Annals of the Rheumatic Diseases, 1977, **36**, 560–562

Polymyalgia rheumatica

Assessment of disease activity using erythrocyte sedimentation rate and plasma viscosity

W. ESSELINCKX, R. C. BUCKNALL, AND A. ST. J. DIXON

From the Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath BA1 1RL

SUMMARY Comparison of clinically assessed activity of disease with 112 paired readings of the erythrocyte sedimentation rate (ESR) and the plasma viscosity (PV) in 23 patients with polymyalgia rheumatica (PMR) showed the following. (1) A correlation between ESR and PV in both sexes, reaching the significance obtained in a comparison group of patients with rheumatoid arthritis (RA) (109 paired readings), with no significant difference between the PMR and RA groups on analysis of variance of the regression slopes. (2) A degree of scatter of readings around the regression lines so that they could not be used for prediction of ESR from the PV or vice versa. (3) χ^2 analysis of normal and abnormal values of ESR and PV which showed a highly significant correlation. However 10 readings were abnormally high for ESR in the presence of a normal PV. 5 of these 10 observations were associated with clinical features of disease activity. 20 readings were abnormally high for PV in spite of a normal ESR with only one instance of clinical activity. These data indicate that it is not possible to provide exact guidelines for a 'safe' level of ESR or PV applicable to the individual patient, and measurement of both these indices of disease activity is recommended.

Corticosteroid treatment used to treat active polymyalgia rheumatica (PMR) and to avoid complications such as blindness secondary to associated arteritis (Easterbrook *et al.*, 1967; Wadman and Werner, 1967) may itself induce adverse effects such as compression fractures of vertebrae. Clearly a reliable laboratory test of disease activity is required. The erythrocyte sedimentation rate (ESR) has been widely used but occasional patients with active PMR have a normal ESR and in some of these, active, biopsy-proven arteritis has been reported (Dick and Freeman, 1940; Roux, 1954; Bruk, 1967; A. St. J. Dixon, unpublished; Rynes *et al.*, 1977).

Plasma viscosity (PV) has supplanted ESR in many laboratories as a routine test of disease activity since it can be automated and the results are not influenced by age, sex, or haematocrit (Eastham and Morgan, 1965). Lawrence (1961) and Harkness (1971) have suggested that it might be a more sensitive indicator of disease activity than the ESR. As soon as the PV was proposed as a substitute for the ESR in our laboratory we performed a few comparative measurements on patients with PMR and met some discrepancies between ESR, PV, and clinical activity of disease. This prompted us to undertake a more extensive comparison, the results of which are reported here, in parallel with those obtained in a group of patients with rheumatoid arthritis (RA).

Accepted for publication March 28, 1977
Correspondence to Dr. A. St. J. Dixon

Patients and methods

ESR (mm in 1 hour) was measured by the Westergren method. We accepted 20 mm as the upper limit of normal for males and 30 mm for females aged 50 or more (Böttiger and Svedberg, 1967). PV was measured using the Coulter viscometer (normal range 1·5–1·72 centipoises). 112 paired readings of ESR and PV were obtained from 23 patients with PMR (46 in males, 66 in females). Disease activity was also assessed clinically by morning stiffness, pain on movement, and general well being at the time of each venesection. 109 paired readings of ESR and PV were obtained from 53 patients with RA (40 in males, 69 in females). In both groups all patients were aged 50 years or more and had a haemoglobin concentration of 11g/dl or more. No patient was polycythaemic.

The following statistical analyses were made: (a) Calculation of the correlation coefficient and of

regression lines in both sexes in both groups and analysis of variance between RA and PMR on the regression lines. (b) Analyses of χ^2 with Yates's correction, except in the males with RA, when a Fisher's exact test was used because of the small number of observations in the extreme positions.

Results

PMR PATIENTS

A significant correlation between ESR and PV was found ($r = 0{\cdot}59$; $P<0{\cdot}001$) for all patients, and for males ($r = 0{\cdot}617$) and females ($r = 0{\cdot}626$) calculated separately. A comparison was made between normal and abnormal values using the χ^2 test, assuming a normal PV<1·72 cp and a normal ESR<20 mm/h and <30 mm/h for males and females respectively. There was a better correlation in the female group ($\chi^2 = 11{\cdot}95$; $P<0{\cdot}001$) than in the male group ($\chi^2 = 9{\cdot}89$; $P<0{\cdot}01$). For both groups combined correlation was more significant ($\chi^2 = 23{\cdot}22$; $P<0{\cdot}001$). It is important to note, however, that in 10 paired readings a raised ESR was associated with a normal PV. 2 of these observations referred to one male and 5 of 8 paired observations in females referred to one patient. 5 (1 male, 4 female) of the total 10 paired readings referred to patients who at the time showed clinically active disease as judged by proximal limb stiffness after rest and aching pain in one or both limb girdles, with or without weight loss and anorexia, muscle tenderness, and impaired active movements at shoulders and hips.

In 20 other paired readings (10 in males, 10 in females) a raised PV was associated with a normal ESR. 4 of these paired observations were made in one male patient. Among these patients clinical evidence of disease activity was found in only one.

There were 37 paired readings (13 in males, 24 in females) in which both the ESR and PV were raised. In 23 of these observations (7 in males, 16 in females) there was no clinical evidence of active disease. In 45 paired observations (21 in males, 24 in females) both the PV and ESR were within the normal range. There was clinical evidence of disease activity in 6 of these patients (4 male, 2 female).

The regression equations linking ESR with PV were as follows.

Male:	PV	=	1·6233	+	0·0034	×	ESR
	ESR	=	−162·56	+	115·13	×	PV
Female:	PV	=	1·6278	+	0·0043	×	ESR
	ESR	=	−134·20	+	87·94	×	PV

Examination of the slopes of the prediction lines confirmed that whereas there was no sex difference for PV there was for ESR at all levels. Since scatter around the regression lines was often over a clinically important change in ESR or PV, the equations were not suitable to predict the PV from the ESR and vice versa.

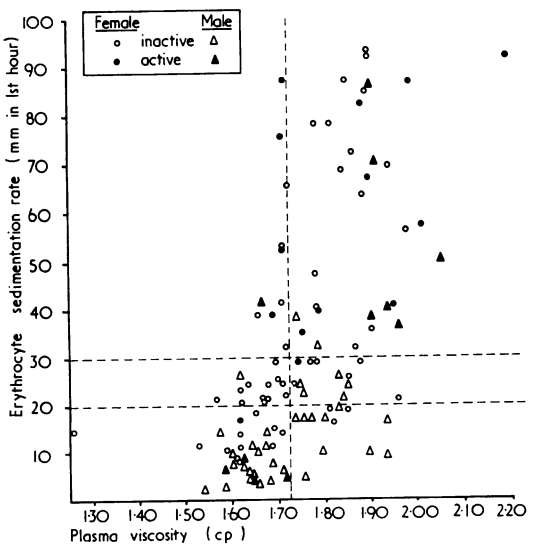

Fig. *112 paired readings of ESR (upper limit of normal. 20 mm in males and 30 mm in females) and PV (upper limit of normal 1·72) in 23 patients with PMR, all aged 50 years or more.*

RA PATIENTS

The correlation between ESR and PV for the whole group was highly significant ($r = 0{\cdot}678$; $P<0{\cdot}001$) and also when males ($r = 0{\cdot}661$; $P<0{\cdot}001$) and females ($r = 0{\cdot}691$; $P<0{\cdot}001$) were calculated separately. Discrepancies, with one exception, all occurred in females, and this was shown by the fact that when comparing normal and abnormal values (Fisher's exact test for males and χ^2 for females) the significance of the correlation was greater in males ($P<0{\cdot}001$) than in females ($\chi^2 = 4{\cdot}18$; $P<0{\cdot}5$). The same comparison made for males and females together yielded a significance of $P<0{\cdot}001$ ($\chi^2 = 21{\cdot}72$).

The regression equations linking ESR and PV were as follows.

Male:	PV	=	1·711	+	0·0035	×	ESR
	ESR	=	−180·29	+	124·47	×	PV
Female:	PV	=	1·666	+	0·0037	×	ESR
	ESR	=	−186·50	+	130·44	×	PV

Analysis of variance of the regression results showed no significant difference ($P>0{\cdot}1$) between the PMR and RA slopes for the male or female groups.

Discussion

Crockson and Crockson (1974) studied ESR and PV as indices of disease activity in patients with RA and showed a highly significant correlation between the two methods. However we concluded from our results that although we could confirm a statistically significant correlation between results of the PV and ESR in both RA and PMR we could not safely predict the PV from the ESR and vice versa. This was borne out by the wide scatter around the regression lines, and by the number of instances where the PV was raised in the presence of a normal ESR and vice versa.

These discrepancies occurred about twice as often in the PMR group as in the RA group. An accurate assessment of disease activity in patients with RA is perhaps of relatively little importance. However the situation is very different in the case of PMR where inadequate corticosteroid therapy may result in a significant morbidity or even mortality.

The PMR patients presenting with a normal ESR in the presence of clinical features of active disease resembled others reported previously (Russell, 1958; Harrison and Bevan, 1967; Paulley and Hughes, 1960; Mowat and Hazleman, 1974; A. St. J. Dixon, unpublished). Among these 7 patients only one had a raised PV, which suggests that this does not represent a more sensitive indicator of disease activity than the ESR in this situation. However the most important aspect of these observations was that 5 patients with active disease assessed clinically showed a raised ESR in the presence of a normal PV. The use of the PV alone to assess corticosteroid dosage was more likely to result in inadequate treatment.

A recent study of the abrupt and gradual withdrawal of corticosteroids from patients with PMR (Esselinckx *et al.*, 1977) showed that patients with clinically inactive disease had a normal PV and ESR, whereas when one or both of these was raised a relapse on attempting to withdraw corticosteroid therapy was much more likely.

We therefore conclude that in the individual patient with PMR one cannot rely on either the PV or ESR, to assess the activity of disease. It is safer to use both tests. It also seems impossible to provide clear guidelines for a safe level of ESR or PV, applicable to all patients with PMR.

We thank Drs. J. A. Cosh and P. A. Bacon for permission to study their patients; Mrs. J. Crockett for performing the ESRs and Mrs. E. Collins for carrying out statistical analysis of the data.

References

Böttiger, L. E., and Svedberg, C. A. (1967). Normal erythrocyte sedimentation rate and age. *British Medical Journal*, **2**, 85–87.

Bruk, M. I. (1967). Articular and vascular manifestations of polymyalgia rheumatica. *Annals of the Rheumatic Diseases*, **26**, 103–113.

Crockson, R. A., and Crockson, A. P. (1974). Relationship of the erythrocyte sedimentation rate to viscosity and plasma proteins in rheumatoid arthritis. *Annals of the Rheumatic Diseases*, **33**, 53–56.

Dick, C. F., and Freeman, G. (1940). Temporal arteritis. *Journal of the American Medical Association*, **114**, 645–647.

Easterbrook, W. M., Baxter, D. W., and Martin, J. A. (1967). Temporal arteritis, development during indomethacin therapy. *Canadian Medical Association Journal*, **97**, 296–299.

Eastham, R. D., and Morgan, E. G. (1965). Plasma viscosity in clinical laboratory practice. *Journal of Medical Laboratory Technology*, **22**, 70–73.

Esselinckx, W., Doherty, S. M., and Dixon, A. St. J. (1977). Polymyalgia rheumatica. Abrupt and gradual withdrawal of prednisolone treatment. *Annals of the Rheumatic Diseases*, **36**, 219–224.

Harkness, J. (1971). The viscosity of human blood plasma: its measurement in health and disease. *Biorheology*, **8**, 171–193.

Harrison, M. J. G., and Bevan, A. T. (1967). Early symptoms of temporal arteritis. *Lancet* **2**, 638–640.

Lawrence, J. S. (1961). *Assessment of Activity of Disease*. Lewis, London.

Mowat, A. G., and Hazleman, B. L. (1974). Polymyalgia rheumatica—a clinical study with particular reference to arterial disease. *Journal of Rheumatology*, **1**, 190–202.

Paulley, J. W., and Hughes, J. P. (1960). Giant cell arteritis of the aged. *British Medical Journal*, **2**, 1562–1567.

Roux, J. K. (1954). La syndrome de l'arterite temporale. *Helvetica Medica Acta*, **21**, Suppl. 34, 1–82.

Russell, R. W. R. (1958). Giant cell arteritis, a review of 35 cases. *Quarterly Journal of Medicine*, **28**, 471–489.

Rynes, R. I., Mika, P., and Bartholomew, L. E. (1977). Development of giant cell (temporal) arteritis in a patient 'adequately' treated for polymyalgia rheumatica. *Annals of the Rheumatic Diseases*, **36**, 88–90.

Wadman, B., and Werner, I. (1967). Therapeutic hazards of phenylbutazone and oxyphenbutazone in polymyalgia rheumatica. *Lancet*, **1**, 597–598.