Prognostic factors are biologic or physical characteristics of a patient or a cancer that can be used to predict the outcome for the individual. They are of value for the management of mesothelioma because patients need a prognosis in order to be able to make informed decisions about treatment options and to make plans for themselves and their families. Prognostic factors also assist in the selection of patients more likely to benefit from intensive treatments, especially in the context of clinical trials (1). Recently it has become clear that prognostic factors may have an additional benefit: they may give insights into the biology of the cancer being studied, and lead to improved understanding of the molecular pathogenesis (2). This new role for prognostic factors may prove to be the most important of all.

The Cancer and Leukemia Group B and European Organization for Research and Treatment of Cancer Prognostic scoring systems are the two most useful prognostic scoring systems currently available for malignant mesothelioma (3,4). These systems rate performance status, age, histologic subtype, weight loss, and hematologic parameters as the most important prognostic factors for malignant mesothelioma. In the future, molecular biologic markers and DNA expression profiles may be able to give us more insight into mesothelioma and will help in prognostication.

Prognostic factors are especially important in the context of malignant mesothelioma because, until recently, treatment has had relatively little impact on the natural history of the disease. This chapter discusses the known clinical prognostic factors for malignant mesothelioma, focusing on the two best-known current systems, and describes some of the new molecular knowledge that will lead to the development of effective targeted therapies.

**Diagnosis of Malignant Mesothelioma**

Confirmation of the diagnosis is an essential prerequisite to giving a mesothelioma patient a prognosis. Unfortunately, obtaining a diagnosis of mesothelioma may not be straightforward. The likelihood
of reaching a reliable diagnosis is increased if a multidisciplinary approach is used. Ideally, a thoracic physician, a thoracic surgeon, a medical oncologist, and a specialist pathologist should all be involved. Repeated biopsies may be required to obtain sufficient quantities of high-quality tumor tissue. Most specialists take the view that computed tomography (CT)-guided biopsy or video-assisted thoracoscopic biopsy are the most reliable techniques for obtaining tissue for histology. Blind pleural biopsy has an unacceptably high false-negative rate. Histology must be verified by a pathologist experienced in making the diagnosis of mesothelioma using the relevant immunohistochemistry stains. It is important that the pathologist not only establishes the diagnosis but defines a cell type for the tumor, i.e., epithelioid (also known as epithelial), sarcomatoid (also known as sarcomatous), or mixed histology.

Natural History of Malignant Mesothelioma

Before discussing specific prognostic factors in mesothelioma, it is necessary to give an idea of the typical prognosis for patients with the disease. Most series have shown that the median survival for a patient with mesothelioma is between 4 and 18 months. Three recent phase II chemotherapy trials with response rates greater than 20% reported median overall survivals of 6.0 months (5), 9.5 months (6), and 10.6 months (7). The large international randomized phase III trial of chemotherapy published recently (8), reported a median survival of 12.1 months for the experimental group (treated with pemetrexed and cisplatin) and 9.3 months for the control arm (treated with cisplatin only). This large trial included mainly good performance status patients; patients seen in a mesothelioma clinic will have a wider variety of performance status and some will have a much shorter survival than these data suggest. Despite the suggestion that survival is, at best, about 1 year, it is worth adding that most mesothelioma physicians have patients who survive significantly longer than this, and the occasional patient lives for many years.

Clinical Prognostic Factors for Malignant Mesothelioma

What are the clinical factors that predict a longer survival? There have been many articles published about clinical prognostic factors in mesothelioma in the past 20 years. Table 27.1 summarizes some of the data from these trials. The commonest prognostic factors identified have included histologic cell type, performance status, age, gender, weight loss, chest pain, and clinical stage. Unfortunately, some of these data have conflicted, probably because many of the studies have been of small size and from single centers. Disease staging, treatments given, response assessment methods, and patient eligibility have varied substantially.
Table 27.1. Prognostic factors in malignant mesothelioma—major published series

<table>
<thead>
<tr>
<th>First author, year (reference)</th>
<th>Median survival</th>
<th>No. of patients</th>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, age, PS, histology, asbestos exposure, stage, disease status</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, age, histology, smoking, first symptoms, pleural effusion, weight loss, delay in diagnosis</td>
</tr>
<tr>
<td>Antman, 1988 [17]</td>
<td>15</td>
<td>180</td>
<td>S: PS, histology, chest pain, age</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, stage, symptoms to diagnosis time, year of diagnosis, smoking, asbestos exposure</td>
</tr>
<tr>
<td>Spirtas, 1988 [19]</td>
<td>7</td>
<td>1475</td>
<td>S: age, gender, treatment, stage, geographic area</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: ethnic group, site, histology, year of diagnosis</td>
</tr>
<tr>
<td>Chahinian, 1982 [14]</td>
<td>7</td>
<td>69</td>
<td>S: histology, age, pleural site</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, asbestos exposure, delay in diagnosis</td>
</tr>
<tr>
<td>Boutin, 1993 [10]</td>
<td>7-32.7</td>
<td>188</td>
<td>S: absence of weight loss, aspect of visceral pleura, stage, histology</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: age, gender, site of disease, asbestos exposure, symptoms to diagnosis, surgery</td>
</tr>
<tr>
<td>De Pangher Manzini, 1993 [16]</td>
<td>13</td>
<td>80</td>
<td>S: age, stage, histologic type</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, PS, period of diagnosis, site of disease, pleural fluid cytology</td>
</tr>
<tr>
<td>Calavrezos, 1988 [18]</td>
<td>5-13</td>
<td>132</td>
<td>S: age stage, histology, PS, pain, treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender, asbestos exposure, duration of symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: age, stage, treatment, asbestos exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: age</td>
</tr>
<tr>
<td>Herndon, 1998 [3]</td>
<td>3.9-9.8</td>
<td>337</td>
<td>S: PS, chest pain, high platelet count, weight loss, high LDH, high WBC count, age, histology</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: gender</td>
</tr>
<tr>
<td>Edwards, 2000 [23]</td>
<td>5.9</td>
<td>142</td>
<td>S: gender, weight loss, PS, low Hb, high WBC count, high platelets, histology</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS: weight loss</td>
</tr>
</tbody>
</table>

S, significant; NS, nonsignificant; WBC, white blood cell; PS, performance status; LDH, lactate dehydrogenase.

Curran et al (4) made the interesting comment that the statistical analyses commonly used, such as the Cox model (9), are unstable with small series. Because mesothelioma has been a relatively rare form of cancer (at least until recent years), sample sizes have been small, and thus this statistical method may be unreliable. Curran discussed the conflicting data on the importance of patient age in predicting a poor outcome. At least four studies showed that age is not of importance (10–13), whereas several others suggested that it is (14–19). The same is true of gender, performance status, and histologic subtype (4).

Studies have also disagreed on the importance of stage as a prognostic marker. Perhaps surprisingly, stage was not found to be important as a prognostic factor in several studies (4,11,17). The main problem with the existing staging systems is that to obtain full information patients should have had cytoreductive surgery such as extrapleural pneumonectomy. Even at surgical referral centers, most patients are unable to have this operation, thus staging data reported in nonsurgical series are likely to be estimates based on radiology. Recent updates of the two largest surgical series (20,21) have confirmed that, as expected, patients staged surgically as stage I or II survive longer than those with advanced stage mesothelioma. Patients with epithelial cell type did so much better than those with nonepithelial cell type that some surgeons would not consider surgery for this latter group. Since 1998, two important studies have been published that have significantly clarified the important prognostic factors in mesothelioma (3,4). These are discussed below.

The Cancer and Leukemia Group B (CALGB) Prognostic Scoring System

The Cancer and Leukemia Group B (CALGB) examined the individual and joint effect of various pretreatment clinical characteristics on the survival of patients with mesothelioma treated with chemotherapy in a series of sequential phase II trials (3). Over a 10-year period, 337 untreated patients with malignant mesothelioma were registered in phase II studies of 10 different treatment regimens. The median overall survival for patients in these trials ranged from 3.9 to 9.8 months with 1-year survival figures ranging between 14% and 50%. The investigators then used Cox survival models and exponential regression trees to examine the prognostic importance of various pretreatment patient characteristics. The following factors were included:

1. ECOG performance status (PS 0, 1, 2)
2. Epithelial histology (yes/no)
3. Presence of chest pain (yes/no)
4. Presence of dyspnea (yes/no)
5. Duration of symptoms (<3 months, 3–6 months, >6 months)
6. Weight loss in the past 6 months (none or >5%)
7. Asbestos exposure (no/yes/unknown)
8. Smoking history (yes/no)
9. Lactate dehydrogenase (LDH) level >500 IU/L (yes/no)
10. Platelet count >400,000 /µL (yes/no)
11. Hemoglobin (Hb) level /µL (<14.6, ≥14.6)
12. White blood cell count (WBC) /µL (<8.7, ≥8.7)
13. Location of disease involvement (pleural/peritoneal/pericardial)
14. Extent of disease (local or regional/distant)

Survival curves were generated for subgroups defined by these putative prognostic factors, and survival comparisons were made. Patients were split into subgroups using an algorithm that maximized differences in the survival distribution measured by the log rank test. A stepwise analysis generated a regression tree with successive stratification into groups according to prognostic factor with progressively decreasing risk ratio.

**Univariate Analysis**

Comparison of the subgroups stratified by prognostic factor using the log rank test showed that the following factors were associated with worse outcome:

**Poor performance status (PS):** Median survival time got worse with increasing PS: for PS 0 survival was 10.9 months, for PS 1 survival was 7.6 months, and for PS 3 survival was only 3.3 months.

**Presence of chest pain:** Presence of chest pain was associated with a reduced median survival time of 5.4 months compared with 8.8 months for patients without chest pain.

**History of dyspnea:** A history of dyspnea was associated with reduced median survival time of 6.3 months compared with 8.3 months in the absence of dyspnea.

**High platelet count:** A platelet count >400,000 /µL was associated with a reduced median survival time of 6.2 months compared with 9.4 months for patients with a platelet count <400,000 /µL.

**Weight loss:** The median survival time in patients with significant weight loss was 5.1 months, and 7.9 months for patients not experiencing weight loss.

**Elevated LDH level:** An elevated LDH level of >500 IU/L was associated with a median survival time of 3.4 months, compared with 7.6 months for patients with an LDH level of <500 IU/L.

**Pleural involvement:** The presence of pleural involvement was associated with a reduced median survival time of 7.1 months compared with 12.3 months for patients without pleural involvement.

There was a statistically significant linear relationship for white blood cell count and hemoglobin with survival ($p < .001$ for both). An elevated hemoglobin and a low white blood cell count were associated with better prognosis. Age exhibited a statistically significant nonlinear relationship with survival, modeled by a combination of a linear effect of age, and a linear effect for the number of years older than 75 years of age.
Multivariate Analysis

Multivariate analysis was conducted for all variables on a subset of 195 patients in which all factors were measured. A raised serum LDH > 500 IU/L, poor performance status (i.e., PS 1 or 2), the presence of chest pain, an elevated platelet count > 400,000/μL, nonepithelial histology, and increasing age > 75 years were predictive of a greater risk of dying early. The six prognostic groups determined by using the regression tree and stepwise algorithm are shown in Table 27.2.

In conclusion, the CALGB prognostic scoring system was able to derive various factors strongly linked with a poor outcome for patients with mesothelioma. The most important predictors of a poor prognosis were poor PS, the presence of chest pain, the presence of pleural involvement, breathlessness as a major symptom, high platelet count, significant weight loss, raised LDH, low Hb, high WBC count, age over 75 years, and nonepithelioid histology. On the positive side, the statistical analysis was able to define the best prognostic groups as those containing patients with excellent performance status, age less than 49 years, and normal hemoglobin level.

The European Organization for Research and Treatment of Cancer (EORTC) Prognostic Scoring System

The European Organization for Research and Treatment of Cancer (EORTC) examined data from 204 adult patients with malignant mesothelioma entered into five consecutive EORTC phase II clinical trials from 1984 to 1993 (4). The drugs tested were mitoxantrone, epirubicin, etoposide, and paclitaxel. The Cox model was used to assess 13 factors related to biology and disease history with respect to survival.
The median survival duration was 8.4 months from trial entry and 12.6 months measured from diagnosis.

The putative prognostic factors studied in a total of 204 patients (all with pleural primary tumors) were:

1. Age (≤55 years, >55 years)
2. Interval since first diagnosis (≤50 days, >50 days)
3. Gender (female, male)
4. ECOG performance status (0, 1–2)
5. White blood cell count (<8.3 × 10⁹/L, ≥8.3 × 10⁹/L)
6. Platelet count (≤350 × 10⁹/L, >350 × 10⁹/L)
7. Hemoglobin difference (variance of <1 or ≥1 g/dL from stated normal)
8. Modified Butchart staging (I, II, III, IV)
9. Prior treatment (no, yes)
10. Alkaline phosphatase level (normal, abnormal)
11. Lactate dehydrogenase (normal, abnormal)
12. Histologic subtype (epithelial, sarcomatoid, mixed)
13. Certainty of histologic diagnosis (definite, probable/possible)

Continuous variables were divided into two groups with the median as the cutoff point. In the univariate analysis, poor prognosis was associated with five variables. In a multivariate analysis, poor prognosis was associated with:

1. Poor performance status (1 or 2)
2. High white blood cell count (≥8.3 × 10⁹/L)
3. Low hemoglobin level (<1 g/dL lower than normal)
4. Probable/possible histologic diagnosis of mesothelioma (i.e., uncertain diagnosis)
5. Sarcomatoid histology

Using these five factors the EORTC classified patients into two groups: a good-prognosis group (with a 1-year survival rate of 40%) and a poor-prognosis group (with a 1-year survival rate of 12%).

**Multivariate Analysis of the EORTC Prognostic Factors**

In a multivariate analysis the Cox multivariate model was based on all of the variables; the model retained the prognostic factors of age, performance status, certainty of histologic diagnosis, histologic subtype, and gender. Based on these five variables, a prognostic score ranging from 0.00 to 2.94 was determined by the following formula:

\[
\text{Prognostic score} = 0.55 \text{ (if WBC} > 8.3 \times 10^9/L) + 0.60 \text{ (if performance status 1 or 2)} + 0.52 \text{ (diagnosis is probable/possible)} + 0.67 \text{ (if sarcomatoid subtype)} + 0.6 \text{ (male gender)}
\]

Based on prognostic score, patients were divided into two groups: a good-prognosis group with a score ≤1.27 (corresponding to having zero, one, or two poor prognostic factors), and a poor-prognosis group.
with a score >1.27 (corresponding to having three, four, or five poor prognostic factors. Relative to patients in the low-risk group the high-risk group had a relative risk of 2.9 [95% confidence interval (CI) = 2.0% to 4.1%; \( p < .001 \)]. The median survival times were 10.8 months and 5.5 months for the low- and high-risk groups, respectively. The 1-year survival rates were 40% and 12%, respectively.

It is of concern that patients were randomized into phase II chemotherapy trials with “uncertain” diagnosis. Recent advances in our understanding of the immunohistochemistry of mesothelioma and the more widespread adoption of the multidisciplinary approach to diagnosis and treatment should make this a much rarer occurrence in the future. The EORTC authors made the interesting observation that patients with “uncertain” diagnosis may have appeared to live less long because more time was spent in trying to obtain a diagnosis prior to registration on trial (“lead time bias”).

**Validation of the CALGB and EORTC Prognostic Models by Other Groups**

Fennell et al (22) from the mesothelioma unit of St. Bartholomew’s Hospital, London, validated the EORTC model in a group of 145 patients treated in three sequential phase II chemotherapy trials. For the 70 patients treated with single-agent vinorelbine, those predicted as having good prognosis by the EORTC system had a median survival of 19.2 months (95% CI = 14.7–23.7) and those in the poor prognosis group had a median survival of 9.9 months (95% CI = 8.5–11.3).

In 2000 Edwards et al (23) from Leicester, United Kingdom, published a retrospective analysis of a series of 142 mesothelioma patients. Interestingly, some of these patients had had surgical intervention, whereas others were treated with chemotherapy or supportive care. Univariate analysis of prognostic variables was performed using a Cox proportional hazards regression model and statistically significant variables were analyzed further in a forward, stepwise multivariate model. The authors then derived EORTC and CALGB prognostic groups, plotted Kaplan-Meier survival, and calculated survival rates from life tables to see if these prognostic groups predicted outcome for their patients.

Significant poor prognostic factors in univariate analysis included male sex, older age, weight loss, chest pain, poor performance status, low hemoglobin, leukocytosis, thrombocytosis, and nonepithelial cell type. The prognostic significance of cell type, low Hb, high WBC, performance status, and gender was retained in the multivariate model. The overall median survival was 5.9 months. Median 1- and 2-year survival data within prognostic groups from Leicester were comparable to the EORTC and CALGB series. The authors concluded that the EORTC and CALGB prognostic scoring systems should be used both in the assessment of survival data of series in different countries and in the stratification of patients into randomized clinical studies.
Further observational data have been reported from the German Mesothelioma Register by Neumann et al (24). From 1987 to 2000, the German register recorded 4455 patients with malignant mesotheliomas. Survival data were only available for 498 patients of whom 156 survived for more than 2 years. The authors undertook a multivariate analysis using the Cox proportional hazards regression model and showed that the favorable prognostic factors were epithelioid subtype, age less than 60 years, and female gender.

What is interesting about these studies is the importance of systemic biologic measures of disease activity as prognostic factors. Low hemoglobin, high white blood cell count, elevated platelets, and elevated LDH were shown to be important in the CALGB, and high white blood cell count was important in the EORTC system. These parameters are likely to be markers of disease activity and may prove less subjective than some of the prognostic factors described previously such as age and approximate clinical stage. All specialists treating patients with mesothelioma are aware of the importance of systemic symptoms: weight loss, anorexia, lethargy, and night sweats are all frequently seen and refute the common view that mesothelioma is a localized disease that metastasizes only in the end stages. It is likely that these constitutional symptoms reflect the cytokine-rich nature of mesothelioma as described by Fitzpatrick (25). These reports may represent real progress in our understanding of malignant mesothelioma.

Novel Molecular Predictors of Prognosis

There have been a number of publications reporting biologic markers of prognosis in mesothelioma. Many of these markers are overexpressed in malignant mesothelioma and often there are statistical correlations with clinical outcome. The insights provided by such data are exciting and suggest real therapeutic progress is not far away. Some of the most interesting molecular factors are discussed below.

Cyclooxygenase (COX)-2

Cyclooxygenase-2 (COX-2) is an enzyme that catalyzes the initial rate-limiting reaction step in the synthesis of prostaglandins. Cyclooxygenase-2 expression is upregulated in several cancer types, including lung (26), breast (27), and colorectal (28), and is associated with increased tumor cell proliferation and invasiveness (2). Other studies have shown that COX-2 overexpression is a significant poor prognostic factor by univariate analysis in colorectal and gastric cancer, and in stage I adenocarcinoma of the lung. Cyclooxygenase-2 has been implicated in carcinogenesis through the promotion of angiogenesis, formation of carcinogenic metabolites such as malondialdehyde, and the downregulation of cell-mediated immunity via T-cell anergy (2).

Cyclooxygenase-2 is a target for novel, selective therapeutic intervention and is under investigation for the treatment of solid tumors. Marrogi et al (29) showed that COX-2 is overexpressed in malignant mesothelioma as well as in nonmalignant mesothelial tissues, and
demonstrated in vitro antiproliferative effects of the COX-2 inhibitor NS398. Nonmalignant mesothelial tissues—despite having similar levels of COX-2—were less sensitive to the antiproliferative activity of NS398. Marrogi et al suggested that COX-2 might therefore be a therapeutic target for mesothelioma.

Edwards et al (2) examined the expression of COX-2 and its prognostic significance in snap frozen malignant mesothelioma tissue collected at video-assisted thoracoscopic biopsy or thoracotomy. In 48 cases studied for COX-2 expression by immunohistochemistry, strong cytoplasmic staining was identified in all tissues studied. Expression did not correlate with measured levels of the stable prostaglandin E2 (PGE2) derivative bicyclo-PGE2. Specific COX-2 expression was identified using Western analysis. In univariate statistical analysis, high COX-2 expression on Western blot band densitometry correlated significantly with poor survival \( (p = .008) \). In multivariate analysis, high COX-2 expression \( (p = .0005) \), nonepithelioid subtype and chest pain were independent predictors of poor prognosis. The authors concluded that COX-2 expression is a prognostic factor for mesothelioma and is a possible therapeutic target. The studies by Edwards et al and Marrogi et al (29) suggest that COX-2 expression may independently predict survival in malignant mesothelioma and may provide a novel target for therapeutic intervention.

**Cyclin-Dependent Kinase Inhibitor p27**

The proliferation-associated antigen p27 (kip) is a cell-cycle regulator and cyclin-dependent kinase (CDK) inhibitor. It acts to regulate cell cycle entry into S-phase via direct interaction with cyclin and CDK. The prognostic value of the proliferation-associated antigen p27 has been investigated in malignant pleural mesothelioma (MPM). In a study by Beer et al (30), sections from 36 patients with MPM were immunohistochemically stained for the p27 antigen. Univariate survival analysis was used to determine the effect of p27 on survival. Low p27 expression (<53% of cells positive) was associated with a statistically significant decrease in survival compared with high p27 expression \( (p = .04) \). Median survival of patients with low p27 was 4 to 6 months, compared with those with high p27 for whom it was 10 to 11 months. The authors conclude that p27 may be an independent prognostic variable in patients with malignant mesothelioma.

Bongiovanni et al (31) also investigated p27 in 63 patients taken from a larger group of 621 pleural mesothelioma patients. Twenty-seven patients were selected with relatively long survival (>24 months), and 36 cases were selected as having a relatively shorter survival (<24 months). The expression of p27 was significantly higher in the long-term surviving group (81%) compared with the short survival group (32%; \( p < .0001 \)). Interestingly, epithelioid histology was associated with higher p27 expression compared with the biphasic type. It was concluded in both studies that p27 may be a useful marker for identifying patients with a more favorable prognosis.
Proliferation Marker MIB-1

MIB-1 is a marker of proliferation. Its expression and prognostic significance was evaluated by Comin et al (32) in a study comparing the immunoreactivity of a series of seven long-term survivors with MPM and a group of control cases with short-term survival. All cases showed MIB-1–positive cells determined by the percentage of nuclear staining. A statistical difference in expression of MIB-1 was observed with significantly greater proliferative activity in the shorter surviving group compared with the controls. A similar finding was also observed by others (31) and suggests that proliferative index may predict outcome for MPM patients.

Angiogenic Cytokines

Angiogenesis is essential for solid tumor proliferation. Malignant mesothelioma is associated with high intratumoral microvascular density, suggesting active angiogenesis. Vascular endothelial growth factor (VEGF), acidic and basic fibroblast growth factors (FGF-1 and -2), and transforming growth factor-β (TGF-β) are all potent angiogenic cytokines. In a study by Kumar-Singh et al (33), increased levels of VEGF, FGF-1, FGF-2, and TGF-β were detected in malignant mesothelioma compared to nonneoplastic mesothelium. When studied together, the levels of these angiogenic cytokines correlated with intratumoral microvascular density and prognosis. Of the cytokines studied individually only FGF-2 correlated with increased tumor invasiveness and worse prognosis.

Ohta et al (34) investigated the prognostic significance of the messenger RNA expression of VEGF, VEGF type C, and their receptors, together with microvessel and microlymphatic density. Fifty-four patients were studied. Vessel density was a negative prognostic indicator that correlated with VEGF expression, indicating an important role for angiogenesis in malignant mesothelioma and the use of vascular density as a prognostic marker.

Glycoprotein 90K

Strizzi et al (35) examined the levels of tumor-associated glycoprotein 90K in the pleural effusions and sera of patients with malignant mesothelioma using enzyme-linked immunosorbent assay (ELISA). This was correlated with immunocytochemistry in malignant mesothelioma sections and compared with benign pleural disease. The average level of glycoprotein 90K was increased in pleural effusions from patients with malignant mesothelioma compared with those of patients with benign pleural disease. Expression of 90K was observed using immunohistochemistry. A positive correlation between 90K and patient survival was reported; using Kaplan-Meier univariate analysis a high serum level of 90K was shown to be associated with a statistically significant increase in survival probability.
Conclusion

Patients with good and poor prognosis can now be determined by well-validated prognostic factors based on the EORTC and CALGB scoring systems. These distinct, but closely related systems, have clarified much contradictory data accrued over the past two decades. The most important poor prognosis predictors are poor performance status, nonepithelial histology, male gender, low hemoglobin, high platelet count, high white blood cell count, and high LDH. In addition to prognostic information these systems have led to insights into the biology of mesothelioma, in particular, the possible role played by cytokine networks in the symptoms experienced by patients with mesothelioma. Prognostic factors may, at last, not simply enable us to predict a worse outcome for some patients compared to others, but help us understand mesothelioma and develop new treatments. Numerous molecular biologic markers of prognosis are under investigation. Overexpression of various cellular proteins has been demonstrated to correlate with the clinical outcome in the source patients. Understanding the importance of these markers in predicting prognosis will lead to better understanding of malignant mesothelioma and will help improve therapy.

References


