists were severely affected with grade 4 or 5 changes. The mean radiographic score for the right and left wrists in the 3 racial groups is summarised in Table 11.1.2. The mean score for both wrists was highest in the Africans, followed by the Coloureds and then the Caucasians.

## DISCUSSION

The wrist and the hand operate together as a functional unit and only in recent years has greater attention been paid to the effects of the wrist disease on the function of the hand (Flatt 1983). A history of pain in the wrists was obtained in 98,4% of our patients and radiographic changes (Larsen grade 2 or more) were present in 81,7% of the wrists. Jacoby et al reported that the wrists were involved in 82% of their 100 patients (Jacoby et al 1973).

Proliferative synovitis in the wrists begins in the region of the ulnar styloid. The characteristic clinical changes were described under the name 'caput ulnae syndrome' (Backdahl 1963). The fibrous ligament holding the distal radioulnar joint together is weakened and destroyed by synovitis, thereby allowing the ulna to migrate dorsally. The ulna can be easily depressed manually and this 'piano key sign' was present in 74 patients (28,9%).

The synovitis of the wrists also leads to weakening and destruction of the ligaments of the wrist joint and the intercarpal ligaments; zig-zag collapse and instability of the wrists then occurs (Flatt 1983, Linscheid and Dobyns 1971). In the present study, subluxation of the wrists was noted in 102 joints (19,9%) and this was irreducible in 76,5% of these joints.

In conclusion, wrist involvement was very common and clinical abnormalities were also frequently detected. Radiographic changes were noted in 81,7% of the wrists and they were severe in 40%. The radiographic changes were more severe in Africans when compared to Coloureds and Caucasians.

TABLE 11.1.1DISTRIBUTION OF THE SEVERITY OF RADIOGRAPHIC CHANGES IN THE WRISTS

GRADE*	NUMBER OF JOINTS INVOLVED (n=442)	JOINTS INVOLVED PERCENT
0	21	4,8
1	64	14,5
2	87	19,7
3	93	21,0
4	95	21,5
5	82	18,6

\* Radiographic grading according to the Larsen et al (1977) standard radiographs.

TABLE 11.1.2MEAN RADIOGRAPHIC GRADES FOR THE DIFFERENT RACES

	COLOUREDS (n=89)	CAUCASIANS (n=85)	AFRICANS (n=47)	TOTAL (n=221)
Right hand	2,933	2,753	3,404	2,964
Left hand	2,966	2,729	3,319	2,950
TOTAL	5,899	5,482	6,723	5,914

## CHAPTER 11.2

### ELBOWS

All the patients in the study were examined to determine the findings on clinical examination and the prevalence of deformities of the elbows.

#### RESULTS

A history of past or present pain in the elbows was obtained in 215 patients (84%).. The clinical findings in the elbows are summarised in Table 11.2.1. Synovial swelling in one or both elbows was present in 87 patients (34%), crepitus of the superior radioulnar joint in 116 patients (45,3%) while epicondylitis was infrequently found at the time of assessment.

The degree of extension of the elbows is shown in Table 11.2.2. Hyperextension of the elbows (greater than 10 degrees) was noted in only 6 elbows (1,2%). Flexion deformity of the elbow (ie extension of the elbow to less than 0 degree) was noted in 308 elbows (60,2%) and 271 of these (52,9%) had a flexion deformity of greater than 10 degrees.

## DISCUSSION

The elbow was involved in 21% of 100 patients studied by Jacoby et al while Laine and Vainio found elbow involvement in 67% (Jacoby et al 1973, Laine and Vainio 1969). The loss of full extension of the elbow is one of the earliest findings and is often not noticed by the patient (Harris 1981). However, limitation of elbow movement is well tolerated and studies at the Mayo Clinic have shown that only 90 degrees of flexion and extension are required for 80% of the activities of daily living provided that the range of motion lies in the optimal functional range of 40° to 130° (Flatt 1983).

In a functional study of 416 elbows in 208 patients with RA, Amis et al found that 71% of the joints had a flexion deformity of more than 5° and 10% had a deformity of more than 50° (Amis et al 1982). In this study a flexion deformity of the elbows was detected in 60,2% and a deformity of more than 10° was detected in 52,9% of the joints. However, most of the patients had retained a good range of movement. Amis et al found that more than 80° of movement was present in 92% of the joints and that about 3% had less than 60° of movement (Amis et al 1982). A range of movement of less than 50% of normal (ie less than 73°) was noted in only 21 joints (4,1%), while the range of movement was more than 60% of normal (ie more than 88°) in 465 joints (90,8%).

In conclusion, over half of the patients in this survey had a flexion deformity of more than 10°. However, most of the patients retained a good functional range of movement.

TABLE 11.2.1CLINICAL FINDINGS IN THE ELBOWS

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
Swelling	42	25	20	87	34,0
Medial epicondylitis	1	1	1	3	1,2
Lateral epicondylitis	1	2	1	4	1,6
Superior radio-ulnar crepitus	46	42	28	116	45,3

TABLE 11.2.2

PREVALENCE OF FLEXION DEFORMITY OF RIGHT AND LEFT ELBOWS  
(BASED ON EXTENSION OF THE ELBOWS IN DEGREES)

EXTENSION IN DEGREES	COLOUREDS (n=208)	CAUCASIANS (n=200)	AFRICANS (n=104)	TOTAL (n=512)	TOTAL %
>10	3	1	2	6	1,2
1 to 10	4	6	5	15	2,9
0	67	80	36	183	35,7
-1 to -10	19	10	8	37	7,2
-11 to -20	42	51	29	122	23,8
-21 to -30	30	32	14	76	14,8
-31 to -40	26	11	7	44	8,6
< -40	17	9	3	29	5,7

## CHAPTER 11.3

### HIPS

#### INTRODUCTION

Involvement of the hip joint is less common in adult RA than in juvenile chronic arthritis. Pain in the lateral aspects of the hips in adults is often a manifestation of the trochanteric bursitis rather than synovitis of the hip.

Radiographic changes in the hips were detected in 40% of 84 patients (Duthie and Harris 1969). Hastings and Parker reviewed the records and x-rays of 694 patients with seropositive RA and found clinical or radiological evidence of hip involvement in 36% (Hastings and Parker 1975).

The prevalence of radiographic involvement of the hip was studied in the Coloured and African patients in this survey.

#### RESULTS

A history of pain in the hips was obtained in 59 patients (37,8%); 27 patients had pain at the time of assessment and 32 had a past history of pain. There were 15 patients who had pain on motion at the time of assessment; the pain was bilateral in 5 of these patients.

All the radiographs were graded according to the Larsen standard radiographs (Larsen et al 1977) by two observers and there was 98,6% agreement in the findings by the two observers. The radiographs of 151 patients (302 joints) were available for analysis and the results of the radiographic findings are shown in Table 11.3.1.

Twelve patients (7,9%) had hip replacement, which was bilateral in 6 patients. A grade 2 or more severe change was noted in 22,2% of the hips. There were 39 patients (25,8%) who had a grade 2 or more severe change in at least one of the hip joints. Two of these patients had a grade 2 change in only one hip and 3 patients had grade 2 changes in both hips. The remaining 34 patients (22,5%) had surgery or a grade 3 or more severe change in at least one of the hips.

## DISCUSSION

RA is characterised by symmetrical arthritis of predominantly the small joints and involvement of the larger joints such as the shoulder and the hip is less common. However, hip involvement has been reported in about 40% of patients with RA (Duthie and Harris 1968, Hastings and Parker 1975).

A history of pain in the hips was obtained in only 37,8% of the patients and was the lowest for any of the joints in the upper or lower limb. Sharp et al found radiographic abnormalities of the hip in 35,6% of 87 patients with peripheral RA who were all seropositive and nearly half of whom had nodules (Sharp et al 1964). Duthie and

Harris found radiographic changes in the hips in 40% of 84 patients with seropositive RA (Duthie and Harris 1969). Their radiographic changes were documented in detail and joint space narrowing, diffuse osteoporosis and subchondral sclerosis were the most common abnormalities. Protrusio acetabuli was noted in 14 patients (16,7%), 11 of whom also had changes in the femoral head. Radiographic changes were noted in 39 patients (25,8%) in this survey.

In conclusion, even though hip pain was noted in only 37,8%, radiographic changes in the hips were noted in 25,8% and 12 patients (7,9%) had a replacement arthroplasty of one or both hips.

TABLE 11.3.1RADIOGRAPHIC CHANGES IN THE HIPS

Grade*	Right Hip (n=151)	Left Hip (n=151)	Total (n=302)	Total Percent
0	58	57	115	38,1
1	60	60	120	39,7
2	7	8	15	5,0
3	5	5	10	3,3
4	2	2	4	1,3
5	10	10	20	6,6
Surgery	9	9	18	6,0

## CHAPTER 11.4

### ASSESSMENT OF THE RADIOGRAPHIC INVOLVEMENT

#### INTRODUCTION

In the management of patients with RA, it is necessary to assess the radiographs to quantify the extent of involvement and also monitor the progression of the disease. The earliest grading system was proposed by Steinbrocker et al using a four point scale but this did not provide an accurate assessment of overall joint damage (Steinbrocker et al 1949). Subsequently the use of various other scoring systems have been reported (Sharp et al 1971, Kellgren et al 1963, Larsen et al 1977, Amos et al 1977). In recent surveys, the Larsen standard radiographs have been used to report the severity and progression of radiographic changes in patients on anti-rheumatic drugs (Larsen et al 1983, Scott et al 1985).

The aim of this survey was to determine the severity of radiographic involvement in the patients in this study, and to determine whether there were any inter-racial differences in the radiographic changes among the races.

#### RESULTS

The radiographic assessment was based on the results obtained from 188

patients; this group included 75% of the Coloureds in the study (78 patients), 68% of the Caucasians (68 patients) and 83% of the Africans (43 patients). The majority of the patients who were excluded had surgery to the joints, and therefore radiographic grading was not possible in these patients.

#### 1. DISTRIBUTION OF THE RADIOGRAPHIC SCORE

The distribution of the total Larsen radiographic score is shown in Table 11.4.1.

#### 2. INTER-RACIAL COMPARISON OF THE RADIOGRAPHIC SCORE

The mean age, mean duration of RA and the mean values for the hands, wrists, feet and the total score are shown in Table 11.4.2.

A one-way covariate analysis was performed to determine whether there was a relationship between the age and duration of RA, and the radiographic score. There was no significant relationship between the age and the radiographic score but the duration of RA showed a highly significant relationship ( $p < 0,001$ ). Therefore, the radiographic scores were corrected for the duration of RA and then the races were compared with each other. There were no significant differences among the races for the mean radiographic scores of the hands, feet and the total score; however, the wrist score was significantly higher in the Africans in comparison with

the Coloureds ( $p=0,004$ ) and Caucasians ( $p=0,0003$ ).

## DISCUSSION

Surgery is often necessary in the management of patients with RA. In the present survey, there were many patients who had previous surgery. Therefore, it was not possible to grade all the radiographs taken at the time of assessment. The proportion of Caucasians and Coloureds who were excluded, because of previous surgery was higher than Africans. It is possible that the patients who had surgery, had more severe radiographic changes; their exclusion may have lowered the mean radiographic score. Therefore, it is difficult to accurately compare the radiographic findings within the races. However, the remainder of the patients were compared in order to obtain information on the severity of radiographic changes. Only the wrists were found to be more severely involved in the Africans, and no other inter-racial differences were noted. This finding is in keeping with the clinical impression in the rheumatology unit that wrist involvement is more severe in Africans.

Scott et al reported the radiographic findings (total Larsen score) in a group of 56 patients with active RA who were treated with remittive agents (Scott et al 1985). The mean values for the total Larsen score, after patients had received therapy for 12 months was 60,8. The majority of their patients had RA for less than 5 years; only 7 patients (14,2%) had RA for more than 5 years. In our survey the mean value for the total Larsen score was 83,5; the higher value is

probably due to the longer duration of RA (mean 10,6 years). In addition, our survey included patients with long standing burnt out RA who would have a higher Larsen score; these patients would not be considered for remittive agent therapy. This factor could also contribute to the lower Larsen score noted by Scott and co-workers (Scott et al 1985).

TABLE 11.4.1

DISTRIBUTION OF THE TOTAL SCORE LARSEN SCORE

	COLOUREDS (n=78)	CAUCASIANS (n=67)	AFRICANS (n=43)	TOTAL (n=188)	TOTAL %
0-20	5	1	1	7	3,7
21-40	4	5	0	9	4,8
41-60	15	15	9	39	20,7
61-80	17	13	8	38	20,2
81-100	12	10	12	34	18,1
101-120	11	14	5	30	16,0
121-140	6	5	5	16	8,5
141-160	4	2	0	6	3,2
161-180	3	2	2	7	3,7
181-200	1	0	1	2	1,1

TABLE 11.4.2INTER-RACIAL COMPARISON - RADIOGRAPHIC FINDINGS

	COLOUREDS (n=78)	CAUCASIANS (n=67)	AFRICANS (n=43)	TOTAL (n=188)
Mean age (years)	50,2	58,1	45,1	51,8
Mean duration of RA (years)	10,7	12,3	7,8	10,6
Hands (0-100)	34,84	37,16	34,91	35,70
Feet (0-50)	18,95	19,62	19,64	19,36
Wrists (0-10)	5,59	5,19	6,62	5,69
Hand + feet + (wrists x 5) (0-200)	81,72	82,74	87,67	83,51

## CHAPTER 12

### FRACTURES

#### INTRODUCTION

In 1941, prior to the introduction of steroids, Baer reported that fractures occurred in 1,2 percent of patients with chronic arthritis (Baer 1941). Since then, there have been many reports on the occurrence of spontaneous or stress fractures in RA (Haider and Storey 1962, Miller et al 1967, Taylor et al 1971, Maddison and Bacon 1974, Schneider and Kaye 1975, Young et al 1981, Jones and Jawad 1984). Some of the pathogenetic mechanisms which are considered to play an important role in the development of fractures in RA are osteomalacia (Maddison and Bacon 1974), osteoporosis (Devas 1966), angular joint deformities (Young et al 1981) and increased mobility after reconstructive surgery (Schneider and Kaye 1975). However, there is little information on the prevalence and incidence of fractures in RA in comparison to control populations. Den Oudsten and Speyer found little difference between the number of fractures in a group of RA patients and those in a control group (Oudsten and Speyer 1959).

Cummings reviewed the evidence for osteoporosis in elderly patients who developed hip fractures (Cummings 1985). He critically reviewed 15 case control studies on the subject and noted that the most rigorously designed studies observed less bone mass in the hips of

patients with fractures than in the hips of control subjects. However, the differences were usually small, and measurements at other sites did not consistently show any difference. Therefore, it is likely that, other factors such as a tendency to fall may be important determinants for the development of fractures in elderly patients. In patients with RA, it may be useful to determine the prevalence of fractures, either spontaneously or related to injury, as there may be an increased predisposition to injury due to involvement of many joints in the lower limbs.

The aim of this survey was to determine the prevalence of fractures in the patients in this study.

## RESULTS

Twenty two patients (8,6%) sustained one or more fractures. Two of these patients, both females, were involved in motor vehicle accidents prior to the onset of RA. One of these patients had a fracture of the inferior pubic ramus of the pelvis while the other had a fracture of the scapula. The clinical data on the remaining 20 patients is summarised in Table 12.1. Two of these patients (number 19 and 20) were also involved in motor vehicle accidents but these occurred after the onset of RA. One patient had fractures of both femora while the other patient had a fracture of the right acetabulum. The data on the remaining 18 patients (7,0%) will be analysed further.

There were 16 females and 2 males. The mean age of all the patients at

the time of the fracture was 60,3 years (range 45-77 years), the mean age for females was 61,1 years (range 45-77 years) and 54,5 years (range 47-62 years) for males. The mean duration of RA at the time of the fracture was 13,4 years (range 0,5 to 33,5 years). Six patients (33%) had been on steroids for a mean duration of 46,8 months (range 3 to 95 months) while the remaining 12 patients (67%) had not been on steroids prior to sustaining a fracture.

The fractures occurred at one or more sites involving the upper limb, lower limb, pelvis and spine. Three females aged 56, 58 and 64 years had evidence of spontaneous vertebral collapse. Two patients had fractures of the pelvis, with one of them having a fracture of the superior pubic ramus while the other had a fracture of the ischium on one side and a fracture of the inferior pubic ramus and ischium on the opposite side. Eight patients had fractures of the femoral neck, which were bilateral in one patient. The patient who had fractures of both femurs also had a fracture through the medial malleolus of the ankle. Two other patients had fractures involving the lower limb, one had a stress fracture of the lower third of the tibia and the other had a spiral fracture of the lower tibia and a transverse fracture of the fibula. Therefore, a total of ten patients had fractures involving the lower limbs. Six patients had fractures of the upper limb which involved the radial styloid (2 patients), capitellum of the elbow, shaft of the humerus, forearm and a colles fracture. Only one patient (number II) had a spontaneous or stress fracture of the lower third of the tibia and three patients (number 7,10 and 18) had vertebral collapse without any history of preceding trauma. All the remaining

fractures were related to trauma or injury, which was usually a fall.

All these patients had complained of pain over the involved site and a fracture was diagnosed on radiographs of the painful area. Four patients had fractures of more than one site with one patient having fractures at four different sites.

### DISCUSSION

It is important to recognise spontaneous or stress fractures in RA so that they can be appropriately managed. If a patient has a history of a sudden increase in pain, then a fracture may be suspected but the diagnosis may be delayed in some patients who may have a slower onset of pain (Haider and Storey 1962, Miller et al 1967). In other patients, it may be mistaken for an acute synovitis or septic arthritis (Fam et al 1983, Young et al 1981).

In the present study, 22 patients (8,6%) had a history of fractures at one or more sites and four of these patients had a history of fractures related to motor vehicle accidents. The remaining 18 patients (7%) had either a traumatic or a spontaneous fracture. Only one patient had a spontaneous fracture of the tibia and 3 patients had spontaneous vertebral fractures.

The factors which may contribute to fractures in RA are osteoporosis, osteomalacia, angular joint deformities and increased mobility after reconstructive surgery. The occurrence of generalized and

periarticular osteoporosis in RA has been recognised (Duncan et al 1965, Kennedy et al 1977). In RA, the osteoporosis may be related to steroid therapy, age and sex of the patient, immobility and disuse and the disease process (Young et al 1981).

The majority of the patients with fractures in our study were females (88,8%) and a similar finding has been noted in other studies of patients with spontaneous fractures (Taylor et al 1971, Maddison and Bacon 1974, Schneider and Kaye 1975, Young et al 1981, Fam et al 1983). Only 6 (33%) of our patients had been treated with steroids. Twelve patients (67%) were not on steroids and eleven of them were females whose mean age was 60,5 years (range 45-77 years). It is likely that post menopausal osteoporosis was a contributory factor in the development of fractures in some of these patients.

Most of the recent studies have documented stress fractures involving the lower limbs and pelvis (Taylor et al 1971, Schneider and Kaye 1975, Fam et al 1983, Jones and Jawad 1984, Maddison and Bacon 1974, Young et al 1981). We found that 6 of our patients had fractures involving the upper limbs and 3 patients had vertebral collapse.

Eight of the 18 patients (44,4%) had fractures of the femoral neck and the mean age of these patients was 65,3 years (range 55 to 77 years). Seven of the patients with femoral neck fractures were Caucasians and one patient was Coloured. The increased prevalence of femoral neck fractures in Caucasians may partly be due to the fact that their mean age was much higher than the Coloureds and the Africans. Solomon has

found that the incidence of femoral neck fractures in Africans was less than one tenth the incidence in Caucasians even though bone density was higher in Caucasians for most of the age ranges from 5 to 75 years (Solomon 1968, Solomon 1979). He noted that among patients with femoral neck fractures, there was a high prevalence of bone losing disorders such as chronic illness, vitamin D deficiency, malabsorption syndromes and alcoholism. He suggested that patients who developed femoral neck fractures are a part of the population who have the usual post climacteric bone loss and some superimposed metabolic disorder which weakens the bone, and that this secondary disorder was less common in Africans than in Caucasians.

Cummings has noted that the role of osteoporosis in the development of hip fractures remains controversial and that other factors such as a tendency to fall may be important in determining which elderly patients will have fractures (Cummings 1985). Therefore, it is important that in patients with RA, attention should be focused on the occurrence of all fractures and not only those which are considered to be stress or spontaneous fractures. It is possible that apart from age, post menopausal osteoporosis and steroid therapy, some of the fractures in the present study were related to the disease process per se or angular deformities and a tendency to fall.

It is necessary for further prospective studies with a control population to determine the prevalence and causes of fractures in RA in comparison to controls. If there is an increase in the prevalence of fractures in RA, then more attention should be directed to the predisposing factors to try and reduce the prevalence of fractures.

TABLE 12.1

## CLINICAL DATA ON PATIENTS WHO HAD FRACTURES

NO	STUDY NO	AGE	SEX	DURATION OF RA (years)	STEROID THERAPY	INJURY	SITE OF FRACTURE
1	10	52	F	4		YES	Spiral fracture of lower tibia & transverse fracture of fibula
2	12	55	F	16	3 mths	YES	Shaft of upper humerus
3	56	77	F	16,5		YES	Femoral neck
4	77	60	F	21		YES	Pubic symphysis
5	208	61	F	28,3		YES	Femoral neck
6	212	77	F	18		YES	Femoral neck
7	216	64	F	14,5		YES	Femoral neck, vertebral collapse colles fracture
8	225	62	M	5		YES	Radial styloid
9	242	66	F	5	48 mths	YES	Capitellum of elbow
10	245	58	F	1		YES	Forearm and vertebral collapse
11	252	47	M	8	24 mths	NIL	Stress fracture of lower third of tibia
12	278	65	F	33,5	72 mths	YES	Femoral neck
13	282	55	F	4		YES	Femoral neck
14	284	60	F	0,5		YES	Bilateral femoral neck, medial malleolus, radial styloid
15	320	45	F	24,5		YES	Shaft of lower humerus
16	273	63	F	22,5	95 mths	YES	Pubic ramus, ischium on R and L
17	241	63	F	18,2	39 mths	YES	Femoral neck
18	211	56	F	1,2		NIL	Vertebral collapse
19	295	54	F	12		MVA	Femoral neck
20	35	35	F	4,5	12 mths	MVA	Acetabulum

## CHAPTER 13

### UPPER GASTROINTESTINAL SYMPTOMS AND PEPTIC ULCERS

#### INTRODUCTION

An increased prevalence of peptic ulcers in patients with RA has been noted in several studies (Kern et al 1957, Gedda and Moritz 1958, Bowen et al 1960, Atwater et al 1965, Sun et al 1974). In 1978, Cooke reviewed the prospective and retrospective studies in RA and concluded that there was possibly a higher frequency of peptic ulceration but the cause was uncertain (Cooke 1978). The factors which have been considered to play a role include not only the disease itself but also therapeutic agents such as corticosteroids, salicylates and other nonsteroidal anti-inflammatory drugs (NSAIDs).

The association of corticosteroids with peptic ulcers in RA has been noted in some studies (Kern et al 1957, Bowen et al 1960, Black et al 1957) but has not been confirmed in others (Atwater et al 1965, Meltzer et al 1958). Cooke reviewed 23 studies of 4278 patients with RA who were treated with steroids and found that the prevalence of ulcers was similar to the general population (Cooke 1967). Other reviews of published reports on the association of steroids, used for a variety of medical disorders, and peptic ulcers, have produced conflicting results (Conn and Blitzer 1976, Messer et al 1983). An association of gastric ulcers with chronic aspirin therapy (Silvoso et

al 1979) and other NSAIDs (Taylor et al 1968, Caruso and Porro 1980) has been reported in patients with rheumatic diseases.

The aims of this survey were to:-

- i) determine the prevalence of upper gastrointestinal symptoms in RA
- ii) determine the number of patients in whom a peptic ulcer was diagnosed during their management in a rheumatic diseases unit
- iii) study the clinical data of the patients with peptic ulcers to determine the prevalence of gastric ulcers (GU) and duodenal ulcers (DU), the mode of diagnosis, the iron status and prevalence of complications such as gastrointestinal haemorrhage and perforation.

## RESULTS

There were 122 patients (47,7%) who experienced upper gastrointestinal symptoms such as epigastric pain and dyspepsia.

Eighty eight of these 122 patients had symptoms such as epigastric pain or dyspepsia but no documented peptic ulcers. Barium meal or endoscopic examination was performed in only 22 of these 88 patients. Gastric erosions were observed in two of the four patients who had endoscopy. Barium studies were performed in 19 patients; 8 had an uncomplicated hiatus hernia and the remainder were normal. Forty one

of the 88 patients had taken antacids in the past, 24 were on regular antacid therapy, 17 took intermittent therapy and 6 patients had not been on any therapy.

All the patients who had peptic ulcers were symptomatic. The diagnosis of a peptic ulcer was made on barium meal examination in 11 patients, during endoscopy in 7 patients and, by both investigations in 14 patients. A GU was diagnosed at post mortem in one of the selected patients who died during the course of the survey and at surgery for an acute abdomen in another patient.

Twenty three of the 34 patients with peptic ulcers had a GU and the remaining 11 patients had a DU. The ratio of GU to DU was 2,1 : 1. The overall female to male ratio was 2,1 : 1, being 3,6 : 1 for GU and 0,8 : 1 for DU. The mean age of the patients was 51,6 years (range 32-73 years) for GU, 50,9 years (range 35-70 years) for DU and 51,4 years (range 32-73 years) for all the patients with peptic ulcers. The prevalence of peptic ulcers in the different racial groups was 18% for Caucasians, 12,5% for Coloureds and 5,8% for Blacks.

The ulcers perforated in 5 patients (4 GU and 1 DU). Three of these 5 patients were known to have a peptic ulcer at the time of perforation (GU in 2 patients and DU in 1 patient), the diagnosis of a GU was made for the first time at surgery in one patient and only at post mortem in another patient who died after perforation of her GU. There were 5 patients who developed acute gastrointestinal haemorrhage and one of these patients later had a perforation. Thus, a total of 9 of the 34

patients (26,5%) with peptic ulcers developed a perforation and/or haemorrhage. Ten patients (29,4%) had surgery for peptic ulcer disease. Four patients had emergency surgery for perforation and one of them later had a vagotomy and pyloroplasty. Six other patients had surgery for intractable symptoms (3 for GU and 3 for DU).

Fourteen of the patients with peptic ulcers were on regular therapy for peptic ulcers, 6 were on intermittent therapy and 14 patients had past treatment. All the patients with peptic ulcers had received antacids, 12 had also taken cimetidine and 4 patients had received sodium carboxolone. Seventeen of the 34 patients (50%) with peptic ulcers had received steroids at some stage of their disease compared with 67 (30,2%) of the remaining 222 patients in the study.

The haemoglobin, red cell indices, serum iron, total iron binding capacity and serum ferritin were normal in 22 of the 34 patients with peptic ulcers. Four of the remaining 12 patients had evidence of iron deficiency anaemia with a low serum ferritin (mean value 8,5 ng/ml). The remaining 8 patients had microcytic hypochromic red cell indices. (mean MCV 71,0 fl, mean MCH 23,1 pg) and reduced iron saturation (mean 5,2%). The serum ferritin values were normal (mean 63 ng/ml), the mean erythrocyte sedimentation rate was 107 mm/hour and five of the eight patients were anaemic.

## DISCUSSION

Upper gastrointestinal symptoms were noted in 122 patients (47,7%)

indicating that they occur commonly in RA. There were 54 patients (32 of the patients with peptic ulcers and 22 of the symptomatic patients with no documented ulcers) who had barium studies and or endoscopy during the course of their disease.

In an autopsy study of a general hospital population over a 20 year period, Watkinson found that the prevalence of peptic ulcers was 18,4% for men and 9,5% for women (Watkinson 1960). The prevalence of peptic ulcers in this study was 16,4% for men and 12,2% for women. The true prevalence of peptic ulcers is probably much higher as over half of the symptomatic patients had not been investigated and also because some patients with peptic ulcers may be asymptomatic. Farah et al reported an endoscopic study of unselected patients with RA and osteoarthritis, and found peptic ulcers in 67 (36,2%) of the 185 RA patients and 12 (26,7%) of the 45 patients with osteoarthritis (Farah et al 1986). They found that GU was commoner in the RA group and 55% of the patients with GU were asymptomatic.

Epidemiological studies have shown that DU is approximately 3 times more common than GU in the general population (Bonnievie 1975a, Bonnievie 1975b). The ratio of DU to GU was 2,2 : 1 in a study of 140 patients with RA (Sun et al 1974) and 1,5 : 1 in another survey of 169 patients with RA (Kern et al 1957). In the present survey there was a reversal of the ratio with the ratio of GU to DU being 2,1 : 1. In a recent report, Malone et al found a similar prevalence of peptic ulcers in RA and osteoarthritis, and suggested that the high incidence of peptic ulcer disease was probably related to drug therapy (Malone

et al 1986). Therefore, the increased prevalence of gastric ulcers in the present survey was probably related to NSAIDs.

The prevalence of peptic ulcers in the different communities in South Africa is not known but the incidence of peptic ulcers per thousand of population has been estimated to be 10,1 for Caucasians, 9,82 for Asians, 1,64 for Coloureds and 0,22 for Blacks (Oosthuizen 1978). The lower prevalence of peptic ulcers in Blacks in the present study may be due to the younger mean age and shorter duration of RA, or a true ethnic difference which was noted previously.

Gastrointestinal haemorrhage or perforation was noted in 26,5% of the patients with peptic ulcers, which is similar to the 31,6% prevalence in steroid treated patients with peptic ulcers (Conn and Blitzer 1976).

Four (11,8%) of the patients with peptic ulcers had iron deficiency anaemia. It is also likely that some of the 8 patients with microcytic hypochromic red cell indices and a low iron saturation also had iron deficiency even though the serum ferritin was normal. Serum ferritin behaves as an acute phase reactant and was probably elevated because of disease activity, as the mean erythrocyte sedimentation rate in these patients was 107 mm/hour. The development of iron deficiency in patients with peptic ulcers emphasizes the need for close monitoring of these patients to detect the presence of gastric erosions, recurrence of peptic ulcers or gastrointestinal bleeding so that they could be appropriately managed.

The inadequacy of the literature on the relationship between drugs, ulcers and gastrointestinal bleeding have been reviewed by Kurata et al (Kurata et al 1982). Cooke reviewed the effects of drugs on the gastroduodenum and noted that while unbuffered aspirin, indomethacin and other non steroidal anti-inflammatory drugs may cause erosions, there was no conclusive evidence to show an increased prevalence of gastric ulcers with these drugs apart from possibly unbuffered aspirin (Cooke 1978). Long term prospective clinical surveys of a large group of RA patients, together with control data, are not available.

In conclusion, dyspepsia and epigastric pain are common in RA. They were noted in 47,7% of the patients and 13,3% had peptic ulcers. It is likely that the prevalence of peptic ulcers is higher as many symptomatic patients had not been investigated. The increased prevalence of symptomatic GU may be related to NSAIDS. The frequent occurrence of perforation, gastrointestinal haemorrhage and/or iron deficiency in patients with peptic ulcers, emphasizes the need for careful assessment and management of upper gastrointestinal symptoms in RA.

## CHAPTER 14

### LABORATORY FINDINGS

- 14.1 Biochemical abnormalities
- 14.2 Immunological abnormalities
- 14.3 Iron status and anaemia

## CHAPTER 14.1

### BIOCHEMICAL ABNORMALITIES

#### INTRODUCTION

Biochemical abnormalities are frequently noted in RA and some of them may be due to the disease per se while others are related to complications of the disease or therapy. Raised alkaline phosphatase and gamma glutamyl-transpeptidase (GGT) have been frequently detected in RA and have been correlated with the activity of the disease (Spooner et al 1982, Lowe et al 1978, Kendall et al 1970). A reduction in the serum creatinine concentration, possibly due to a reduction in muscle mass, has been noted in patients with rheumatic diseases (Nived et al 1983). In addition, abnormalities of calcium and cholesterol have also been reported (London et al 1963, Reid et al 1982).

The aim of the survey was to determine the prevalence of biochemical abnormalities in RA and to determine whether there were any differences in the three different racial groups.

#### RESULTS

The mean values of the biochemical tests for the 3 racial groups and the total group are shown in Table 14.1.1. The prevalence of abnormal biochemical tests is shown in Table 14.1.2. Twenty three patients

(9,1%) had serum albumen values of less than 35g/l (Table 14.1.3). An increase in the serum globulins ( $> 35\text{g/l}$ ) was noted in 100 patients (39,7%). The serum alkaline phosphatase was elevated in 107 patients (42,3%) and 102 of these patients had a less than two fold increase from 116 to 200 units. The GGT was measured in 216 patients and was elevated in 14 patients (6,5%). Twelve of the patients with an elevated GGT also had an elevated alkaline phosphatase. The LDH was elevated in 2 patients (0,9%), the AST in 2 patients (0,8%) and the ALT in 3 patients (1,2%). The elevation of the LDH, AST and ALT was less than two fold in all the patients. The total bilirubin was marginally elevated ( $19\mu\text{mol/l}$ , normal  $0-17\mu\text{mol/l}$ ) in one patient.

Seventy two patients (28,1%) had an elevated urea ( $> 6,7\text{mmol/l}$ ) but the degree of elevation was mild in the majority of the patients as the mean value ( $\pm$  standard deviation) was  $5,9 \pm 2,5\text{mmol/l}$  (Table 14.1.2). An elevated urea of more than  $10\text{mmol/l}$  was present in 17 patients (6,6%). The serum creatinine was elevated in 17 patients (mean value  $133,4\mu\text{mol/l}$ , all of whom had an elevated urea (mean value  $10,7\text{mmol/l}$ ). A reduction in the serum creatinine (less than  $75\mu\text{mol/l}$ ) was much more common and was noted in 111 patients (43,4%). The serum creatinine was correlated with age, Ritchie articular score, ESR, CRP, upper arm muscle circumference (UAMC) and the body mass index (Table 14.1.4). There was a significant increase in the serum creatinine with increasing age ( $r=0,431$ ;  $p<0,001$ ) but there was no correlation with the ESR and CRP. There was a negative correlation with the articular index score but the  $r$  value was only  $0,163$  and  $r^2$  was  $0,027$ . There was no correlation with the UAMC, which is an index

of body protein stores.

The serum uric acid was elevated ( $> 0,45\text{mmol}/\ell$ ) in 31 (12,1%) patients with 14 patients having a mild elevation from 0,46 to 0,50mmol/ $\ell$  and the remaining 17 patients had levels greater than 0,50 mmol/ $\ell$ . Eighteen of the 31 patients with an elevated uric acid were on diuretic therapy or had an elevated serum creatinine. One patient had a mild elevation of the urea (7,4mmol/ $\ell$ ) with a normal serum creatinine and the remaining 12 patients (4,7%) had an elevated uric acid without any obvious secondary cause.

A raised serum calcium ( $>2,6\text{mmol}/\ell$ ) was detected in 7 patients. None of the patients had a reduction in the serum calcium after correction for hypoalbuminaemia. The serum cholesterol was raised in 20 patients ( $>7,8\%$ ), while 4 patients had a low serum cholesterol.

The biochemical tests in the 3 races were compared to detect the prevalence of abnormalities between the races. The statistical test used was the Pearson Chisquare test followed by pairwise comparison if there were any significant differences among the races. The serum globulins were significantly higher in the Coloureds and Africans in comparison to Caucasians ( $p < 0,0001$ ) but there was no difference between the Coloureds and Africans ( $p=0,3398$ ). The serum creatinine values were significantly higher in Coloureds ( $p=0,006$ ) and Caucasians ( $p < 0,0001$ ) in comparison to Africans. The blood urea was higher in Caucasians than Africans ( $p=0,0017$ ). The serum cholesterol was higher in Caucasians ( $p=0,0023$ ) and Coloureds ( $p=0,0279$ ) than in Africans.

There were no significant differences among the races for the serum albumen, alkaline phosphatase, GGT and serum calcium.

### DISCUSSION

The liver function tests were studied in 100 patients with RA and an elevation of the serum globulin and depression of the serum albumen were the most frequent abnormalities (Lefkovits and Farrow 1955). Fernandes et al found low serum albumen levels in 5% of 100 patients with RA while Cockel et al found a reduction in the serum albumen in 25% and elevation of the globulin in 44% of their 100 patients with RA (Fernandes et al 1979, Cockel et al 1971). The serum albumen levels were reduced (less than 35g/l) in 23 patients (9,1%) in this study and 100 patients (39,7%) had globulins greater than 35g/l. Studies of the serum protein patterns in Africans and Caucasians in Cape Town, Durban and Kampala have shown a reduction in the serum albumen and a rise in globulins in Africans in all three centres (Powell 1958, Arens and Brock 1954, Holmes et al 1951). However, with improvement in the nutrition, there was a rise in the serum albumen but hyperglobulinaemia persisted (Powell 1958). The factors which are considered likely to contribute to the raised globulins are poor nutrition, infection and chronic liver disease (Powell 1958). A rise in the serum globulins may be due to the RA itself but the higher values noted in Africans and Coloureds in comparison to Caucasians are probably related to the factors discussed above.

Hyperuricaemia was detected in 31 patients (12,1%) although only 12

patients (4,7%) had an elevated uric acid in the absence of any possible secondary cause. This could be related to the prevalence of hyperuricaemia in approximately 5% of the normal population (Dieppe and Calvert 1983). The factors which may contribute to hyperuricaemia in rheumatoid arthritis are salicylate therapy, rapid tissue breakdown and silent pyelonephritis (Cockel et al 1971, Grayzel et al 1961). Cockel et al found an elevated uric acid in 8 of their 100 patients with RA; it was attributed to renal impairment in 7 patients as there was a correlation of the uric acid with the urea and creatinine (Cockel et al 1971).

A reduction in the serum creatinine has been reported in patients with rheumatic diseases (Nived et al 1983). The serum creatinine was reduced (less than  $75\mu\text{mol}/\ell$ ) in 111 patients (43,4%) and this observation supports the suggestion by Nived et al that lower normal values may need to be considered when assessing the significance of serum creatinine values in RA (Nived et al 1973). The reduction in the serum creatinine was considered to be due to a reduction in the muscle mass. However, there was no correlation of the creatinine with the UAMC (which is used to assess the skeletal muscles) in this study. Since muscle wasting initially occurs adjacent to involved joints, it may not have been detected by measurement of the UAMC.

A mild elevation of the blood urea was common while only 17 patients (6,6%) had a value of more than  $10\text{ mmol}/\ell$ . Richards et al studied the renal function in 167 outpatients with RA and found that 9 patients (5,4%) had an elevated urea of  $>10\text{ mmol}/\ell$  (Richards et al 1986).

Sorensen found a reduction in the creatinine clearance in 32% of 203 patients with RA in comparison to a prevalence of 13,8% in a control group of 447 patients (Sorensen 1961). The impaired renal function in these patients was dependent on the duration and severity of the disease. The factors which contribute to impaired renal function in RA are the older age of the patients studied, the presence of coexistent hypertension and cardiac disease, and nephrotoxicity related to non steroidal anti-inflammatory drugs (NSAIDs) or slow acting anti-rheumatic drugs such as gold and penicillamine. A variety of renal effects have been reported with NSAIDs and they now constitute an important and potentially reversible cause of impaired renal function in RA (Clive and Stoff 1984).

An analysis of the published data indicates that a raised alkaline phosphatase is noted in up to 46% of patients with RA as shown in Table 14.1.5. A raised alkaline phosphatase was detected in 42,3% of the 253 patients in this study and this finding is similar to other studies (Spooner et al 1982, Sullivan et al 1978). Kendall et al studied a group of 15 patients with raised alkaline phosphatase and found that this was associated with a raised serum 5-nucleotidase and with the activity of the rheumatoid disease (Kendall et al 1970). Sullivan et al found that the origin of the raised alkaline phosphatase was attributed to the liver in two thirds of the patients and 58% of these patients had concomitant elevation of the GGT (Sullivan et al 1978).

Lowe et al found an elevated GGT in 73% of their 62 patients with RA

(Lowe et al 1978). In a separate study of 28 patients they found that the levels of GGT correlated significantly with objective indices of activity and that there was a significant drop after treatment with penicillamine. Spooner et al found an elevated GGT in 23,5% of their 98 patients and 12% had an elevated GGT and alkaline phosphatase (Spooner et al 1982). An elevated GGT was detected in only 14 (6,5%) of our patients and 12 of these patients also had an elevated alkaline phosphatase. An elevated GGT was noted much less frequently than in other studies. In a recent study, Thompson et al noted that the AST, ALT and GGT levels were generally normal in RA, but alkaline phosphatase and 5-nucleotidase were elevated in 25% and 31% respectively (Thompson et al 1986). They also suggested that the elevated 5-nucleotidase was due to diffusion from the joints as the synovial fluid to serum ratio was 6,9 and the alkaline phosphatase probably came from the osteoblasts involved in the repair of erosions.

In conclusion, biochemical abnormalities are common in RA. Elevation of the blood urea ( $> 10$  mmol/l) and serum creatinine were each noted in 17 patients (6,6%) but a reduction of the serum creatinine was much more common, being noted in 43,3%. Hyperuricaemia was present in 31 patients (12,1%) but unexplained hyperuricaemia was noted in only 12 patients (4,7%). A mild elevation of the alkaline phosphatase was noted in 107 patients (42,3%) but a rise in the GGT was present in only 6,5%, which is much lower than the prevalence in other studies. There were 23 patients (9,1%) who had a reduction in the serum albumen and hyperglobulinaemia was present in 39,7%.

TABLE 14.1.1

COMPARATIVE BIOCHEMICAL FINDINGS (mean values  $\pm$  SD) IN  
THE THREE RACIAL GROUPS

	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL
Albumen g/l	40,0 $\pm$ 4,2	39,9 $\pm$ 4,7	38,4 $\pm$ 3,6	39,6 $\pm$ 4,3
Globulin g/l	36,6 $\pm$ 8,7	29,9 $\pm$ 7,1	38,5 $\pm$ 7,9	34,4 $\pm$ 8,7
Cholesterol mmol/l	5,36 $\pm$ 1,15	5,65 $\pm$ 1,27	4,54 $\pm$ 0,97	5,30 $\pm$ 1,23
Calcium mmol/l	2,40 $\pm$ 0,11	2,38 $\pm$ 0,13	2,36 $\pm$ 0,12	2,39 $\pm$ 0,12
Urea mmol/l	5,8 $\pm$ 2,5	6,7 $\pm$ 2,5	4,5 $\pm$ 1,7	5,9 $\pm$ 2,5
Creatinine $\mu$ mol/l	80,7 $\pm$ 19,5	87,3 $\pm$ 22,6	70,7 $\pm$ 15,8	81,3 $\pm$ 20,9
Uric acid mmol/l	0,36 $\pm$ 0,10	0,34 $\pm$ 0,09	0,32 $\pm$ 0,98	0,34 $\pm$ 0,09
Alkaline phosphatase (units)	111,1 $\pm$ 34,2	113,5 $\pm$ 38,4	114,6 $\pm$ 36,1	112,8 $\pm$ 36,2

TABLE 14.1.2

PREVALENCE OF BIOCHEMICAL ABNORMALITIES

	NORMAL RANGE	MEAN VALUE + SD	NUMBER TESTED	PERCENT ABNORMAL	
				PRESENT STUDY	COCKEL ET AL (1977)
Urea mmol/l	1,7-6,7	5,9 + 2,5	256	28,1% high	16% high
Creatinine µmol /l	75-115	81,3 + 20,9	256	6,6% high 43,4% low	7% high
Uric Acid mmol/l	0,12-0,45	0,34 + 0,09	256	9,1% low	8% high
Albumen g/l	35-50	39,6 + 4,3	253	8,1% low	25% high
Globulin g/l	25-35	34,4 + 8,7	252	39,7% high	44% high
Cholesterol mmol/l	3,1-7,1	5,30 + 1,23	256	7,8% high	
Calcium mmol/l	2,10-2,60	2,39 + 0,12	252	2,8% high	1% high 20% low
Alkaline					
Phosphatase Units	30-115	112,8 + 36,2	253	42,3% high	26% high
LDH units l/l	100-350	201,1 + 46,6	232	0,9% high	
AST	0-40	15,8 + 6,3	250	0,8% high	
ALT	0-53	17,3 + 11,1	243	1,2% high	
GGT	0-50	15,9 + 23,1	216	6,5% high	

TABLE 14.1.3

	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL	TOTAL %
SERUM ALBUMEN					
<35 g/l	6	14	3	23	9,1
>35 g/l	98	85	48	230	90,9
	103	99	51	253	100,0
SERUM GLOBULINS					
<35 g/l	53	77	22	152	60,3
36-40 g/l	23	15	11	49	19,4
41-45 g/l	12	3	11	26	10,3
46-50 g/l	9	1	4	14	5,6
>50 g/l	6	2	3	11	4,4
	103	98	51	252	100,0
ALKALINE PHOSPHATASE					
<115 u/l	59	60	27	146	57,7
116-150 u/l	30	24	16	70	27,7
151-200 u/l	12	13	7	32	12,6
201-250 u/l	2	1	1	4	1,6
251-300 u/l	0	1	0	1	0,4
	103	99	51	253	100,0

TABLE 14.1.4.

CORRELATION OF SERUM CREATININE WITH OTHER PARAMETERS

	<u>NUMBER</u>	<u>r</u>	<u>r<sup>2</sup></u>	<u>p VALUE</u>
ESR	215	-0,030	0,0009	0,664
CRP	218	0,013	0,0002	0,848
Articular Index				
Score	220	-0,163	0,0266	0,015
BMI	220	0,065	0,0042	0,336
UAMC	220	0,087	0,008	0,200
AGE	220	0,431	0,186	0,001

TABLE 14.1.5

PREVALENCE OF A RAISED ALKALINE PHOSPHATASE IN RA

	NO. OF PATIENTS	PERCENT WITH ELEVATED ALKALINE PHOSPHATASE
Akesson et al (1980)	253	20,4
Webb et al (1975)	216	18,1
Spooner et al (1982)	98	46,0
Cockel et al (1971)	100	26,0
Sullivan et al (1978)	100	45,0
Present Study (1986)	253	42,3

## CHAPTER 14.2

### IMMUNOLOGICAL ABNORMALITIES

#### INTRODUCTION

Rheumatoid arthritis is a systemic disease which is characterised by the occurrence of articular and extra-articular manifestations. The presence of a positive rheumatoid factor is a feature of the disease, which is noted in 70%-80% of patients with RA. In addition, these patients may also have other immunological abnormalities such as a positive antinuclear factor, raised serum immunoglobulins, raised circulating immune complexes and less frequently hypocomplementaemia.

The aim of the survey was to determine the prevalence of immunological abnormalities in RA and to determine whether there were any differences in the three different racial groups.

#### RESULTS

The mean values of the serum immunoglobulins in the 3 racial groups is shown in Table 14.2.1. One hundred and six patients (43,3%) had a raised IgG, 63 (25,9%) had a raised IgA and 23 (10,5%) had raised IgM. Only one patient had a reduction in the immunoglobulins with a reduction of both IgG and IgA.

The results of the latex and the sheep cell agglutination tests for rheumatoid factor are shown in Table 14.2.2 and Table 14.2.3. A positive latex test for rheumatoid factor (titre of 1/80 or higher) was present in 156 patients (61,5%) and 67 patients (26,4%) had a positive SCAT (titre of 1/16 or higher) at the time of assessment. A positive latex and/or SCAT test for rheumatoid factor were present in 202 patients (78,9%) at some stage of the disease while the remaining 54 patients (21,1%) were persistently seronegative (Table 14.2.4).

The results of the antinuclear factor are summarised in Table 14.2.5. Ninety one patients (36,0%) had a positive ANF in a titre of 1/10 or higher. The pattern of nuclear fluorescence was speckled in 75 patients (29,6%), homogenous in 13 (5,2%) and this information was not available in 3 patients.

There was mild elevation of the double stranded DNA (DS DNA) in 6 patients (mean value 28 $\mu$ g/ml bound DNA per ml of serum; range 22-40 $\mu$ g/ml). Two of these patients had a positive rheumatoid factor (latex test) and antinuclear factor, one patient had a positive ANF alone and one patient had a positive rheumatoid factor alone. Two patients had a negative rheumatoid factor and antinuclear factor.

The smooth muscle antibody was positive in a titre of 1/10 in 14 patients (5,5%) while 18 patients (7,0%) had a titre of 1/20 to 1/80. The antimitochondrial antibody was positive in only one patient in a titre of 1/10. One of the patients with a positive smooth muscle antibody in a titre of 1/10, had an elevated LDH of 513 $\mu$ / $\ell$  but the

transaminases were normal. The LDH and transaminases were normal in the other patients who had a positive smooth muscle antibody and the patient who had a positive antimitochondrial antibody.

The immunological tests in the 3 races were compared to determine whether there were any differences among the races. The mean serum IgG was significantly higher in Coloureds ( $p=0,0004$ ) and Africans ( $p<0,0001$ ) than Caucasians, but there was no difference between the Coloureds and Africans. There were no significant differences among the races for the mean IgA, IgM and DS DNA, and the presence of a positive rheumatoid factor (latex and SCAT), antinuclear factor and smooth muscle antibody.

## DISCUSSION

Kapoor et al studied the serum immunoglobulins in 23 patients with RA and found that the mean IgA levels were significantly higher than controls while the IgG and IgM levels were similar to controls (Kapoor et al 1981). Tilve et al studied 50 patients with RA and found elevated IgM in 14%, elevated IgG and IgM in 22%, a reduction in IgG in 10% and a reduction in both IgG and IgM in 6% (Tilve et al 1977). Pruzanski et al studied the sera of 80 patients with RA, and found increased IgG in 15% and IgM in 6%, and a reduction in IgG in 1% and IgA in 19% (Pruzanski 1973). In the present study, only one patient had a reduction of both IgG and IgA while a raised IgG (43,3%), IgA (25,9%) and IgM (10,5%) were common. A rise in the IgG was noted more frequently in our study and this is probably due to the increased

prevalence of malnutrition, infection and chronic liver disease in the Coloured and African communities and these factors contribute to the hyperglobulinaemia (Powell 1955).

A positive rheumatoid factor occurs in about 75% of patients with rheumatoid arthritis (Davis 1979). In this survey 78,9% had a positive rheumatoid factor during the course of their disease but only 61,5% had a positive rheumatoid factor at the time of assessment. An increased prevalence of a positive rheumatoid factor (using the latex and sheep cell agglutination tests) has been reported in hospitalised Africans without any joint disease (Chalmers et al 1977, Chalmers et al 1978). The increased prevalence has been attributed to chronic liver disease and chronic infections. There was no significant difference in the prevalence of a positive rheumatoid factor among the RA patients from the 3 races.

Antinuclear antibodies were detected in 24% of 72 patients with RA by Pollak (Pollak 1964). He also reviewed previously reported surveys and noted a prevalence of 24% in 638 patients with RA. Webb et al found a positive antinuclear factor in 34,4% of their 216 patients with RA (Webb et al 1975). Antinuclear factor was positive in 91 (36%) of the 253 patients in the present study. Ward et al found that subcutaneous nodules, positive rheumatoid factor, vascular lesions, infections, ocular lesions and Felty's syndrome were commoner in ANF positive patients (Ward et al 1964). However, Condemi et al found that more ANF positive patients had nodules and severe disease but no other difference was detected (Condemi et al 1965).

Antibodies to DS DNA are characteristically found in patients with SLE but may also be present in other connective tissue diseases (Bell et al 1975). Antibodies to denatured (single stranded) DNA do not have the same specificity as antibodies to DS DNA and have been reported in over 50% of patients with RA (Koffler et al 1971). Bell et al found antibodies to DS DNA in 9% of RA patients and Johnson et al detected them in 16% of RA patients (Bell et al 1975, Johnson et al 1973). Rochmis et al found increased DNA binding in 3 (4,8%) out of their 62 patients with definite or classical RA; all three patients had negative antinuclear antibodies and two patients had negative rheumatoid factor tests (Rochmis et al 1974). Mild elevation of antibodies to DS DNA were detected in 6 patients (2,4%) in the present study.

Antimitochondrial antibody was detected in 10% of 71 patients with RA studied by Doniach and co-workers (Doniach et al 1966). Whaley et al estimated a prevalence of antimitochondrial antibodies in 0,94% of 997 patients with RA alone and 1,5% of 71 patients with RA and Sjogren's syndrome (Whaley et al 1970). Only one patient (0,4%) in the present survey had a positive antimitochondrial antibody (titre 1/10) with normal transaminases, LDH and bilirubin.

A positive smooth muscle antibody was detected in 16% of the 32 patients with RA studied by Doniach et al (Doniach et al 1966). There were 32 patients (12,5%) who had a positive smooth muscle antibody in the present survey. Only one of these patients had an isolated elevation of the LDH of 513  $\mu/\ell$  but the transaminases and bilirubin

were normal in all the patients.

In conclusion, abnormalities of immunological tests were present in the 3 communities studied. A rise in the serum immunoglobulins, especially IgG, was much more common than in other studies. The IgG values were significantly higher in Coloureds and Africans than in Caucasians. A positive rheumatoid factor was present in 202 patients (78,9%) during the course of the disease and 91 patients (36,0%) had a positive antinuclear factor. A rise in the DS DNA, antimitochondrial antibody and smooth muscle antibody levels were uncommon.

TABLE 14.2.1

SERUM IMMUNOGLOBULIN LEVELS (mean values  $\pm$  SD) IN  
THE THREE RACIAL GROUPS

	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL
IgG g/l (n=245)	19,81 $\pm$ 8,18	14,98 $\pm$ 5,3	22,45 $\pm$ 6,77	18,40 $\pm$ 9,47
IgA g/l (n=243)	4,51 $\pm$ 2,46	3,49 $\pm$ 1,95	4,44 $\pm$ 2,13	4,09 $\pm$ 2,24
IgM g/l (n=220)	2,28 $\pm$ 1,65	1,93 $\pm$ 1,09	2,33 $\pm$ 1,55	2,15 $\pm$ 1,44

TABLE 14.2.2

RHEUMATOID FACTOR LATEX TEST

<u>TITRE</u>	<u>COLOUREDS</u> (n=103)	<u>CAUCASIANS</u> (n=100)	<u>AFRICANS</u> (n=51)	<u>TOTAL</u> (n=254)	<u>TOTAL%</u>
0	28	20	9	57	22,4
40	12	21	8	41	16,1
80	10	17	7	34	13,4
160	14	9	9	32	12,6
320	19	16	6	41	16,1
640	10	7	10	27	10,6
1280	5	5	1	11	4,3
2560	2	2	1	5	2,0
5120	3	3	0	6	2,4

TABLE 14.2.3

RHEUMATOID FACTOR SHEEP CELL AGGLUTINATION TEST

<u>TITRE</u>	<u>COLOUREDS</u> (n=103)	<u>CAUCASIANS</u> (n=100)	<u>AFRICANS</u> (n=51)	<u>TOTAL</u> (n=254)	<u>TOTAL%</u>
0	77	76	34	187	73,6
16	7	7	3	17	6,7
32	6	3	4	13	5,1
64	3	5	7	15	5,9
128	2	2	1	5	2,0
256	2	5	1	8	3,1
512	2	1	0	3	1,2
1024	4	1	1	6	2,4

TABLE 14.2.4

THE NUMBER OF PATIENTS WHO HAD A POSITIVE LATEX OR SCAT FOR RHEUMATOID FACTOR AT ANY STAGE OF THE DISEASE - PAST OR PRESENT  
(PERCENTAGES IN PARENTHESES)

	<u>COLOUREDS</u> n=104	<u>CAUCASIANS</u> n=100	<u>AFRICANS</u> n=52	<u>TOTAL</u> n=256
Latex				
< 80	25 (24)	24 (24)	8 (15,4)	57 (22,3)
> 80	79 (76)	76 (76)	44 (84,6)	199 (77,7)
SCAT				
< 16	47 (45,2)	41 (41)	16 (30,8)	104 (40,6)
> 16	57 (54,8)	59 (59)	36 (69,2)	152 (59,4)
Latex <80+				
SCAT <16	24 (23,1)	22 (22)	8 (15,4)	54 (21,1)
Latex >80 or				
SCAT >16	80 (76,9)	78 (78)	44 (84,6)	202 (78,9)

TABLE 14.2.5

<u>ANTINUCLEAR ANTIBODIES</u>					
<u>TITRE</u>	<u>COLOUREDS</u> (n=103)	<u>CAUCASIANS</u> (n=99)	<u>AFRICANS</u> (n=51)	<u>TOTAL</u> (n=253)	<u>TOTAL%</u>
0	66	56	40	162	64,0
10	13	12	3	28	11,1
20	5	14	1	20	7,9
100	8	5	5	18	7,1
500	5	8	1	14	5,5
2500	6	4	1	11	4,3

## CHAPTER 14.3

### ASSESSMENT OF IRON STATUS AND PREVALENCE OF ANAEMIA

#### INTRODUCTION

Anaemia is common in RA and may be due to several factors (Mowat 1971). It is most commonly due to the anaemia of chronic disorders which is considered to result from a defect in bone marrow iron supply as the iron stores are characteristically normal or increased (Cartwright and Lee 1971). Iron deficiency has been reported in 30% - 70% of patients with RA (Hansen et al 1983). It is often difficult to differentiate between the anaemia of chronic disorders and iron deficiency because similar abnormalities of red cell indices and iron studies may occur in either type of anaemia. Therefore, an assessment of the body stores is essential and this usually requires examination of the stained bone marrow particles. Serum ferritin concentration provides a reliable index of iron stores in normal subjects (Jacobs et al 1972, Walters et al 1973). A close relationship between the serum ferritin and stainable iron deposits has been reported in RA but some of the patients had a serum ferritin concentration above the level normally associated with iron deficiency even though there were no visible iron deposits (Bentley and Williams 1974, Smith et al 1977). The rise in the serum ferritin may be related to its role as an acute phase reactant in RA (Blake et al 1981, Rothwell and Davis 1981).

The aim of this survey was to determine the prevalence of anaemia and abnormalities of the red cell indices and iron studies in RA.

## RESULTS

The mean values of the haemoglobin, red cell indices, serum iron, total iron binding capacity, percent iron saturation and serum ferritin in the 3 racial groups is shown in Table 14.3.1. There were no differences in the mean values for any of the variables among the 3 races (Table 14.3.1). The prevalence of anaemia in the different races is shown in Table 14.3.2 and there were no significant differences among the races. There were 73 patients (37,8%) who were anaemic; a more severe anaemia with a haemoglobin of less than 10,0 g/dℓ in females and less than 12,0 g/dℓ in males was noted in 29 patients (15,0%).

The prevalence of abnormalities of the iron studies and red cell indices in patients with anaemia and the remainder of the patients is shown in Table 14.3.3. Abnormalities of the red cell indices and iron studies were significantly more common in the anaemic group.

Sixteen patients (8,3%) had a reduction in the serum ferritin of less than 15 µg/ℓ and they were considered to have iron deficiency. Twelve of the 16 patients (75%) with iron deficiency were anaemic and they also had a reduction in the red cell indices. Four patients had a normal haemoglobin; one of them had a normal serum iron, TIBC, iron saturation and red cell indices, one patient had a reduction of the

red cell indices and iron saturation and two patients had only a reduction of the iron saturation.

A reduction in the red cell indices was present in 62 patients (32,1%). Forty patients (20,7%) had a more severe abnormality (MCV less than or equal to 78 fl and MCH of less than or equal to 28 pg); 37 of these 40 patients also had an iron saturation of less than 15%. This latter group of 37 patients included 24 patients who had a serum ferritin of less than 60 µg/l; 7 had values of 15 µg/l or less, 7 had values between 16 µg/l and 20 µg/l and the remaining 10 ranged from 21 - 59 µg/l.

A reduction in the iron saturation (less than 15%) was present in 122 patients (63,2%). A more severe reduction (less than 10%) was present in 82 patients (42,5%). A reduction in the serum iron, rise in the TIBC and fall in the iron saturation consistent with iron deficiency were noted in 45 patients (23,3%). The distribution of the serum ferritin levels in the 3 races is shown in Table 14.3.4. A reduction in the serum ferritin level below 60 µg/l was present in 111 patients (57,5%).

A comparison of some of the clinical and laboratory parameters in the anaemic group and the remainder of the patients is shown in Table 14.3.5. There was a significant reduction in the mean MCV, MCH, serum iron and iron saturation in the anaemic group but there were no differences in the serum ferritin and total iron binding capacity..

There was also a rise in the mean ESR, CRP and articular index score in the anaemic patients but there was no difference in the duration of RA. There was also a significant difference in the functional classification in the 2 groups and this was mainly due to the finding that there were fewer patients in functional class I in the anaemic group. There was no difference in the prevalence of seropositivity and nodules in the two groups.

### DISCUSSION

Anaemia is common in RA and in developed countries it may be noted in 65% of the women and 45% of men (Mowat 1971). In the present survey anaemia was noted in 37,8% of the patients at the time of assessment. Furthermore, it is likely that many other patients had anaemia during the course of the disease. There was a significant increase in the indices of activity (ESR, CRP and articular index score) in the anaemic patients and these findings are in agreement with the observations by others (Cartwright 1971, Mowat 1971). There was no difference in the serum ferritin in the anaemic patients in comparison with the remainder of the patients. This may be related to the fact that ferritin behaves as an acute phase reactant and was higher than expected in the anaemic group as these patients also had higher indices of activity.

Iron deficiency (serum ferritin 15  $\mu\text{g}/\ell$  or less) was detected in 16 patients (8,3%). However, only 12 (75%) of these patients were anaemic. Therefore, in the other 4 patients, a reduction of the serum

ferritin was detected before the development of anaemia.

Several studies have suggested that in patients with RA, a higher value should be used as the lower limit of normal for the serum ferritin in order to detect patients with iron deficiency and an iron responsive anaemia (Hansen and Hansen 1986, Rajapakse 1980, Blake et al 1981). The diagnostic value of the ferritin was studied by Hansen et al using 60  $\mu\text{g}/\ell$  as the lower limit of normal (Hansen et al 1983). They found that serum ferritin was a reliable indicator of iron deficiency in RA with a sensitivity and specificity of 86% and 88% respectively. In a recent study, they reported that in anaemic patients, a serum ferritin value below 60  $\mu\text{g}/\ell$  was a good indicator of iron responsive anaemia with a predictive value of 83% (Hansen and Hansen 1986). If a serum ferritin of less than 60  $\mu\text{g}/\ell$  was used as the lower limit of normal in the present survey, then 111 patients (57,5%) would be considered to have iron deficiency. Hansen et al found evidence of iron deficiency in 55,3% of their patients with RA (Hansen et al 1983). In an endoscopic study of a randomly selected group of 185 patients with RA, a peptic ulcer was detected in 36,2%; over half of the patients who had a GU were asymptomatic (Farah et al 1986). Therefore, it is possible that gastrointestinal bleeding may be an important contributory factor to the development of iron deficiency.

In conclusion, the present survey of a large group of patients with RA shows that anaemia is common, and it was noted in 37,8% of the patients. Although definite iron deficiency was diagnosed in 16

patients (8,3%) who had a serum ferritin of 15  $\mu\text{g}/\ell$  or less, the prevalence of iron deficiency may be as high as 57,5% if a serum ferritin of 60  $\mu\text{g}/\ell$  or less is used as the diagnostic criterion. It may be impractical to subject such a large percentage of predominantly outpatients to bone marrow examination in order to establish a definite diagnosis. Therefore, it is necessary to formulate guidelines for the management of these patients and a trial of iron therapy may be more practical in patients with anaemia and a serum ferritin of less than 60  $\mu\text{g}/\ell$ , especially if there is evidence of disease activity. It is also necessary to investigate patients with iron deficiency or an iron responsive anaemia to determine the cause of the iron deficiency so that they can be appropriately treated.

TABLE 14.3.1

COMPARISON OF THE MEAN AND STANDARD DEVIATION OF THE HAEMOGLOBIN,  
RED CELL INDICES AND IRON STATUS IN THE 3 RACIAL GROUPS

	COLOUREDS (n=75)	CAUCASIANS (n=78)	AFRICANS (n=40)	TOTAL (n=193)	p VALUE
Hb	12,5 <sub>±</sub> 1,8	12,6 <sub>±</sub> 1,9	11,9 <sub>±</sub> 1,9	12,4 <sub>±</sub> 1,9	0,1249
MCV	82,5 <sub>±</sub> 7,1	84,7 <sub>±</sub> 8,4	83,5 <sub>±</sub> 6,4	83,6 <sub>±</sub> 7,6	0,1972
MCH	27,3 <sub>±</sub> 2,8	28,2 <sub>±</sub> 3,1	27,6 <sub>±</sub> 2,7	27,7 <sub>±</sub> 2,9	0,1560
Iron	9,2 <sub>±</sub> 6,1	10,5 <sub>±</sub> 7,7	10,1 <sub>±</sub> 7,9	9,9 <sub>±</sub> 7,2	0,5318
TIBC	68,5 <sub>±</sub> 19,0	68,5 <sub>±</sub> 15,7	66,6 <sub>±</sub> 14,8	68,1 <sub>±</sub> 18,8	0,8092
SATURATION	13,5 <sub>±</sub> 8,5	15,0 <sub>±</sub> 9,7	15,8 <sub>±</sub> 12,0	14,6 <sub>±</sub> 9,8	0,4324
FERRITIN	90,9 <sub>±</sub> 210,4	78,8 <sub>±</sub> 91,2	111,2 <sub>±</sub> 214,1	90,2 <sub>±</sub> 172,8	0,6317

TABLE 14.3.2

PREVALENCE OF ANAEMIA IN THE 3 RACES  
(Percentages in parentheses)

	COLOUREDS n=75	CAUCASIANS n=78	AFRICANS n=40	TOTAL n=193
Females Hb < 11,6 g/dℓ + males < 13,3 g/dℓ	28 (37,3)	25 (32,1)	20 (50,0)	73 (37,8)
Females Hb < 10,0 g/dℓ + males < 12,0 g/dℓ	9 (12,0)	11 (14,1)	9 (22,5)	29 (15,0)

TABLE 14.3.3

PREVALENCE OF ABNORMALITIES OF IRON STATUS AND RED CELL INDICES IN  
 PATIENTS WITH ANAEMIA AND THE REMAINING PATIENTS  
 (Percentages within each group in parentheses)

	ANAEMIC GROUP n=73	REMAINDER n=120	TOTAL n=193	p VALUE
Iron <8 $\mu\text{mol}/\ell$				
TIBC >67 $\mu\text{mol}/\ell$				
Saturation <15%	28 (38,4)	17 (14,2)	45 (23,3)	0,0002
Saturation <10%	51 (69,9)	31 (25,8)	82 (42,5)	< 0,0001
Saturation <15%	62 (84,9)	60 (50,0)	122 (63,2)	< 0,0001
MCV <81 fl				
MCH <28 pg	43 (58,9)	19 (15,8)	62 (32,1)	< 0,0001
MCV <78 fl				
MCH <28 pg	31 (42,5)	9 (7,5)	40 (20,7)	> 0,0001
Iron <8 $\mu\text{mol}/\ell$				
TIBC >67 $\mu\text{mol}/\ell$				
Saturation <15%				
MCV <81 fl				
MCH <28 pg	19 (26,0)	8 (6,7)	27 (14,0)	0,0004
Saturation <15%				
MCV <78 fl				
MCH <28 pg	29 (39,7)	8 (6,7)	37 (19,2)	< 0,0001
Saturation <15%				
MCV <81 fl				
MCH <28 pg	39 (53,4)	17 (14,2)	56 (29,0)	< 0,0001
Ferritin <15 $\mu\text{g}/\ell$	12 (16,4)	4 (3,3)	16 (8,3)	0,0022

TABLE 14.3.4

DISTRIBUTION OF SERUM FERRITIN ( $\mu\text{g}/\ell$ ) LEVELS IN THE 3 RACES

	COLOUREDS (n=75)	CAUCASIANS (n=78)	AFRICANS (n=40)	TOTAL (n=193)	TOTAL Percent
<15	5	7	4	16	8,3
16-20	6	6	3	12	7,8
21-30	10	8	8	26	13,5
31-40	14	12	5	31	16,1
41-50	7	6	1	14	7,3
51-59	4	4	1	9	4,7
>60	29	35	18	82	42,5
TOTAL	75	78	40	193	

TABLE 14.3.5

COMPARISON OF THE FINDINGS IN PATIENTS WITH ANAEMIA  
AND THE REMAINDER OF THE PATIENTS  
 (Percentages in parentheses)

	ANAEMIC GROUP n=73	REMAINDER n=120	p VALUE
MCV (fl)	78,9 $\pm$ 7,7	86,5 $\pm$ 5,9	< 0,0001
MCH (pg)	25,8 $\pm$ 2,9	28,8 $\pm$ 2,3	< 0,0001
Iron ( $\mu$ mol/l)	6,6 $\pm$ 6,9	11,9 $\pm$ 6,6	< 0,0001
TIBC ( $\mu$ mol/l)	68,4 $\pm$ 20,3	67,9 $\pm$ 14,4	0,8619
Saturation (percent)	9,4 $\pm$ 8,0	17,7 $\pm$ 9,5	< 0,0001
Ferritin ( $\mu$ g/l)	95,0 $\pm$ 215,8	87,3 $\pm$ 141,2	0,7671
Duration of RA (months)	148,7 $\pm$ 115,3	155,0 $\pm$ 114,5	0,7159
Articular index score	7,6 $\pm$ 5,9	5,6 $\pm$ 5,7	0,0204
ESR (mm/hour)	106,9 $\pm$ 43,7	59,8 $\pm$ 44,1	< 0,0001
CRP (percent)	31,3 $\pm$ 25,9	19,6 $\pm$ 16,9	0,0008
Functional class*			0,0094
1	10 (13,7)	40 (33,3)	
2	46 (63,0)	53 (44,2)	
3	11 (15,1)	22 (18,3)	
4	6 ( 8,2)	5 ( 4,2)	
TOTAL	73	120	
RF positive	49 (67,1)	74 (61,7)	0,4445
Nodules	17 (23,3)	35 (29,4)	0,3828

## CHAPTER 15

### THERAPEUTIC REQUIREMENTS IN RHEUMATOID ARTHRITIS

#### INTRODUCTION

The role of a multidisciplinary team in the management of patients with RA is well recognised (Ehrlich 1973, Capell et al 1983). The therapeutic goals in the management of RA include the relief of pain, preservation of function, prevention of structural joint damage and attempts to allow the patients to maintain a normal life style. The education of the patient is the single most important aspect of the management of RA (Lightfoot 1985). The control of disease activity and preservation of function may require a combination of physical therapy, occupational therapy, drug therapy and hospitalization. Emotional support and therapy for depression and/or anxiety are often required. Complications of drug therapy such as gastrointestinal adverse effects and anaemia also require specific therapy. In addition, patients may also require therapy for co-existent disease such as hypertension and cardiovascular diseases, asthma or diabetes.

The aims of this study were to determine the therapeutic requirements of patients with RA with reference to the following forms of therapy:

- 1) Physiotherapy
- 2) Occupational therapy

- 3) RA related drug therapy eg. analgesics, anti-inflammatory drugs
- 4) Remittive agent therapy
- 5) Intra-articular or intralesional corticosteroids
- 6) Therapy for concomitant diseases such as hypertension and cardiovascular disease
- 7) Surgery - the surgical requirements are discussed in detail in the next chapter.

## RESULTS

### (1) PHYSIOTHERAPY

About two thirds of the patients (67,6%) had been referred to physiotherapy during the course of their illness and only 18 patients (7,0%) were attending physiotherapy at the time of assessment. The frequency with which the patients used the different modalities of physical therapy are summarised in Table 15.1.

### (2) OCCUPATIONAL THERAPY

Fifty percent of the patients had been referred to an occupational therapist. Most of these patients (86%) had used one or more splints. One third of the patients had used some form of aids and the activities for which the aids were used are shown in Table 15.2.

(3) DRUG THERAPY FOR RHEUMATOID ARTHRITIS (EXCLUDING REMITTIVE AGENT THERAPY)

All the patients had taken non steroidal anti-inflammatory drugs (NSAIDs) during the course of their illness and 87,5% were on oral NSAIDs at the time of assessment. The patients who were not on oral NSAIDs were in remission, on treatment with low dose corticosteroids or were using only NSAID suppositories. The number of different NSAIDs taken in the year preceding the survey is shown in Table 15.4. The current NSAID medication taken by the patients is shown in Table 15.5 (oral NSAIDs) and Table 15.6 (NSAID suppository). Most of the patients had taken analgesics and 60,6% were on current analgesic medication. Antidepressant drugs and tranquilizers were taken by 24,2% and 31,3% respectively.

(4) INTRA-ARTICULAR OR INTRALESIONAL CORTICOSTEROIDS

The number of articular or peri-articular injections of steroids and local anaesthetic is shown in Table 15.7. Thirty eight patients (20,9%) received 9 or more injections at various sites.

(5) REMITTIVE AGENT THERAPY

There were 104 patients (40,6%) who were on a remittive

agent at the time of assessment and a further 59 patients (23,1%) were on remittive agents in the past (Table 15.8). Sixty Coloureds (57,7%), 69 Caucasians (69%) and 34 Africans (65,4%) were treated with remittive agents in the past or present; there were no significant differences among the races. The number of different remittive agents taken by the patients is shown in Table 15.9. The majority of the patients (41,4%) had taken only one remittive agent while 22,3% had used 2 or more remittive agents.

The frequency of the use of the different remittive agents at present and in the past, the response to therapy and the reasons for stopping therapy are shown in Table 15.10. Ninety one patients (35,5%) had received injectable gold (Sodium aurothiomalate : 'Myocrisin'), 15 patients (5,9%) oral gold (Auranofin: 'Ridaura'), 54 patients (21,1%) penicillamine, 54 patients (21,1%) chloroquine and 16 (6,3%) sulphasalazine. There were 3 patients who were treated with cyclophosphamide, 2 with azathioprine and one with dapsone.

(6) CORTICOSTEROID THERAPY (Table 15.11)

Thirty nine patients (15,2%) were on steroids for a mean duration of 4,3 years; the present mean daily dose was 7,4 mg. Another 45 patients (17,6%) had been on steroids in the past for a mean duration of 2,1 years.

(7) OTHER DRUG-THERAPY

Apart from the medication for RA, the frequency of use of other medication at the time of the study is shown in Table 15.12. The prevalence of hypertension was 21,5% and therefore drugs for hypertension were frequently prescribed. Twenty five patients (9,8%) were on oral iron therapy and 9 patients (3,5%) were on folate. The other medication which the patients received were for the treatment of asthma, diabetes, ischaemic heart disease, peptic ulcers etc. Thirty eight patients (14,8%) were on regular medication for dyspepsia or peptic ulcers and a further 23 patients (9,0%) took intermittent antacid therapy.

DISCUSSION

The management of a chronic disease such as RA, where the cause is not known, presents a challenge to the clinician. Once the diagnosis of RA has been made, education of the patients, their family and employers is basic to the planning of any treatment program. A positive approach by the patient may be the single most important factor in the successful management of RA (Lightfoot 1985).

Although physical therapy is an essential part of the treatment of many rheumatic diseases, it is often neglected (Pigg 1985). It is important for patients to be advised about an exercise program to

maintain range of motion, prevent disuse atrophy of muscles and to prevent or correct deformity. The major concern of the occupational therapist is to maintain the patient's ability to function independently and it may be necessary to provide aids to assist the patient to perform tasks which would otherwise be difficult. In the present survey only 50% of the patients had been referred to an occupational therapist and 67,6% were referred for physiotherapy. One would expect a higher proportion of patients who attend a specialist arthritis clinic to be referred for physiotherapy and occupational therapy. About half of the patients in the study were attending the arthritis clinic at Groote Schuur Hospital where there is a great demand for physiotherapy and occupational therapy from other medical disciplines. Therefore, most of these patients would not be referred routinely for advise about exercise programs or activities of daily living assessment. Patients were only referred when specific therapy such as paraffin wax, ultrasound, splints etc. were required.

All the patients had taken oral NSAIDs during the course of their disease and 87,5% were currently on an oral NSAIDs. There is a marked variation among individuals in their response to NSAIDs and therefore there were a wide variety of NSAIDs which were being taken by the patients as shown in Table 15.5. Furthermore, it was also frequently necessary for patients to change their NSAID medication and the number of different NSAIDs taken during the year preceding the survey is shown in Table 15.4. Only 32,4% were on one or no NSAIDs while the remainder had used 2 or more NSAIDs. The use of NSAID suppositories was also frequent in this survey and 109 patients (42,6%) were

currently using suppositories, usually in combination with an oral agent.

Psychosocial problems are common in RA (Vignos 1973, Swezey and Wainer 1985). Antidepressant medication and tranquilisers had been used during the course of the disease in 24,2% and 31,3% of the patients respectively.

Intra-articular injections of corticosteroids are effective in the management of rheumatoid synovitis while intralesional injections may be used in peri-arthritis, tendinitis or tenosynovitis. In the present survey there were 179 patients (69,9%) who had received one or more injections of intra-articular or intralesional steroids. The use of local corticosteroids is effective in controlling inflammation, preventing joint contracture, improving function and may delay the need for starting a disease modifying antirheumatic drug (Shapiro et al 1985).

There were 104 patients (40,6%) who were currently taking a disease modifying antirheumatic drug and a further 59 patients (23,1%) were on treatment in the past. The results of therapy with injectable gold (Sodium aurothiomalate: 'Myocrisin'), oral gold (Auranofin : 'Ridaura') and penicillamine in the arthritis unit have been published (Majoos et al 1981, Smith et al 1982, Grobbelaar and Meyers 1984) and are similar to the findings in other published series.

Anaemia is common in patients with RA and may be due to many factors.

Twenty five patients (9,8%) were currently on oral iron therapy, 9 patients (3,5%) were on folic acid and one patient with pernicious anaemia was on vitamin B12 injections. The prevalence of hypertension in this study was 21,5% and therefore many patients were on diuretics, beta-blockers and/or other hypotensive drugs.

The management of patients with RA often requires the use of many different drugs, apart from the need for physiotherapy and occupational therapy. Treatment for inflammation may require the use of analgesics, NSAIDs and disease modifying antirheumatic drugs while the use of haematinics, anti-depressants and antacids may be necessary for the accompanying manifestations or complications of RA. Furthermore, concomitant diseases such as hypertension, ischaemic heart disease, asthma and diabetes will further increase the number of medications which the patients have to take.

TABLE 15.1

	<u>PHYSIOTHERAPY</u>				TOTAL %
	NO	PAST	PRESENT	PAST OR PRESENT	
Physiotherapy	83	155	18	173	67,6
Hydrotherapy	173	75	8	83	32,4
Exercises	107	135	14	149	58,2
Heat	162	87	7	94	36,7
Cold (ice)	224	30	2	32	12,5
Electrical (Ultra-sound, lamp etc)	169	83	4	87	34,0

TABLE 15.2

	<u>OCCUPATIONAL THERAPY</u>				TOTAL %
	NO	PAST	PRESENT	TOTAL PAST OR PRESENT	
1. Occupational Therapy	128	116	12	128	50
2. Splints	146	79	31	110	43
3. Aids	171	76	9	85	33,2
4. Types of Aids					
a) personal (dressing, feeding)	232	5	19	24	9,4
b) hygiene (both, toilet)	221	12	23	35	13,7
c) general household, cooking	187	19	50	69	27
d) walking stick	197	30	29	59	23
e) elbow crutches	232	15	9	24	9,4
f) axillary crutches	223	27	6	33	12,3
5. Wheelchair	239	7	10	17	5,6

TABLE 15.3DRUG THERAPY FOR RHEUMATOID ARTHRITIS

(Figures as Percentages)

	PAST	PRESENT	TOTAL
Analgesics	36,7	60,5	97,2
Antidepressants	16,8	7,4	24,2
Tranquilizers	13,3	18,0	31,3
NSAID (Oral)	12,5	87,5	100,0

TABLE 15.4NUMBER OF DIFFERENT NSAIDs TAKEN OVER THE PAST YEAR

NUMBER	PERCENT
0	4,3
1	28,1
2	35,2
3	16,8
4	10,9
5	3,1
6	1,6

TABLE 15.5CURRENT ORAL NSAID THERAPY

DRUG	NUMBER	PERCENT
Diclophenac Sodium	61	25,3
Naproxen	23	9,5
Piroxicam	22	9,1
Indoprofen	20	8,3
Froben	12	5,0
Fenclofenac	10	4,2
Sulindac	9	3,7
Ketoprofen	8	3,3
Indomethacin	7	2,9
Tolmetin sodium	5	2,1
Ibruprofen	4	1,7
Fenoprofen	1	0,4
Other	2	0,8
Combination	15	6,2
Nil	42	17,4

TABLE 15.6CURRENT NSAID SUPPOSITORY

DRUG	NUMBER	PERCENT
Indomethacin	78	32,5
Diclophenac Sodium	23	9,6
Ketoprofen	7	2,9
Naproxen	1	0,4
Nil	131	54,6

TABLE 15.7

NUMBER OF INTRA-ARTICULAR / INTRALESIONAL INJECTIONS OF STEROID  
AND LOCAL ANAESTHETIC

NUMBER OF INJECTIONS	NUMBER (n=179)	PERCENT
1	33	18,1
2	37	20,3
3	18	9,9
4	25	13,7
5	12	6,6
6	10	5,5
7	3	1,6
8	6	3,3
9	38	20,9

TABLE 15.8

USE OF REMITTIVE AGENT THERAPY IN THE 3 RACIAL GROUPS

	COLOUREDS (n=104)	CAUCASIANS (n=100)	AFRICANS (n=52)	TOTAL (n=256)	TOTAL %
Present	37	40	26	103	40,2
Past	23	29	8	60	23,4
Nil	44	31	18	93	36,3

TABLE 15.9NUMBER OF DIFFERENT REMITTIVE AGENTS USED

NUMBER	COLOURED	CAUCASIANS	AFRICANS	TOTAL	TOTAL %
0	44	31	18	93	36,3
1	43	36	27	106	41,4
2	14	23	6	43	16,8
3	3	8	1	12	4,7
4	0	2	0	2	0,8
	104	100	52	256	100,0

TABLE 15.10

REMITTIVE AGENT THERAPY IN RHEUMATOID ARTHRITIS

	INTRAMUSCULAR GOLD	ORAL GOLD	PENICILLAMINE	CHLOROQUINE	SULPHASALAZINE	OTHER
<b>1. PRESENT TREATMENT</b>						
Remission	22	11	5	12	5	2
No response	1	0	1	1	1	1
Partial response	10	0	5	5	1	0
Inadequate therapy	1	0	7	13	1	0
TOTAL	34	11	18	31	8	2
<b>2. PAST TREATMENT</b>						
Remission	17	0	10	6	4	0
No response	9	2	11	8	2	2
Partial response	13	1	9	5	1	1
Inadequate therapy	18	1	6	4	1	1
TOTAL	57	4	36	23	8	4
<b>REASONS FOR STOPPING TREATMENT</b>						
Remission	1	0	0	1	3	0
Side effects	40	1	21	9	3	1
No/inadequate response	10	2	13	7	1	2
Poor compliance	3	1	2	4	0	0
Other	3	0	0	2	1	1
TOTAL	57	4	36	23	8	4
TOTAL NUMBER (PAST AND PRESENT)	91	15	54	54	16	6
Mean duration of treatment (Months)	26,9	39,5	17,9	19,4	12,6	5,9

TABLE 15.11CORTICOSTEROID THERAPY

	COLOUREDS	CAUCASIANS	AFRICANS	TOTAL	TOTAL %
1. Nil	73	59	40	172	67,2
2. Past	17	20	8	45	17,6
3. Present	14	21	4	39	15,2
Mean duration (years)	4,8	4,7	0,4	4,3	
Mean daily dose at present (mg)	6,7	7,6	9,3	7,5	

TABLE 15.12OTHER DRUG THERAPY

	NUMBER (n=256)	PERCENT (n=100)
Iron	25	9,8
Folic Acid	9	3,5
Vit B12	1	0,4
Digoxin	3	1,2
Diuretics	45	17,6
B Blockers	20	7,8
Other hypotensive drugs	18	7,1
Other therapy	61	23,8

## CHAPTER 16

### SURGICAL REQUIREMENTS IN RHEUMATOID ARTHRITIS

#### INTRODUCTION

The major consequences of inflammatory joint disease include pain, loss of function, progressive joint destruction and deformity. Evaluation by a multidisciplinary team is essential to formulate a programme of management with realistic goals for each patient (Capell et al 1983, Sledge 1981, Ehrlich 1973, Pigg 1985, Lightfoot 1985).

The development of the concept of low friction arthroplasty by Charnley in 1961 revolutionised the management of arthritis of the hip and today many different joints are amenable to prosthetic replacement (Charnley 1961). Patients with RA may need to have surgery to multiple joints and careful preoperative evaluation is then essential to determine the optimal timing and sequence of the surgical procedures (Capell et al 1983, Sledge 1981).

The frequency of surgery in RA will depend on a number of factors such as the selection of patients for study, the age of patients, the duration and severity of the disease and the availability of surgical expertise and resources for rehabilitation.

At the Rheumatism Foundation Hospital in Heinola, Finland, close

collaboration between the rheumatologist and orthopaedic surgeons in the management of patients with rheumatic diseases was established in 1952. In 1964, Laine and Vainio reported that one third of their patients with RA had surgery and that most of the patients had more than one operation (Laine and Vainio 1964).

The relevant information concerning the surgical requirements in RA is important to facilitate the long term planning and provision of health care services for patients with rheumatic diseases.

In view of the lack of information about the frequency of surgery in Africa, this study was conducted to determine the following:

- a) the frequency of surgery in patients with RA.
- b) the frequency of surgery to the upper and lower limbs and spine.
- c) the nature and frequency of surgery performed on the various joints.
- d) whether there were any inter-racial differences in the requirements for the different surgical procedures.

## RESULTS

### 1. FREQUENCY OF SURGERY IN RHEUMATOID ARTHRITIS

#### (TABLE 16.1, FIGURE 16.1)

- a. There were 126 patients (49,2%) who had one or more surgical procedures during the course of their disease. Ninety patients (35,2%) had more than one surgical

procedure. The proportion of patients who required surgery in the different racial groups was Caucasians 60%, Coloureds 44,2% and Africans 40%. Surgery was performed significantly more often in Caucasians than in the Africans ( $p=0,012$ ) and Coloureds ( $p=0,024$ ).

- b. The 126 patients who required surgery had 479 surgical procedures (mean 3,8 / patient, range 1 - 20).
- c. The most frequent sites of surgery were the hands, wrists, knees, metatarsophalangeal joints (MTPJs) and the hips.

## 2. HAND AND WRIST SURGERY (TABLE 16.2)

Flexor tenosynovectomy was performed in the hands in 32 patients (12,5%) while 6 patients (2,5%) had extensor tenosynovectomy. Fourteen patients (5,2%) had repair of the extensor tendons following tendon rupture. The other soft tissue surgery (Table 16.2.) which was performed in 13 patients were procedures for the correction of swan neck and boutonniere deformities. The most common procedure in the wrists was excision arthroplasty of the ulnar head in 30 patients (11,7%), and this operation was usually combined with rerouting of the extensor tendons (8,2%). Fourteen patients (5,5%) had carpal tunnel release, which was bilateral in 6 patients (2,3%).

### 3. HIP AND KNEE SURGERY (TABLE 16.3)

A cemented replacement arthroplasty of the hip was performed in 21 patients (8,2%), eight (38%) of whom had bilateral arthroplasty. Replacement arthroplasty of the knee was performed in 29 patients (11,3%) with 14 patients (48,3%) having bilateral arthroplasty. There were 40 patients (15,6%) who had a replacement of one or more of the four major weight bearing joints. The soft tissue procedures on the knees included soft tissue release, excision of a ruptured popliteal cyst and excision of a semimembranous bursa.

### 4. FOREFOOT SURGERY (TABLE 16.4)

Thirty one patients (12,1%) had surgery to the 1st MTPJ and 24 patients (9,4%) had surgery to the 2nd to 5th MTPJs. The most common procedures were osteotomy and arthrodesis of the 1st MTPJ and excision arthroplasty of the 2nd to 5th MTPJs. The soft tissue surgery in the forefoot included tenotomy or tendon transfer.

### 5. OTHER JOINTS

There were only a few patients who had surgery in the other joints. The surgical procedures which were most frequently performed were a Benjamin double osteotomy of the shoulder in 9 patients (3,5%), excision of the radial head in 6 patients

(2,3%), arthrodesis of the ankles in 4 patients (1,6%) and supra-malleolar osteotomy in 3 patients (1,2%).

#### 6. INTER-RACIAL COMPARISON (TABLE 16.5)

There was a statistically significant increase in the frequency of carpal tunnel release (10% vs 0%), flexor tenosynovectomy (22% vs 3,9%), surgery to the 1st MTPJ (15% vs 0%) and excision arthroplasty of the 2nd to 5th MTPJs (16% vs 0%) in Caucasians in comparison with Africans. Flexor tenosynovectomy (22% vs 7,7%) was more frequently performed in Caucasians in comparison with Coloureds ( $p < 0,05$ ).

#### DISCUSSION

Laine and Vainio reported an analysis of 1000 operations on 562 patients from May 1963 to February 1964 (Laine and Vainio 1964). At that time, synovectomy was being performed more frequently and replacement arthroplasty had not been performed on any of their patients. They found that surgical procedures were most frequently performed on the foot and ankle (36,4%), hands (29,0%) and the knees (19,7%). In the present study (Figure 16.1) surgery was most frequently performed in the hands (21,5%), wrists (18,8%), knees (18,8%) and feet and ankles (14,5%). There were 126 patients (49,2%) who had one or more surgical procedures and the mean number of surgical procedures was 3,8 per patient. Ninety patients (35,2%) had more than one surgical procedure. Laine and Vainio noted that about

one third of their RA patients had surgery and most of them had more than one operation (Laine and Vainio 1964).

Only four patients required fusion of the upper cervical spine despite the presence of significant atlanto-axial instability and/or cranial settling in 46,4% of the patients. Arthroplasty of the shoulder was not being performed in the unit at the time of the survey and nine patients had a Benjamin double osteotomy, which provided effective pain relief although there was little improvement in the range of movement.

Replacement arthroplasty of the knee was performed on 43 joints in 29 patients in comparison to replacement arthroplasty of the hip on 29 joints in 21 patients. The greater need for arthroplasty of the knee probably reflects the more frequent involvement of the knee joint in RA.

Rupture of the flexor tendon is not as common as extensor tendon rupture (Helal 1984). Two of our patients had rupture of the flexor pollicis longus and one patient had rupture of the flexor digitorum profundus to the middle finger. However, extensor tendon rupture was more common and was detected in fourteen patients (5,2%).

An increased frequency of surgery in Caucasians and Coloureds in comparison to Africans may be due to several factors. The Africans were younger and had RA for a shorter period than the Caucasians. The severity of RA has been reported to be milder in Africans (Anderson

1970), but there were no differences in the functional disability and severity of radiographic changes in the 3 communities in this study. Some of the patients had been offered surgery to improve function but refused. Many of the Africans were unemployed and were therefore able to cope with their disabilities.

The absence of any surgical procedures in the forefoot in Africans may be related to several factors. Hallux valgus is significantly more common in Caucasians than in urban and rural Africans (Gottschalk et al 1980). The difference has been attributed to either the use of footwear or a basic abnormality of the feet which may be established at an early age. Other studies in St Helena and in the Chinese population have shown that hallux valgus is commoner in shod feet than unshod feet (Shine 1965, Lam Sim-Fook 1958).

The difference in the need for soft tissue surgery such as flexor tenosynovectomy and carpal tunnel release among the different races cannot be readily explained. In the prospective clinical assessment of the hand, flexor tenosynovitis was less common in Africans than Coloureds or Caucasians but these values were not statistically significant.

The need for a replacement arthroplasty of the major weight bearing joints in 15,6% of the patients reflects the need to achieve better medical control and prevent joint destruction. It is likely that with the present trends towards earlier and more aggressive medical management, the need for surgery may be lessened in some patients. The

frequency of surgery depends on various factors and 49,2% of the patients in the present study had one or more surgical procedure. If a similar survey is conducted among patients who had RA for a longer period, then the frequency of surgery would be higher. Many of the patients in this study had further surgery after the completion of the survey.

Surgery plays an important role in the long-term management of patients with RA; 126 patients (49,2%) had one or more surgical procedures and the mean number of procedures was 3,8. The most frequent sites of surgery were the hands, wrists, MTPJs and hips. Forty patients (15,6%) had a replacement arthroplasty of one or more of the major weight bearing joints. There was a significant increase in the frequency of surgery to the 1st MTPJ, 2nd to 5th MTPJ, carpal tunnel release and flexor tenosynovectomy in Caucasians compared to Africans.

The polyarticular involvement in RA and the need for multiple surgical procedures per patient emphasizes the view that collaboration and cooperation between the Rheumatologist and the Orthopaedic Surgeon is not merely desirable but mandatory.

FIGURE 16.1

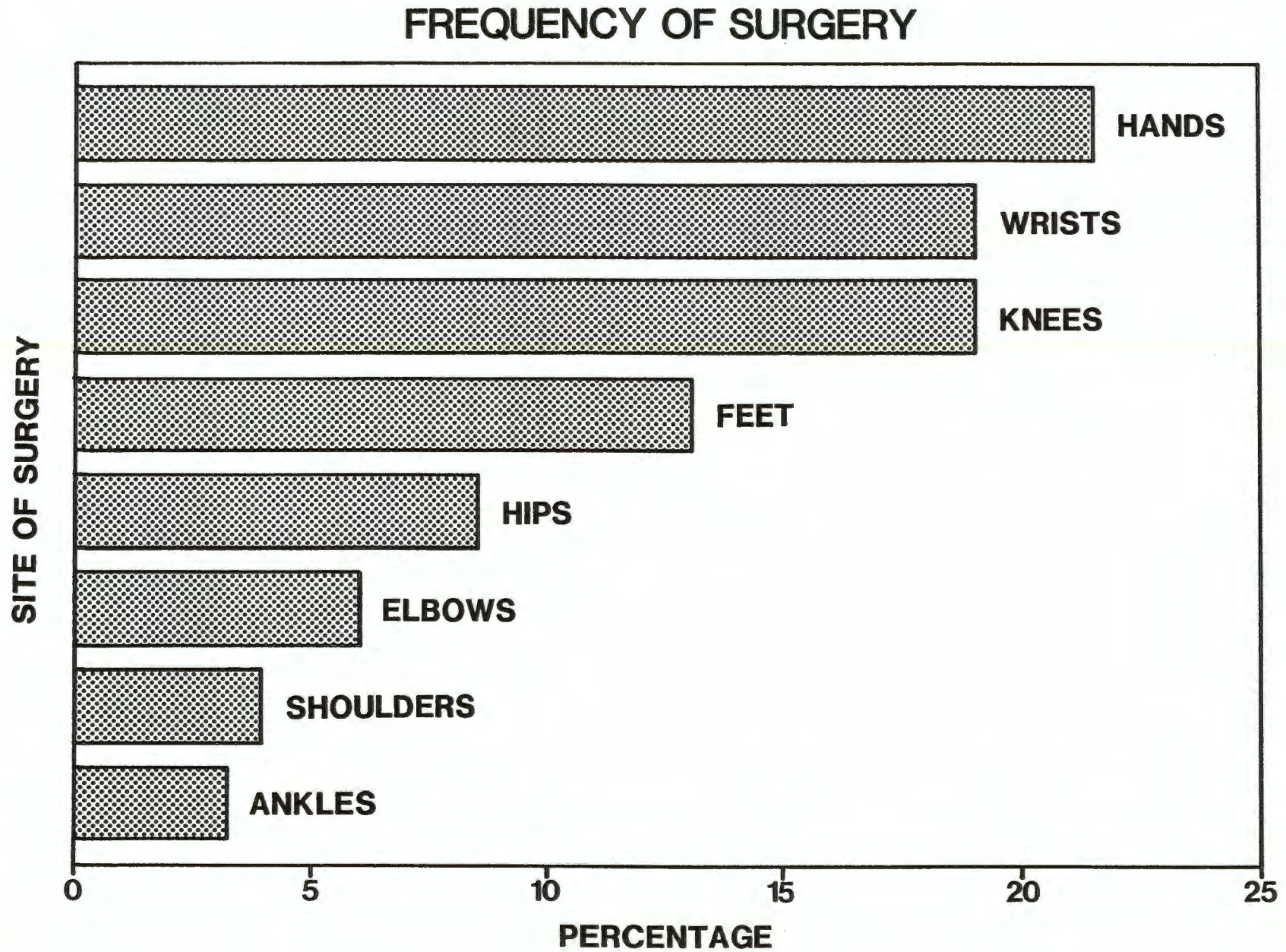


TABLE 16.1FREQUENCY OF SURGERY IN RHEUMATOID ARTHRITIS

	<u>Coloureds</u> (n=104)	<u>Caucasians</u> (n=100)	<u>Africans</u> (n=52)	<u>Total</u> (n=256)	<u>Total %</u>
Upper limb	15	18	7	40	15,6
Lower limb	18	11	10	39	15,2
Upper and lower	8	28	3	39	15,2
Soft tissue only	5	3	0	8	3,1
TOTAL	46	60	20	126	49,2

N.B. Four patients had surgery to the cervical spine and 1 patient to the lumbar spine - all these patients had other surgical procedures and are included in the above table.

TABLE 16.2

FREQUENCY OF SURGICAL PROCEDURES  
IN THE HANDS AND WRISTS

	<u>Number of</u> <u>Hands or Wrists</u>	<u>Number of</u> <u>Patients</u>	<u>Number of</u> <u>Patients %</u>
<b>A) <u>HAND SURGERY</u></b>			
1) Synovectomy			
Flexor tendon	47	32	12,5
Extensor tendon	6	6	2,3
PIP	4	4	1,6
MCP	8	7	2,7
2) Extensor tendon repair	14	14	5,5
3) Other soft tissue surgery	16	13	5,1
4) Arthrodesis MCP, PIP and or DIP	6	4	1,6
5) Excision Arthroplasty-MCP	1	1	0,4
6) Replacement Arthroplasty-MCP	14	10	3,9
<b>B) <u>WRIST SURGERY</u></b>			
1) Carpal tunnel release	20	14	5,5
2) Synovectomy wrist	7	7	2,7
3) Extensor tendon surgery	31	21	8,2
4) Excision arthroplasty of ulnar styloid	44	30	11,7
5) Osteotomy-radius	2	1	0,4
6) Arthrodesis	7	5	2,0

TABLE 16.3

HIP AND KNEE SURGERY

	<u>Number of Joints</u>	<u>Number of Patients</u>	<u>Number of Patients %</u>
1) HIP			
a) Replacement arthroplasty	29	21	8,2
b) Osteotomy	1	1	0,4
c) Other	2	2	0,8
2) KNEE			
a) Synovectomy	23	17	6,6
b) Other soft tissue	7	6	2,3
c) Osteotomy	13	8	3,1
d) Replacement arthroplasty	43	29	11,3
e) Arthrodesis	2	2	0,8

TABLE 16.4

FORE FOOT SURGERY

	<u>Number of Feet</u>	<u>Number of Patients</u>	<u>Number of Patients %</u>
1ST MTPJ			
Exostectomy	8	7	2,7
Osteotomy	10	8	3,1
Arthrodesis	14	11	4,3
Excision arthroplasty	5	3	1,2
Replacement arthroplasty	1	1	0,4
Soft tissue	6	4	1,6
Other	2	2	0,8
2ND to 5TH MTPJs			
Excision arthroplasty	36	23	9,0
Osteotomy	1	1	0,4
Arthrodesis	1	1	0,4
Soft tissue	7	5	2,0

TABLE 16.5

INTER RACIAL COMPARISON OF SURGERY IN THE DIFFERENT RACES(figures as percentages)

PROCEDURE	CAUCASIANS	COLOUREDS	AFRICANS
1. Carpal tunnel release	<u>10,0</u>	<u>2,9</u>	0,0
2. Flexor tenosynovectomy	22,0	<u>7,7</u>	<u>3,9</u>
3. 1st MTPJ surgery	<u>15,0</u>	<u>6,7</u>	0,0
4. 2nd - 5th MTPJ surgery	<u>16,0</u>	<u>7,7</u>	0,0

NB: Statistical test used was the Fisher's exact test for pairwise comparison. The continuous line represents groups between whom there was no significant difference.

## CHAPTER 17

### EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

#### IN COLOURED

- 17.1 Introduction
- 17.2 Cardiac involvement - clinical and echocardiographic study
- 17.3 Keratoconjunctivitis sicca
- 17.4 Peripheral neuropathy - clinical and electrophysiological study
- 17.5 Pulmonary involvement - clinical and lung function tests
- 17.6 Prevalence of extra-articular manifestations - summary

## CHAPTER 17.1

### INTRODUCTION

The 104 Coloured patients in the survey were chosen for further study to determine the prevalence of extra-articular manifestations of RA based on a history, clinical assessment, laboratory findings, review of clinical records and specialised tests such as pulmonary function tests, echocardiography, nerve conduction studies and ophthalmological assessment to detect the presence of KCS.

The mean age of the patients was 51,1 years (range 21-80 years) and the mean duration of RA was 12,4 years (range 1,1 - 50 years) as shown in Table 3.1. The female to male ratio was 2,3 : 1. The age group and sex ratio at the time of assessment and the duration of RA are shown in Figure 17.1.1 and Figure 17.1.2 respectively.

The majority of the patients (89%) were outpatients, 9 (9%) were in hospital for medical management and were assessed prior to discharge from hospital. One patient (1%) was seen prior to surgery and another patient was seen prior to discharge from hospital after arthrodesis of her wrist.

Fifty six patients (54%) had been admitted to Groote Schuur or Princess Alice Orthopaedic Hospital and the mean number of admissions in this group was 2,6 per patient. Thirty eight (68%) of the 56

patients had one or more admissions for surgery while the remaining 18 patients (32%) had been admitted for medical management only. The marital status, history of smoking and alcohol intake, occupational history, family history of RA and associated diseases are discussed in Chapter 3. The functional classification (ARA) is shown in Figure 17.1.3.

Sixty patients (58%) had been treated with a remittive agent, 37 (36%) were currently on therapy and 23 patients (22%) had therapy in the past. Forty three patients (41%) used only one remittive agent, 14 (14%) had used 2 agents and 3 (3%) had been on 3 different remittive agents.

The remittive agents used by the patients are shown in Table 17.1.1.

TABLE 17.1.1

FREQUENCY OF USE OF THE DIFFERENT REMITTIVE AGENTS

DRUG	PAST	PRESENT	TOTAL (n=104)	TOTAL %
Injectable gold	23	11	34	32,7
Oral gold	2	7	9	8,7
Penicillamine	9	5	14	13,5
Chloroquine	7	12	19	18,3
Sulphasalazine	1	2	3	2,9
Azathioprine	1	0	1	1,0

FIGURE 17.1.1

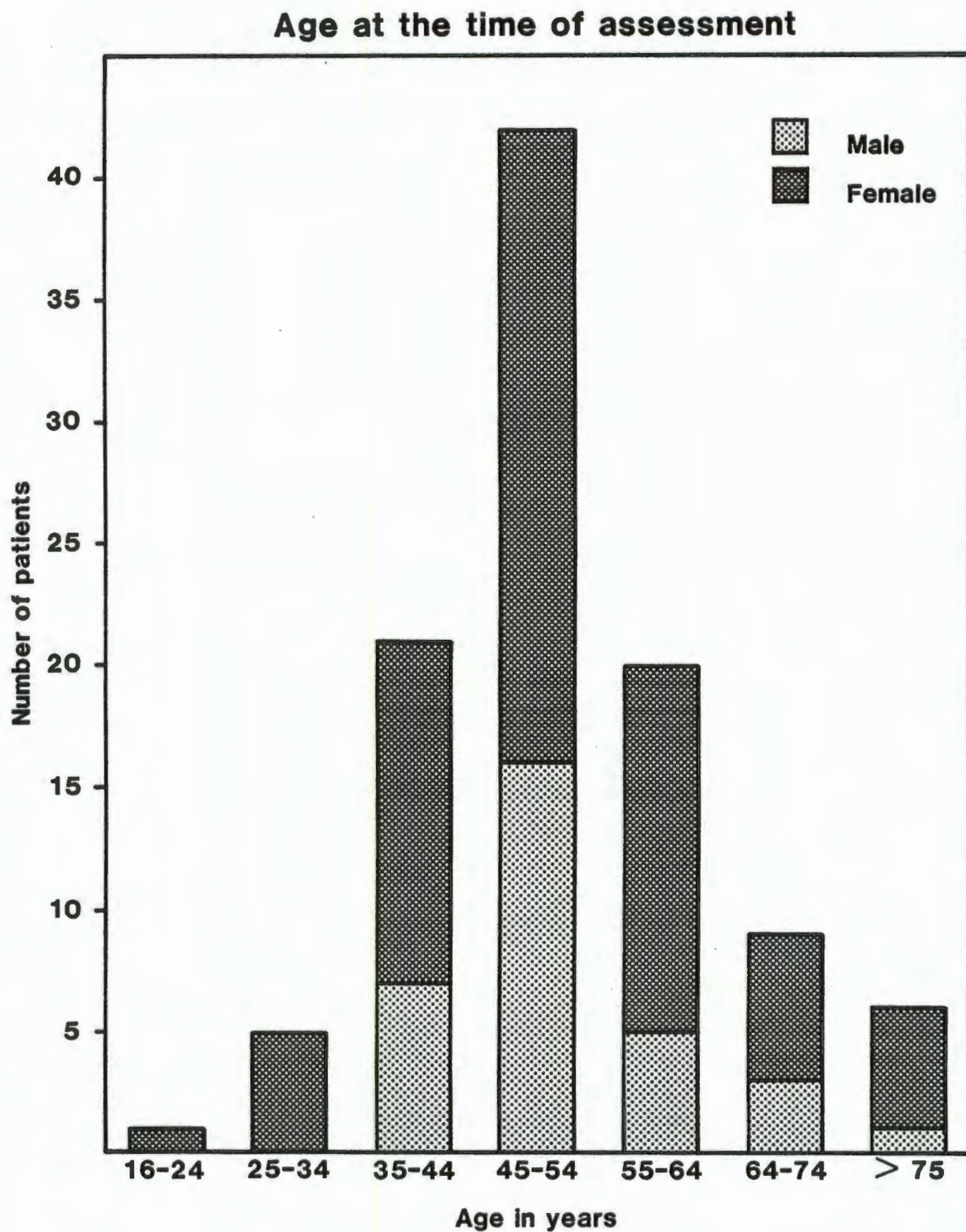


FIGURE 17.1.2

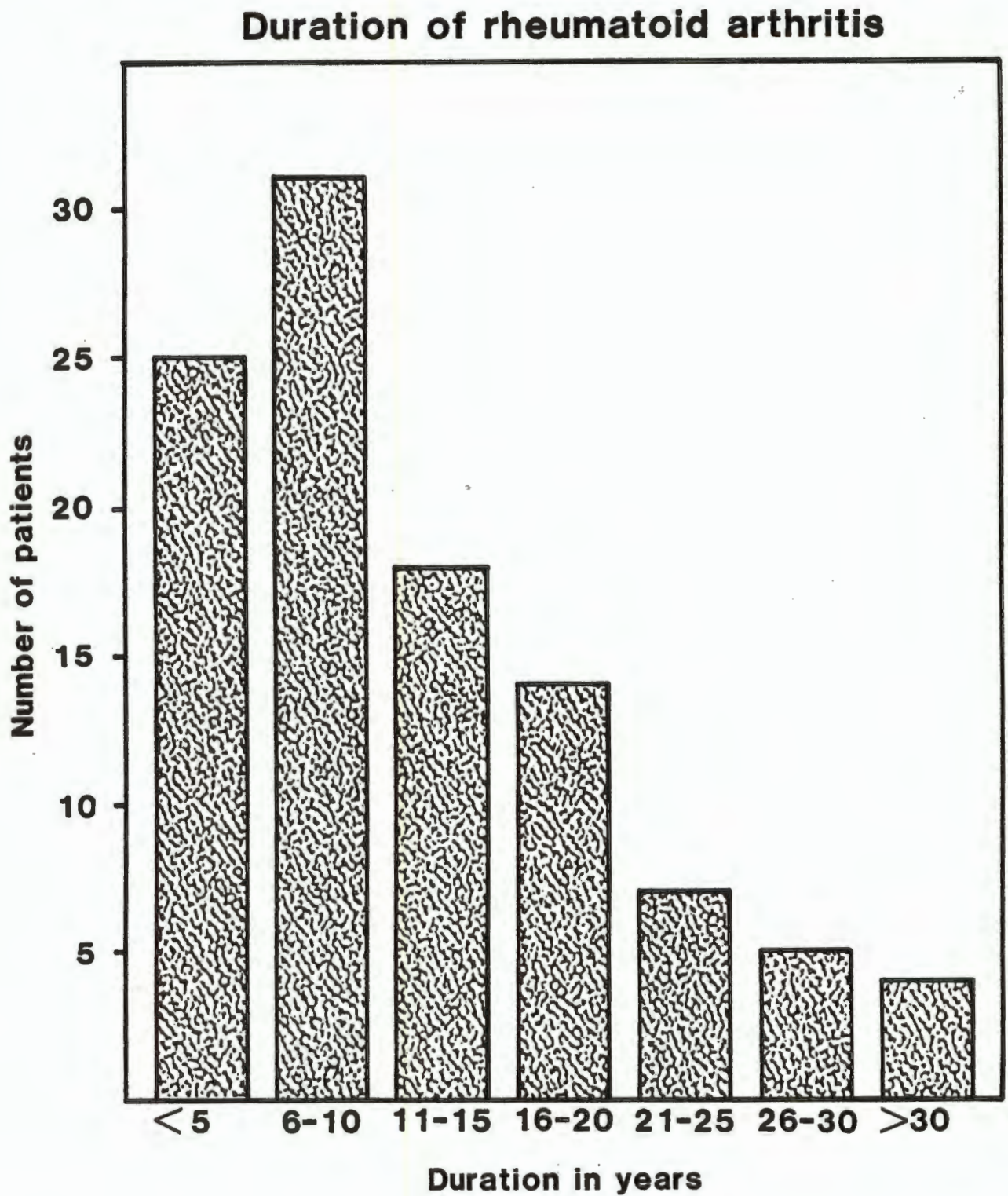
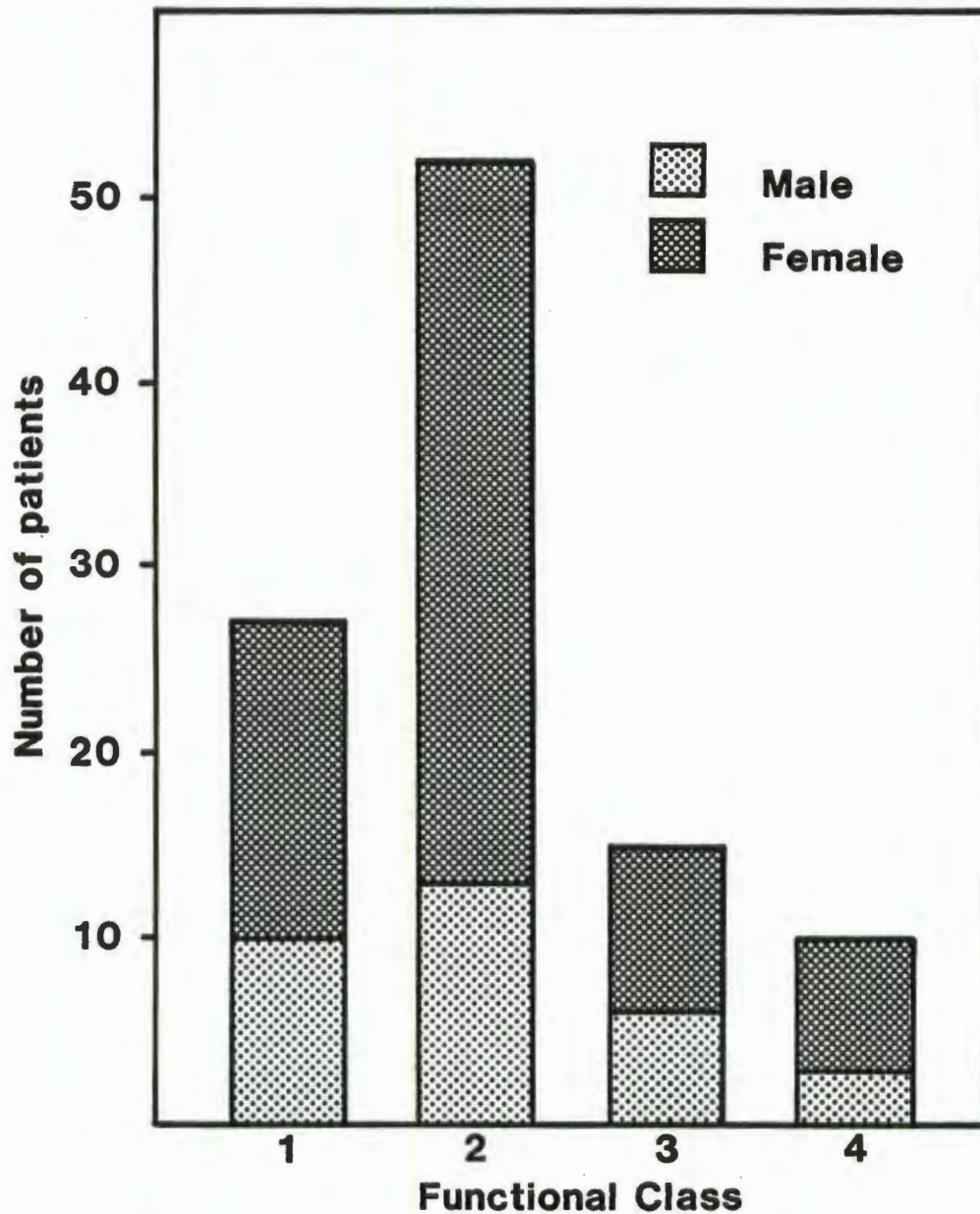


FIGURE 17.1.3

**FUNCTIONAL CLASSIFICATION (ARA)  
IN COLOURED**

CHAPTER 17.2CARDIAC INVOLVEMENT IN RHEUMATOID ARTHRITIS- A CLINICAL AND ECHOCARDIOGRAPHIC STUDYINTRODUCTION

The association of chronic arthritis and heart disease has been recognised for nearly 200 years, although it was only in 1941 that Baggenstoss and Rosenberg described the presence of typical rheumatoid granulomas in the heart (Baggenstoss and Rosenberg 1941). In 1950, Bywaters discussed the concept of rheumatoid heart disease as a pathologically distinct entity and this was confirmed in subsequent necropsy and clinical studies (Bywaters 1950).

The prevalence of cardiac involvement in RA was 30%-50% in necropsy studies but clinical involvement has been noted in only 2%-10% of cases (Pizarelllo and Goldberg 1985). Kirk and Cosh reviewed the pooled data from 8 major autopsy series of patients with RA and found pericarditis in 30% of 400 patients (Kirk and Cosh 1969). The advent of echocardiography has provided a non-invasive method for the detection of cardiac abnormalities such as pericardial effusion, pericardial thickening and mitral valve anomalies which may not be suspected on clinical or radiological assessment. Early echocardiographic studies showed evidence of pericarditis (effusion and or thickening) in 34% to 46,6% of patients with RA and these

findings were similar to the prevalence noted in autopsy studies (Prakash et al 1973, Bacon and Gibson 1974, Nomeir et al 1973). Abnormalities of mitral valve motion (a reduction in the E-F slope) which were noted in some studies (Prakash et al 1973, Bacon and Gibson 1974, Nomeir et al 1973, Schorn et al 1976) have not been confirmed in other studies (Hernandez-Lopez et al 1977, Davia et al 1975, MacDonald et al 1977).

The present study was undertaken to further define the cardiac abnormalities occurring in a randomly selected group of patients with RA.

## RESULTS

Two of the original 104 patients had died prior to their cardiac assessment. The cause of death in one patient was a perforated peptic ulcer which was proven at post-mortem. The other patient had a sudden death at home (a post-mortem was not performed). One patient with severe RA, who was bedridden and depressed, refused permission for the cardiac study. The remaining 101 patients were assessed clinically and had chest radiographs and electrocardiographs. Echocardiography was attempted in all 101 patients but 17 patients were considered to have failed echocardiographic studies. These failures were usually due to obesity, skeletal abnormalities and difficulty in positioning patients with fixed deformities of the joints. Seven patients had adequate 2-dimensional studies but adequate M-mode echocardiograms could not be obtained. One of these seven patients had evidence of a

pericardial effusion but no other abnormalities were noted in the patients who had 2-dimensional studies alone. The remaining 77 patients had adequate 2-dimensional studies and most of the parameters could be assessed on the M-mode echocardiogram in these patients. The mitral valve morphology, E-F slope, aortic valve and left atrial dimension were assessed in all 77 patients. The measurement of fractional shortening and left ventricular diastolic dimension was possible in 74 of the 77 patients and the right ventricular dimension was measured in 60 patients.

The mean age of the 77 patients who had adequate 2-D and M-mode echocardiograms was 48,7 years and the mean duration of RA was 11,4 years. The female to male ratio was 3,1 : 1. Ninety (89%) of the 101 patients who had echocardiograms were outpatients at the time of assessment. A comparison of the demographic data, functional classification, frequency of subcutaneous nodules and rheumatoid factor in the 77 patients who had adequate 2-D and M-mode echocardiograms and the total number who were selected for the study is shown in Table 17.2.1. There were 25 patients who were in ARA functional classes 3 and 4 and only 11 of these patients had adequate echocardiographic studies.

The associated diseases which were present in the 77 patients with adequate echocardiogram studies were: hypertension - 16 patients (20,8%), ischaemic heart disease - 3 patients (3,9%), diabetes - 4 patients (5,2%), tuberculosis - 8 patients (10,4%), asthma - 8 patients (10,4%) and rheumatic fever - 4 patients (5,2%). None of the

four patients with a history of rheumatic fever had evidence of rheumatic heart disease. One patient had Kartagener's syndrome with dextrocardia and bronchiectasis.

### ECHOCARDIOGRAPHIC FINDINGS

The abnormalities which were detected on echocardiography are summarised in Table 17.2.2. The clinical data on the patients who had abnormal echocardiographic findings is summarised in Table 17.2.3.

#### (1) PERICARDIAL EFFUSION OR THICKENING

A pericardial effusion was detected in four of the 77 patients who had adequate 2-D and M-mode echocardiograms and in 1 of the 7 patients who had adequate 2-D studies only. Therefore, pericardial effusion was detected in 5 of the 84 patients (6,0%) but pericardial thickening was not detected in any of the patients. Four of these 5 patients had a positive latex test for rheumatoid factor and 2 patients had subcutaneous nodules.

#### (2) FRACTIONAL SHORTENING

The fractional shortening could be calculated in 74 of the 77 patients. Only one patient (No. 2) had an abnormal fractional shortening of 11% (normal 25% to 35%). This patient developed acute aortic incompetence following infective endocarditis and required an aortic valve replacement; he subsequently developed

a myopathic ventricle.

(3) RIGHT VENTRICULAR ENLARGEMENT

The size of the right ventricle could be measured in 60 patients. Enlargement of the right ventricle was present in only one patient (No. 35) who had fibrosing alveolitis and pulmonary hypertension.

(4) LEFT VENTRICULAR SIZE

The left ventricle was dilated in 5 of the 74 patients who were assessed. Four of these 5 patients had coexistent cardiac diseases. The abnormalities which were present in these patients were aortic valve replacement and a myopathic left ventricle (No. 2), previous inferior myocardial infarct (No. 63), hypertension (No. 91) and hypertension and mitral incompetence due to dysfunction and dilatation of the left ventricle (No. 104). The remaining patient (No. 79) had deviation of the heart to the right with loss of lung markings in the right base but no evidence of cardiac disease.

(5) LEFT ATRIAL ENLARGEMENT

The left atrial dimension was increased in 5 of the 77 patients and the mean value was 53 mm (range 47 to 64 mm, normal 20 to 40 mm). The abnormalities which were noted in these patients were

aortic valve replacement and a myopathic left ventricle (No. 2), hypertension, diabetes and previous cardiac failure (No. 5), hypertension and left anterior hemiblock (No. 77), hypertension with aneurysmal dilatation of the aorta and aortic incompetence (No. 37) and mitral annular calcium with mitral incompetence and left bundle branch block (No.15).

(6) AORTIC VALVE

The aortic valve was assessed in 77 patients. One patient (No. 2) had a prosthetic aortic valve and 4 patients had thickening of the aortic valve. Two of the patients with aortic valve thickening had hypertension (No. 5 and 15), one patient (No. 37) had hypertension and aortic incompetence and one patient (No. 7) had an aortic ejection click and non specific ST-T wave changes on ECG.

(7) MITRAL VALVE

(a) MORPHOLOGY

The morphology was assessed in 77 patients and 11 abnormalities were detected in 10 patients. Three patients (No's 11, 20 and 32) had mitral valve prolapse, one patient (No. 48) had hypertrophic obstructive cardiomyopathy and one patient (No. 37) with hypertension and aortic incompetence had flutter on the mitral valve. Mitral annular calcium was detected in 6

patients and their mean age was 63.7 years (range 50-78 years). The abnormalities which were noted in these patients were hypertension and hypertrophic obstructive cardiomyopathy (No. 48), hypertension and mitral incompetence (No. 15), diabetes and hypertension (No. 5 and 43), hypertension alone (No. 76) and one patient (No. 47) did not have any associated abnormality.

(b) MITRAL VALVE MOTION (E-F SLOPE)

The E-F slope was reduced (less than 70 mm / sec) in 12 of the 77 patients (15,6%). There were 6 patients who had hypertension. One of these patients had only hypertension and left ventricular hypertrophy (No. 55). The associated findings which were noted in the remaining 5 patients with hypertension were diabetes and mitral annular calcium (No. 5), mitral incompetence (No. 15), aortic incompetence (No. 37), hypertrophic obstructive cardiomyopathy and mitral annular calcium (No. 48) and an old anteroseptal infarct (No. 31). One patient (No. 22) had aortic incompetence and left ventricular hypertrophy and another patient (No. 6) with an E-F slope of 57 mm / sec had a sinus tachycardia but no associated cardiac disease. The remaining four patients (No's 4, 26, 65 and 72) had a mild reduction in the E-F slope with a mean value of 65,5 mm / sec. Two of these patients (No's 4 and 26) had been previously treated for pulmonary tuberculosis and one patient (No

72) had an axis of  $+ 100^\circ$  and an inferiorly directed p wave vector consistent with underlying lung disease.

## DISCUSSION

Pericarditis has been detected in 30% of RA patients in autopsy studies (Kirk and Cosh 1969) but the frequency of clinical pericarditis varies from 2% to 10% (Kirk and Cosh 1969, Cathcart and Spodick 1962, Gordon et al 1973). Clinical pericarditis has characteristically been found in patients with high titre rheumatoid factor, subcutaneous nodules, anaemia and high sedimentation rate (Pizarelli and Goldberg 1985). Franco et al found a male to female ratio of 1,1 : 1 in their 17 patients with clinically diagnosed pericarditis and a ratio of 1,4 : 1 in a review of 41 cases reported in the literature (Franco et al 1972).

The majority of the patients with pericarditis diagnosed at post mortem, were found to have adhesive or obliterative pericarditis and most reports did not describe effusions even when the pericarditis was of the acute fibrinous type (Kirk and Cosh 1969). In one of the largest autopsy studies, Cruikshank studied 100 patients with RA, 49 of whom were admitted to hospital because of their RA (Cruikshank 1958). He found evidence of acute fibrinous pericarditis in only one patient and 15 patients had evidence of previous pericarditis. Pericardial effusion or thickening has been detected in 15% to 46,6% in echocardiographic studies (Bacon and Gibson 1974, Nomeir et al 1973, Hernandez-Lopez et al 1977). It is interesting that these

workers found that with echocardiography, the prevalence of pericarditis was similar to that found at autopsy. This is perhaps surprising since the echocardiographic studies were done on predominantly outpatients with RA who were likely to have less active disease than those studied at autopsy by Cruickshank (Cruikshank 1958).

Prakash et al studied 16 outpatients with RA and found that 7 patients (44%) had pericardial effusion (Prakash et al 1973). However, 15 of their patients (94%) were males and 69% had subcutaneous nodules; therefore the prevalence of pericardial effusion in this study is not representative of the general RA population. Hernandez-Lopez et al studied 26 patients, of whom 23 (89%) were males and 4 patients (15%) had pericardial effusion or thickening (Hernandez-Lopez et al 1977). Nomeir et al found pericardial effusion or thickening in 14 (46,7%) of their 30 patients, half of whom were males and 13 (43,3%) had subcutaneous nodules (Nomeir et al 1973). Bacon and Gibson found pericardial effusion in 50% of their 22 patients with nodules and 18% of their 22 patients without nodules, but the sex ratio of the patients in this study was not reported (Bacon and Gibson 1974).

The majority of the patients in the present study were outpatients and the prevalence of pericardial effusion was only 6%, which is much lower than the findings in other studies. There was a high failure rate among patients who were in ARA functional classes 3 and 4, and the exclusion of these patients may have lowered the prevalence of pericardial effusion. However, the overall success rate of 84% in

this study was similar to the 84% to 89% noted in other studies (Hernandez-Lopez et al 1977, Davia et al 1975). It is also possible that there is a difference in the prevalence of pericardial effusion in our patients due to racial or genetic factors. Alternatively, the higher prevalence in other studies may be related to patient selection as there was a higher proportion of males or patients with nodules in some of these studies or that the small number of patients studied is not representative of the general RA population.

Mitral annular calcification (MAC) is found in 8,5% to 10% of adult autopsies and can be reliably diagnosed by echocardiography even though the findings may sometimes be mistaken for a posterior pericardial effusion (Gabor et al 1976, D'Cruz et al 1977, Hirschfield and Emilson 1975). Mitral annular calcification may be associated with a reduction in the E-F slope in the absence of mitral stenosis and D'Cruz et al noted a reduction of less than 40 mm / sec in 74% of 38 patients with MAC (Gabor et al 1976, D'Cruz et al 1977, Dashkoff et al 1977). Mitral annular calcification may be considered a degenerative change and be idiopathic, or it may be accelerated by systemic hypertension, aortic stenosis and diabetes, and is usually detected in the elderly (Braunwald 1980). The initial echocardiographic studies in RA, which showed a reduction in the E-F slope, had been performed before the echocardiographic features of MAC had been described. The presence of MAC has not been reported in any of the previous studies and therefore its contribution to a reduction in the E-F slope might have been overlooked. Six (7,8%) of our patients had MAC. One 64 year old patient with MAC had no associated

disease but the other 5 patients had hypertension and two of them were also diabetic. Three of the patients with MAC had a reduction in the E-F slope and one of these patients also had HOCUM.

A reduction in the E-F slope was noted in 25% of the patients by Prakash et al and 30% of the patients by Nomeir et al; all these patients had an E-F slope of 60 mm / sec or less (Prakash et al 1973, Nomeir et al 1973). Bacon and Gibson noted a reduction in the mean values for the E-F slope in patients with RA and nodules (Bacon and Gibson 1974). A reduction in the E-F slope is not specific for mitral stenosis and may be noted with decreased left ventricular compliance eg, asymmetric septal hypertrophy, aortic valve lesions, systemic hypertension, pulmonary hypertension, atrial myxoma and with vegetations on the mitral valve. Twelve (15,6%) of our patients had a reduced E-F slope and 7 of these patients had associated cardiac diseases. One patient had an E-F slope of 57 mm / sec and a sinus tachycardia which may also reduce the E-F slope. Four patients (5,2%) had a mild reduction (mean value 65,5 mm / sec) without any cardiac disease. It was not possible for us to assess the left ventricular compliance to determine the possible source of the reduction in the E-F slope. The lack of any significant abnormalities of the E-F slope, in the absence of cardiac disease, is similar to the some of the recent studies (MacDonald et al 1977, Hernandez-Lopez et al 1977, Davia et al 1975) but differs from the earlier studies (Prakash et al 1973, Bacon and Gibson 1974, Nomeir et al 1973).

Cathcart and Spodick studied 254 RA patients with age and sex matched controls and found that there was an increased prevalence of coronary artery disease in RA (Cathcart and Spodick 1962). Other studies have suggested that the incidence of atherosclerotic coronary artery disease was at least equal to that seen in age matched controls (Pizarelli and Goldberg 1985). MacDonald et al found that 11 (21,6%) of his patients had ischaemic heart disease, which was detected in only 3 patients (3,9%) in this study (MacDonald et al 1977). Hypertension was common and was detected in 20,8% of our patients. There were 4 patients who had a history of rheumatic fever but none of them had any clinical or echocardiographic abnormalities.

Aortic incompetence was noted in 3 patients in the study. One patient developed acute aortic incompetence following infective endocarditis and required aortic valve replacement, one patient had positive serological tests for syphilis and the third patient had hypertension with aneurysmal dilatation of the aorta. Two patients had mitral incompetence, one of whom had hypertension and MAC, and the other patient had hypertension and a dilated left ventricle. The aortic and mitral valvular incompetence in these 5 patients could be related to factors other than valvulitis associated with RA.

In conclusion, a randomly selected group of 101 patients with RA were studied to determine the prevalence of cardiac abnormalities on clinical assessment and echocardiography. Although 45 abnormalities were detected in 31 patients, most of them could be related to coexistent diseases such as hypertension. Apart from the presence of

pericardial effusion in 5 patients (6%) and minor abnormalities of the E-F slope in 4 patients (5,2%), no other significant abnormalities were noted.

TABLE 17.2.1

COMPARATIVE FINDINGS IN THE TOTAL GROUP AND PATIENTS  
WITH ADEQUATE ECHOCARDIOGRAPHIC STUDIES  
(PERCENTAGE IN PARENTHESES)

	<u>TOTAL GROUP</u>	<u>PATIENTS WITH ADEQUATE</u>
	n=104	<u>2-D and M-MODE STUDIES</u>
		n=77
Female : Male Ratio	2,3 : 1	3,1 : 1
Mean age (years)	51,1	48,7
Range	21-80	21-78
Mean duration of RA (years)	12,4	11,4
Range	1,1-50	1,1-38
Functional class (ARA)		
1	27 (26,0)	23 (29,9)
2	52 (50,0)	43 (55,8)
3	15 (14,4)	7 (9,1)
4	10 (9,6)	4 (5,2)
Subcutaneous nodules	31 (29,8)	23 (29,9)
Positive rheumatoid factor		
Present	63 (61,0)	42 (54,5)
past or present	82 (78,9)	59 (76,6)

TABLE 17.2.2PREVALENCE OF ECHOCARDIOGRAPHIC ABNORMALITIES

<u>ECHOCARDIOGRAPHIC FINDINGS</u>	<u>NO. STUDIED</u>	<u>NO. ABNORMAL</u>	<u>% ABNORMAL</u>
Pericardial effusion	84	5	6,0
Fractional shortening	74	1	1,4
Left ventricular diastolic dimension	74	5	6,8
Right ventricular diastolic dimension	60	1	1,6
Left atrial dimension	77	5	6,5
Mitral valve a) morphology	77	10**	13,0
b) EF slope	77	12	15,6
Aortic valve	77	5	6,0

\*\* Eleven abnormalities were detected in 10 patients as one patient with hypertrophic obstructive cardiomyopathy also had mitral annular calcium

TABLE 17.2.3.

## AGE, SEX AND CLINICAL FINDINGS IN THE PATIENTS WITH ECHOCARDIOGRAPHIC ABNORMALITIES

STUDY NO	AGE	SEX	ECHOCARDIOGRAPHIC FINDINGS	CLINICAL DIAGNOSIS	STUDY NO	AGE	SEX	ECHOCARDIOGRAPHIC FINDINGS	CLINICAL DIAGNOSIS
40	36	F	Pericardial effusion	Previous PTB, Effusion right base	37	56	F	LA enlarged, MV flutter, AV thickening, EF - 40 mm / sec	Hypertension, AI
57	78	M	Pericardial effusion	Hypertension, fibrosing alveolitis	77	76	F	LA enlarged, EF - 44 mm / sec	Hypertension
61	52	F	Pericardial effusion	CTR 52%	7	56	F	AV thickening	Aortic ejection click
64	57	F	Pericardial effusion	Hypertension	43	71	F	MAC	Diabetes, hypertension
81	47	F	Pericardial effusion	Previous PTB, CTR 54%	47	64	F	MAC	
2	38	M	FS 11%, LV dilated, AV prosthesis, LA enlarged	AV prosthesis, myopathic LV	76	50	F	MAC	Hypertension
48	53	M	MAC, HOCUM EF - 10 mm / sec	Hypertension, asthma HOCUM	11	21	F	MV prolapse	MV prolapse
35	39	F	RV enlarged	Fibrosing alveolitis and pulmonary hypertension	20	52	F	MV prolapse	MV prolapse
63	48	M	LV dilated	Old inferior infarct	32	55	F	MV prolapse	MV prolapse
79	37	M	LV dilated	Heart deviated to right with loss of lung markings on right	6	37	F	EF - 57 mm / sec	Asthma past
91	52	F	LV dilated	Hypertension	31	72	F	EF - 44 mm / sec	Hypertension, old anteroseptal infarct
104	68	F	LV dilated	Hypertension, MI	22	59	F	EF - 18 mm / sec	AI
5	66	F	LA enlarged, MAC, AV thickening, EF - 52 mm / sec	Diabetes, hypertension CCF	26	44	F	EF - 68 mm / sec	Previous PTB
15	78	F	LA enlarged, AV thickening MAC	Hypertension, MI	65	49	F	EF - 60 mm / sec	Asthma
					72	42	M	EF - 68 mm / sec	Mild reduction of transfer factor. Inferior p wave vector
					4	49	F	EF - 66 mm / sec	Previous PTB
					55	47	M	EF - 60 mm / sec	Hypertension

## ABBREVIATIONS

Sex: F - female; M - male; PTB - pulmonary tuberculosis; CTR - cardiothoracic ratio; FS - fractional shortening; LV - left ventricle; RV - right ventricle; AV - aortic valve; MV - mitral valve; LA - left atrium; MAC - mitral annular calcium; HOCUM - hypertrophic obstructive cardiomyopathy; MI - mitral incompetence; AI - aortic incompetence; CCF - congestive cardiac failure.

## CHAPTER 17.3

### KERATOCONJUNCTIVITIS SICCA IN RHEUMATOID ARTHRITIS

#### INTRODUCTION

Sjogren's syndrome comprises the clinical triad of keratoconjunctivitis sicca (KCS) or dry eyes, xerostomia (with or without salivary gland enlargement) and rheumatoid arthritis (RA) or another connective tissue disease. The term may be applied when only two of the major components of the triad are present (Bloch and Bunim 1963). The term sicca complex or sicca syndrome is used to refer to KCS and xerostomia in the absence of associated connective tissue diseases.

The terms secondary and primary sicca syndrome or secondary and primary Sjogren's syndrome have been used to differentiate the occurrence of sicca features with or without a connective tissue or auto immune disease respectively (Gumpel 1982, Lyons et al 1983, Moutsopoulos 1980).

Keratoconjunctivitis sicca refers to a condition in which the eyes are deficient in aqueous tear secretion secondary to hypofunction of the lacrimal gland (Forstot et al 1982). Sjogren reported that the frequency of arthritis in patients with the sicca syndrome varied from 17% to 87% in different series and that 62% of his own 80 patients had

arthritis (Sjogren 1951). Manifestations of the sicca complex have been noted in 11% to 35% of patients with RA, the higher incidence being noted in patients with advanced joint disease (Burke 1985). Lenocho et al found KCS in 58,4% of 250 patients with active RA who had slit lamp examination after the instillation of Bengal red and the atropine provocation test (Lenocho et al 1964).

The aim of this study was to determine the prevalence of KCS in a randomly selected group of patients with RA and document the value of the various tests used in the diagnosis.

## RESULTS

The study group consisted of 72 females and 32 males giving a female to male ratio of 2,3 : 1. The mean age of patients was 51,1 years (range 21 to 80 years) and the mean duration of RA was 12,4 years (range 1,1 to 50 years). The ARA functional classification of the patients was as follows: class I - 26%, II - 50%, III - 14,4% and IV - 9,6%.

A history of symptoms suggestive of KCS was obtained in 33 patients (31,7%). Twenty two of these patients (67%) were found to have evidence of ocular surface desiccation damage as shown by corneal and / or conjunctival epithelial staining with Rose Bengal. These patients were considered to have KCS.

The results of the findings in these 33 patients will be considered in

2 groups. Patients who had symptoms of KCS but no epithelial staining (Group A) and patients who had corneal and/or conjunctival staining with symptoms of KCS (Group B).

#### GROUP A

Eleven patients (10,6%) had symptoms suggestive of KCS but no staining of the cornea or conjunctiva. Six of these patients had experienced only one or two symptoms compatible with KCS. Two of the eleven patients had abnormal Schirmer's test values between 5 and 15 mm and reduced tear film but the B.U.T. was normal in both. No other abnormalities were detected in these patients.

#### GROUP B

Twenty two patients (21,2%) had symptoms of KCS with epithelial staining. The staining of the right and left cornea and conjunctiva were each scored separately as 0 - nil, 1 - mild, 2 - moderate and 3 - severe (maximum possible score 12). The mean staining score was 5,0 (range 1 - 12).

The frequency of the different symptoms in the patients who had KCS is summarised in Table 17.3.1.

Patients who had abnormalities of the marginal tear film, Schirmers test or B.U.T. in at least one of the eyes, were considered to have abnormalities of these tests. The marginal tear film was reduced in

15 patients (68,2%) and normal in 7 patients. The Schirmer's test was abnormal in 21 patients (95,5%), 8 (36,4%) had values of 5 mm or less and 13 (59%) had a mild abnormality (6 mm to 15 mm). The B.U.T. was abnormal (less than 10 seconds) in 13 patients (59%) while the remaining 9 patients had normal values.

Nineteen of the 22 patients with epithelial staining had abnormalities of at least 2 of the other 3 tests ie, Schirmer's less than 15 mm, reduced tear film and/or reduced B.U.T. The remaining 3 patients had an abnormality of only one of these tests. The presence of debris in the tear film was noted in 5 patients and a further 2 patients had mucus strands. Three patients had mucus filaments on the cornea, two of whom also had tear debris and the third patient had corneal melting.

The results of the erythrocyte sedimentation rate, serum immunoglobulins, latex test for rheumatoid factor and antinuclear factor are summarised in Table 17.3.2. Three groups are tabulated as follows:- group A - patients with symptoms but no signs of KCS, group B - patients with symptoms and signs of KCS and group C - patients with no symptoms or signs of KCS. The mean value of the IgG, IgM and ESR were higher in patients who had KCS (group B) than the other 2 groups but these values were not statistically significant. The prevalence of a positive rheumatoid factor (86,4%) and anti-nuclear factor (31,8%) were also more frequent in group B, but these values were also not statistically significant. Smooth muscle antibodies and thyroid antibodies (microsomal and thyroglobulin) were not detected

more frequently in the patients with KCS. When the results of the patients in group A and B were combined and compared with group C, then there was still no statistically significant difference for any of the above tests.

## DISCUSSION

The prevalence of KCS in RA varies depending on the criteria used for the diagnosis of KCS. Henderson reported a series of 121 patients with KCS, all of whom had erosions or filaments of the corneal epithelium (Henderson 1950). He noted that, with the Schirmer's test, there was a frequent occurrence of false positive and false negative results and that negative results may occur even in patients with severe eye involvement. The Schirmer's test is a crude functional evaluation of tear production and the results are dependent on temperature, hydration and the age of the patient (Kassan and Gardy 1978). There is also a wide variation in the normal population and although 15mm or less of wetting is generally considered abnormal, many authors feel a lower value of 5 mm or less is more significant (Michels 1974, Mackie and Seal 1981). The predictive value of the unstimulated Schirmer test, using wetting of filter paper of 5 mm or less in 5 minutes, is limited since 17% false positive and 15% false negative results may occur (de Roethth 1954). The Schirmer's test should not be used to make a diagnosis of KCS without symptoms or signs (Laibson 1980) and because of the various problems, some physicians have abandoned its use (Kearns 1980). In the present study, 95,5% of the patients with corneal staining had an abnormal

Schirmer's test of less than 15 mm. Only 8 (36,4%) of the patients with KCS had an unstimulated Schirmer's test of 5mm or less while the remaining 13 patients had a mild abnormality (6mm to 15mm). Therefore, if an abnormal Schirmer's test of 5 mm or less was used as the main criterion for the diagnosis of KCS, then the majority of the patients with corneal staining would have been incorrectly diagnosed.

Objective evidence of desiccation changes, in addition to a compatible history, should be present to make a diagnosis of KCS (Michels 1974). The best objective clinical test for desiccation changes is topical staining with Rose Bengal, which is invariably present in KCS and can be roughly quantitated to improve reliability in interpreting this test (Michels 1974, Van Bijsterveld 1969). Rose Bengal staining of the cornea may be associated with 4% false positive and 5% false negative results (Van Bijsterveld 1969) and is more reliable than fluorescein staining which does not stain degenerate cells in-situ. The diagnosis of KCS in this study was based on the presence of symptoms of KCS and evidence of epithelial desiccation on Rose Bengal staining. The prevalence of KCS was 21,2% which accords well with other studies where a prevalence of 11% to 35% has been reported (Burke 1985). Reddy et al found evidence of KCS in 3 of 40 patients with RA who had no ocular symptoms (Reddy et al 1977). Asymptomatic patients with epithelial staining would not have been detected in this survey as only symptomatic patients were studied. It is also likely that two of the patients with symptoms of KCS, without any epithelial staining, may have early KCS as they had a reduced tear film and a Schirmer's test of less than 15 mm. Therefore, the true prevalence of KCS may be

higher than reported here.

Other tests used in the diagnosis of KCS, such as assessment of the marginal tear film, B.U.T. and Schirmer's test are not consistently abnormal and are therefore less reliable. Only 15 of the patients with KCS (68,2%) had a reduced marginal tear film and 13 patients (59%) had a reduced B.U.T. Vanley and co-workers found that the B.U.T. was not of conclusive value and its reproducibility could not be maintained within reasonable limits (Vanley et al 1979). Although a reduction in the volume of the tear wedge may suggest reduced tear flow (Wright 1971) no correlation exists between meniscus height and the Schirmer's test (Lamberts et al 1979). The presence of debris in the tear strip or other evidence of mucin abnormality were unreliable predictors of KCS.

Assessment of the tear lysozyme content and tear film osmolarity are also of value in the diagnosis of KCS (Mackie and Seal 1976, Avisar et al 1979, Gilbard et al 1978) but neither of these tests is used routinely by most ophthalmologists. Mackie and Seal found that a low lysozyme concentration (tear lysozyme ratio  $<1,0$ ) is associated with KCS and is a useful test in diagnosing questionably dry eyes, a term used for borderline cases (Mackie and Seal 1981). It is possible, that in the future, these tests may become established as routine tests for the diagnosis of KCS.

Gumpel and Hobbs found that the level of serum IgG, IgA and IgM were significantly higher in 50 patients with Sjogren's syndrome than a

control population and the elevation was most marked for IgG and least for IgA (Gumpel and Hobbs 1970). They did not detect any difference between patients with sicca syndrome alone and those with associated RA. We noted that the levels of IgG, IgA and IgM were higher in patients with KCS and RA than with RA alone, but these values were not statistically significant. In primary Sjogren's syndrome, a positive rheumatoid factor has been detected in 70%-80% and positive antinuclear antibodies in 50%-70% (Mason et al 1973). A positive latex test for rheumatoid factor was detected in 19 out of our 22 patients (86,4%) with KCS and RA in comparison to a prevalence of 98,9% of 94 patients with RA and Sjogren's syndrome in another study (Whaley et al 1973).

In conclusion, a randomly selected group of 104 patients with RA were studied and 33 patients were found to have symptoms of KCS. Two thirds of these patients were found to have KCS (overall prevalence of 21,3%) which was diagnosed by the presence of epithelial desiccation after Rose Bengal staining. The majority of the patients (95,5%) had an abnormal Schirmer's test, but generally accepted values of 5 mm or less were only present in 8 patients (36,4%). Therefore, in order to make a definite diagnosis of KCS, slit lamp examination is necessary to detect epithelial desiccation, and the marginal tear film and break up time could also be assessed. There were no significant differences in the mean ESR, immunoglobulins and the prevalence of a positive rheumatoid factor in RA patients with or without KCS in this survey.

TABLE 17.3.1

PREVALENCE OF OCCULAR SYMPTOMS IN PATIENTS WITH KCS

<u>SYMPTOMS</u>	<u>NUMBER</u> (n=22)	<u>PERCENT</u>
Burning	18	82
Itching	17	77
Dryness	17	77
Sore	16	73
Gritty	16	73
Foreign body sensation	12	55
Visual disturbance	11	50
Photophobia	9	41
Tearing	9	41

TABLE 17.3.2

THE MEAN IMMUNOGLOBULINS AND ESR AND PREVALENCE  
OF POSITIVE ANTINUCLEAR AND RHEUMATOID FACTOR TESTS AS A  
PERCENTAGE IN EACH GROUP

	<u>Symptoms of KCS</u> (n=11)	<u>KCS</u> (n=22)	<u>NO KCS</u> (n=71)	<u>Total</u> (n=104)
IgG g/l	18,3	23,2	18,9	19,8
IgA g/l	3,7	4,9	4,5	4,5
IgM g/l	2,4	2,6	2,2	2,3
ESR mm/hour	68,2	91,3	76,2	78,5
Rheumatoid factor				
(latex) positive - %	72,7	86,4	77,5	78,9
Anti-nuclear factor				
(positive) - %	18,2	31,8	45,5	18,3

## CHAPTER 17.4

### PERIPHERAL NEUROPATHY IN RHEUMATOID ARTHRITIS: A CLINICAL AND ELECTRO-PHYSIOLOGICAL STUDY

#### INTRODUCTION

In RA peripheral neuropathy may take several different forms such as entrapment neuropathy, digital neuropathy, distal sensory neuropathy, distal sensori-motor polyneuropathy and mononeuritis multiplex (Pallis and Scott 1965, Hart and Golding 1960). Fortunately, apart from the entrapment neuropathies, overt clinical evidence of other forms of neuropathies is uncommon.

An awareness of the presence of a neuropathy is important as symptoms such as neuritic pain and weakness, and clinical evidence of wasting and weakness are difficult to evaluate in patients with severe deforming RA.

Electrophysiological studies have shown that entrapment neuropathies (carpal tunnel syndrome and tarsal tunnel syndrome) and peripheral sensory and motor neuropathies are common in RA (Moritz et al 1963, Good et al 1965, Chamberlain and Bruckner 1970, Chamberlain and Corbett 1970, Herbison et al 1973, Baylan et al 1981, Lang et al 1981).

The aim of this survey was to study a large group of randomly selected patients with classical or definite RA to determine:

- i) the prevalence of carpal tunnel syndrome (CTS) based on an electrophysiological study of the median motor and sensory distal latency.
- ii) the prevalence of abnormalities of the peripheral nerves based on a study of the lateral popliteal conduction velocity and the sural nerve conduction studies.

## RESULTS

The median nerve motor and sensory recordings were performed in 103 patients, the lateral popliteal conduction studies in 95 patients and sural nerve recordings in 94 patients. Thirty six abnormalities were recorded in 27 patients and the results are summarised in Table 17.4.1.

### 1. CARPAL TUNNEL SYNDROME

Eighteen patients (7,5%) had CTS, with 13 patients having abnormal motor and sensory distal latency and 5 patients had abnormal sensory distal latency (DL) alone. Two of the 18 patients with CTS had diabetes which may have contributed to the CTS. Therefore, if these 2 patients are excluded, the prevalence of CTS was 14,9%. The clinical findings and electrical abnormalities detected in the 18 patients were as follows:

- i) Six patients had symptoms and signs of CTS; five had prolonged motor and sensory DL, while one had prolonged sensory DL alone.
- ii) Five patients had past symptoms of CTS; four had prolonged sensory DL alone and one of them previously required a carpal tunnel release.
- iii) Seven patients were asymptomatic; six had prolonged motor and sensory DL and one had prolonged sensory DL alone.

Six of the patients (33,3%) with CTS also had abnormalities of the lateral popliteal and/or sural nerve as shown in Table 17.4.1.

In addition to the 18 patients who had abnormal electrical studies, there were a further 5 patients who had been diagnosed as having symptomatic CTS during the course of their disease. Two of these patients had carpal tunnel release while the other 3 patients responded to the use of splints and/or intra-lesional corticosteroid injections.

## 2. LATERAL POPLITEAL CONDUCTION VELOCITY

Normal conduction studies were obtained in 84 patients (88,4%). One patient had cardiac failure with oedema of the lower limbs and the lack of response in this patient was presumed to be technical. Ten patients (10,5%) had abnormal slowing of the conduction velocities. None of these 10 patients had any

clinical abnormalities due to weakness of the muscles supplied by the lateral popliteal nerve. Five patients had abnormal conduction velocity of the lateral popliteal alone while the remainder had abnormalities of the median and/or sural nerves.

### 3. SURAL NERVE

Abnormal sural nerve recordings were obtained in 13 patients (13,8%). One patient had slowing of the conduction velocity while a recording could not be obtained in the other 12 patients. Four of the 13 patients had oedema of the feet and one patient had previous surgery and deformity of the foot. Therefore, technical factors may have contributed to the failure to obtain a sural nerve recording in these 5 patients while the remaining 8 patients were considered to have true pathology. Two of the 5 patients who were considered to have technical reasons for the absent sural nerve studies, also had abnormal lateral popliteal conduction velocity and a third patient had diabetes, CTS and an unrecordable lateral popliteal conduction velocity due to oedema of the lower limbs from cardiac failure.

Six of the 8 patients who were considered to have true pathology also had other coexistent abnormal electrophysiological studies as shown in Table 17.4.1. Two of these 8 patients had a history of heavy alcohol intake; one had slowing of sural nerve conduction and a distal symmetrical sensory neuropathy while the other patient had abnormal median nerve conduction and a previous

history of numbness and paraesthesiae of both feet but no abnormality was present at the time of assessment.

#### OTHER SIGNIFICANT CLINICAL NEUROLOGICAL FINDINGS

Apart from the two patients who had a history of heavy alcohol intake (one of whom had clinical evidence of a distal sensory neuropathy) and abnormal sural nerve studies, there were 2 other patients who also had a history of heavy alcohol intake with clinical evidence of a sensory neuropathy but sural nerve studies were normal. Therefore, a total of 3 patients had clinical evidence of a distal sensory neuropathy but only one of them had abnormal sural nerve studies. All the patients who had a history of heavy alcohol intake were Coloured males and the neurological abnormalities in these patients were probably related to alcohol.

Two patients had evidence of basilar invagination or cranial settling on radiographs of the cervical spine and bilateral pyramidal tract signs on clinical examination. One of these patients had occipitocervical fusion while the other patient refused surgery and was managed conservatively with a cervical collar. There was one other patient who had spastic paraparesis of both lower limbs with hyperreflexia, ankle clonus and an extensor plantar response. This patient had a history which suggested a diagnosis of meningovascular syphilis had been made 20 years earlier and his neurological abnormalities were therefore considered to be unrelated to his RA.

One patient was found to have a digital neuropathy of the thumb one year before the survey, and although there was improvement, she had mild numbness of the medial side of the right thumb at the time of assessment.

One patient had an ulnar entrapment neuropathy at the time of the survey and this was confirmed on nerve conduction studies. One other patient had been previously diagnosed as having an ulnar entrapment neuropathy.

#### DISCUSSION

Carpal tunnel syndrome is common in RA and may be detected by electromyography in up to 50% of the patients (Barnes and Currey 1967). At the Mayo Clinic, CTS was diagnosed in 56 (8,9%) of the 627 patients with RA (Conn 1985). Clinical evidence of carpal tunnel syndrome was detected in 23% of 72 patients in another study (Chamberlain and Corbett 1970). However, in the latter study, electrophysiological confirmation of CTS was obtained in only 2 of the 6 patients with clinically diagnosed CTS who were studied. Thomas et al noted that in many cases of CTS there were no abnormalities on clinical examination, and the electromyogram provided the only objective evidence of CTS (Thomas et al 1967). In patients who have early RA, objective signs of CTS are reported to be uncommon (Wells and Johnson 1962, Moritz 1964).

In the present survey, CTS was detected in 18 (17,5%) of the 103

patients studied, and if the two patients with diabetes are excluded, the prevalence of CTS was 14,9%. There was a poor correlation between clinical and electrophysiological tests as 7 of the 18 patients (39%) were asymptomatic, 5 patients (28%) had symptoms in the past and only 6 patients (33%) had symptoms and signs of CTS. In a recent survey, the usefulness of 5 clinical tests which are most commonly used for the diagnosis of CTS were assessed (Golding et al 1986). There was no physical sign that was useful in the diagnosis of CTS and the authors suggested that CTS should be suspected on the basis of presenting symptoms and confirmed by standard electrodiagnostic tests. Hoffman has emphasized the importance of sensory nerve conduction studies in the diagnosis of CTS as only about two thirds of patients with verified CTS have prolonged median motor latencies whereas 85%-95% will have median sensory abnormalities (Hoffman 1975). Thirteen patients had abnormal motor studies (72,2%) and 17 patients had prolonged sensory distal latency (94,4%). There were 5 patients (27,8%) in the present study in whom the diagnosis of CTS was based on abnormal sensory studies alone.

The peroneal nerve motor conduction velocity (PCV) and latency were studied in a group of 70 patients who were admitted to a Veterans Administration Hospital (Good et al 1965). The majority (98%) of the patients were males and 71% had nodules, and therefore they represented a select group of RA patients. There was a highly significant reduction in the mean PCV in RA patients in comparison with controls, and paraesthesiae and/or sensory signs were detected in 64% of the patients and 21% of the control group. There was a poor

correlation between the symptoms and signs of a peripheral neuropathy and abnormal electrical findings. In the present study 10 patients (10,5%) had reduced lateral popliteal conduction velocity but none of the patients had any clinical abnormalities.

The neuroelectrophysiological function of six sensory nerves were studied in a selected group of 23 RA patients (Lang et al 1981). Ten patients (43%) had abnormalities and 4 of these patients had abnormalities of more than one nerve. There were 27 patients (26,0%) who had 36 abnormalities in this study and 7 patients (25,9%) had abnormalities of two or more nerves. Hoerner et al tested 287 various nerves and found one or more abnormal values in the majority of the 72 patients examined (Hoerner et al 1963). The association of abnormalities of the median nerve and the lateral popliteal and/or sural nerve is interesting as it may be related to active synovitis in the wrist, knee or ankle joints, or in the absence of active inflammation, it may suggest the presence of a distal neuropathy affecting the upper and lower limbs, or a combination of these 2 factors.

Hart et al have reported their experience of patients with overt peripheral neuropathy (Hart et al 1957, Hart and Golding 1960, Hart 1969). In the present study 3 patients had clinical evidence of a peripheral neuropathy but all of them also had a history of heavy alcohol intake.

In conclusion, electrophysiological abnormalities were detected in 27

patients (26,2%) with RA when one median nerve (motor and sensory), lateral popliteal and sural nerve were studied. It is likely that the prevalence would be higher if more nerves were studied in the same patients. The abnormalities of conduction which were considered to be related to RA were CTS in 14,9%, reduced lateral popliteal conduction velocity in 10,5% and sural nerve abnormalities in 6,9%. Seven of the 27 patients (25,9%) with abnormal studies had involvement of more than one nerve. There was a poor correlation between the clinical findings and electrophysiological tests.

TABLE 17.4.1

SUMMARY OF ABNORMAL ELECTROPHYSIOLOGICAL STUDIES

NERVE TESTED	NUMBER ABNORMAL	PERCENT ABNORMAL
<b>Median motor and or sensory</b>		
<b>Carpal tunnel syndrome (CTS)</b>	18	17,5
Alone	12	
+ abnormal lateral		
popliteal	2	
+ abnormal sural	2	
+ abnormal lateral		
popliteal and sural	2	
<b>Lateral Popliteal</b>	10	10,5
Alone	5	
+ CTS	2	
+ CTS and sural	2	
+ sural	1	
<b>Sural</b>	8	9,0
Alone	2	
+ CTS	2	
+ lateral popliteal	2	
+ CTS + lateral popliteal	2	

## CHAPTER 17.5

### PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS

#### INTRODUCTION

The recognition of the pulmonary complications of RA and the association of pneumoconiosis and RA were first reported in 1948 and 1951 respectively (Ellman and Ball 1948, Caplan 1953). The lungs may be affected in a variety of ways such as pleurisy, pulmonary nodules, diffuse pulmonary fibrosis and obliterative bronchiolitis (Turner-Warwick and Courtney 1977).

Most of the previous surveys on pulmonary involvement in RA have focused on a single or few aspects only. Furthermore, they tended to study a small number of patients who were highly selected as smokers and patients with pre-existing lung diseases were excluded. Hyland et al studied the pulmonary abnormalities in a randomly selected group of 155 patients with RA and 95 controls (Hyland et al 1983). An increased frequency of chest crackles, chest radiographic abnormalities and evidence of a restrictive ventilatory defect were noted in the patients with RA. They did not find any increase in chronic airways obstruction as reported in previous studies (Collins et al 1976, Geddes et al 1979).

The aim of this survey was to determine the prevalence of pulmonary

abnormalities in a randomly selected group of patients with RA, by clinical examination, assessment of chest radiographs and pulmonary function tests. The study numbers of the patients with abnormalities is reported; some patients had cardiac and pulmonary abnormalities and their data could be compared in Table 17.2.3.

## RESULTS

The results of the lung function tests were subdivided into groups depending on the sex, smoking status (smokers, ex-smokers and non-smokers), the presence or absence of tuberculosis and other abnormalities which were detected such as bronchiectasis, fibrosing alveolitis, pneumonia, asthma, pleural disease or cardiac disease (Table 17.5.1). The mean values of the pulmonary function tests, expressed as a percentage of the predicted values, and the number of patients who responded to bronchodilators in the various subgroups are shown in Table 17.5.2.

Thirty one patients had evidence of airways obstruction; 25 of them were smokers or ex-smokers and the remaining 6 non-smokers had a mild abnormality of airways obstruction. The clinical data of these 6 patients was as follows: one patient (No. 94) had a history of tuberculosis and asthma and evidence of old TB on x-ray; one patient (No. 4) had a history of TB and x-ray evidence of old TB; two patients had evidence of cardiac disease (No. 59 had a coronary artery by-pass graft and cardiomegaly and No. 104 had hypertension and mitral incompetence with left ventricular hypertrophy and a dilated left

ventricle); one patient (No. 56), who had a marked response to a bronchodilator, had a unilateral radiolucent lung and the remaining patient (No. 89) had no obvious cause for airways obstruction.

There were 11 patients who had evidence of a restrictive lung defect. Three patients had interstitial lung disease (No's 4, 35, 52); 4 had pleural disease, one of whom also had bronchiectasis and another had pneumonia (No's 10, 20, 40, 49); 2 had a history of tuberculosis (No's 18 and 26) and the remaining 2 patients had cardiac disease (No. 15 had hypertension, mitral incompetence and cardiomegaly and No. 87 had hypertension with left axis deviation).

The KCO was abnormal in 21 patients and all of them were smokers. There were 57 patients who had a reduced  $T_LCO$ ; 47 of them had a history of smoking and/or TB. Three of the remaining 10 patients had cardiac disease (No. 37 had hypertension and aortic incompetence, No. 59 had a coronary artery bypass graft and No. 104 had hypertension and mitral incompetence) and one patient (No. 20) had pleural disease. The remaining 6 patients (No's 3, 39, 50, 54, 59 and 99) had no obvious explanation for the reduced  $T_LCO$ , which may be related to occult interstitial or vascular disease. The abnormalities of MIP and MEP were minor in the majority of the patients and no clinical correlates could be found.

Five patients had interstitial lung disease which was diagnosed on the basis of radiographic changes and abnormal pulmonary function tests (No's 4, 35, 52, 57 and 83). All of them had a reduction in the

transfer factor and 3 of them (No's 4, 35, 52) had evidence of restrictive lung disease on the assessment of their volumes. Two of these 5 patients were smokers (No's 57 and 83). One of the patients (No. 35) had evidence of pulmonary hypertension on cardiac assessment.

Seventeen patients had evidence of pleural disease; four of these patients (No's 12, 38, 40, and 66) had tuberculosis based on a history and/or chest radiograph, one patient (No. 52) had interstitial lung disease and previous TB, 2 patients had pneumonia (No's 9 and 20), one patient had cardiac disease (No. 104) and one patient (No. 35) had interstitial lung disease. There were no coexistent diseases in the remaining 8 patients with pleural abnormalities.

One asymptomatic patient (No. 92) had evidence of a cavitating rheumatoid nodule which regressed on subsequent follow up examination. Two patients had evidence of bronchiectasis, one of whom had Kartagener's syndrome with dextrocardia. Six patients had evidence of a recent or past pneumonia (No's 9, 20, 48, 90, 91 and 96). Nine patients had a history of asthma and all of them had evidence of airways obstruction and response to bronchodilator therapy.

There were 22 abnormalities in 21 patients (20,2%) which were considered to be due to RA; 4 patients had interstitial lung disease, one patient had interstitial lung disease and pleural involvement, 8 patients had pleural involvement alone, 6 patients had a diffusion defect, one had airways obstruction and one had a nodule. There was no significant increase in the prevalence of nodules and

seropositivity in the patients who had interstitial lung disease, pleural involvement or diffusion defects.

## DISCUSSION

Twenty two abnormalities were detected in 21 patients (20,2%) who did not have any evidence of an associated disease to explain the abnormality; therefore they were considered to be related to RA. One patient had interstitial lung disease and pleural involvement.

Tuberculosis is very common in Coloureds in the Western Cape and constitutes a major health problem among the poorer communities throughout South Africa. Therefore, it was not surprising that 25 patients (24%) had a history or radiographic evidence of TB. An analysis of the chest radiographs in 309 patients with RA in Denmark showed evidence of healed TB in 9,1%, previous pleurisy in 18,8% and evidence of pleural effusions in 0,6% (Jurik et al 1982). Seventeen patients (16,3%) had pleural abnormalities in this survey but only 9 patients (8,7%) had no evidence of any other pulmonary disease or any cardiac disease. However, it is possible that some of these patients may have had previous asymptomatic pleural involvement due to TB but this could not be determined with certainty. In one study a history of pleurisy was obtained in 21% of 516 RA patients, and pleural effusion which was attributed to RA was noted in 3,3% (Walker and Wright 1967). Hyland et al did not find any evidence of an increased prevalence of pleurisy in RA patients compared to controls (Hyland et al 1983). However, the characteristic changes in the pleural fluid in

RA provides convincing evidence that it is a definite entity (Hunder et al 1972, Luthra et al 1975, Gordon et al 1985).

Diffuse pulmonary fibrosis has been reported in association with seropositive nodular disease and is more common in males (Gordon et al 1985). The prevalence of pulmonary fibrosis varies, depending on the selection of patients and methods of assessment. It was detected in 1,6% of 516 patients in one study (Walker and Wright 1969) and 1,1% in another survey of 702 patients (Patterson et al 1965). It was detected more often when the investigations included lung biopsy (Cervantes-Perez et al 1980). Diffuse interstitial lung disease may also be related to gold salts and penicillamine but no relationship was noted in this study.

The association of infection with RA has been noted in several reports (Huskisson and Hart 1972, Anonymous 1972, Baum 1971). An increased prevalence of pulmonary infection has been noted in patients with RA, with or without parenchymal disease (Gordon et al 1985). Apart from the presence of TB in 25 patients (24%), 6 patients (5,8%) had evidence of pneumonia and 2 patients had bronchiectasis.

A reduction in  $T_LCO$  was very common (54,8%) but the majority were related to smoking. A direct relationship between smoking and a reduction in  $T_LCO$  has also been noted in other studies (Hyland et al 1973, Frank et al 1978, Davidson et al 1974). Only 6 patients (5,8%) did not have any other contributory factor and this abnormality may therefore be due to occult interstitial or vascular disease. A

significant reduction in the diffusion capacity has been noted in RA (Whorwell et al 1975, Oxholm et al 1982) but Hyland et al failed to detect any evidence of a reduction in  $T_LCO$  in RA when compared to controls (Hyland et al 1973).

Acute obliterative bronchiolitis in RA has been reported by Geddes et al and the majority of the patients had a rapidly progressive course (Geddes et al 1977). Airflow obstruction was noted in 31 patients in this survey and the majority of these patients were smokers. Only one patient had airflow obstruction which could not be related to any other disease. This finding is similar to the observation by Hyland et al who failed to detect any increase in the prevalence of airflow obstruction (Hyland et al 1983). In earlier studies by Collins et al and Geddes et al, airways obstruction was detected in 61% and 32% respectively (Collins et al 1976, Geddes et al 1979). These differences may be related to an inadequate smoking history or differences in the interpretation of the pulmonary function tests, and they have been reviewed in other reports (Gordon et al 1985, Hyland et al 1983).

Pulmonary manifestations such as pleural involvement and interstitial lung disease, have been reported to occur more commonly in association with nodules and a positive rheumatoid factor. However, in the present survey, there was no relationship between the prevalence of nodules and seropositivity in the patients with or without the abnormalities which were considered to be related to RA.

The present survey shows that it is important to select a random

population of patients with RA when screening for the prevalence of pulmonary involvement. There were 69 patients (66,3%) who were current smokers or ex-smokers and 25 patients (24%) had a history or radiographic evidence of tuberculosis. Therefore, if patients who had a history of smoking and/or tuberculosis had been excluded, then only 28 patients (26,9%) would have been eligible for the study and this would represent a highly selected group. Furthermore, if patients with a history of cardiac disease or other respiratory diseases were omitted then there would have been even more exclusions.

In conclusion, pulmonary involvement is common in RA and was detected in 21 patients (20,2%). It is possible that the true prevalence is higher; some of the abnormalities, which were noted in smokers and patients with other diseases such as TB, may be due to a combination of factors, including RA, but this cannot be determined with certainty. The abnormalities which were detected were pleural involvement (8,7%), interstitial lung disease (4,8%), diffusion defect (5,8%), airways obstruction (1%) and pulmonary nodule (1%).

TABLE 17.5.1

THE PREVALENCE OF ABNORMALITIES OF LUNG FUNCTION ACCORDING  
TO SEX, SMOKING STATUS, PRESENCE OR ABSENCE OF TUBERCULOSIS  
AND OTHER DISEASES

	NO.	OBST.	REST.	UAO	T <sub>L</sub> CO	KCO	MIP	MEP
TOTAL	104	31	11	4	57	21	10	31
NON-SMOKERS	35	6	5	3	12	0	3	15
EX-SMOKERS	17	6	2	0	10	2	2	6
SMOKERS	52	19	4	1	35	19	5	10
MALES	32	10	3	1	22	11	4	13
FEMALES	72	21	8	3	35	10	6	18
TUBERCULOSIS	25	9	6	0	14	4	3	8
ABSENCE OF TB	79	22	5	4	43	17	7	23
NON-SMOKER AND ABSENCE OF TB	28	4	2	3	10	0	2	13
BRONCHIECTASIS	2	1	1	0	2	1	0	0
FIBROSING ALVEOLITIS	5	4	3	0	4/4	3/4	1	1
PNEUMONIA	6	2	1	1	2	1	0	2
ASTHMA	9	9	0	0	2	1	1	1
PLEURAL DISEASE	17	6	5	1	13	6	1	5
CARDIAC DISEASE	10	3	1	0	5/9	0/9	2	3

ABBREVIATIONS: No. - number; OBST. - obstructive defect; REST. - restrictive defect; UAO - upper airway obstruction, T<sub>L</sub>CO - transfer factor of carbon monoxide; KCO - transfer coefficient for carbon monoxide; MIP - maximum inspiratory pressure; MEP - maximum expiratory pressure.

TABLE 17.5.2

THE MEAN VALUES FOR THE PULMONARY FUNCTION TESTS EXPRESSED AS A PERCENTAGES OF THE PREDICTED VALUES,  
AND THE NUMBER OF PATIENTS WHO RESPONDED TO BRONCHODILATORS IN THE VARIOUS SUB-GROUPS

GROUPS	NUMBER	FEV <sub>1</sub> %	FVC%	FEV <sub>1</sub> /FVC RATIO	DEF%	PIF%	RESPONSE TO BRONCHODILATOR	RV%	FRC%	TLC%	RV/TLC RATIO	MIP%	MEP%	T <sub>L</sub> CO <sub>2</sub>	KCO <sub>2</sub>
							NUMBER								
TOTAL	104	85,1	86,8	77,0	107,2	94,7	30	123,0	108,7	97,1	36,9	109,6	90,2	77,4	94,5
NON-SMOKERS	35	87,0	86,2	79,6	114,4	88,3	5	127,8	111,2	99,6	37,3	112,7	85,9	86,5	106,2
EX-SMOKERS	17	80,7	83,0	76,5	99,1	94,8	6	122,8	103,1	94,0	40,0	111,8	96,1	74,2	96,8
SMOKERS	52	85,2	88,5	75,3	105,2	98,7	19	120,2	109,1	96,7	35,6	106,9	91,3	72,5	86,4
MALES	32	83,0	87,5	73,6	107,0	108,1	10	97,1	91,6	89,7	34,3	110,1	89,2	73,3	86,4
FEMALES	72	86,0	86,6	78,5	107,3	88,1	20	134,3	116,2	100,4	38,0	109,4	90,7	79,3	98,3
TB	25	79,7	83,4	75,0	100,5	96,8	8	110,2	96,9	90,5	36,7	113,8	92,4	74,6	95,3
ABSENCE OF TB	79	86,8	87,9	77,6	109,2	94,0	22	127,4	112,7	99,3	37,0	108,4	89,5	78,2	94,3
NON-SMOKERS AND ABSENCE OF TB	28	91,4	89,6	80,2	119,6	88,0	4	137,1	118,4	105,2	37,9	109,6	82,8	88,7	105,6
BRONCHIECTASIS	2	42,2	45,5	78,5	58,3	54,0	1	136,1	89,3	65,7	46,5	122,9	121,8	44,2	85,3
INTERSTITIAL LUNG DISEASE	5	62,5	67,8	74,4	84,6	91,9	3	117,8	100,6	82,5	42,6	113,4	99,8	39,3	62,3
PNEUMONIA	6	81,3	86,5	73,0	100,8	104,5	2	125,0	109,4	100,4	38,6	114,9	91,3	83,3	96,3
ASTHMA	9	68,8	81,4	66,2	83,6	88,2	9	147,3	118,0	100,1	43,5	115,7	104,6	82,5	97,7
PLEURAL DISEASE	17	77,2	80,0	75,0	103,1	96,1	6	118,3	107,4	91,8	40,7	117,7	89,5	68,8	90,4
CARDIAC DISEASE	10	86,8	87,5	75,8	102,4	86,2	3	133,8	110,3	99,0	43,0	100,9	86,1	79,8	95,9

CHAPTER 17.6PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS - SUMMARYINTRODUCTION

In 1948, Ellman and Ball coined the term rheumatoid disease to include patients with RA who have both articular and systemic manifestations of the disease (Ellman and Ball 1948). Joint inflammation is the cardinal manifestation of the disease and therefore, the term rheumatoid arthritis is still widely used.

Most of the extra-articular manifestations of RA can be ascribed to serositis, vasculitis and rheumatoid nodules, which are themselves probably due to vascular inflammation. These manifestations usually tend to occur in patients with a positive rheumatoid factor and are most frequently associated with a higher titre of rheumatoid factor (Decker and Plotz 1985).

Most of the previous surveys on extra-articular manifestations of RA have tended to study one or a few of the extra-articular features.

The aim of this survey was to determine the prevalence of extra-articular manifestations of RA based on clinical assessment, a review of the hospital records and specialised tests such as nerve conduction studies, echocardiography and pulmonary function tests in a

randomly selected group of patients. Renal abnormalities are not generally regarded as an extra-articular manifestation. Some information about the renal function in Coloureds was available and is also included in this chapter.

## RESULTS

The prevalence of the various extra-articular manifestations is summarized in Table 17.6.1. Ninety two patients (88,5%) had one or more extra-articular manifestations.

Anaemia was the commonest manifestation; 33 patients (31,7%) were anaemic at the time of assessment and a further 24 patients (23,1%) were anaemic in the past.

Keratoconjunctivitis sicca was the most common ocular manifestation and was detected by Rose Bengal staining in 22 (21,2%) of the patients. Lymphadenopathy was detected in 24 patients (23,1%) and the most frequent site was the axilla. Most of the patients had enlarged lymph nodes in a single region, such as the axilla, and only 5 patients had involvement of 2 or more regions. Five patients had splenomegaly but one of these patients had a history of heavy alcohol intake and portal hypertension, which was probably on the basis of cirrhosis of the liver. The liver was enlarged (on palpation or percussion) in 43 patients (41%) and measured approximately 1 cm in 9 patients (8,7%), 2 cm in 19 patients (18%), 3 cm in 13 patients (12,5%) and 4 cm in 2 patients (2%).

Rheumatoid nodules were present in 31 patients (29,8%). Two of these patients previously had subcutaneous nodules, which were not present at the time of assessment. The most common sites were the elbows and upper forearms, and only a few nodules were detected at other sites. Cutaneous or digital vasculitis were noted in 4 patients (3,8%) at the time of assessment. Leg ulcers had developed in 7 patients; one patient had pyoderma gangrenosum, 2 patients had ulcers which were due to stasis and pressure and the remaining 4 ulcers were probably related to RA.

The cardiac, neurological and pulmonary abnormalities which were noted are discussed in chapters 17.2, 17.4 and 17.5 respectively and the manifestations which were related to RA are summarised in Table 17.6.1. The abnormalities of the E-F slope, noted in 4 patients were minor and not of any practical significance; all these patients had one or more of the other extra-articular manifestations.

The renal abnormalities which were noted were as follows:

- 1) BLOOD UREA: Twenty seven patients (26%) had an elevated urea; 11 patients had a mild elevation from 6,8 - 8,0 mmol/l, 11 had values between 8,1 and 10,0 mmol/l and the remaining 5 patients had values more than 10,0 mmol/l. Fifteen of the patients with an elevated urea had hypertension or were on diuretic therapy.
- 2) SERUM CREATININE: Six patients had a mild elevation of the serum creatinine from 121 to 131 umol/l. All these patients had an elevated urea and four of them had a blood urea of more than 10,0 mmol/l. Five of the six patients with a raised creatinine had

hypertension.

- 3) PROTEINURIA: Five patients had proteinuria at the time of assessment. One of these patients had an aortic valve replacement and a myopathic ventricle, and another had hypertension and aortic incompetence. The remaining 3 patients had transient proteinuria and all of them had normal serum creatinine.
- 4) RENAL BIOPSY: Three patients had a renal biopsy during the course of their illness. Two of them had a membranous nephropathy whilst on gold therapy and the third patient had evidence of pyelonephritis.

The prevalence of some of the milder extra-articular manifestations such as anaemia, lymphadenopathy or nodules, either alone or in combination, is shown in Table 17.6.2. There were 6 patients (5,8%) who had nodules alone, and anaemia was the only extra-articular manifestation in 12,5%.

There were 31 patients who had nodules (past or present) and 80 patients had a positive rheumatoid factor (past or present). There was a significant increase ( $p=0,0270$ ) in the prevalence of a positive rheumatoid factor in patients with nodules (28/31; 90,3%) when compared to the remainder of the patients (52/73; 71,2%). Two patients had rheumatoid nodules in the past and therefore, nodules were detected at the time of assessment in 29 patients. A positive rheumatoid factor was present at the time of assessment in 63 patients (60,6%). There was also a significant increase ( $p=0,0031$ ) in the

prevalence of a positive rheumatoid factor (at the time of the study) in patients who had nodules at the time of assessment (24/29 : 82,8%) in comparison with the remainder of the patients (39/75 : 52%).

The prevalence of nodules and a positive rheumatoid factor (past or present) in association with the various extra-articular manifestations is shown in Table 17.6.3. There was a significant increase in the prevalence of nodules in patients with lymphadenopathy ( $p=0,0467$ ) but no other significant relationships were noted with nodules. Patients with abnormal lateral popliteal and/or sural nerve conduction studies had a significant increase in the prevalence of a positive rheumatoid factor either at the time of assessment ( $p=0,0035$ ) or at any stage of the disease ( $p=0,0139$ ); none of the other extra-articular features were associated with an increased prevalence of seropositivity.

## DISCUSSION

Studies on the prevalence of a spectrum of extra-articular manifestations in the same population have not been frequently reported. The prevalence of extra-articular manifestations were studied in a group of 127 hospitalised patients with classical and definite RA (Gordon et al 1973). The demographic data and the prevalence of extra-articular manifestations are compared with the findings in the present survey (Table 17.6.4). The groups were compared, even though the selection and methods of assessment were different, as there are no other studies for comparison. All the

patients studied by Gordon et al were hospitalised patients, 93% had a positive rheumatoid factor and 53% had nodules (Gordon et al 1973). The majority (approximately 90%) of the patients in the present survey were outpatients, 76,9% had a positive rheumatoid factor at some stage of their disease and 29,8% had nodules. However, there were similarities in the demographic data as shown in Table 17.6.3. It is surprising that keratoconjunctivitis sicca and pleural involvement, which were the commonest ocular and pulmonary abnormalities in the present survey, were not reported by Gordon et al (Gordon et al 1973). Diffuse pulmonary fibrosis is detected more often in patients with active disease and was detected less often in the present survey (Gordon et al 1985). This difference may have occurred because hospitalised patients were more likely to have active disease and also because the prevalence of nodules and a positive rheumatoid factor in the hospitalised patients was higher than is generally reported in RA (Gordon et al 1973). One or more extra-articular manifestations were noted in 76% of the hospitalised patients (Gordon et al 1973) and a similar high prevalence of 88,5% was noted in the present survey.

Anaemia is the commonest extra-articular manifestation of RA and may be noted in two thirds of women and about half of the men with RA (Mowat 1971). Anaemia was noted in 54,7% of the patients during the course of their disease.

The prevalence of lymphadenopathy varies from 19% to 96% in different series (Short et al 1957). Short et al found a prevalence of 29,4% in RA subjects and 4% of controls (Short et al 1957). Lymphadenopathy

was noted in 23,1% in the present survey. The observation that lymphadenopathy was rarely generalised and usually confined to a single anatomical region is in agreement with the findings by Robertson et al (Robertson et al 1968).

Cutaneous or digital vasculitis has been reported in up to 8% of hospitalised RA patients (Bernhard 1985) and was present in 3,8% in this survey. Hart has noted that leg ulcers in RA may be related to trauma, stasis, Felty's syndrome or rheumatoid vasculitis (Hart 1969). In this survey, two patients had stasis ulcers and 4 patients (3,8%) had ulcers which were considered to be due to rheumatoid vasculitis.

Keratoconjunctivitis sicca was detected in 14,3% of 216 patients by Thompson and Eadie and was considered to be the most common ocular manifestation of RA (Thompson and Eadie 1956). These findings were confirmed in this study and KCS was present in 21,2%.

An increased prevalence of a peripheral neuropathy in RA was noted in the 1950-1960 period and corticosteroids were considered to contribute to the development of neuropathy (Hart et al 1957, Hart and Golding 1960). In the present survey, 3 patients had evidence of a symmetrical distal sensory neuropathy; all were males who had a history of heavy alcohol intake and alcohol was considered the likely cause. The prevalence of carpal tunnel syndrome varies from 8,9% in a clinical study of 627 patients to as much as 50% on electromyography (Conn 1985, Barnes and Currey 1967). Abnormalities of conduction studies of the peroneal nerve and sensory nerves have also been

reported (Good et al 1965, Lang et al 1981, Hoerner et al 1981). In the present survey, 27 patients (26,2%) had abnormal electrophysiological studies and seven of these patients had involvement of more than one nerve. Abnormalities of the median nerve were recorded in 16 patients; the lateral popliteal in 10 and the sural in 8 patients. There was a poor correlation between the clinical and neurophysiological tests.

Pericarditis has been detected in 2%-10% of patients in clinical studies and about 30% in autopsy studies (Pizarelli and Goldberg 1985, Kirk and Cosh 1969). Pericardial effusion and/or thickening and abnormalities of mitral valve motion (E-F slope) have been frequently noted in echocardiographic studies (Prakash et al 1973, Bacon and Gibson 1974, Nomeir et al 1973). Forty five echocardiographic abnormalities were noted in 31 patients in this study. Apart from the presence of pericardial effusion in 5 patients (6%) and minor abnormalities of the E-F slope in 4 patients (5,2%), all the other abnormalities could be related to associated cardiac diseases.

Pulmonary involvement in RA has been reported in many studies but most of them have tended to study one or a few aspects only. The abnormalities which were detected and considered to be related to RA were pleural involvement in 9 patients (8,7%), pulmonary fibrosis or fibrosing alveolitis in 5 patients (4,8%), a reduction in the  $T_LCO$  in 6 patients (5,8%), airways obstruction in 1 patient and a pulmonary nodule in 1 patient. A history of pleurisy was obtained in 21% of 516 patients in one study and involvement of the pleura has been

considered to be the commonest pulmonary abnormality (Walker and Wright 1967). Some studies have failed to detect any increase in pleural involvement (Hyland et al 1983) but 9 patients (8,9%) in this survey had pleural involvement without any other secondary cause. There was only one patient who had evidence of airways obstruction in the absence of a history of smoking, tuberculosis or cardiac disease. Airways obstruction has been noted in 32% and 61% of patients in different studies but Hyland et al failed to detect any increase in airways obstruction (Collins et al 1976, Geddes et al 1979, Hyland et al 1973). A reduction in the  $T_LCO$  was noted in 57 patients, and the 6 patients who did not have any other contributory factors, may have occult interstitial or vascular disease. Infection was common and 25 patients (24%) had evidence of TB, 6 had previous pneumonia and 2 had bronchiectasis.

Sorensen studied the endogenous creatinine clearance in a group of 203 patients with RA and 387 controls (Sorensen 1961). He found that there was impairment of renal function which was related to the severity and duration of the disease. However, impaired renal function in RA is usually due to drug therapy (gold salts, penicillamine, analgesics and NSAIDs), coexistent cardiac or renal disease and amyloidosis. Mild elevation of the blood urea was not uncommon, but nearly all the patients who had a raised creatinine or significant proteinuria, were found to have associated diseases.

The extra-articular manifestations of RA are associated with a positive rheumatoid factor, especially in patients with a high titre,

and rheumatoid nodules, which themselves are common in patients with high titres of rheumatoid factor (Hurd 1979, Decker and Plotz 1985, Scott et al 1981, Schmid et al 1961, Mongan 1969, Gordon et al 1973).

Rheumatoid nodules occur in about one-third of the patients with RA (Hurd 1979, Bernhard 1985, McKenna and Wright 1985, Stevens 1985) and a positive rheumatoid factor is detected in 70% or more patients with RA (Carson 1981). In the present survey, rheumatoid nodules were noted in 31 patients (29,8%) and a positive rheumatoid factor was present in 63 patients (60,6%) at the time of assessment and 80 patients (76,9%) at any stage of the disease. These findings are similar to their prevalence in other studies. There was a significant increase in the prevalence of a positive rheumatoid factor in patients with nodules when compared with the remainder of the patients. However, apart from the association of lymphadenopathy with rheumatoid nodules, and abnormalities of lateral popliteal and sural nerve conduction with a positive rheumatoid factor, there was no significant increase in the prevalence of a positive rheumatoid factor or nodules with the other extra-articular manifestations.

The association of seropositivity with pulmonary involvement and pericarditis have been frequently reported (Gordon et al 1985, Bernhard 1985). The association of nodules and seropositivity with extra-articular manifestations has been reported in 3 large studies (Schmid et al 1961, Scott et al 1981, Gordon et al 1973). Schmid et al reported 34 RA patients with arteritis, of whom 17 had histological evidence of arteritis (Schmid et al 1961)). Eleven of these 17

patients had evidence of necrotizing arteritis. Many of the patients had severe systemic illness and 5 (29,4%) of the 17 patients with histological evidence of arteritis had died. Peripheral neuritis occurred in 16 of the 34 patients, of whom 7 had foot drop and 2 had quadriplegia. Scott et al reported 50 patients with RA and systemic vasculitis; histological evidence of vasculitis was noted in 60% and the overall mortality was 30% (Scott et al 1981). They defined systemic vasculitis clinically by the presence of deep cutaneous ulcers, peripheral gangrene, acute peripheral neuropathy or mononeuritis, or severe systemic diseases occurring in the presence of typical nail fold or digital infarcts (Scott et al 1981). Gordon et al also reported an association between seropositivity and extra-articular manifestations (Gordon et al 1973). However, there was a high prevalence (93%) of rheumatoid factor and nodules (53%) in their hospitalised patients and this may have contributed to the association which was noted with the various extra-articular manifestations.

Many of the patients in the present survey had extra-articular features which were only detected with the use of specialised investigations such as echocardiography, pulmonary function tests and nerve conduction studies. In addition, milder abnormalities such as anaemia, lymphadenopathy and keratoconjunctivitis sicca were often present without evidence of systemic vasculitis. Therefore, the spectrum of extra-articular manifestations in the present survey were milder than those reported in other surveys (Schmid et al 1961, Scott et al 1981). Thus, the lack of a strong relationship between the

presence of nodules and seropositivity with the extra-articular features, may be related to the relatively milder spectrum of extra-articular manifestations noted in a mainly outpatient population. Furthermore, some of the manifestations were only present in a small number of patients and therefore, significant relationships may not have been detected.

In conclusion, extra-articular manifestations of RA are common and were detected in 92 patients (88,5%). The commonest manifestations which were detected were anaemia, nodules and keratoconjunctivitis sicca. The use of specialised tests results in the detection of many manifestations which would not be suspected on clinical examination and routine tests. However, as many of the patients were asymptomatic or had only mild symptoms, these tests are not of much practical value in the routine medical management of patients with RA. Nevertheless, they do provide valuable information in surveys of this nature and show that non-articular manifestations are commoner than expected. Furthermore, apart from lymphadenopathy and abnormal conduction studies of the lateral popliteal and/or sural nerves, the other extra-articular manifestations were not associated with an increased prevalence of nodules and seropositivity. This may be related to the milder spectrum of extra-articular features seen in this survey when compared to those reported in patients with systemic vasculitis.

TABLE 17.6.1

EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

ABNORMALITY	NUMBER (n=104)	PERCENT
1) ANAEMIA Present	33	31,7
Past	24	23,1
2) EYES		
a) Ketatoconjunctivitis sicca	22	21,2
b) Episcleritis (Present 2, Past 3)	5	4,8
c) Scleritis (Present 1, Past 1)	2	1,9
d) Retinal vasculitis	1	1,0
3) LYMPHADENOPATHY	24	23,1
4) SPLENOMEGALY	4	3,8
5) NODULES	31	29,8
6) CUTANEOUS VASCULITIS	4	3,8
7) LEG ULCERS	4	3,8
8) CARDIAC		
Pericardial effusion	5	6,0
Reduced E-F slope	4	5,2
9) NEUROLOGICAL		
a) Digital neuropathy	1	1,0
b) Entrapment neuropathy - median	16	15,8
- ulnar	2	1,9
c) Lateral popliteal abnormality	10	10,5
d) Sural nerve abnormality	6	6,9
10) PULMONARY		
a) Interstitial lung disease	5	4,8
b) Pleural involvement	10	9,6
c) Diffusion defect	6	5,8
d) Airways obstruction	1	1,0
e) Nodules	1	1,0

TABLE 17.6.2

PREVALENCE OF VARIOUS EXTRA-ARTICULAR MANIFESTATIONS -  
EITHER ALONE OR IN COMBINATION

	NUMBER (n=104)	PERCENT
1) Anaemia alone	13	12,5
2) Anaemia + LN*	4	3,8
3) Anaemia + LN + CTS	1	1,0
4) CTS alone	3	2,9
5) Nodules alone	6	5,8
6) Nodules + anaemia	4	3,9
7) Nodules + LN	1	1,0
8) Nodules + anaemia + LN	4	3,8
9) Any one of the other manifestations (Alone or in combination with any of the above)	56	53,8
10) NIL	12	11,5

\* LN = lymphadenopathy

TABLE 17.6.3.

THE PREVALENCE OF NODULES AND SEROPOSITIVITY IN PATIENTS  
WITH THE VARIOUS EXTRA-ARTICULAR MANIFESTATIONS  
(PERCENTAGES IN PARENTHESES)

<u>ABNORMALITY</u>	<u>NUMBER</u>	<u>NODULES</u>	<u>SEROPOSITIVITY</u>		
			<u>PRESENT</u>	<u>PAST</u>	<u>PAST OR PRESENT</u>
Anaemia Present	33	8 (24,2)	18 (54,5)	10 (30,3)	28 (84,8)
Past	24	7 (29,2)	16 (66,7)	1 ( 4,2)	17 (70,8)
KCS	22	4 (18,2)	16 (72,7)	4 (18,2)	20 (90,1)
Episcleritis / Scleritis	5	2 (40,0)	3 (60,0)	1 (20,0)	4 (80,0)
Leg ulcers	4	1 (25,0)	4 (100,)	0	4 (100 )
Cutaneous vasculitis	4	1 (25,0)	3 (75,0)	1 (25,0)	4 (100 )
Pericardial effusion	5	2 (40,0)	4 (80,0)	1 (20,0)	5 (100 )
Lateral popliteal or sural	15	6 (40,0)	14 (93,3)	1 ( 6,7)	15 (100 )
Splenomegaly	4	2 (50,0)	4 (100,)	0	4 (100 )
Lymphadenopathy	24	11 (45,8)	16 (66,7)	3 (12,5)	19 (79,2)
Interstitial lung disease	5	2 (40,0)	4 (80,0)	1 (20,0)	5 (100..)
Pleural involvement	10	3 (37,5)	8 (80,0)	0	8 (80,0)
Diffusion defect	6	0	3 (50,0)	0	3 (50,0)
Airways obstruction	1	0	0	0	0
Nodule	1	1 (100,)	1 (100,)	0	1 (100 )
Any one of the pulmonary abnormalities	21	6 (28,6)	12 (57,1)	1 (4,8)	13 (61,9)

TABLE 17.6.4.

COMPARISON OF THE DEMOGRAPHIC DATA AND THE PREVALENCE OF  
EXTRA-ARTICULAR FEATURES WITH GORDON et al (1973)

	<u>GORDON et al (1973)</u> n=127	<u>PRESENT STUDY</u> n=104
Females to males	1,9 : 1	2,3 : 1
Mean age	55,0 + 1,0	51,1 + 12,0
Mean duration	11,5 + 0,8	12,4 + 9,3
ARA Criteria - classical %	16	16,3
- definite %	84	83,7
Functional class 3 and 4 (%)	37	24,0
Rheumatoid factor (% positive)	93	76,9
 <u>EXTRA-ARTICULAR MANIFESTATIONS</u>		
Subcutaneous nodule (%)	53	29,8
Digital vasculitis (%)	15	3,8
Skin ulceration (%)	13	3,8
Lymphadenopathy (%)	12	23,1
Splenomegaly (%)	9	3,8
Episcleritis (%)	9	4,8
KCS (%)	-	21,2
Pericarditis (%)	2	6,0
Non-compressive neuropathy (%)	10	14,4
Pulmonary fibrosis (%)	20	4,8
Pleural disease (%)	-	9,6
Pulmonary nodule (%)	-	1,0
Airways obstruction (%)	-	1,0
Diffusion defect (%)	-	5,8
Any of the above extra-articular features	76	88,5*

\* The prevalence in the present survey includes other features listed in Table 17.6.1.

## CHAPTER 18

### SUMMARY AND CONCLUSION

#### SUMMARY OF RESULTS

The spectrum of RA was studied in a group of 256 patients with classical or definite RA from 3 different South African Communities (104 Coloureds, 100 Caucasians and 52 Africans). Eighty four percent of the patients fulfilled the criteria for classical RA and 16% had definite RA. The majority of the patients (91,8%) were outpatients at the time of assessment. The mean age of onset of RA was nearly a decade earlier in Africans in comparison with Caucasians. The mean age of the Coloureds was intermediate between that of the Caucasians and Africans. The mean duration of RA was also significantly longer in Caucasians and Coloureds in comparison with Africans. The ratio of females to males was 2,8 : 1 and there were no statistically significant differences among the races.

Only 80 patients (31,3%) were working at the time of assessment. Seventy eight patients (30,5%) were dependent on state support (9,4% were pensioners and 21,1% received a disability grant). The majority of the Coloureds and Africans belonged to the poorer social class and 38,5% of the Coloureds and 19,2% of the Africans received a disability grant from the state in comparison with only 4% of the Caucasians. A family history of RA in a first degree relative was obtained in 30% of

the Caucasians, 13,5% of the Coloureds and 7,7% of the Africans.

Malnutrition was present in 23,2% of the patients and obesity was noted in 23 patients (10,5%). Malnutrition was commoner in men, and malnourished patients tended to have a higher mean ESR and more severe functional disability. There was no significant difference in the prevalence of malnutrition in the 3 communities. Obesity was significantly more common in African females than Caucasians. There were no differences in the functional status, activity of the disease and the use of steroids in obese patients in comparison with the remainder of the patients.

The ARA functional classification of the patients was as follows: Class 1 - 25,8%; 2 - 52,3%; 3 - 14,5% and 4 - 7,4%. There was a highly significant correlation when the ARA and Joint Committee classification were compared with each other, and with the total score and separate scores for the upper and lower limb using the Swezey functional disability classification and the modified Lee functional index score.

The most frequent sites of joint pain were the hands (98,4%), wrists (98%), knees (93,8%) and the shoulders (93,4%). A Ritchie articular index score of 0 was recorded in 17,2% and a total of 51,2% had a score of 5 or less.

Atlanto-axial subluxation and/or impaction were detected in 115 patients (46,4%) and a history of neck pain was obtained in 78,5%.

However, only four patients (1,6%) developed a myelopathy. There was a poor correlation between neurological abnormalities and the presence of AAS and/or AAI.

A history of injections of corticosteroids and local anaesthetic for articular or periarticular involvement of the shoulder was obtained in 44,5%. A Larsen grade 2 or more severe radiographic involvement of at least one of the shoulders was present in 41,9% of the patients.

The prevalence of resorptive arthropathy was 5,1% and there were no differences among the races. Patients with resorptive arthropathy tended to have their disease for a longer period but the age, sex ratio and the prevalence of nodules in the resorptive arthropathy group was similar to the remainder of the patients.

A z-shaped deformity of the thumb was noted in 12,2% of the hands. The prevalence of deformities of the fingers, with involvement of one or more fingers, was 28,9% for SND, 23,8% for BD and 17,2% had ulnar deviation. The mean number of fingers involved in those who had deformities was 3,5 for SND, 2,1 for BD and 4,4 for ulnar deviation. Boutonniere deformity was commoner in Africans in comparison to Caucasians but ulnar deviation of the fingers was commoner in Caucasians. Flexor tenosynovitis of one or more fingers was present in 145 patients (56,6%) and the mean number of fingers involved was 2,9. The function of the fingers was most severely impaired in the index finger followed by the middle, ring and little fingers. There was significantly less severe impairment of hand function in Africans

in comparison with the Coloureds and Caucasians.

An analysis of only the right handed patients showed that there was no significant difference of the prevalence of SND, BD, UD or FTS in the dominant and non-dominant hand. However, the mean radiographic score was higher in the dominant hand, which also showed more severe impairment of function. The most important factors which contributed to impaired function of the fingers were the severity of radiographic changes and the presence of a SND.

A Larsen grade 2 or more severe radiographic score was noted in 81,7% of the wrists, and 40% had very severe involvement with a Larsen grade 4 or 5. The mean radiographic score for the wrist was significantly higher in Africans in comparison with Caucasians and Coloureds. Flexion deformity of the elbows was common and a deformity of more than 10° was present in 52,9% of the elbows. A history of pain in the hips was obtained in 37,8%. Thirty nine patients (25,8%) had either surgery or a Larsen grade 2 or more severe change in at least one of the hip joints.

Foot involvement is an important source of pain and disability in RA. Radiographic changes (Larsen grade 2 or more severe involvement) in at least one of the toes occurred in 90,2% of the patients even though pain in the forefoot was present in 76,1%. Subluxation of the MTPJs joints was present in 71%, and 37,1% had callosities under the metatarsal heads. Seventy two patients (28,2%) had some modification of their footwear even though deformities of the feet were noted in

47,6%. The commonest deformities were planovalgus (29,3%) and planus (14,3%).

The prevalence of fractures in this survey was 8,6%; if the fractures which were related to motor vehicle accidents were excluded, the prevalence was 7%. The mean age of the patients with fractures was 60,3 years and the female to male ratio was 8 : 1. Fractures occurred in the lower limbs in 10 patients, the upper limbs in 6 patients and 3 patients had vertebral collapse. Only one patient had a spontaneous fracture of the lower third of the tibia and 3 patients had spontaneous vertebral collapse. The fractures in the remaining patients were related to injury, which was usually a fall. Corticosteroid therapy was not a major predisposing factor as only one-third of the patients had been on steroids.

Seventy two patients (28,1%) had an elevated urea (>6,7 mmol/l) but a significant elevation of more than 10 mmol/l was present in only 17 patients (6,8%). The serum creatinine was elevated in 17 patients (6,6%) and all these patients had an elevated blood urea. A reduction in the serum creatinine was much more common and 111 patients (43,4%) had values below 75  $\mu$ mol/l. A mild rise (less than two fold) in the alkaline phosphatase was present in 42,3% but only 6,5% had a raised GGT. There was a significant rise in the total serum globulins in Coloureds and Africans in comparison with the Caucasians.

A positive rheumatoid factor was noted during the course of their disease in 202 patients (78,9%); 156 (61,5%) had a positive rheumatoid

factor at the time of assessment. A positive anti-nuclear factor was present in 91 patients (36%) and a mild elevation of DS DNA was present in 6 patients. There was no significant difference in the prevalence of rheumatoid factor, antinuclear factor or DS DNA among the races. A smooth muscle antibody was present in 12,5% but only one patient had a positive antimitochondrial antibody. A rise in the IgG was present in 43,3%, IgA in 25,9% and IgM in 10,5%. The IgG values were significantly higher in Coloureds and Africans in comparison with Caucasians.

Anaemia was present in 37,8% at the time of assessment. Definite iron deficiency, with a serum ferritin below 15 ng/ℓ was present in 16 patients (8,3%), but the prevalence may be as high as 57,5% if a serum ferritin of 60 ng/ℓ or less is used as the diagnostic criterion as recommended in some surveys. The anaemic patients had a significantly higher mean ESR, CRP and articular index score.

About two thirds of the patients attended physiotherapy and half of the patients were seen by an occupational therapist. Oral NSAIDs were currently taken by 87,5% and 45,4% were using a NSAID suppository. Thirty nine patients (15,2%) were on oral steroid therapy at the time of assessment and a further 17,6% had taken steroids in the past. A history of antidepressant medication was obtained in 24,2% and 31,3% had taken tranquilizers. There were 179 patients (69,9%) who had received one or more injections of intra-articular or intralesional steroids. Slow acting anti-rheumatic drugs (remitive agents) had been taken by 163 patients (63,7%), and 57 patients (22,3%) had 2 or

more agents during the course of their disease.

One hundred and twenty six patients (49,2%) had one or more surgical procedures and the mean number of procedures per patient was 3,8. The most frequent sites of surgery were the hands, wrists, MTPJs and hips. Forty patients (15,6%) had a replacement arthroplasty of one or more of the four major weight bearing joints. There was a significant increase in the frequency of surgery to the 1st MTPJ, 2nd to 5th MTPJs, carpal tunnel release and flexor tenosynovectomy in Caucasians in comparison with Africans.

The extra-articular manifestations were studied in the group of 104 Coloureds with the use of specialised tests. There were 92 patients (88,5%) who had at least one or more extra-articular manifestation.

Anaemia was the commonest extra-articular manifestation and was present in 31,7%, and a further 23,1% had anaemia in the past. Eye involvement was also common and 21,2% of the patients had KCS, 5 (4,8%) had episcleritis, 2 (1,9%) had scleritis and one patient had retinal vasculitis. Hepatomegaly was detected in 41,3%, lymphadenopathy in 23,1% and splenomegaly in 3,8%. Subcutaneous nodules were detected in 29,8%, cutaneous vasculitis in 3,8% and 4 patients (3,8%) had leg ulcers which were probably related to RA.

A survey on the cardiac involvement in RA showed that 45 echocardiographic abnormalities were noted in 31 patients (37%). Pericardial effusion was detected in 5 patients (6%), 5 patients

(6,8%) had an enlarged left ventricle, 5 patients (6,5%) had an enlarged left atrium and one patient had an enlarged right ventricle. One patient had reduced fractional shortening. Eleven abnormalities of mitral valve morphology were present in 10 patients (13%) and 12 patients (15,6%) had a reduced E-F slope. Abnormalities of the aortic valve were detected in 5 patients. The only significant abnormalities which may be related to RA were pericardial effusion in 5 patients (6%) and a mild reduction in the E-F slope in 4 patients (5,2%).

Abnormal electrophysiological tests of nerve conduction were detected in 27 patients (26,2%), with seven of these patients (25,9%) having abnormalities of more than one nerve. The abnormalities which were considered to be related to RA were CTS in 14,9%, reduced lateral popliteal conduction velocity in 10,5% and sural nerve involvement in 6,9%. There was a poor correlation between the clinical findings and electrophysiological tests. Three patients had clinical evidence of a distal sensory neuropathy but all of them had a history of heavy alcohol intake. Although involvement of the cervical spine was common, only 2 patients developed a myelopathy as a result of basilar invagination.

Abnormalities of pulmonary function were common and the number of patients who had impaired tests were as follows: airflow obstruction (31), restrictive defect (11), reduced  $T_LCO$  (57), reduced KCO (21), reduced maximum inspiratory pressure (10) and reduced maximum expiratory pressure (31). However, the majority of these abnormalities could be due to factors such as smoking, respiratory

diseases such as TB, asthma or pneumonia and cardiac diseases. The clinical data, radiographic findings and pulmonary function tests were analysed together, and the following were considered to be related to RA: interstitial lung disease (5 patients), rheumatoid nodule (1 patient), pleural involvement (9 patients), airways obstruction (1 patient) and a diffusion defect (6 patients). A total of 22 abnormalities were noted in 21 patients (one patient had interstitial lung disease and evidence of pleural involvement). There were 25 patients who had TB, 6 had pneumonia, 9 had asthma and 2 had bronchiectasis.

There was a significant increase in the prevalence of a positive rheumatoid factor (either at present or at any stage of the disease) in patients with rheumatoid nodules. The various extra-articular manifestations were analysed to determine whether they were related to the presence of nodules or a positive rheumatoid factor. There was a significant increase in the prevalence of nodules in patients who had lymphadenopathy but none of the other features were related to nodules. A positive rheumatoid factor was noted more often in patients who had abnormal lateral popliteal or sural nerve conduction studies but no relationship was noted for any of the other extra-articular features.

## CONCLUSION

The present survey was undertaken to study many different aspects of RA in a large population of patients and also to compare the different communities to determine whether there were any inter-group differences. Although prospective surveys of a single or few manifestations of RA are extensively reported, an indepth analysis of a large group of patients with RA is infrequently documented.

In South Africa there is a high unemployment rate and an abundance of unskilled and semi-skilled workers. Therefore, the job opportunities for patients with a disabling disease such as RA are limited and this may explain why less than one third of the patients were employed. The findings that 30% of the Caucasians had a first degree relative with RA warrants further family studies as genetic factors may be more important here than is generally observed in other Westernized communities.

Surprisingly there is little information on the nutritional status of patients with RA. Further surveys are necessary to determine the prevalence of malnutrition in hospitalised RA patients and the variation of the nutritional status during the course of the disease. It may be important to improve the nutritional status of patients, especially during active systemic disease with severe constitutional disturbances, and during the rehabilitation and management of patients who require multiple surgical procedures.

The functional assessment of patients has shown that the ARA functional classification, which is brief, concise and widely used, adequately describes the functional status of patients in clinical surveys when compared to the Swezey functional disability classification and the Lee functional index. The majority of the patients (78,8%) belonged to the mild ARA functional classes 1 and 2. The milder functional classification of the patients in this survey is partly related to patient selection as the majority of the patients were outpatients at the time of assessment. Many of the earlier surveys which studied several different aspects of RA, were performed in hospitalised patients who were more likely to have severe functional disability. However, the overall severity of the disease in the study population is comparable to other studies with reference to the severity of radiographic findings and the use of remittive agent therapy. The findings of this study suggest that with proper medical care, the outcome is relatively good for the majority of the patients with RA of sufficient severity to warrant referral to a rheumatology unit. The frequent use of slow acting drugs (63,7%), the need for surgery in 49,2%, referral to physiotherapy and occupational therapy and the overall management by a health care team probably contribute to the successful outcome. Therefore, until the cause of RA is known and a cure is available, it will be necessary to have adequate staff and facilities in urban areas throughout the country in order to control the disease, prevent joint destruction and preserve or improve function.

Although atlanto-axial subluxation and basilar invagination are very

common, only 1,6% developed a myelopathy. Since all the patients who developed a myelopathy had severe AAS or impaction, it is necessary to closely monitor patients with severe involvement. There was a poor correlation between clinical and radiological findings. Therefore, there is still a need for better methods to detect patients who are likely to develop a myelopathy. Further long term studies are necessary, using possibly computerised axial tomography and nuclear magnetic resonance.

Most of the previous surveys on shoulder involvement in RA studied patients who had symptoms referable to the shoulder. When randomly selected patients were studied in this survey, radiographic changes were common (41,9%). Periarticular or soft tissue problems around the shoulder are also very common as shown by the high prevalence of shoulder pain and the frequent need for intra-lesional corticosteroids with local anaesthetic.

The prevalence of resorptive arthropathy in RA has not been previously documented. It was detected in 5,1% of the patients, which is similar to its prevalence in psoriatic arthritis. Apart from the longer duration of RA, the more severe joint damage and lower prevalence of seropositivity in patients with resorptive arthropathy, no other significant differences were noted. The prevalence and distribution of FTS and deformities of the fingers, severity of radiographic changes and function of the hand have been extensively documented in this survey. Previous surveys have shown conflicting results between handedness and the distribution of deformities. In this large study,

there were no differences in the prevalence of FTS and deformities of the fingers in the dominant and non-dominant hand. However, the increased severity of radiographic changes in the dominant hand has been reported in two small studies, and was confirmed in this large study. In addition, the function of the hand was also more severely impaired in the dominant hand.

A greater awareness of foot deformities is necessary so that with more attention to footwear it may be possible to achieve better control of symptoms and prevent progressive deformities. Radiographic changes are detected more often in the forefoot than suggested by symptoms alone. Although the hips were less frequently involved than the hands, feet and shoulders, significant radiographic changes were noted in 25,8%. As the hip is a major weight bearing joint, this finding is important in the long term management, because many patients will progress despite control of the disease activity and they will later require surgery.

The high prevalence of upper gastrointestinal symptoms and the increased frequency of gastric ulcers in comparison to duodenal ulcers, suggests that they may be related to NSAIDs. Patients with peptic ulcers need close monitoring because complications such as gastrointestinal haemorrhage, perforation or iron deficiency anaemia were common.

Fractures were not uncommon in this survey and they contributed to increased morbidity in some patients. Recent reports have suggested

that even in elderly patients with femoral neck fractures, factors other than osteoporosis, such as a tendency to fall may determine which patients will develop fractures. Only one third of the patients were on corticosteroids and as the majority of the patients were elderly females, postmenopausal osteoporosis was probably a contributory factor. However, prospective surveys with control data are necessary to determine whether there is an increased prevalence of fractures in RA.

A frequent rise in the serum alkaline phosphatase is in agreement with previous reports. However, unlike previous studies, a concomitant elevation of the GGT was uncommon. The present findings are similar to those recently reported by Thompson and co-workers (Thompson et al 1986).

A reduction in the serum creatinine was common and this finding is in agreement with another study (Nived et al 1983). Therefore, when the renal function is assessed in RA, it is important to be aware of this finding. A reduction in the serum creatinine has been considered to be related to a reduction in the muscle mass in RA. However, when the upper arm muscle circumference (which is used to assess the skeletal muscle mass) and the body mass index were compared with the serum creatinine, there was no significant correlation. In RA, muscle wasting mainly occurs adjacent to the involved joints. Therefore, it is possible that a reduced muscle mass may be present but may have been detected with the measurements which are conventionally used to assess muscle mass.

Anaemia was commonly noted and although definite iron deficiency was detected in 8,3%, the prevalence may be as high as 57,5% depending on the diagnostic criteria used. It is probably necessary for bone marrow examination to be performed more often, depending on the clinical findings and results of the red cell morphology and iron studies.

This survey shows that there was underutilization of physiotherapy and occupational therapy in the study population. Corticosteroids played an important role in the control of disease activity as nearly one third of the patients received oral corticosteroids and about 70% had intra-articular or intralesional steroids. The frequent need for surgery in RA emphasizes the need for close collaboration with the orthopaedic surgeons in the management of RA. Since 15,6% of the patients had arthroplasty of one or more of the four major weight bearing joints, the use of aggressive medical therapy is necessary to control disease activity and prevent joint destruction.

A survey on the extra-articular manifestations of RA in Coloureds has shown that they are very common (88,5%). The prevalence of the extra-articular manifestations increases with the use of specialised tests. Anaemia is the commonest extra-articular manifestation of RA. Keratoconjunctivitis sicca is the commonest ocular manifestation and would be detected if all symptomatic patients are screened. The prevalence of splenomegaly and lymphadenopathy were similar to other studies but hepatomegaly was detected more often.

The clinical and echocardiographic study of the heart has shown that although abnormalities were frequently detected, they were usually due to coexistent diseases. The only significant abnormalities which may be related to RA are the presence of a small pericardial effusion in 5 patients (6%) and a mild reduction in the E-F slope in 4 patients (5,2%). The prevalence of these findings was much lower than reported in other surveys.

Abnormalities of nerve conduction are common and would be detected more often if more nerves were tested. Many of the patients with abnormal studies were asymptomatic and there was a poor correlation between the clinical findings and electrophysiological tests. Abnormalities of more than one nerve were detected in a quarter of the patients who had abnormal studies. Clinical evidence of a peripheral neuropathy is uncommon.

Pulmonary function tests show that abnormalities are very common but are often due to other factors such as smoking or coexistent pulmonary or cardiac diseases. There were 21 patients (20,2%) who were found to have abnormalities which were probably related to RA. The true prevalence of abnormalities related to RA is probably higher as some of the abnormalities may be due to a combination of factors such as smoking and RA. The importance of selecting a random sample for assessment is shown in this survey because if smokers and patients with TB were excluded, then only 26,9% of the patients would have been eligible for the study and they would represent a highly selected group.

Apart from the association of nodules with lymphadenopathy and seropositivity, and abnormalities of lateral popliteal and/or sural nerves with seropositivity, no other significant relationship was noted with the other extra-articular manifestations and nodules or seropositivity. It is possible that this is related to the 'milder' extra-articular manifestations which were present in this study and many of them were only detected with the use of specialised tests.

The present survey has shown that although abnormalities are frequently detected with the use of specialised tests, they are however, of little clinical significance in the majority of patients. Therefore, they do not have a role in the routine management of these patients but are helpful in surveys of this nature because they show that abnormalities are present more often than would be suspected on clinical assessment alone. Longitudinal follow up of these patients is necessary to determine whether they persist, progress or resolve.

There has been only one published survey on Africans with RA in South Africa (based on 22 patients) and they were found to have a mild remitting disease, severe radiographic changes were uncommon and involvement of the ankles was common. In the present survey the spectrum of RA in Africans was similar in comparison with Caucasians and Coloureds with reference to sex, functional classification, pattern of joint involvement, the use of remittive agent therapy and the prevalence of nodules and seropositivity. However, certain differences which were noted were:

1. The age of onset of RA was nearly a decade earlier when compared with Caucasians. It is possible that RA begins at an earlier age in Africans but other factors may have contributed to this difference.
2. The total serum globulins and immunoglobulin G were significantly higher in Africans in comparison with Caucasians and this may be related to an increased prevalence of malnutrition and infection in childhood and/or chronic liver disease.
3. An increased prevalence of a positive rheumatoid factor has been noted in hospitalised Africans without arthritis. However, there was no significant difference in the prevalence of a positive rheumatoid factor in the 3 communities with RA in this study.
4. The prevalence of malnutrition in hospitalised medical and surgical patients from the same 3 communities included in this survey have shown that malnutrition is commoner in Africans and Coloureds. In the present survey, there was no significant difference in the prevalence of malnutrition in the 3 communities. However, the majority of the Coloureds and Africans in both the studies belonged to the poorer social classes. Obesity has been found to be commoner in a control population of African females and a significant increase in the prevalence of obesity was also noted in the African females with RA.
5. The prevalence of peptic ulcers and fractures have been noted to

be lower in the general population of Africans. A similar lower prevalence was noted in Africans with RA in comparison to Caucasians.

6. The prevalence of ischaemic heart disease is lower in Africans and the mean serum cholesterol, which is one of the risk factors for ischaemic heart disease, was significantly lower in Africans in comparison with Caucasians.
7. The mean radiographic score was corrected for the duration of RA and there was no significant difference in the severity of changes in the hands and feet among the races but wrist involvement was significantly more severe in Africans in comparison with Coloureds and Caucasians.
8. There was significantly less severe impairment of hand function in Africans even though there was no significant difference in the severity of radiographic changes on the hands.
9. Surgery was performed less frequently in Africans but this may be related to the shorter duration of RA. However, the only procedures where there was a significant difference among the races were for surgery to the forefoot, carpal tunnel release and flexor tenosynovectomy.

This survey was undertaken to determine the spectrum of manifestations of RA patients in the Western Cape and also whether there were any inter-group differences. Both of these aspects have been studied and are reported. In addition, this study provided information about certain areas for further study. The importance of anaemia, iron deficiency and peptic ulcers are another area where greater attention is necessary during the management of patients. There is a need to make greater use of existing physiotherapy and occupational therapy services or even improve the facilities further. The importance of surgery in the total patient management has been shown by the finding that nearly half of the patients had surgery and about 15% had arthroplasty of one or more of the major weight bearing joints. The outcome of management policies in the Unit have produced a relatively successful outcome regarding the functional status of patients. Although the majority of the Coloureds and Africans belonged to the poorer social class, the overall spectrum of the manifestations were remarkably similar to Caucasians and the areas of difference have been recorded. The Africans account for about two-thirds of the population of South Africa; therefore the findings of the present survey suggest that when Africans have better access to health care facilities countrywide, there would be a great demand on the inadequate resources presently available.

APPENDIX 1

COMMITTEE FOR THERAPEUTIC CRITERIA OF THE AMERICAN RHEUMATISM  
ASSOCIATION (ARA): CLASSIFICATION OF FUNCTIONAL CAPACITY  
(STEINBROCKER et al 1949)

- Class 1     Complete  
              Ability to carry on all usual duties without handicaps
- Class 2     Adequate for normal activities  
              Despite handicap or discomfort or limited motion at one or more joints
- Class 3     Limited  
              Only to little or none of duties of usual occupation or self care
- Class 4     Incapacitated, largely or wholly  
              Bedridden or confined to wheelchair; little or no self care

APPENDIX 2

FUNCTIONAL GRADING USED BY THE JOINT COMMITTEE OF THE  
MEDICAL RESEARCH COUNCIL AND NUFFIELD FOUNDATION  
ON CLINICAL TRIALS OF CORTISONE, A.C.T.H., AND OTHER  
THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES  
(Joint Committee: UK, 1954)

- Grade 1     Fully employed or employable in usual work and able to undertake normal physical recreation.
- Grade 2     Doing light or part-time work and only limited physical recreation. For housewives, all except the heaviest housework.
- Grade 3     Not employed and unemployable. No physical recreation. Housewives, only light housework and limited shopping.
- Grade 4     Confined to house or wheel-chair, but able to look after themselves in essentials of life. Hospital patients confined to bed.
- Grade 5     Completely bedridden

APPENDIX 3SEWZEY FUNCTIONAL DISABILITY CLASSIFICATION  
(Swezey 1978)

- a) UPPER EXTREMITY: (Self-care and communication). Includes feeding, grooming, toileting, bathing, dressing, typing or writing and telephoning.
1. NORMAL: Can perform all activities efficiently and at a level compatible with normal recreational and vocational needs.
  2. INDEPENDENT: Performs all activities without assistance or assistive devices but may have some discomfort, awkwardness, or inefficiency in accomplishing task.
  3. PARTIALLY INDEPENDENT: Requires assistive devices or special preparation or scheduling of activities because of pain, weakness, fatigue or limitation of motion.
  4. PARTIALLY DEPENDENT: Requires assistance or supervision in some activities.
  5. DEPENDENT: Requires assistance or supervision in most functions.
- b) LOWER EXTREMITY: (Mobility). Includes walking indoors and outdoors, up and down stairs; transferring from supine to sitting and sitting to standing, to tub or toilet; bending, moving in bed, operating a wheelchair or automobile.
1. NORMAL: Can perform all activities efficiently and at a level compatible with normal recreational and vocational needs.
  2. INDEPENDENT: Performs all activities without assistance or assistive devices but may have some discomfort, awkwardness, or inefficiency in accomplishing task.
  3. PARTIALLY INDEPENDENT: Requires an aid such as a cane, crutch or walker, or is unable to handle irregular terrain, steps, prolonged walking or standing, or certain architectural barriers, or has difficulty transferring from a low seated position.
  4. PARTIALLY DEPENDENT: Requires a wheelchair or assistance in some transfers, or practical ambulation is restricted to household.
  5. DEPENDENT: Bedridden or requires assistance with most transfers.

APPENDIX 4LEE FUNCTIONAL INDEX  
(Lee et al 1973)

1. Can you turn your head from side to side?
2. Can you comb your hair (at the back of your head)?
3. Can you close drawers (with arms only)?
4. Can you open doors?
5. Can you lift a full teapot?
6. Can you lift a cup with one hand and drink from it?
7. Can you turn a key in a lock?
8. Can you cut meat with a knife?
9. Can you butter bread?
10. Can you wind a watch?
11. Can you walk?
12. Can you walk without:
  - a) someone's help?
  - b) crutches?
  - c) a walking stick?
13. Can you walk up a flight of stairs?
14. Can you walk down a flight of stairs?
15. Can you stand up with your knees straight?
16. Can you stand on your toes?
17. Can you bend down to pick something up off the floor?

The answers are scored: 0 = Yes, with no difficulty;  
 1 = Yes, but with difficulty, eg, pain,  
 weakness or stiffness  
 2 = No

APPENDIX 5RHEUMATOID THUMB DEFORMITIES  
(Flatt 1983)

- Type 1 Fixed flexion of the metacarpophalangeal joint and hyperextension of the interphalangeal joint.
- Type 2 The metacarpal is fixed in adduction and there is hyperextension of the interphalangeal joint with compensatory flexion of the metacarpophalangeal joint.
- Type 3 The interphalangeal joint is in flexion and the metacarpophalangeal joint is in extension.
- Type 4 The metacarpal is in adduction with radial abduction of the proximal phalanx.

APPENDIX 6RADIOGRAPHIC EVALUATION OF RHEUMATOID ARTHRITIS BY  
STANDARD REFERENCE FILMS  
(Larsen et al 1977)

The following descriptions of the stages should be considered as a supplement to the standard radiographs:

- GRADE 0 Normal conditions. Abnormalities not related to arthritis, such as marginal bone deposition, may be present.
- GRADE I Slight abnormality. One or more of the following lesions are present: periarticular soft tissue swelling, periarticular osteoporosis and slight joint space narrowing. When possible, use for comparison a normal contralateral or a previous film of the joint in the same patient, as demonstrated in the standard series. The standard series illustrates a characteristic osteoporosis and joint space narrowing, whereas no attempt was made to demonstrate the appearance of soft tissue. Soft tissue swelling and osteoporosis may be reversible. This stage represents an early, uncertain phase of arthritis or a later phase without destruction. Compatible appearances may occur without arthritis in old age, traumatic conditions, Sudeck's atrophy, etc.
- GRADE II Definite early abnormality. Erosion and joint space narrowing corresponding to the standards. Erosion is obligatory except in the weight-bearing joints.
- GRADE III Medium destructive abnormality. Erosion and joint space narrowing corresponding to the standards. Erosion is obligatory in all joints.
- GRADE IV Severe destructive abnormality. Erosion and joint space narrowing corresponding to the standards. Bone deformation is present in the weight-bearing joints.
- GRADE V Mutilating abnormality. The original articular surfaces have disappeared. Gross bone deformation is present in the weight-bearing joints. Dislocation and bony ankylosis, being late and secondary, should not be considered in the grading; if present, the grading should be made according to the concomitant bone destruction or deformation.

There may sometimes, especially in the erosive phase of arthritis, be some disparity between the degree of erosion and the narrowing of the joint space, because loosening of joint ligaments and the presence of excess joint fluid may cause widening of the joint space. If so, the degree of erosion should be the decisive factor when using the present grading system.

APPENDIX 7

## REFERENCE RANGE FOR LABORATORY TESTS

Urea	1,7 - 6,7	mmol/l
Creatinine	75 - 115	umol/l
Albumen	35 - 50	g/l
Globulins	25 - 30	g/l
Calcium	2,10 - 2,60	mmol/l
Inorganic phosphorus	0,80 - 1,40	mmol/l
Urate	0,12 - 0,45	mmol/l
Alkaline phosphatase	30 - 115	Units
LDH	100 - 250	Units/l
AST	0 - 40	Units/l
ALT	0 - 53	Units/l
Gamma glutamyl-transpeptidase	0 - 50	Units/l
Immunoglobulin G	4,08 - 17,88	g/l
Immunoglobulin A	0,64 - 5,44	g/l
Immunoglobulin M	0,50 - 3,55	g/l
Haemoglobin g/dl		
Males	13,3 - 17,3	g/dl
Females	11,6 - 15,6	g/dl
White cell count	4 - 11	$\times 10^9/l$
Mean cell volume	81 - 93	fl
Mean corpuscular haemoglobin	28 - 30	pg
Platelets	140 - 420	$\times 10^9/l$
Erythrocyte sedimentation rate		
Males	0 - 5	mm/hour
Females	0 - 7	mm/hour

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