# Discriminating ability of the erythrocyte sedimentation rate: a prospective study in general practice

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*SUMMARY. Despite its frequent use, little is known about the ability of the erythrocyte sedimentation rate to discriminate between 'pathology' (inflammatory diseases and malignancies) and 'no pathology' in general practice. This has been studied by following 362 patients who presented to their general practitioner with a new complaint, for which the general practitioner considered determination of the erythrocyte sedimentation rate to be indicated. The test was performed at the local hospital laboratory and the patients were seen again after three months, in order to establish the follow-up diagnoses. By comparing the test results with the follow-up diagnoses, combined with receiver operating characteristic curves and regression analysis, the erythrocyte sedimentation rate was found to have a reasonable discriminating ability with respect to malignancies and inflammatory diseases (sensitivity 53%, specificity 94%, positive predictive value 48%, negative predictive value 91%, odds ratio 15.1). The upper limit for the normal erythrocyte sedimentation rate should be set at approximately 12 mm hour$^{-1}$ for men and 28 mm hour$^{-1}$ for women, and needs no correction for age. It is concluded that the erythrocyte sedimentation rate still deserves a place in the general practitioner's daily routine.*

## Introduction

DESPITE its frequent use,[1] little is known about one of the most important aspects of the erythrocyte sedimentation rate in general practice — its ability to discriminate between serious diseases requiring therapy ('pathology') and harmless often self limiting diseases ('no pathology').[2]

Reference values and sensitivity, specificity and predictive values of the erythrocyte sedimentation rate have been described in healthy,[3-7] and diseased people.[8-13] The suggested upper limits of a normal erythrocyte sedimentation rate vary from 5 to 50 mm hour$^{-1}$, depending on the patient's age, sex and the disease concerned. Authors tend to disagree on the appropriate reference values in the elderly and on the ability of the erythrocyte sedimentation rate to rule out disease. In addition, the erythrocyte sedimentation rate is influenced by the red cell volume, for example in anaemia or polycythaemia, pregnancy, which elevates the rate, and certain medication, such as steroids and oral contraceptives.

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Because of these uncertainties, alternative tests have been recommended.[14-17] However, until now, no study of erythrocyte sedimentation rate has included the full spectrum of patients attending the general practitioner with a new complaint for which the general practitioner considers determination of erythrocyte sedimentation rate to be indicated. By investigating this rather undifferentiated population prospectively, as in the present study, the discriminating ability of the erythrocyte sedimentation rate is tested to the full.[18-21] Moreover, such a study may cast some light on the indications for determining erythrocyte sedimentation rate in general practice and may enable a proper assessment of predictive values. The prevalences of the diseases concerned and the appropriate reference values can be derived.[22]

## Method

Nine general practitioners participated in the study. They were willing to participate following positive experiences in previous studies. All patients presenting to these general practitioners over five successive months in 1987 with a new complaint for which the general practitioner considered determination of the erythrocyte sedimentation rate to be indicated were included in the study. After informed consent had been obtained, the name, date of birth and sex of the patient, and the possible diagnosis before determination of the erythrocyte sedimentation rate were recorded by the general practitioner. A venous blood sample was then taken from the patient's arm. To prevent clotting, the blood was collected in ethylene diaminetetra-acetate (EDTA-K3) tubes. The samples were collected daily and Westergren's erythrocyte sedimentation rate determined at the local hospital laboratory. All the patients received normal care from their general practitioner and were also requested to visit the general practitioner after three months. Where necessary, patients received a written reminder or a telephone call after three months had expired. During the visits, a general practitioner-investigator (G J D) established the follow-up diagnosis by interviewing the patient, reviewing the chart and hospital letters, and asking for additional information from the general practitioner if necessary. The diagnoses were classified according to the *International classification of health problems in primary care (ICHPPC-2-defined).*

Prior to the study, a questionnaire concerning reference values and indications for determining erythrocyte sedimentation rate in general practice was completed by 20 general practitioners. The results were also used to define 'pathology'. Later, the same questions were answered by the nine general practitioners who participated in the study.

The prevalence, sensitivity, specificity and predictive values of the test (which together constitute its discriminating ability) have been calculated according to the current definitions of these terms.[23] Receiver operating characteristic curves have been used to study the relation between sensitivity, specificity and reference values (cut-off points).[23] Odds ratios, with their 95% confidence intervals, have been used in estimating the joint value of sensitivity and specificity in discriminating 'pathology' from 'no pathology'. Furthermore, the logistic regression function for the simultaneous contributions of erythrocyte sedimentation rate,

age and sex in predicting 'pathology' has been calculated, using the *BMDP-LR* computer programme.[24] A further explanation of the data analysis techniques and the results obtained, is given in Appendix 1.

## Results

On the basis of the results of the questionnaire completed by 20 general practitioners, 'pathology' was defined as inflammatory diseases and malignancies. 'No pathology' covered the categories 'signs, symptoms and ill-defined conditions', as well as 'adverse effects', 'supplementary classification' and 'preventive medicine'. These diagnoses concern minor and spontaneously resolving problems.[25] The remaining disease categories were defined as 'all other diseases'.

Using these definitions, the *ICHPPC-2-defined* categories were modified slightly. Pneumonia, arthritis and fever of unknown cause were added to the category 'inflammatory and parasitic diseases', hereafter referred to as 'inflammatory diseases'. As far as possible, inflammations of other bodily systems were included in the 'inflammatory diseases' category. The neoplasms found were referred to as malignancies. The category 'genitourinary system diseases' was divided into 'urinary system diseases' and 'diseases of the genital organs'. 'Preventive medicine' covered medical examinations requested by the patient and this category was separated from the 'supplementary classification'.

In total, 362 patients, aged 4–87 years (mean and median 47 years, standard deviation 19 years) participated in the study. Two thirds of the patients (67.4%) were female. The diagnoses made before the determination of the erythrocyte sedimentation rate are given on Table 1. The follow-up diagnosis could not be established for four patients (most were tourists) and Table 1 shows the distribution of the follow-up diagnoses which were found for the remaining 358 patients.

**Table 1.** Distribution of the diagnoses established before determination of the erythrocyte sedimentation rate and during the follow-up period.

| | % of patients ($n = 362$) | |
|---|---|---|
| | Initial diagnosis | Follow-up diagnosis |
| Inflammatory diseases | 13.3 | 13.3 |
| Malignancies | 1.9 | 2.5 |
| Endocrinological, nutritional and metabolic diseases | 1.4 | 0.3 |
| Blood diseases | 0.8 | 0.8 |
| Mental disorders and diseases of the nervous system and sense organs | 3.0 | 4.4 |
| Circulatory system diseases | 0.3 | 1.7 |
| Respiratory system diseases | 13.3 | 11.0 |
| Digestive system diseases | 5.8 | 9.9 |
| Urinary system diseases | 0.8 | 1.4 |
| Diseases of the genital organs | 0.6 | 2.2 |
| Skin and subcutaneous tissue diseases and congenital anomalies | 2.5 | 3.6 |
| Musculoskeletal and connective tissue diseases | 17.4 | 16.9 |
| Signs, symptoms and ill-defined conditions | 25.7 | 24.6 |
| Adverse effects and supplementary classification | 2.8 | 2.8 |
| Preventive medicine | 2.8 | 3.6 |
| Unknown | 7.7 | 1.1 |

$n$ = total number of patients.

Table 1 demonstrates the wide range of disorders found in patients presenting with new complaints in general practice for whom the determination of the erythrocyte sedimentation rate was considered to be indicated. The most common diagnosis was 'signs, symptoms and ill defined conditions'. 'Musculoskeletal and connective tissue diseases', 'inflammatory diseases', 'respiratory system diseases' and 'digestive system diseases' were also frequent diagnoses. These latter four categories mostly concerned cases of myalgia, inflammatory intestine disease, minor respiratory tract inflammation and irritable bowel syndrome, respectively. The nine malignancies diagnosed were carcinoma of the stomach (two patients), colon (two), lung (two), prostate (one), testis (one) and peritoneum (one). In three of these patients metastases were also found. There was only one diagnosis of diabetes mellitus and one congenital anomaly (an additional lobe of the liver).

Owing to accidental blood sample mismanagement, the erythrocyte sedimentation rate was not determined for six of the 358 patients with a follow-up diagnosis and since in children higher erythrocyte sedimentation rates can be independent of disease activity, 11 patients aged 4–15 years were excluded. Thus data for 341 (109 men and 232 women) were used for further analysis. In order to verify the definition of 'pathology' and to establish the appropriate upper limits of reference values for these patients, we used receiver operating characteristic curves. The ability of the erythrocyte sedimentation rate to discriminate the more frequently found follow-up diagnoses from 'no pathology', is illustrated by the curves shown in Figure 1. Owing to the numerically small contribution of malignancies, the 'pathology' (inflammatory diseases and malignancies) curve followed the inflammatory diseases curve almost exactly and therefore the former was not included on Figure 1(b). The most important cut-off points at which the computer programme calculated the corresponding sensitivities and specificities are given in Appendix 1, Table II. The arithmetically optimal cut-off points are found at the erythrocyte sedimentation rate values when the sum of the sensitivity and specificity is greatest. In choosing these upper limits of reference values the test outcomes are considered to be of equal usefulness, which means that a false positive and false negative test result are seen as equally serious and harmful for the patient. However, this situation will not always correspond to clinical reality. Therefore the extent to which sensitivity and specificity changed after choosing the greatest sum but one was also examined. Table 2 shows the sensitivity and specificity at the cut-off points in the 'pathology' receiver operating characteristic curve where the greatest and greatest but one sum of sensitivity and specificity were found (differences for inflammatory diseases, malignancies and 'pathology' 0.21%, 0.93% and 0.14%, respectively). The corresponding prevalences and predictive values are also given. Predictive values were calculated by comparing 'pathology' and 'no pathology' plus 'all other diseases'. By inspection of the positive predictive values it can be concluded that the upper limit of the cut-off point when diagnosing 'pathology' corresponds to an erythrocyte sedimentation rate of around 27 mm hour$^{-1}$. This conclusion is supported by the odds ratios (the joint parameters of the likelihood ratios for a positive and negative test result) which improve considerably at the higher cut-off points for inflammatory diseases, malignancies and 'pathology'.

Sex was found to be relatively important in predicting 'pathology', as can be seen from Table 3 and from the receiver operating characteristic curves in Figure 2. From Figure 2 the optimal and suboptimal cut-off points for erythrocyte sedimentation rate were calculated to be 12 and 14 mm hour$^{-1}$ in men, and 28 and 27 mm hour$^{-1}$ in women, respectively. The sensitivities and specificities at these cut-off points are given in Table 4. Age seemed to be relatively unimportant. The results are

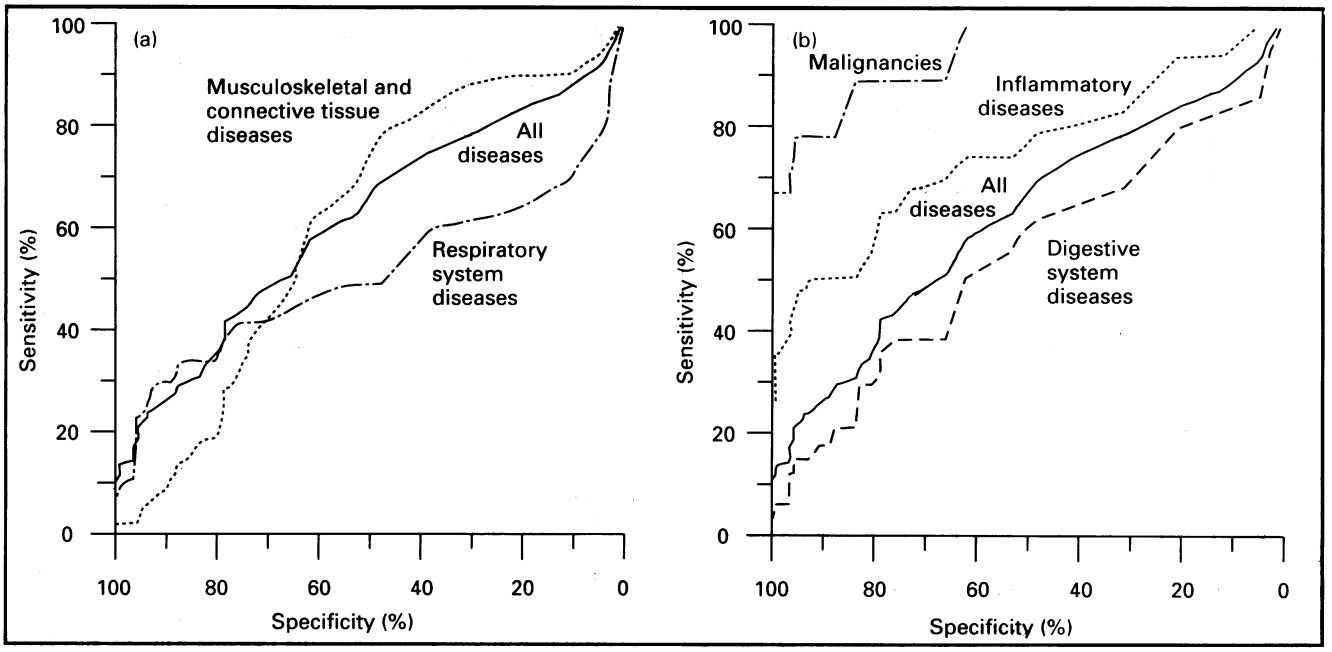


**Figure 1.** *Receiver operating characteristic curves, illustrating the relation between cut-off points, sensitivity and specificity of the erythrocyte sedimentation rate with regard to (a) 'all diseases', 'respiratory system diseases' and 'musculoskeletal and connective tissue diseases', and (b), 'all diseases', 'malignancies', 'inflammatory diseases' and 'digestive system diseases', using 'no pathology' as a reference group.*

illustrated even better by the logistic regression function, which was found to be:

$$\ln p/(1-p) = -4.76 + 3.14 \times \text{logESR} - 0.86 \times \text{sex}$$

where $p$ = chance of 'pathology', sex: male = 0; female = 1. The 95% confidence intervals of the coefficients of logESR and sex were calculated as (2.15 to 4.12) and (−1.54 to −0.19), respectively. Erythrocyte sedimentation rate was tranformed to logESR because of its skew distribution; most of the values found were low. Age did not appear in this function. The regression coefficient of sex (0.86) is equivalent to an odds ratio of 2.4. The regression function also illustrates the ability of the erythrocyte sedimentation rate to predict 'pathology', independent of the choice of cut-off point. The chances of patients having a diagnosis of 'pathology', given their sex and erythrocyte sedimentation rate were calculated from the logistic regression function and are given in Table 5. The results from the questionnaire, completed by the nine general practitioners, showed that three general practitioners did not regard age as relevant to the cut-off point for erythrocyte sedimentation rate, and one general practitioner mentioned neither age nor sex as being relevant.

**Table 3.** Frequency distribution of pathology (inflammatory diseases and malignancies) and all diagnoses other than pathology in relation to age and sex.

| Age (years) | No. of patients | % of patients with pathology | | % of patients with all other diagnoses | |
|---|---|---|---|---|---|
| | | Men | Women | Men | Women |
| 15–30 | 68 | 4.4 | 10.3 | 23.5 | 61.8 |
| 31–40 | 62 | 6.5 | 9.7 | 30.6 | 53.2 |
| 41–50 | 45 | 6.7 | 6.7 | 35.6 | 51.1 |
| 51–60 | 63 | 4.8 | 6.3 | 27.0 | 61.9 |
| 61–70 | 49 | 6.1 | 10.2 | 22.4 | 61.2 |
| 71–80 | 43 | 14.0 | 7.0 | 16.3 | 62.8 |
| 81–87 | 11 | 0.0 | 45.5 | 27.3 | 27.3 |
| Total | 341 | 6.5 | 9.7 | 26.1 | 57.8 |

Among the nine participating general practitioners only one reported using a cut-off point above 20 mm hour$^{-1}$. Since several reference laboratories advise the use of cut-off points up to 10 mm hour$^{-1}$, we also calculated the discriminating ability at this limit (Table 6). The results show a considerable

**Table 2.** The sensitivity and specificity of the erythrocyte sedimentation rate in detecting 'pathology' (inflammatory diseases and malignancies), calculated at the optimal and suboptimal cut-off points from the receiver operating characteristic curves in Figure 1. The corresponding prevalences, positive predictive values and negative predictive values together with the odds ratios and their 95% confidence intervals are also given.

| | | Cut-off points for ESR (mm h$^{-1}$) | Sensitivity (%) | Specificity (%) | Sensitivity + specificity (%) | Prevalence (%) | Positive predictive value (%) | Negative predictive value (%) | Odds ratio[a] | Confidence interval |
|---|---|---|---|---|---|---|---|---|---|---|
| Inflammatory diseases | Optimal | 24 | 50 | 92 | 142 | 13 | 40 | 92 | 9.2 | 3.6– 24.3 |
| | Suboptimal | 27 | 48 | 94 | 142 | 13 | 41 | 91 | 12.4 | 4.4– 36.7 |
| Malignancies | Optimal | 28 | 78 | 94 | 172 | 3 | 18 | 99 | 56.0 | 7.9–192.0 |
| | Suboptimal | 19 | 89 | 82 | 171 | 3 | 16 | 99 | 37.3 | 4.2–162.9 |
| 'Pathology' | Optimal | 27 | 53 | 94 | 147 | 16 | 48 | 91 | 15.1 | 5.5– 43.2 |
| | Suboptimal | 24 | 55 | 92 | 147 | 16 | 46 | 91 | 11.0 | 4.4– 28.1 |

[a]Odds ratios are calculated using the original two by two tables not the rounded figures for sensitivity and specificity given here.

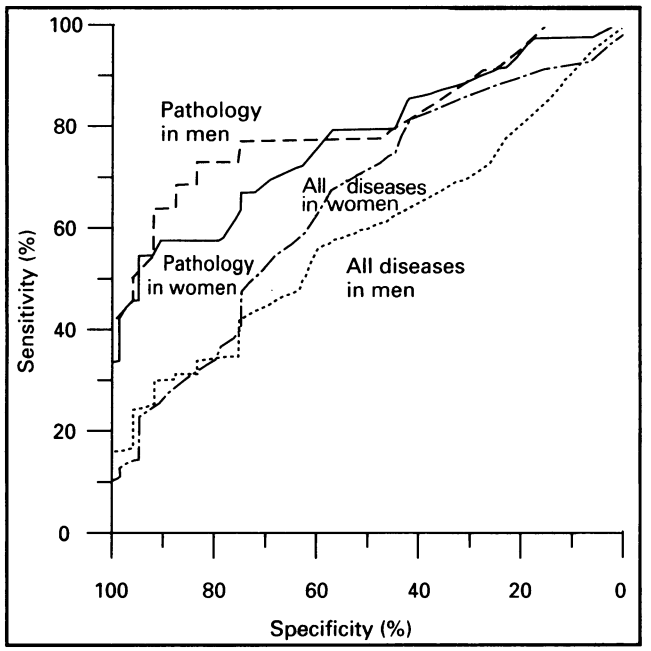


**Figure 2.** *Receiver operating characteristic curves, illustrating the relation between cut-off points, sensitivity and specificity of the erythrocyte sedimentation rate with regard to all diseases in men and women, as well as 'pathology' (inflammatory diseases and malignancies) in men and women, using 'no pathology' as a reference group.*

**Table 4.** The sensitivity and specificity of the erythrocyte sedimentation rate in detecting 'pathology' (inflammatory diseases and malignancies), calculated at the optimal and suboptimal cut-off points from the receiver operating characteristic curves in Figure 2.

| | Cut-off point for ESR (mm $h^{-1}$) | Sensitivity (%) | Specificity (%) |
|---|---|---|---|
| *Men* | | | |
| Optimal | 12 | *73* | *84* |
| Suboptimal | 14 | *68* | *88* |
| *Women* | | | |
| Optimal | 28 | *55* | *95* |
| Suboptimal | 24 | *58* | *91* |

**Table 5.** Percentage chance of a diagnosis of 'pathology' (inflammatory diseases and malignancies) given patients' sex and erythrocyte sedimentation rate.

| | | % chance of 'pathology' | |
|---|---|---|---|
| ESR (mm $h^{-1}$) | No. of patients | Men | Women |
| 0–10 | 163 | *16* | *8* |
| 10–20 | 97 | *33* | *17* |
| 20–30 | 32 | *46* | *27* |
| 30–40 | 25 | *56* | *36* |
| 40–60 | 15 | *69* | *50* |
| 60–80 | 6 | *77* | *58* |
| 80–100 | 3 | *82* | *65* |

increase in sensitivity and a decrease in specificity at this lower cut-off point. Hence, using an upper limit of 10 mm $hour^{-1}$ in this study would mean that the erythrocyte sedimentation rate becomes better at ruling out than ruling in 'pathology'. Table 6 also shows the 95% confidence intervals of the discriminating ability figures at the 27 mm $hour^{-1}$ cut-off point. The relatively low number of patients suffering from 'pathology' is reflected in large confidence intervals around sensitivity and positive predictive value.

**Table 6.** Figures for discriminating ability at the optimal cut-off point of the erythrocyte sedimentation rate of 27 mm $hour^{-1}$ compared with the cut-off points of 10 mm $hour^{-1}$ used by the local hospital. The results from the study by Stayer and colleagues[13] ($n$ = 368) who used a cut-off point of 30 mm $hour^{-1}$ are also given.

| Cut-off point (mm $h^{-1}$) | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | Positive predictive value (%) (95% CI) | Negative predictive value (%) (95% CI) |
|---|---|---|---|---|
| 27 | *53 (40–66)* | *94 (89–99)* | *48 (35–61)* | *91 (88–94)* |
| 10 | *78* | *62* | *52* | *84* |
| 30 (ref. 13) | *61* | *76* | *46* | *85* |

CI = confidence interval.

## Discussion

Erythrocyte sedimentation rate was found to be a useful test for general practitioners in diagnosing patients who are suspected of having an inflammatory disease or malignancy. For these diagnoses, the upper limit of the erythrocyte sedimentation rate should be around 12 mm $hour^{-1}$ in men and 28 mm $hour^{-1}$ in women. Using the overall limit of the 27 mm $hour^{-1}$, the chances of a diagnosis of 'pathology' are twice as high in men as in women. The erythrocyte sedimentation rate needs no further correction for age.

The receiver operating characteristic curves demonstrated that the erythrocyte sedimentation rate had a reasonably high sensitivity and specificity with respect to inflammatory diseases and malignancies only (Figure 1). In comparison with the reference group, receiver operating characteristic curves for the other diseases generally showed the erythrocyte sedimentation rate to be far less discriminatory.

Since the erythrocyte sedimentation rate was most frequently determined in patients suffering from minor and spontaneously resolving problems, the general practitioners apparently used the test to rule out rather than rule in disease. Consequently, the false negative rate of the erythrocyte sedimentation rate should be low. A reasonable sensitivity for the erythrocyte sedimentation rate was found only with respect to malignancies and not inflammatory diseases and only at the suboptimal cut-off point (Table 2). However, at higher cut-off points, the specificity with regard to malignancies and inflammatory diseases improved. Considering the relatively low prevalence of malignancies and inflammatory diseases in general practice, a high specificity would be useful. This dilemma was partly solved by considering the predictive values. Whereas the negative predictive values of the erythrocyte sedimentation rate hardly changed on altering the cut-off points, all positive predictive values improved at the higher cut-off points. It can therefore be concluded that the upper limit of the cut-off point of the erythrocyte sedimentation rate when diagnosing 'pathology' lies around 27 mm $hour^{-1}$. This conclusion is supported by the odds ratios which improve considerably at the higher cut-off points for inflammatory diseases, malignancies and 'pathology'. The odds ratios also illustrate the much greater discriminating ability of the erythrocyte sedimentation rate with regard to malignancies than inflammatory diseases. Although the cut-off point of 27 mm $hour^{-1}$ specificity was found to be higher than sensitivity, an erythrocyte sedimentation rate of more than 27 mm $hour^{-1}$ may be considered a better predictor of

'pathology' than an erythrocyte sedimentation rate below 27 mm hour$^{-1}$ is of 'no pathology'.

From the logistic regression function it can be seen that age is unimportant in predicting 'pathology', independent of the chosen cut-off point of the erythrocyte sedimentation rate. It was also found that the frequency distribution of 'pathology' hardly changed with age. Hence, an intercollinearity between age and sex cannot be held responsible for the findings presented here. The influence of sex is best illustrated by its regression coefficient (0.86) and by the percentage chance of having 'pathology' which increases with higher erythrocyte sedimentation rate. The chances of having 'pathology' is consistently higher for men than for women, the largest differences being found at erythrocyte sedimentation rates between 10 and 30 mm hour$^{-1}$.

Table 6 shows a comparison between our results and those of a recent Israeli study.[13] Despite the almost equal size of the study populations and the very similar cut-off points, Stayer found a lower specificity and better sensitivity. It is possible that serious diseases were more frequently included in his study. However, his report does not clearly differentiate between 'disease' and 'no disease', and the population was studied retrospectively.

Several investigators have demonstrated a clear relation between age and cut-off points for erythrocyte sedimentation rate. Using the results obtained by Bottiger and Svedberg[3] the 27 mm hour$^{-1}$ cut-off point would apply only to women who are almost 50 years old, whereas using Miller's results it would apply to women aged 44 years or men aged 54 years.[5] Lewis considers an erythrocyte sedimentation rate of 27 mm hour$^{-1}$ to be abnormal at any age in men or women.[16] Among the nine general practitioners taking part in this study three did not regard age as relevant to the cut-off point of erythrocyte sedimentation rate used and one doctor considered neither age nor sex to be relevant.

Determination of erythrocyte sedimentation rate is cheap, relatively simple and easy to incorporate into daily general practice. However, a false negative or positive may result in potentially harmful policies for the patient. Studying the discriminating ability of the erythrocyte sedimentation rate is therefore clinically relevant. In general, the discriminating ability of diagnostic techniques is best evaluated by measuring the therapeutic impact of the test results.[26] This criterion was met to some extent in this study because detecting malignancies and inflammatory diseases will usually lead to therapeutic action, whereas 'no pathology' and sometimes 'all other diseases' justify a wait-and-see policy. Others have preferred to evaluate a diagnostic test by means of medical decision analysis.[27,28] However, clinical utilities and benefit-to-cost ratios are difficult to assess and need further investigation.[29]

In this study, each general practitioner collected a blood sample for erythrocyte sedimentation rate determination nearly twice a week. The frequency is approximately what was estimated before the study and makes it less likely that bias by indication for the test or dilution of the study population occurred. Bias by indication may have occurred if the general practitioners had entered patients into the study selectively instead of including all patients for whom the determination of the erythrocyte sedimentation rate was indicated. Furthermore, because the inclusion criteria were not defined beforehand, and the general practitioners were not asked to exclude children and tourists from the study, clear information was obtained on the composition of the population for whom determination of erythrocyte sedimentation rate was indicated. Since the index ('pathology') and control ('no pathology') groups both derived from this population, the results may be considered applicable to daily general practice.

The number of patients in this study can be seen as a compromise between desirability and feasibility. Whereas a bigger study population could have decreased the confidence intervals of the figures for discriminating ability the necessarily prolonged study period would have diminished the amount of attention the general practitioners paid to the study and therefore could have resulted in bias by indication for the test. Similar compromises were made in the follow-up procedure selected. A panel of clinicians might have been able to provide a more accurate follow-up diagnosis. However, such a panel would have deterred patients from entering the study, which, again, could result in bias by indication for the test. Furthermore, a follow-up period of more than three months could have enabled the investigator to establish more appropriate diagnoses, but at the same time it would have increased chances of recall bias and intercurrent new pathology. Finally, not knowing what kind of pathology is to be expected makes it far more difficult to organize a set of standardized follow-up investigations. These dilemmas concerning sample size and gold standard are particularly relevant to general practice studies, in which scientific research can easily lead to a considerable interference with a general practitioner's normal routine. However, this study illustrates that these problems can be overcome by cooperating with enthusiastic general practitioners.

**Appendix 1.**

The diagnostic data is interpreted using two by two tables in which the distributions of high and normal test outcomes in diseased and non-diseased patients are compared. Sensitivities, specificities, positive predictive values and negative predictive values are then calculated using the distributions summarized in Table I.

What we want to know is what is a high erythrocyte sedimentation rate, or, in other words, which cut-off point results in the fewest false positive and false negative results. To answer this question, a series of two by two tables is created, using different cut-off points. Receiver operating characteristic curves can be seen as a summary of such a series of two by two tables. The curves illustrate the extent to which sensitivity and specificity change on altering the cut-off point. The most important cut-off points (and corresponding sensitivities and specificities) used to construct the curves in Figure 1 are given in Table II.

In general, a curve following the diagonal from bottom left to top right represents a test that does not discriminate between diseased and

**Table I.** Numerical distribution of the follow-up categories in relation to the corresponding values of the erythrocyte sedimentation rate (ESR).

| ESR (mm h$^{-1}$) | Number of patients | | | | |
|---|---|---|---|---|---|
| | Inflammatory diseases | Malignancies | 'Pathology' | 'No pathology' | All other diseases |
| 0–5 | 3 | 0 | 3 | 21 | 36 |
| 6–10 | 9 | 0 | 9 | 42 | 53 |
| 11–15 | 6 | 1 | 7 | 17 | 37 |
| 16–20 | 5 | 1 | 6 | 9 | 19 |
| 21–25 | 1 | 0 | 1 | 6 | 13 |
| 26–30 | 2 | 0 | 2 | 2 | 9 |
| 31–35 | 3 | 1 | 4 | 4 | 8 |
| 36–40 | 5 | 0 | 5 | 1 | 3 |
| 41–45 | 2 | 3 | 5 | 0 | 1 |
| 46–50 | 5 | 0 | 5 | 0 | 1 |
| 51–55 | 0 | 1 | 1 | 0 | 0 |
| 56–60 | 0 | 0 | 0 | 0 | 2 |
| 61–65 | 1 | 0 | 1 | 0 | 1 |
| 66–70 | 3 | 0 | 3 | 0 | 0 |
| 71–75 | 0 | 0 | 0 | 0 | 0 |
| 76–80 | 0 | 1 | 1 | 0 | 0 |
| 81–85 | 0 | 0 | 0 | 0 | 0 |
| 86–90 | 0 | 1 | 1 | 0 | 0 |
| 91–95 | 0 | 0 | 0 | 0 | 1 |
| 96–100 | 1 | 0 | 1 | 0 | 0 |
| Total | 46 | 9 | 55 | 102 | 184 |

**Table II.** The most important cut-off points used in constructing the receiver operating characteristic curves shown in Figure 1. The corresponding sensitivities and specificities are also given.

| Upper limits of reference values of ESR (mm $h^{-1}$) | All diseases[a] | | Malignancies | | Inflammatory diseases | | Pathology | | Digestive system diseases | | Respiratory system diseases | | Musculoskeletal and connective tissue diseases | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) | Sensitivity (%) | Specificity (%) |
| 8 | *69* | *48* | *100* | *47* | *78* | *48* | *82* | *48* | *62* | *48* | *49* | *48* | *79* | *48* |
| 10 | *58* | *62* | *100* | *62* | *74* | *62* | *78* | *62* | *50* | *62* | *46* | *62* | *61* | *62* |
| 12 | *47* | *73* | *89* | *72* | *67* | *73* | *71* | *73* | *38* | *73* | *41* | *73* | *39* | *73* |
| 14 | *41* | *78* | *89* | *78* | *63* | *78* | *67* | *78* | *35* | *78* | *38* | *78* | *28* | *78* |
| 16 | *36* | *79* | *89* | *79* | *59* | *79* | *64* | *79* | *29* | *79* | *36* | *79* | *20* | *79* |
| 19 | *31* | *83* | *89* | *82* | *50* | *83* | *56* | *83* | *21* | *83* | *33* | *83* | *16* | *83* |
| 24 | *24* | *92* | *78* | *91* | *50* | *92* | *55* | *92* | *15* | *92* | *28* | *92* | *1* | *92* |
| 27 | *22* | *94* | *78* | *94* | *48* | *94* | *53* | *94* | *15* | *94* | *23* | *94* | *1* | *94* |
| 28 | *21* | *95* | *78* | *94* | *46* | *95* | *51* | *95* | *15* | *95* | *23* | *95* | *0* | *95* |
| 31 | *17* | *96* | *67* | *95* | *41* | *96* | *45* | *96* | *12* | *96* | *18* | *96* | *0* | *96* |

[a] Except 'no pathology'.

non-diseased patients, because, independent of the chosen cut-off point the false positive and false negative rates will both be 50%. Tossing a coin would be equally as effective. This situation is illustrated in Figure 1b: the erythrocyte sedimentation rate does not discriminate between patients suffering from digestive system diseases and patients having 'no pathology'. The opposite is true for malignancies where the test discriminates reasonably well. The curve shows that, independent of the chosen cut-off point, the sensitivity and specificity are always relatively high. Receiver operating characteristic curves thus enable the reader to see quickly which diseases are best detected by the test: those with curves in the top left of the figure.

Up to now, we have presumed a simple relationship between test outcomes and follow-up diagnoses. However, age and sex determine the erythrocyte sedimentation rate to some extent, independent of the presence of 'pathology'. Furthermore, the presence of a disease might relate to age and sex rather than to the erythrocyte sedimentation rate. Logistic regression analysis, however, allows the relationship between the erythrocyte sedimentation rate, sex and age (the so called independent variables) on the one hand and the chances of 'pathology' (the dependent variable) on the other to be established. The function can only be derived by using an advanced computer programme. The input to the programme must include all independent variables and the follow-up diagnosis for each patient in the study. After taking account of the interrelationships of the independent variables, the computer programme determines the best model approximating to clinical reality in the study. The output is in the form of an algebraical function. Each independent variable receives a coefficient. The magnitude of the coefficients represent the relative importance of the variable in predicting 'pathology'.

Logistic regression analysis can also predict the chance of an individual patient having 'pathology' given his or her erythrocyte sedimentation rate, sex and age. Establishing cut-off points is no longer needed and the prediction is probably more accurate in daily practice than positive and negative predictive values.

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