phalangeal index falls slightly with age ($P > 0.1$); this fall was pronounced in the spondylitics ($P < 0.05$).

A group of 33 acromegalics studied in the same way were found to have phalangeal indices significantly lower than normal ($P < 0.001$).

Factors influencing measures of slimness of the hand bones in a normal population include age, occupation, hand dominance, sex, and radiographic technique. It has become apparent that careful matching for such variables is essential in the study of diseased groups.

Discussion

DR. R. GRAHAME (*London*) I feel that one possible explanation for the disparity between the metacarpal indices found by yourself and by Parish is that he derived his index in a slightly different way. He used the mean of the individual ratios of the four metacarpals and did not take the ratio of the sums of the lengths over the widths.

DR. CHAPUT DE SAINTONGE It comes to the same thing; we calculated the metacarpal index both ways and obtained the same results.

DR. J. G. PARISH (*Clacton*) I believe you have used the same method for calculating the metacarpal index as I used. There was, however, a difference in calculating the proximal phalanx index—I think you have used the mid-point here. The method of measuring bones is becoming very complicated and we have reached the stage now where the whole process will have to be put on computer. The University of Essex is at present devising a machine for scanning hand films electronically and we are hoping to be able to measure not only the length and breadth of the bones and the various indices, but also the shape of the head, the base, and other factors.

DR. M. I. V. JAYSON (*Bath and Bristol*) Do you think that it is fair to use normal subjects as your controls? Do you not think that you should use patients with other chronic inflammatory disorders? Slimness of the bones might simply be a function of chronic disease.

DR. CHAPUT DE SAINTONGE None of these patients had chronic inflammatory disease of their hands. It is a very difficult problem and I am not sure that I can answer it or suggest a suitable control group.

DR. W. W. BUCHANAN (*Glasgow*) You made the point that the metacarpal length correlated strongly with the height, when in fact the correlation coefficient for the third metacarpal was 0.67. The square of r gives us a coefficient of determination of 0.51, which means that you have only accounted for 51 per cent. of the observations; in other words there are 49 per cent. for which you cannot account and this therefore suggests that the correlation with height is rather poor even though it is statistically significant.

DR. CHAPUT DE SAINTONGE Our study shows that hand bone dimensions are determined by many other factors apart from height. This lowish coefficient of variation is therefore exactly what we should expect. The point

is that, of the variables we measured, the third metacarpal length was the best indirect measure of height.

Reference

Parish, J. G. (1966) *Brit. J. Radiol.*, 39, 52 (Radiographic measurements of the skeletal structure of the normal hand)

Phagocytic Activity of Macrophages and Polymorphs in Inflammatory Exudates studied by a 'Skin Window' Technique in Rheumatoid and Control Patients. By J. D. JESSOP, B. VERNON-ROBERTS, and J. HARRIS (*University Hospital of Wales and The London Hospital*)

The macrophages and polymorphs which appear at sites of inflammation, such as joints involved by active rheumatoid disease, are known to be derived from precursors situated in the bone marrow and to migrate *via* the blood stream to inflamed areas. It would seem likely that reliable methods of assessing various parameters of the functional activity of cells migrating to inflammatory sites in rheumatoid patients could provide useful information.

We have studied the phagocytic activity of macrophages and polymorphs migrating to areas of sterile inflammation using a 'skin window' technique in rheumatoid and control subjects. Glass coverslips coated with colloidal carbon were placed on abraded areas of skin on the upper arm and were removed 24 hours later. The percentages ('scores') of macrophages and polymorphs containing visible phagocytosed carbon aggregates was assessed by microscopic examination of the cells adhering to the glass.

- (1) Repeated tests on a healthy non-rheumatoid control subject over short and prolonged intervals up to a year showed that macrophage and polymorph scores varied over a range of 10 per cent.
- (2) The macrophage scores were significantly elevated (Table) in untreated RA patients when compared with non-rheumatoid controls ($P < 0.001$), were markedly decreased in RA patients receiving prednisolone ($P < 0.001$), and were decreased in RA patients receiving gold when compared with untreated RA ($P < 0.001$) or non-rheumatoid controls ($P < 0.05$). Similar changes were observed with the polymorph scores.

Group	No. in group	Percentage cells containing carbon (mean $\pm$ s.e.)	
		Macrophages	Polymorphs
Controls	50	53 $\pm$ 2	24 $\pm$ 1
Untreated RA	61	73 $\pm$ 2	37 $\pm$ 2
RA + Gold	51	45 $\pm$ 2	27 $\pm$ 1
RA + Prednisolone	31	26 $\pm$ 2	11 $\pm$ 1

- (3) Serial studies of patients receiving weekly gold injections showed that macrophage scores fell progressively as treatment continued. There was a significant degree of correlation between macrophage scores and the total dose of gold.
- (4) In a patient receiving monthly gold injections, there was an initial fall in macrophage and polymorph scores in the three days following injection, and a return to pre-injection levels by the end of the month.
- (5) Gold was demonstrable within inflammatory macrophages and polymorphs during gold therapy.

The findings indicate that the phagocytic activity of inflammatory macrophages and polymorphs is increased in untreated RA and may be suppressed below non-rheumatoid control levels by prednisolone or gold therapy. They also suggest that the coverslip technique may be a useful means of assessing the efficacy of anti-inflammatory drugs and the response of individual patients to treatment with gold and prednisolone.

Effects of Gold and Prednisolone on Inflammation and Phagocytosis in the Rat. By B. VERNON-ROBERTS and J. D. JESSOP (*The London Hospital and University Hospital of Wales*)

It is widely recognized that, unlike corticosteroids, gold salts must be administered for some length of time before any diminution of inflammatory activity can be clinically detected in joints exhibiting active inflammation in rheumatoid disease. In view of this apparent difference in the mechanisms whereby gold salts and corticosteroids suppress inflammation in man, we have carried out studies, in rats, of the effects of both anti-inflammatory agents on the cellular and fluid phases of the inflammatory response and on the phagocytic activity of macrophages and polymorphs migrating into inflamed areas.

After 14 days of treatment with various doses of sodium aurothiomalate ('Myocrisin') or prednisolone, the fluid and cellular phases of the inflammatory response were quantitatively assessed by a cotton pellet implantation technique (Nicol, Quantock, and Vernon-Roberts, 1967) and phagocytosis was measured by assessing the percentages of carbon-containing macrophages and polymorphs among the inflammatory cells adhering to the glass 24 hours after the application of carbon-coated coverslips to abraded areas of skin. The results showed that:

- (1) Gold salts and prednisolone both suppress the fluid and cellular phases of inflammation, and reduce the numbers of macrophages and polymorphs containing endocytosed carbon
- (2) Prednisolone is more effective than gold salts in suppressing inflammation and phagocytic activity
- (3) The amounts of fluid and cellular exudate and the percentages of carbon-containing cells exhibit a linear dose-response relationship with the daily dose of prednisolone and the total dose of gold.

Using the carbon-coated coverslip technique, phagocytic activity was assessed at intervals after a single injection of sodium aurothiomalate (5 mg.) or prednisolone (1 mg.). The results showed that:

- (1) Phagocytosis was suppressed during the first 24 hours after the injection of prednisolone, but thereafter did not differ significantly from control levels, whereas
- (2) Although phagocytosis was not significantly reduced until 48 hours after the injection of sodium aurothiomalate, it was maximally depressed from 6 to 10 days after injection, and did not return to the control level until 24 days after injection.

In rats injected with ^{198}Au -sodium aurothiomalate, light microscope autoradiography revealed the label

located within macrophages situated at inflammatory sites and elsewhere in the body; electron microscope autoradiography revealed the label located to the plasma membranes, lysosomes, nuclear envelopes, and mitochondria of macrophages.

It is concluded that, although gold salts are effective suppressants of inflammation and inflammatory cell activity, they differ from prednisolone in that they are less potent, take longer to exert their effects, and exhibit a different type of dose-response relationship. The fact that gold localizes to many different regions within the macrophage suggests that gold salts may affect a variety of cellular functions.

Discussion

DR. A. K. THOULD (*Cornwall*) Was there any difference in the response of macrophages or polymorphs in patients who subsequently developed gold sensitivity?

DR. JESSOP We only had one patient who developed serious haematological complications and there was no difference in her scores.

DR. VERNON-ROBERTS I have not presented the results of the differential counts in these patients, but a high proportion of patients on gold treatment showed a significant increase in eosinophil counts in inflammatory exudates, although they did not show blood eosinophilia.

DR. W. W. BUCHANAN (*Glasgow*) You expressed the number of cells which contained carbon particles as a percentage of the macrophages or polymorphs, but was the total number of these cells always the same? Did you always count three hundred macrophages and three hundred polymorphs?

DR. VERNON-ROBERTS Yes, we did.

DR. W. W. BUCHANAN And was the total number of polymorphs in the window constant?

DR. VERNON-ROBERTS We used the pellet technique in the rat because in the exudate on cover slips there are millions of cells and it is not possible to assess the number. I must add that the colloidal carbon used has a diameter of about 300 Å; it is therefore not possible to see individual particles by light microscopy but most of the cells from the cover slip exudates do in fact contain carbon by electron microscopy. There must be an aggregate of at least three hundred of these particles in order to see them with a light microscope and therefore the suppression or elevation of phagocytosis is a relative, not an absolute, term.

DR. A. J. PALFREY (*London*) It seems to me that, particularly in the pellet count, there is a change in proportion of the polymorphs to monocytes. Did you notice the same thing in the exudates under the cover glasses?

DR. VERNON-ROBERTS No, there was not a significant change in the differential count.

DR. R. N. MAINI (*London*) In the untreated rheumatoid patients, was there any correlation between disease activity and your count, and did you study the effect of