confirmed (McConkey, Fraser, and Bligh, 1965). Furthermore, the skin of many patients is friable, resists shear stresses poorly, and may produce problems in wound healing. Previous studies on skin collagen in these patients have been confined to measurements of soluble or total content. However, although total collagen is reduced, particularly in patients receiving corticosteroids, measurements on the small soluble fraction (<5 per cent) have been inconclusive. The major fraction of skin collagen is polymeric collagen, and having developed methods of measuring quantities and stability of this collagen in biopsies (85 sq. mm.) of human skin, we have applied them to patients with rheumatoid arthritis (Francis and Macmillan, 1971).

So far 19 biopsies have been performed, including repeat biopsies in two patients after 6 months' penicillamine therapy. Compared with matched normal controls, a modest reduction in total skin collagen, particularly in patients on prolonged corticosteroid therapy has been confirmed. However, the stability of the polymeric collagen was not clearly altered by these drugs but was reduced in patients with active disease. With penicillamine, skin thickness and total collagen content were dramatically reduced. In addition, there was a reduction in collagen stability. In patients on corticosteroids there was an increased proportion of soluble collagen.

It will be suggested that important changes in collagen metabolism occur in these patients which may influence skin strength, integrity and wound healing (and perhaps renew interest in the 'collagen diseases').

Discussion

DR. B. MCCONKEY (Birmingham) There is a distinction which is in danger of being lost between two different kinds of skin abnormality seen in patients with rheumatoid disease and sometimes in the elderly. One is the abnormality in which you get senile or steroid purpura and fragile skin, and the other is what we have called 'transparent skin' (McConkey, Fraser, Bligh, and Whiteley, 1963). Although patients with one tend also to have the other, I think the conditions are quite distinct and ought to be considered separately in studies of this sort.

DR. R. GRAHAME (London) One of your earlier slides suggested that there was no difference in total skin collagen in normal subjects and in patients who have not had steroids. This is different to the results of Shuster, Raffle, and Bottoms (1967).

DR. FRANCIS No, they showed in fact, that total skin collagen in patients with rheumatoid arthritis who had not been on steroid therapy was lower, but not significantly so.

DR. T. C. HIGHTON (New Zealand) Some years ago (Highton, 1963) I did some relevant work using the granuloma pouch system in rats and measuring the amount and weights of granulation tissue produced following injection of serum from rheumatoid and normal subjects. I also measured the strength of a standard wound. The results indicated that serum derived from patients with active rheumatoid arthritis, when injected into rats, leads to their producing significantly less new tissue in the granuloma pouches, and these rats had wounds of less tensile strength than those injected with normal serum or saline.

DR. L. E. GLYNN (Taplow) Would it not be valid to measure the stability of collagen at different temperatures?

DR. FRANCIS It could be done on isolated samples of collagen fibre, but we have not attempted this.

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Post-operative Wound Healing in Patients with Rheumatoid Arthritis. By R. W. GARNER, A. G. MOWAT, and B. L. HAZLEMAN (Nuffield Orthopaedic Centre, Oxford)

It is often supposed that surgical wounds are more liable to become infected or to heal poorly in patients with rheumatoid arthritis compared with controls and that corticosteroid therapy is likely to exaggerate these tendencies. There is considerable indirect evidence to support these concepts and this will be presented.

Since orthopaedic surgical procedures are being increasingly used in the management of rheumatoid arthritis, it seemed valuable to compare postoperative wound healing in these patients and control subjects.

In a retrospective study covering a period of 20 months, 100 patients with rheumatoid arthritis undergoing a variety of orthopaedic operations were matched with others undergoing operation for conditions other than rheumatoid arthritis and other inflammatory joint diseases. Of the patients with rheumatoid arthritis, 49 were receiving corticosteroids. Details of wound infection, wound haematoma formation, and wound healing were obtained from the medical and nursing records.

There were 13 wound infections, all superficial, in the patients with rheumatoid arthritis and eight superficial infections in the control group ($P > 0.10$). Eleven of the 13 patients with rheumatoid arthritis were receiving corticosteroids ($P < 0.02$). Eight of 26 rheumatoid patients undergoing Macintosh knee arthroplasty had wound infections. There were seven wound haematomas in the rheumatoid patients and five in the control group ($P > 0.10$), although in three of the latter anticoagulant therapy was a major cause. Anticoagulants were not given to patients with rheumatoid arthritis. Altogether 31 wounds failed to heal by primary intention in the rheumatoid group and 16 in the control group ($P < 0.02$). There was no difference in the mean number of days ± 1 S.D. to complete wound healing between the rheumatoid patients (16.6 ± 7.5) and the controls (15.2 ± 7.9). There was no correlation between the days to healing and activity of arthritis, duration of disease, or positive serological test for rheumatoid factor. However, patients receiving corticosteroids for more than 3 years took longer to heal their wounds (20.3 ± 11.0 days) compared to those receiving these drugs for 3 years or less (15.2 ± 4.9 days; $P < 0.05$). There was no correlation between haemoglobin concentrations and wound healing in either patient group.

It will be suggested that, although there are several theoretical and a number of practical reasons inherent in a study of this type which can never be truly comparative, which would lead one to expect problems with wound healing in patients with arthritis, only minor differences

between the patient groups were demonstrated. The results may influence the surgical management of these patients.

Discussion

PROF. V. WRIGHT (*Leeds*) I am interested to know how you determine when the wound is healed.

DR. MOWAT We did not find this in the medical notes but on looking carefully through the nursing notes we found enough information.

MR. S. J. BURROUGH (*Stoke Mandeville*) What significance do you attach to separation? Is a separated wound a delayed healing wound as far as you are concerned?

DR. MOWAT It is a delayed healing wound, but we have assessed independently those that were infected and those that were just simply separated with the wound-edge gaping.

MR. S. J. BURROUGH But there were rather more separated wounds in the rheumatoid group?

DR. MOWAT Yes, there were 15 compared with 5 in the control group ($P < 0.05$).

DR. D. A. H. YATES (*London*) You mentioned vasculitis in passing and the possible effects on wound healing. How many of this group had active vasculitis and was this relevant?

DR. MOWAT Something like four or five of our seropositive patients had an overt vasculitis. They did not appear to run into any problems. Overall, it is very difficult to say when a patient has vasculitis or not and indeed, even whether the seronegative patient may really have a vasculitis. Certainly we could not detect any obvious difference between our seropositive or seronegative patients, and similarly no apparent association with the severity of the disease.

DR. A. J. POPERT (*Droitwich*) Serum proteins have been amply demonstrated to be a significant factor in wound healing (Rhoads and Kasinskas, 1942). The severity and activity of the disease is also an important factor and it is closely bound up with related parameters such as haemoglobin concentration and rheumatoid factor titre. All these factors operate adversely in patients with the more severe kind of connective tissue disease and particularly when the disease is active. Such patients with active disease are often anaemic or have disturbed serum proteins with elevated globulin and low albumin or are underweight; they undoubtedly carry a high incidence of wound infection. Treatment with corticosteroids influences wound healing adversely only if it is given in a dose high enough to produce obvious hypercorticism. When the dosage is optimal, there is an improvement in the general condition of the patient and a favourable change in the anaemia and serum protein concentrations with hypercorticism; there will then result an improved wound healing rate and a reduced incidence of infection. Comparable patients not treated with steroids will heal less well. On the other hand, if the dose of steroids is enough to produce the clinical signs of Cushing's syndrome, then there will be a corresponding increase in the rate of wound dehiscence and infection.

DR. MOWAT With respect, sir, these are impressions that people have. They are largely undocumented impressions and we set out to investigate them. Our results suggest the very opposite of what many people think; haemoglobin values had nothing to do with wound healing and serum proteins seemed likely to produce little difference. We looked at the erythrocyte sedimentation rate and the activity of the disease and found no correlation.

DR. A. J. POPERT I was going to point out that yours is not the only paper which has been written on this subject. Peter Davis and I published a paper on this in 1958 (Popert and Davis, 1958) and I presented a paper on some eight cases to the Heberden Society in 1963 (Popert, 1963). There is a vast mass of other data (cited by Popert, 1962) on this subject, which you may not have fully culled.

DR. MOWAT I should be most interested to have those references. Most of the work is on animals and I was not aware that you had published in this field. Our results clearly disagree.

PROF. J. J. R. DUTHIE (*Edinburgh*) I should like to point out that the level of haemoglobin will not be significant until it has fallen to around about the 70 per cent mark. Your mean was 12.8g., which is 84 per cent so you did not have very anaemic patients for a start. The ESR was in the thirties, so that you did not have many active patients. You cannot say that anaemia and severity have anything to do with it when you did not have anaemic or active patients in your group.

MR. A. R. TAYLOR (*Stoke Mandeville*) I should like to make a final comment from the surgeon's point of view: there are very few of us who would operate with that degree of anaemia irrespective of whether the subjects were rheumatoid patients or not.

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Lymphocyte Sensitivity to Human Skeletal Muscle Antigen in Polymyositis. By M. M. ESIRI, B. L. HAZLEMAN, and I. C. M. MACLENNAN (*Radcliffe Infirmary, Oxford*) Evidence has been accumulating which suggests that polymyositis may be due to a breakdown of tolerance to skeletal muscle. If this is so, lymphocytes should be sensitive to muscle and express this sensitivity by undergoing transformation in the presence of muscle *in vitro*. This hypothesis has been tested using a quantitative method of estimating blast transformation.

Peripheral blood lymphocytes were separated from venous blood, suspended in tissue culture fluid, and incubated with varying concentrations of an homogenate of normal human muscle. Tritiated thymidine was added before taking the cultures down on the fifth day. The DNA was extracted and sampled in a liquid scintillation counter for the amount of incorporated tritium present. The amount of tritium incorporated by lymphocytes in the presence of muscle was compared with that incorporated in lymphocytes grown alone, the differences between these figures giving a measure of stimulation or inhibition produced by the muscle antigen. The results are seen in the