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VALUE OF THE ERYTHROCYTE SEDIMENTATION RATE AS A SCREENING TEST

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The erythrocyte sedimentation rate (ESR) is well established as a clinical test in diseased patients (*Brit. med. J.*, 1960; Gibson, 1960). However, little seems to have been published concerning its value as a routine screening test. Borchgrevink, Heistø, and Reimers Reksten (1965) found 41 (2 per cent.) of 2,205 Norwegian male blood donors with an ESR over 20 mm./hr; nineteen of these showed a persistent elevation. The ESR has not usually been included in screening programmes (Jungner, 1966; Collen, 1966), but we have found it of great value and therefore present our experience with 2,000 men. Ever since the appearance of Westergren's paper (1926), there has been considerable dispute over the range of normal values for the ESR. Our experience with 1,739 healthy men suggests that slightly broader limits than usual may be acceptable.

METHODS

The Institute of Directors' Medical Centre opened in June, 1964, and by December, 1965, over 2,000 male patients had been seen. Each visit provides for a detailed history and examination, chest and abdominal *x* rays, 12-lead electrocardiogram, haemoglobin estimation, ESR and serum cholesterol. Results on some other aspects have been published elsewhere (Wright and Pincherle, 1967; Pincherle and Shanks, 1967). The first 2,000 patients seen who had a complete case record were analysed in detail, using an electronic computer. In any case of doubt, further reference was made to the clinical notes.

Blood was taken by venepuncture into sequestrene bottles. For administrative reasons this was kept overnight in a refrigerator, and then read in standard Westergren tubes. A one in five dilution was made with 3·8 per cent. sodium citrate and the fall in mm./hr recorded. Overnight storage tends to give slightly lower readings.

STATISTICAL RESULTS

The first 134 men seen had the ESR determined in a different laboratory. They had a significantly higher mean ESR of 8·12 mm./hr ("t" = 7·62; $P < 0·0001$) and have, therefore, been excluded from the analysis.

Some patients were already aware of disease which might be associated with a raised ESR and others were diagnosed as suffering from such a disease as a result of their visit to the Medical Centre. 127 patients who were in this way known to be liable to have a raised ESR were therefore excluded from the detailed statistical analysis.

The data on the 1,739 normal men were studied by multiple regression analysis. The tendency for the ESR to rise with age is well known (Ansell and Bywaters, 1958; Dawson, 1960; Boyd and Hoffbrand, 1966). Our results (Table I) confirm this and indicate a tendency for the rise to flatten out after age 60 (Hilder and Gunz, 1964).

TABLE I

VARIATION OF ESR WITH AGE IN MEN

Age (yrs)	No. of Patients	Mean ESR (mm./hr)
<30	42	3·19
30–39	369	3·84
40–49	658	4·69
50–59	549	5·19
60–69	112	5·15
70+	9	5·0
Total	1,739	4·66

Regression coefficient $b = 0·0575$ mm./hr per year of age on 1,737 D.F.; S.E. = 0·00845; "t" = 6·8; $P < 0·0001$.

There was a considerable fluctuation in mean value from month to month, but a general pattern of high values in spring and autumn and low values in summer appeared (Table II). Smoking tended to cause a rise in the mean ESR; this was a progressive trend with increasing amounts smoked and was statistically significant (Table III).

TABLE II
VARIATION OF ESR WITH SEASON

Months	No. of Patients	Mean ESR (mm./hr)
Nov.–Jan.	536	4·45
Feb.–Apr.	347	4·93
May–July	353	4·26
Aug.–Oct.	503	4·99

Analysis of variance in monthly groups gives $F=2·13$ on 11 and 1,727 D.F.; $0·05>P>0·01$.

TABLE III
VARIATION OF ESR WITH SMOKING HABITS

Cigarettes Smoked Daily		No. of Patients	Mean ESR (mm./hr)
None	(0)	597	4·03
Given up	(1)	338	4·86
1–19	(2)	354	4·94
20+	(3)	450	5·13

$b=0·354$ mm./hr per change in smoking class; S.E. (b)$=0·0640$; "t"$=5·5$; $P<0·0001$.

Alcohol consumption, mental stress, and a family history of ischaemic heart disease had no significant effect on mean ESR levels. The ESR was found to rise significantly with increasing degrees of overweight. (Table IV).

TABLE IV
CHANGES IN ESR WITH WEIGHT

Weight as Percentage of Expected Weight	No. of Patients	Mean ESR (mm./hr)
Less than 90	174	4·20
90–109	1,067	4·60
110–119	333	4·89
120 or Over	165	5·05

$F=2·66$ on 3 and 1,735 D.F.; $P<0·05$.

Other variables were considered in the multiple regression. Of these cholesterol and haemoglobin levels appeared to be significant, whereas blood pressure values, particularly diastolic, were not (Table V). The original residual mean square was 10·43 and even after taking out the effects of eight variables, this dropped only to 9·52, suggesting that none of these factors are of major importance in determining the final value of the ESR.

The 127 patients with some disease liable to raise the ESR showed no significant variation of the mean ESR with age (Table VI). This suggests, as might be predicted, that the effect of disease is much more significant than the effect of age alone. As expected, too, the proportion of patients with disease liable to raise the ESR rose with increasing age. The diseases were many and various; broadly speaking, 52 per cent. were infective (acute or chronic), 41 per cent. were inflammatory but not infective, 3 per cent. were neoplastic, and the remaining 4 per cent. were due to other causes.

TABLE V
MULTIPLE REGRESSION RESULTS

Variable	Partial Regression Coefficient	"t" for the Partial Regression	P
Age	0·0414	4·67	<0·0001
Month	−0·0370	0·55	>0·5
Smoking	0·358	5·72	<0·0001
Weight	0·271	2·75	<0·01
Blood Pressure			
Systolic	0·0106	2·12	<0·05>0·01
Diastolic	−0·0013	0·17	>0·9
Serum Cholesterol	0·0068	4·36	<0·0001
Haemoglobin	−0·0941	7·74	<0·0001

TABLE VI
ESR IN DISEASED PATIENTS

Age (yrs)	No. of Patients	Mean ESR (mm./hr)	Percentage of Total Number of Patients in that Age Group
<30	1	13·0	2
30–39	17	21·4	4
40–49	33	14·1	5
50–59	48	22·5	8
60–69	25	19·7	18
70+	3	15·0	25
Total	127	19·36	7

The regression coefficient $b=0·0203$ on 126 D.F.; S.E.$=0·0526$; "t"$=0·39$; $P>0·6$.

DISCUSSION

The value of the "normal" ESR in men is usually quoted as 0–9 mm./hr (Dawson, 1960; Wintrobe and Landsberg, 1935; Wintrobe, 1961), and indeed 91 per cent. of our "normal" patients were in this range. However, 17 per cent. of the "abnormal" group were also in this range, so that there is a considerable overlap. For the normal subjects the mean was 4·66 and the standard deviation 3·23 mm./hr, so that a slightly higher upper limit of normal of 11 mm./hr might be justified (mean +2 standard deviations). Of 41 cases with an ESR over 20 mm./hr, only three had no apparent cause, and these showed a considerable fall in ESR at follow up.

None of the abnormal subjects had an ESR of less than 3 mm./hr and in only 4 per cent. was it 6 mm./hr or less. We can, therefore, define four ranges:

0–6 mm./hr, almost certainly normal;
7–11 mm./hr, probably normal;
12–20 mm./hr, doubtful;
Over 20 mm./hr, most probably abnormal.

These ranges agree well with the suggested upper limit of 14 mm./hr for blood donors suggested by Borchgrevink and others (1965).

The effect of age on the ESR is well documented as is the rise produced by lower haemoglobin values (Ham and Curtis, 1938; Miale, 1962). The seasonal changes may be related to increased incidence of mild respiratory infections, and this may also account for the raised values found in smokers. The relationship between smoking and cholesterol (Wright and Pincherle, 1967) may also be of importance, but it is unlikely to be the only factor, as the partial regression coefficient of ESR on smoking is also highly significant.

The relationship we have found between ESR and cholesterol is not well known, despite previous reports (Swank, 1962). Various other authors have reported relationships with other lipid fractions (Canè and Pinamonti, 1959; Hartwig and Cohn, 1960; Ehrly, Gramlich, and Müller, 1965). The mechanism is probably related to increased aggregation of the red blood corpuscles (Swank, 1951, 1962). Wagner and Schlender (1963) did not find a very significant relationship between ESR and weight, perhaps because they used dermatological patients rather than normal men. It is difficult to account for this relationship, but it is unlikely to be an artefact as the partial regression coefficient is significant at the 1 per cent. level. It may possibly be related to some lipid factor other than the cholesterol. While the effect is small (about 0·01 mm./hr/lb.) it would be of interest to investigate this further, in the laboratory as well as epidemiologically. In the malnourished, improved nutrition causes a fall in ESR (Walker, Fletcher, and Reynolds, 1956). It would be interesting if this effect became reversed at improved levels of nutrition.

Clinical Results

The statistical data presented above are of great theoretical interest. However, from the practical point of view, the important point is what information of direct clinical value can be obtained from looking at the ESR. The clinical conditions giving rise to a raised ESR are well known, and space does not allow us to elaborate on individual diseases.

In general, we can say that the ESR is helpful in three ways in the context of routine physical examinations:

(1) It may be the sole pointer to a pathological process. This we have found rare. There was only one case in the 2,000 men considered in this paper who fitted into this category; this was a man with an ESR of 68 mm./hr who turned out to be suffering from multiple myeloma which has responded well to treatment.

(2) Much more commonly, the ESR may be the second prick of the spur that has caused the doctor to decide to investigate some other abnormality. This occurred in eight cases, all with ESRs over 25 mm./hr. The diagnosis ranged from adenoma of the lung to chronic sinusitis.

(3) The ESR may indicate the activity of some previously diagnosed condition. Here a normal ESR is of significance; 44 of our patients had an ESR of 11 mm./hr or less, indicating that their disease was relatively quiescent, and fifteen had an ESR of over 20 mm./hr, indicating that it was active.

There were five patients with cholesterol levels over 300 mg. per cent. and an ESR over 25 mm./hr. One of these was a particularly interesting case. A man aged 57 with familial xanthomatosis, who had had a coronary thrombosis 8 years previously. The blood pressure was 190/105, cholesterol 600 mg. per cent. and ESR 30 mm./hr. When he was treated with Clofibrate (Atromid-S) the cholesterol fell to 195 mg. per cent. and the ESR to 10 mm./hr. We can thus follow the statistical relationship between ESR and cholesterol from the general to the particular.

Conclusions and Summary

We have analysed the ESRs of 2,000 men and have confirmed the variations in ESR caused by age and haemoglobin values reported by previous workers. We suggest that the usually quoted normal range is too narrow, and that an ESR of under 12 mm./hr taken alone may be regarded as normal; conversely, higher values should be taken most seriously. We have found a positive correlation between ESR and obesity and independently between ESR and hypercholesterolaemia. This was apparent in individual cases as well as in the statistical data, and a plea is made for further investigation of this relationship. We feel that as this is a simple investigation that can be carried out relatively quickly and easily with inexpensive

equipment, it should be used more often, especially perhaps by the general practitioner.

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