PSORIASIS AND ARTHRITIS

BY

V. WRIGHT

Leeds

(RECEIVED FOR PUBLICATION JULY 23, 1956)

The literature on this subject shows considerable divergence of opinion on the significance of the association of psoriasis and erosive arthritis, and on what may be said to comprise "psoriatic arthropathy", if the term is to be used at all. The difficulties of the problem are increased by the fact that according to the predominant complaint the patient may fall into the hands of either the rheumatologist or the dermatologist, and escape the statistical eye of one or the other. The difficulty in assessing the incidence is indicated by the diverse figures given in the literature—an aspect recently reviewed by Gribble (1955). Among dermatologists, however, it is generally agreed that atrophic arthritis is commoner among patients with psoriasis (Leczinsky, 1948: 5·8 per cent. males, 7·9 per cent. females; Ingram, 1954: 7 per cent.) than among the general population. Among rheumatologists it is agreed by the majority that psoriasis occurs in about 3 per cent. of patients with atrophic arthritis (Dawson and Tyson, 1937; Bauer, 1939) as compared with 0·7 per cent. in the general population (Ingram, 1954), while there is no significant increase in the incidence among patients with osteo-arthriti.s.

Many workers have endeavoured to define an entity "psoriatic arthropathy", and the following definitions have been suggested:

(1) A form of atrophic arthritis associated with psoriasis and exhibiting a reasonable degree of synchronous activity as evidenced by remissions and relapses in arthritis and cutaneous manifestations (Lane and Crawford, 1937; Jeghers and Robinson, 1937; Epstein, 1939).

(2) Arthritis restricted to the distal interphalangeal joints associated with psoriasis (Bauer, Bennett, and Zeller, 1941).

(3) A syndrome in which both skin lesions and arthritic manifestations are atypical (Dawson, 1937), or in which the joints are improved by treatment of the skin (O"Leary, 1943).

(4) A peculiarly destructive form of arthritis associated with psoriasis (Fawcitt, 1950).

Other authors feel there is no justification for the use of the term, because they think the two conditions are coincidental. The problems therefore are:

(1) Is there an entity "psoriatic arthropathy"?
(2) If there is, what are its characteristics?

Most of the published reports have dealt with cases fulfilling one or other of the diagnostic criteria above, and there have been few broad surveys of the general field of concomitant psoriasis and joint disease. The present study was undertaken in the light of the striking absence of the Waaler-Rose phenomenon in all cases of erosive arthritis associated with psoriasis seen before the start of the survey, and an attempt has been made to answer the problems by contrasting three groups of patients, one with psoriasis and arthritis, one with uncomplicated rheumatoid arthritis and one with uncomplicated psoriasis.

Material and Methods

In all, 42 patients with psoriasis and arthritis have been considered, 34 with erosive arthritis (the term "erosive arthritis" being used in preference to "rheumatoid arthritis" so that the issue may not be prejudiced), six with degenerative joint disease, one with gout, and one with rheumatic fever. In all cases the diagnosis of psoriasis was confirmed by a dermatologist (Dr. D. S. Wilkinson). In five, information was incomplete, two patients having died, the other three having left the district. The others were examined personally, their serum was submitted to certain laboratory tests, and radiographic studies were made. This group has been contrasted with 55 unselected patients with rheumatoid arthritis who were found to have a positive Differential Agglutination Test (Waaler-Rose), and with an unselected group of patients with psoriasis but no joint manifestations (310 patients in all).
**Findings**

I. Erosive Arthritis

**Sex Incidence.**—It is of interest that of the 34 patients, eighteen were men and sixteen were women. While this series is too small to be of statistical significance, the point is of obvious importance, since both rheumatoid arthritis and psoriasis, occurring singly, were found to be commoner in women (Table 1).

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>SEX INCIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series</td>
<td>A</td>
</tr>
<tr>
<td>No. of Patients</td>
<td>34</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Psoriasis and Erosive Arthritis</td>
</tr>
<tr>
<td>Sex (per cent.)</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Male</td>
</tr>
</tbody>
</table>

The increased proportion of males among patients with psoriasis and erosive arthritis has been noted before by French writers (Darier, 1920; Darier, Civatte, and Tzanck, 1947), and Vilanova and Piñol (1951), in reviewing the literature, observed a similar incidence to the present figures (82 males to 68 females; 54.7 to 45.3 per cent.).

**Onset of Psoriasis.**—In terms of site of origin or age at onset the skin lesions differed little from uncomplicated psoriasis, except that in the cases with arthritis there was a tendency towards a later age at onset. In 16 per cent. of patients the nails were affected initially.

**Onset of Skin and Nail Lesions related to Onset of Arthritis.**—Fig. 1 shows that psoriasis usually preceded the onset of arthritis in these patients, developing first in 64 per cent. and preceding the arthritis by anything from 37 years to 2 months. In 13 per cent. the psoriasis and arthritis were synchronous in onset, and in 23 per cent. the skin lesions came second. It is tempting to suggest that some cases of erosive arthritis with a negative differential agglutination test (D.A.T.) are destined to develop psoriasis. The only clue to this may be the family history, for 35 per cent. of the patients with psoriasis and erosive arthritis had a family history of psoriasis as compared with 2 per cent. of the rheumatoid group (Fig. 2).

In some ways joint changes seemed more closely related to lesions of the nails than to psoriasis of the skin. Only 13 per cent. had no nail changes. In cases of psoriasis as a whole (including some with arthritis) the nails are involved in between 10 and 25 per cent. of patients, the figure of 15 per cent.
given by Pardo-Castello (1936) being about the average in the literature. Widely varying figures are however quoted: Crawford (1938) gives an incidence as high as 49·8 per cent. and the next highest figure is 25 per cent. Among the group of patients with uncomplicated psoriasis, 18 per cent. had changes of the finger nails (23 per cent. men, 14·7 per cent. women). Only two patients with psoriasis and erosive arthritis never had nail changes, and two more had lesions of the nails but not of the skin. In relation to the arthritis, nail changes came first in 28 per cent., with a lapse of 4 months to 10 years, and arthritis came first in 40 per cent., with an intervening period of 6 months to 35 years (Fig. 1). Although skin changes and arthritis came on simultaneously in only 13 per cent., nail changes were synchronous with arthritis in 32 per cent. The onset of the various manifestations was closely related (i.e. one occurred within 12 months of the other) in 19 per cent. between joint and skin changes, and 48 per cent. between joint and nail changes. Moreover, exacerbations were more often synchronous in nails and joints than in skin and joints.

Thus in 53 per cent. nail and joint changes either developed simultaneously, or were subject to synchronous exacerbation. Only 24 per cent. had a similar relationship between the skin and joints, an equal number claimed an inverse relationship, and in 52 per cent. there was no relation at all. A topographical association between nail and joint changes was sometimes evident (Fig. 3), but a similar association with the site of skin lesions could not be demonstrated.

**Onset of Arthritis.**—The average age at onset of arthritis in the two groups (Table II) is compared with the results obtained in the Empire Rheumatism Council Survey (1950).

![Fig. 3.](image)

**Fig. 3.**—Topographical association of distal interphalangeal joint and nail lesions in erosive arthritis with psoriasis. The index and middle fingers of the left hand show a contrast between affected and unaffected nails.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Psoriasis with Erosive Arthritis</td>
<td>37</td>
<td>33</td>
</tr>
<tr>
<td>Uncomplicated Rheumatoid Arthritis</td>
<td>41</td>
<td>43</td>
</tr>
<tr>
<td>E.R.C. Survey (Rheumatoid Arthritis)</td>
<td>42</td>
<td>41</td>
</tr>
</tbody>
</table>

Contrasted by decades (Fig. 4, opposite), there is a marked similarity in the age at onset, apart from a higher incidence in the second decade among those with psoriasis.

There was no significant difference in the percentage of those with an acute onset (Table III, opposite), nor was there any difference in the numbers with a history of pyrexia at the onset of the arthritis.
PSORIASIS AND ARTHRITIS

Sherman (1952), in her review of psoriasis with arthritis, comments that the onset is not polyarticular, whereas Jeghers and Robinson (1937) maintain that this is so, but it should be noted that their diagnostic criteria differs. In the present series 31 per cent. of cases were polyarticular at onset and 69 per cent. were not. Among patients with rheumatoid arthritis 41 per cent. are monarticular at the start according to the Empire Rheumatism Council Survey; the proportion was similar in this smaller group of rheumatoid patients. A polyarticular onset is therefore less common in the psoriatic group (Table IV).

The joints involved initially are shown in Fig. 5. The distal interphalangeal joints were the most frequent targets for the initial attack in patients with psoriasis and erosive arthritis. Otherwise the site of onset is virtually the same in both groups.

Course of Arthritis.—From the history two impressions emerged:

(1) That a patient could have severe affection of the joints and then apparently recover completely. Such complete remissions occurred in 50 per cent. One woman, virtually confined to bed for 2 years, recovered and remained fit for the next 8 years with no active joint trouble or residual disability.

(2) The major part played by stiffness in the symptomatology—68 per cent. emphasized this in their history and in 26 per cent. of the total it was the predominant complaint.

From the history the joints involved are virtually the same as in rheumatoid arthritis, apart from a predilection for the distal interphalangeal joints.

Table III

ACUTE ONSET OF ARTHRITIS, BY SEX
(Per cent.)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis and Erosive Arthritis</td>
<td>29</td>
<td>40</td>
<td>34</td>
</tr>
<tr>
<td>Uncomplicated Rheumatoid Arthritis</td>
<td>36</td>
<td>29</td>
<td>32</td>
</tr>
</tbody>
</table>

Table IV

NON-POLYARTICULAR DISEASE AT ONSET, BY SEX

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis with Erosive Arthritis</td>
<td>82</td>
<td>60</td>
<td>72</td>
</tr>
<tr>
<td>Uncomplicated Rheumatoid Arthritis</td>
<td>54</td>
<td>43</td>
<td>45</td>
</tr>
</tbody>
</table>

Fig. 4.—Age at onset: (A) of patients with arthritis and psoriasis; (B) of patients with rheumatoid arthritis.

Fig. 5.—Joints involved initially: (A) in patients with arthritis and psoriasis; (B) in patients with rheumatoid arthritis.
These last joints, if involved, are usually affected at the onset of the arthritis (Fig. 6).

As far as disability is concerned, judging from the time lost from work through the patient’s arthritis, the disease seems to be either severe and crippling, or very mild. Mild cases were commoner than severe ones. Cases of intermediate severity were, however encountered.

Skin and Nail Lesions.—These were typical in distribution. The palms and soles were affected in only 9 per cent, in contrast to many reports giving a higher incidence (Cannon, 1934: Wassmann, 1949). The psoriasis was extensive in only three patients: two of these were completely bedridden with arthritis and the third was severely disabled.

In 81 per cent, changes were present in the nails. In two patients the nails only were involved, an uncommon but recognized phenomenon (White, 1938; MacKenna, 1950). The order of frequency of changes in the nails was:

1. Thickening, beginning in the distal part.
2. Separation from the subungual bed.
3. Ridging and cracking.
4. Pitting.
5. Spoon shape, secondary to hyperkeratosis.

These results disagree with those of some other investigators (Vilanova and Piñol, 1951), who have described pitting as the most common symptom. Pitting may well be the most characteristic feature, although it is occasionally seen in chronic eczema, exfoliative dermatitis, and other inflammatory skin diseases (Pardo-Castello, 1936).

Joints.—Although the arthritic process showed a predilection for the distal interphalangeal joints, in no case was the joint involvement confined to them, and even in a “classical” case where three such joints of each hand were involved with the corresponding nails, one metacarpophalangeal and one...
prosimal interphalangeal joint were also involved. There would therefore seem to be no rational basis for designating patients with distal interphalangeal joint involvement only as suffering from "psoriatic arthropathy", and for excluding patients with more joints involved. When the distal joints of the fingers were involved, the change seemed to affect the whole finger tips, producing spade-like ends with considerable swelling over the joint.

Three patients showed a clinical picture of ankylosing spondylitis with peripheral joint involvement. This high incidence is in accord with recent reports (Sherman, 1952; Sterne and Schneider, 1953; Fletcher and Rose, 1955).

In an attempt to assess the severity of the arthritis special note was made of the state of the joints first involved, and of the presence of ulnar deviation. The latter was present in 36 per cent. of the rheumatoid group as compared with 13 per cent. of those with psoriasis and erosive arthritis. Four broad stages were distinguished in the current state of the joints initially affected:

1. No abnormality;
2. Mild stigmata, including slight limitation of movement, swelling without much tenderness, slight pain on movement, crepitus, and slight deformity without ankylosis or subluxation;
3. Recent exacerbation;
4. Severe involvement, including gross deformity, ankylosis, or subluxation.

Table V shows the relative frequency of these divisions. There is a slight tendency for more of the rheumatoid group to show stigmata in the joints initially affected. This is of interest since the arthritis was of shorter duration than in the psoriatic group. Its significance may be lessened by the fact that the patients with rheumatoid arthritis all sought help because of the condition of their joints, while many of those with psoriasis and erosive arthritis had presented on account of their skin manifestations.

Associated Findings.—Only one arthritic patient of those with psoriasis had subcutaneous nodules and effusions in the extensor tendon sheaths. He had a positive Differential Agglutination Test (D.A.T.). This is of interest since subcutaneous nodules are regarded by many as the most characteristic lesion of rheumatoid arthritis (Bauer, 1939; Bennett, 1943). Among the group of patients with rheumatoid arthritis, 17 per cent. had subcutaneous nodules on examination, and 22 per cent. gave a history of nodules at some time during the course of the arthritis.

The complete absence of subcutaneous nodules among patients with psoriasis and erosive arthritis with a negative D.A.T., strikingly differentiates these patients from those with uncomplicated rheumatoid arthritis.

Laboratory Investigations.—The haemoglobin, E.S.R. (Win trobe), and white cell counts were estimated in the patients with psoriasis and erosive arthritis. No laboratory investigations were done on those with uncomplicated psoriasis, but comparison has been made with results obtained at first attendance from an unselected group of 69 patients with rheumatoid arthritis and a positive D.A.T. The results are not strictly comparable since the patients with psoriasis were sought, whereas those with rheumatoid arthritis attended a rheumatology clinic of their own volition. Under these circumstances the psoriatic group showed less anaemia, a lower E.S.R., and more normal white cell counts.

C-reactive protein was found in the sera of 43 per cent. of the patients with psoriasis and erosive arthritis.

The D.A.T. was positive in only two patients with psoriasis and erosive arthritis (i.e. 94 per cent. negative). The method used was a modification of the techniques of Rose, Ragan, Pearce, and Lipman (1948) and Heller, Kolodny, Lepow, Jacobson, Rivera, and Marks (1955). Sera producing agglutination of sensitized sheep red cells in a dilution of 1:16 or higher were taken to be positive, providing the heterophile antibody was present in minimal quantity or had been absorbed previously. It is interesting that the one patient in the series with nodules and tendon sheath effusions should be one of those with a positive D.A.T. and that in addition he should be one of the two without nail changes. It seems possible that in these patients the occurrence of psoriasis and rheumatoid arthritis was a true coincidence, while in the others the skin and joint features were manifestations of a single disease process.

In patients with erosive arthritis and a negative D.A.T., the history and clinical examination should be carefully searched for psoriasis. In fact the diagnosis of one of this series came to light in such a manner.

<table>
<thead>
<tr>
<th>Grade of Involvement</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis and Arthritis</td>
<td>39</td>
<td>35</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>22</td>
<td>45</td>
<td>13</td>
<td>20</td>
</tr>
</tbody>
</table>
ANNALS OF THE RHEUMATIC DISEASES

The results of other laboratory investigations are given in Table VI.

The serum cholesterol level was estimated by a modification of Sackett's method (King, 1951). The normal range is 140–215 mg per 100 ml. The level was raised in 28 per cent. of the group with psoriasis and erosive arthritis, the values in three patients being over 300 mg per 100 ml. High values are said to occur in psoriasis alone (Epstein, 1939), although this is not universally agreed (Tobias, 1939).

Because many authors regard gross bone destruction as a feature of psoriatic arthropathy, the serum alkaline phosphatase activity was measured in King Armstrong Units, 12 K.A. units being considered the upper limit of normal. In both groups the majority had a raised value; the highest (72 K.A. units) was in a severely crippled psoriatic patient. The increase of serum alkaline phosphatase activity was most closely related to the number of joints involved and to the duration of the arthritis in both groups. There was no evidence of Paget's disease in any of these patients.

The few references in the literature to the level of the serum proteins in psoriasis and erosive arthritis state that they are normal (Shlionsky and Blake, 1936; Sherman, 1952). In the present series the levels were estimated by the method of Martin and Morris (1949), normal values in our laboratory being:

- Serum globulin 1·7–3·8 g. per 100 ml., serum albumin 3·0–4·3 g. per 100 ml.

High globulin values were obtained in 17 per cent. of the psoriatic group and in 22 per cent. of the rheumatoid group. The findings were confirmed by Kunkel's zinc sulphate test (1947) and qualitative electrophoresis. The most common finding with the latter method was an increase in the γ-globulin and β-globulin bands which merged into each other.

Treatment.—Many reports have recorded that the joint symptoms subside with treatment of the psoriasis (Gross, 1928; Jeghers and Robinson, 1937; Epstein, 1939; Franks and Wallace, 1942; O'Leary, 1943), but experience in the present series is sharply at variance with this finding. In fact only one patient had experienced this regression, and it was probably significant that he had been at rest in hospital at the time.

The arthritis responded to the usual methods of salicylate therapy, physiotherapy, cortisone, corticotrophin, and prednisolone in selected cases, local hydrocortisone, and gold. Ragan and Tyson (1946) found a large proportion of toxic reactions in psoriatic patients receiving gold. In none of eleven patients in this series to whom gold had been given had there been any reaction.

II. Osteo-Arthritis

The group of patients with osteo-arthritis sent from the Orthopaedic Department was too small for detailed analysis. It comprised four men and two women. Unexpectedly the four male patients had nail changes. In one patient they had appeared 7 months before the arthritis, but in the remainder they were unrelated to the arthritis in its onset or course. The findings in the joints affected were typical of osteo-arthritis and bore no relation to the skin rash in time of onset or severity of symptoms.

The haemoglobin, E.S.R., and white cell counts were all normal as were the serum alkaline phosphatase levels. One patient had a serum cholesterol value of 260 mg. per 100 ml.

III. Gout and Rheumatic Fever

One patient had gout and one had a typical history of rheumatic fever. In neither were the nails affected. There were no atypical features in the arthritic or skin findings in either, and there was no obvious relation between the skin and joint manifestations.

Conclusions

The one patient with gout and the one with rheumatic fever who were examined showed no features that were not explicable on the basis of a mere coincidence of the psoriasis and the joint condition.

<table>
<thead>
<tr>
<th>Table VI</th>
<th>LABORATORY INVESTIGATIONS</th>
<th>(Per cent. of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Cholesterol (mg/100 ml.)</td>
<td>Alkaline Phosphatase (K.A. Units)</td>
</tr>
<tr>
<td>Amount</td>
<td>180</td>
<td>180–215</td>
</tr>
<tr>
<td>Psoriasis and Erosive Arthritis (32 cases)</td>
<td>32</td>
<td>65</td>
</tr>
</tbody>
</table>
| Rheumatoid Arthritis (69 cases) | 16 | 32 | 29 | 23 | 51 | 27 | 22 | **Note:** Values are rounded for clarity.
PSORIASIS AND ARTHRITIS

The six patients with psoriasis and osteo-arthritis were probably also examples of a chance association. The only unusual feature clinically was the nail involvement in all four male patients.

The group of patients with erosive arthritis and psoriasis show many interesting features when compared with groups having uncomplicated psoriasis and uncomplicated rheumatoid arthritis (with a positive D.A.T.).

The negative D.A.T. in 94 per cent. of these cases suggests that the combination of psoriasis and erosive arthritis is more than the coincidence of two common diseases. It suggests at least that the arthritis is modified by the presence of psoriasis, or, more probably, that it is a distinct entity. The finding of tendon sheath effusions and subcutaneous nodules (both classical manifestations of rheumatoid arthritis) in only one patient of the series—of the two with a positive D.A.T.—lends weight to the suggestion that these two had true rheumatoid arthritis while the others formed a distinct group. There are certain distinctive features of the syndrome of psoriasis and erosive arthritis. Many of the attributes described in the literature could not be substantiated in the present series, viz:

(1) In the majority the psoriasis was not extensive or pustular, nor did it affect the palms and soles; when the skin eruption was extensive the arthritis was severe.

(2) Alleviation of the skin condition seemed to help the arthritis in only one case and the significance of the association was dubious since the patient was in hospital at the time.

(3) The patients did not appear unduly susceptible to toxic gold reactions.

(4) Thickening, not pitting, was the most common nail change encountered.

(5) In no case was arthritis limited to the distal interphalangeal joints.

(6) The arthritis was not unduly resistant to treatment.

(7) The serum protein levels were abnormal in several patients.

From a positive point of view the outstanding features may be summarized as follows:

(1) There was a high incidence of nail changes (87 per cent.), and these were the sites of onset in 16 per cent. Two patients had nails only affected.

(2) The nail changes bore a closer relation to the onset and course of the arthritis than the skin lesions.

(3) A small proportion (13 per cent.) appeared to show a connexion between the skin and joint manifestations as evidenced by the simultaneous onset and exacerbations.

(4) The arthritis was less often polyarticular at onset than classical rheumatoid arthritis.

(5) Distal interphalangeal joint involvement was related topographically to the nail lesions rather than to the skin lesions.

(6) Stiffness played a major part in the symptomatology.

(7) There was a high incidence of complete remissions of the arthritis.

(8) The disease was milder on the whole than rheumatoid arthritis, as shown by fewer joints involved clinically and radiographically, smaller incidence of ulnar deviation, and milder stigmata in the originally affected joints. A mutilating type does however occur rarely.

(9) The disease tends to be either very mild or crippling.

(10) A similarity to gout was noted at some time in the history in 39 per cent.

(11) When the distal interphalangeal joints and nails were involved the fingers had a spade-like appearance.

(12) There was a marked family history of psoriasis in 35 per cent.

(13) There was a high incidence of ankylosing spondylitis.

(14) Nodules and tendon sheath effusions were absent except in one patient with a positive D.A.T.

(15) The incidence in males seemed to be slightly increased.

(16) There was apparently less anaemia, a lower E.S.R., and less tendency to leucocytosis, but this was probably due to the selection of the patients.

Summary

42 cases of psoriasis with arthritis have been studied, 34 with erosive arthritis, six with degenerative joint disease, one with gout, and one with rheumatic fever. They have been compared with 55 unselected patients with rheumatoid arthritis and a positive differential agglutination test (D.A.T.) and 310 patients with psoriasis alone. A close comparison has been made between the three groups clinically and by certain blood tests, including haemoglobin estimation, E.S.R. (Wintrobe), white cell count, serum proteins, Kunkel’s zinc sulphate test, electrophoresis, serum alkaline phosphatase, serum cholesterol, C-reactive protein, and the D.A.T. It is concluded that those with osteoarthritis, gout, and rheumatic fever were examples of a chance association, although the surprising finding of nail changes in all four male patients with osteoarthritis is noted. On the basis of the D.A.T. it is thought that two of the group with erosive arthritis were examples of rheumatoid arthritis and coincidental psoriasis, whereas in the rest the disease probably formed a distinct entity. The significant features of the group with erosive arthritis are set out, as well as findings in the present series which are at variance with those of previous authors.

I am indebted to Dr. A. G. S. Hill, Dr. D. S. Wilkinson, Dr. M. Good, Mr. G. Platt, and other Consultants of Stoke Mandeville Hospital for allowing me to study their patients. My thanks are due especially to Dr. A. G. S. Hill and Dr. D. S. Wilkinson for their invaluable help.
in the preparation and performance of this study in all its stages.

REFERENCES
