A Proposed New International TNM Staging System for Malignant Pleural Mesothelioma*

From the International Mesothelioma Interest Group†

Study objective: Investigation of the behavior and treatment of diffuse malignant pleural mesothelioma (MPM) is hindered by the lack of an accurate universally accepted staging system. To address this problem, the International Mesothelioma Interest Group (IMIG) has developed a new TNM-based staging system.

Methods: The staging system was developed at a consensus meeting of IMIG members involved in clinical research in MPM, including the originators of previously proposed staging systems. The new staging system is based on the analysis of emerging information about the impact of T and N status on survival.

Results: In contrast to five previous staging systems, the T descriptors designated as T1, T2, T3, and T4, provide precise anatomic definitions of the local extent of the primary tumor. The N descriptors, designated as N0, N1, N2, and N3, are virtually identical to those used in the International Lung Cancer Staging System. The stage groupings recognize new data about the better prognosis of T1 and N0 tumors and classify those tumors into stages I and II. The adverse impact of nodal metastases on survival noted in some recent surgical series warrants placing node-positive tumors in stage III. Locally advanced unresectable (T4) tumors and extrathoracic disease (N3 or M1) are classified as stage IV.

Conclusion: This proposed staging system reconciles and updates several earlier systems, and can provide the framework for analyzing the results of prospective clinical trials aimed at improving the currently dismal prognosis of MPM. *(CHEST 1995; 108:1122-28)*

IMIG=International Mesothelioma Interest Group; MPM=malignant pleural mesothelioma; TNM=tumor, node, metastasis

Key words: malignant mesothelioma; prognosis; staging

Diffuse malignant pleural mesothelioma (MPM) is an uncommon cancer. However, management of this disease is becoming important because its worldwide incidence is increasing, and because it is still uniformly fatal. In contrast to other malignancies, prospective clinical trials in the treatment of MPM have been undertaken only recently. They are hindered by the small number of patients seen at any single institution, by a poor understanding of the natural history of MPM, and by the lack of an accurate and uniformly accepted staging system. During the past 20 years, several staging systems have been proposed, but none are completely validated or universally used.[1] Some of these systems are based on a tumor node metastases (TNM) system, whereas others use a classification of stages I through IV without precise TNM descriptors (Tables 1-5). The various staging systems have been erratically applied to survival analyses. Consequently, it is impossible to interpret and compare results of most reported series or to determine if a specific treatment, such as surgical resection, has a true impact on survival. There is a pressing need for prospective multi-institutional clinical trials investigating novel treatment strategies for MPM, but these cannot be performed without an internationally accepted staging system that permits accurate stratification of patients into groups with a relatively similar prognosis.

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The International Mesothelioma Interest Group (IMIG) brings together pulmonary medicine physicians, thoracic surgeons, medical and radiation oncologists, epidemiologists, radiologists, pathologists, and laboratory scientists involved in research in MPM. All

Table 1—*Staging Proposed by Butchart et al*[2]

Stage No.	Description
I	Tumor confined within the "capsule" of the parietal pleura, *ie*, involving only ipsilateral pleura, lung, pericardium, and diaphragm
II	Tumor invading chest wall or involving mediastinal structures, *eg*, esophagus, heart, opposite pleura. Lymph node involvement within the chest
III	Tumor penetrating diaphragm to involve peritoneum; involvement of opposite pleura. Lymph node involvement outside the chest
IV	Distant blood-borne metastases

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Table 2—*Staging Proposed by Mattson*[3]

Stage No.	Description
I	Ipsilateral pleura and lung only
II	Chest wall invasion, mediastinal or pericardial involvement, contralateral lung or pleural involvement
III	Extrathoracic extension (a) Nodes outside chest (b) Diaphragmatic penetration to peritoneum
IV	Distant metastases

Table 3—*Proposed Staging System for Mesothelioma Patients Based on Survival of 52 Patients**

Stage No.	Definition
I	Disease confined to within capsule of the parietal pleura: ipsilateral pleura, lung, pericardium, diaphragm, or chest-wall disease limited to previous biopsy sites
II	All of stage I with positive intrathoracic (N1 or N2) lymph nodes
III	Local extension of disease into: chest wall or mediastinum; heart, or through diaphragm, peritoneum; with or without extrathoracic or contralateral (N3) lymph node involvement
IV	Distant metastatic disease

*Adapted from Sugarbaker et al.[6]

Table 4—*Staging Proposed by Chahinian*[4]

Stage No.	Description*
I	T1N0M0
II	T1-2N1M0 T2N0M0
III	T3, any N,M0
IV	T4, and N,M0, any M1

*T=primary tumor; T1=limited to ipsilateral pleura only (parietal pleura, visceral pleura); T2=superficial local invasion (diaphragm, endothoracic fascia, ipsilateral lung, fissures); T3=deep local invasion (chest wall beyond endothoracic fascia); T4=extensive direct invasion (opposite pleura, peritoneum, retroperitoneum); N=lymph nodes; N0=no positive lymph node; N1=positive ipsilateral hilar nodes; N2=positive mediastinal nodes; N3=positive contralateral hilar nodes; M=metastases; M0=no metastases; M1=metastases, blood-borne or lymphatic.

previously proposed systems for MPM were developed by IMIG members based on their individual institutional experiences.[1-6] The clear need for an internationally accepted staging system prompted a group of IMIG members interested in this issue to hold a consensus meeting in June 1994 during the Seventh World Conference of the International Association for the Study of Lung Cancer. The new International TNM Staging System for MPM presented herein is the re-

Table 5—*Staging System Proposed by UICC**

T—primary tumor and extent		
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1		Primary tumor limited to ipsilateral parietal and/or visceral pleura
T2		Tumor invades any of the following: ipsilateral lung, endothoracic fascia, diaphragm, pericardium
T3		Tumor invades any of the following: ipsilateral chest wall muscle, ribs, mediastinal organs, or tissues
T4		Tumor extends to any of the following: contralateral pleura or lung by direct extension, peritoneum or intra-abdominal organs by direct extension, cervical tissues
N—lymph nodes		
Nx		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastases
N1		Metastases in ipsilateral bronchopulmonary or hilar lymph nodes
N2		Metastases in ipsilateral mediastinal lymph nodes
N3		Metastases in contralateral mediastinal, internal mammary,—supraclavicular, or scalene lymph nodes
M—metastases		
Mx		Presence of distant metastases cannot be assessed
M0		No (known) distant metastasis
M1		Distant metastasis present
Stage grouping		
Stage I	T1N0M0	
	T2N0M0	
Stage II	T1N1M0	
	T2N1M0	
Stage III	T1N2M0	
	T2N2M0	
	T3N0M0	
	T3N1M0	
	T3N2M0	
Stage IV	Any T, N3M0	
	T4, any NM0	
	Any T, any NM1	

*From American Joint Committee on Cancer, Handbook for Staging of Cancer. 4th ed. Philadelphia: JB Lippincott Co, 1993; 137-38.

sult of that meeting. It reconciles the multiple previous staging systems, provides a staging system similar to those used for other solid tumors, and takes into consideration recent data regarding the influence of T and N status on overall survival in MPM.

Materials and Methods

The IMIG members listed in Appendix I who have been primary authors of large retrospective series or principal investigators in clinical trials in MPM presented their data with respect to the influence of T and N status and of other potential prognostic factors on overall survival. These data were used to create a TNM-based system that potentially can be applied to the radiographic, surgical, and pathologic staging of MPM. The precise TNM descriptors were developed by consensus during the meeting and were later critically reviewed by a large number of IMIG members (Appendices 1 and 2), including the originators of five previously proposed staging systems for MPM.

Results

The proposed new International Staging System for MPM is shown in Table 6. It includes precise TNM descriptors that are grouped into a stage I through IV classification. Though potentially applicable to radiographic staging by CT scan, these TNM descriptors are primarily based on surgical and pathologic findings.

T1 is divided into 1a and 1b. T1a describes a very early tumor that involves only the ipsilateral parietal pleura with or without tumor on the diaphragmatic or mediastinal pleura. The visceral pleura is not involved. T1b describes an early but slightly more advanced tumor that involves all pleural surfaces, including the visceral pleura. However, the involvement of the visceral pleura is still minimal, and is manifested by scattered areas of tumor studding. Patients with T1 disease usually have a free pleural space and present with a large pleural effusion.

The distinction between T1a and T1b is based on the unique report of Boutin et al[7] of 66 patients whose tumors were carefully staged by thoracoscopy. In this series, the 23 patients with T1a tumors had a median survival of 32.7 months, whereas the 43 patients with T1b tumors had a median survival of 7 months. The extensive thoracoscopic experience of Boutin et al in MPM suggests that tumor arises in the parietal and diaphragmatic pleura, then spreads to the visceral pleura.[7] The prolonged survival seen in patients with subtle thoracoscopic findings and biopsy specimen-proved T1a tumors explains some of the variation in survival rates in early reports (Table 7). If the tumors of patients are staged noninvasively, it is difficult to determine whether T1a, T1b (or even T2) disease is present. However, these T stages appear to have a different prognosis when documented surgically.

T2 designates a tumor that is more advanced that T1b by virtue of confluent involvement of the visceral pleura and/or extension of the pulmonary parenchyma, such that the pleural tumor cannot be fully removed without resecting the underlying lung. Usually, the diaphragmatic muscle is also involved by tumor. Patients with T2 disease may still have a free pleural space with an effusion, but the parietal and visceral pleural surfaces have often begun to fuse. As such, the pleural effusion may have resolved or be loculated.

Although the difference in tumor extent between T1b and T2 is quite obvious at thoracotomy, it may be difficult to determine at thoracoscopy whether the diaphragmatic muscle is involved or tumor penetrates into the underlying pulmonary parenchyma. The difference between T1b and T2 has important implications for patients being considered for surgical resection. Complete removal of all gross T2 disease may require an extrapleural pneumonectomy, whereas T1b tumor might be amenable to resection by pleurectomy/decortication. Less survival data are available to support the distinction between T1b and T2 than between T1a and T1b tumors. A recent series in which 131 patients underwent thoracotomy for possible resection of malignant pleural mesothelioma showed that the 18 patients with T1 tumors had a significantly better overall survival than did the 36 patients with T2 tumors. However, the number of patients with T1 tumors was too small to allow a statistically valid comparison of survival rates among the subsets of T1a, T1b, and T2 tumors.[8] Pending further survival data comparing T2 with T1b tumors as documented at thoracotomy, IMIG members believed that this distinction was warranted considering the potential therapeutic implications.

T3 describes a locally advanced tumor that is still potentially amenable to surgical resection of all gross disease. In addition to involvement of all the pleural surfaces, there may be areas of tumor extension into the endothoracic fascia or the mediastinal fat. The surface of the pericardium may be involved such that partial pericardiectomy rather than just removal of the mediastinal pleura overlying the pericardium is required. A solitary, completely resectable focus of tumor extending directly into the chest wall is also included in the T3 category. This usually occurs in patients who have a tumor implant in the chest wall at the site of a previous diagnostic thoracentesis, pleural biopsy, or thoracoscopy. It is also occasionally seen in patients who present with a dominant parietal pleural mass. Although to our knowledge there are no data to indicate that a specific size limitation should be placed on the area of chest wall involvement, the concept of focal direct extension of tumor is similar to that employed in the T3 category of the lung cancer staging system. This is surgically quite distinct from a very locally advanced tumor that is technically unresectable because it diffusely invades the intercostal or chest wall muscles.

T4 designates a very locally advanced and technically

unresectable tumor. In addition to involvement of all the pleural surfaces, T4 is characterized by features including diffuse extension of tumor into the chest wall, direct extension through the diaphragm to the underlying peritoneum, or direct extension to the contralateral pleura, the mediastinal organs, the spine, the myocardium, or the internal surface of the pericardium.

Among patients with more locally advanced tumors,

Table 6—*New International Staging System for Diffuse MPM*

T1	
	T1a Tumor limited to the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura No involvement of the visceral pleura
	T1b Tumor involving the ipsilateral parietal pleura, including mediastinal and diaphragmatic pleura Scattered foci of tumor also involving the visceral pleura
T2	Tumor involving each of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features: • involvement of diaphragmatic muscle • confluent visceral pleural tumor (including the fissures) or extension of tumor from visceral pleura into the underlying pulmonary parenchyma
T3	Describes locally advanced but potentially resectable tumor Tumor involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features: • involvement of the endothoracic fascia • extension into the mediastinal fat • solitary, completely resectable focus of tumor extending into the soft tissues of the chest wall • nontransmural involvement of the pericardium
T4	Describes locally advanced technically unresectable tumor Tumor involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral) with at least one of the following features: • diffuse extension or multifocal masses of tumor in the chest wall, with or without associated rib destruction • direct transdiaphragmatic extension of tumor to the peritoneum • direct extension of tumor to the contralateral pleura • direct extension of tumor to one or more mediastinal organs • direct extension of tumor into the spine • tumor extending through to the internal surface of the pericardium with or without a pericardial effusion; or tumor involving the myocardium
N—Lymph nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastases in the ipsilateral bronchopulmonary or hilar lymph nodes
N2	Metastases in the subcarinal or the ipsilateral mediastinal lymph nodes, including the ipsilateral internal mammary nodes
N3	Metastases in the contralateral mediastinal, contralateral internal mammary, ipsilateral, or contralateral supraclavicular lymph nodes
M—Metastases	
MX	Presence of distant metastases cannot be assessed
M0	No distant metastasis
M1	Distant metastasis present

Stage:	Description:
Stage I	
Ia	T1aN0M0
Ib	T1bN0M0
Stage II	T2N0M0
Stage III	Any T3M0 Any N1M0 Any N2M0
Stage IV	Any T4 Any N3 Any M1

the distinction between T3 and T4 has obvious implications with respect to surgical resection and, apparently significant differences in survival. In one series, the median survival for T3 tumors was 13 months and for T4 tumors 6.5 months.[8] MPM, particularly the epithelial form, often progresses to T4 status before distant metastatic disease is present, but T4 tumors appear to be associated with an equally dismal prognosis as M1 disease.[7,9]

The descriptors for the N status are virtually identical to those used in the International Lung Cancer Staging System.[10] N1 describes involvement of the ipsilateral bronchopulmonary and hilar lymph nodes, and N2 of the subcarinal or ipsilateral mediastinal lymph nodes and the ipsilateral internal mammary nodes. N3 designates metastases in the contralateral mediastinal, contralateral internal mammary, or the ipsilateral or contralateral supraclavicular lymph nodes.

The frequency of nodal involvement and its prognostic implications have only recently been investigated. Among patients undergoing a relatively uniform treatment regimen of extrapleural pneumonectomy and adjuvant chemotherapy and radiation, Sugarbaker et al[6] found that the 39 patients with normal nodes had a significantly better survival than the 13 patients with abnormal nodes. The adverse influence of nodal involvement is not evident in some other surgical series.[11] However, analysis of this variable is confounded by the small numbers of patients in most reports, a lack of routine complete nodal sampling, and the retrospective nature of many analyses. The true incidence of nodal involvement and the routes of lymphatic spread are poorly understood. It is possible that N2 nodes, and the internal mammary nodes, may become involved before N1 nodes because of the anatomic extent of MPM and the fact that it apparently arises in the parietal and diaphragmatic pleurae. Recent analysis of another surgical series of 89 patients who underwent systematic mediastinal lymph node dissection confirms that nodal involvement is associated with a significantly worse median survival (18.3 months for N0 tumors vs 9.4 months for any nodes that are abnormal).[8] The frequency of nodal metastases was substantially higher in this series (50% of patients) than in the experience of Sugarbaker et al (25% of patients) and emphasizes the importance of systematic nodal dissection in elucidating the impact of nodal metastases on survival. The anatomic distinction among N1, N2, and N3 nodes is familiar to all physicians caring for patients with thoracic neoplasms. It is preserved in this staging system in order to facilitate further study of the prognostic implications of metastatic disease in these nodal subsets. However, the currently available survival data are insufficient to distinguish among these nodal subsets with respect to staging. Therefore, both N1 and N2 disease are grouped with stage III.

Table 7—*Results of Supportive Care Only

Study	No. of Patients	% Survival 1-yr	% Survival 2-yr	Median, mos
Law et al[24]	64	77	31	15.0†
Hulks et al[15]	68	NS§	NS	7.0
Ruffie et al[25]	176	NS	NS	6.8
Caensler et al	15	NS	20	15.8†
Lewis et al[23]	14	NS	NS	9.6†

*Adapted from Allen et al.[11]
†Survival calculated from onset of symptoms rather than diagnosis.
‡Average rather than median survival.
§NS=not stated.

The descriptors for M status are identical to those used for all other solid tumors. M0 designates no evidence of metastatic disease, whereas M1 describes the presence of metastases outside of the ipsilateral hemithorax. A common site of progression or recurrence in patients with MPM is the peritoneum. This may occur by direct extension of tumor through the diaphragm (T4 tumor) or as a result of lymphatic or hematogenous dissemination. However, the prognosis appears to be similar no matter what the route of tumor spread.

These TNM descriptors are used to characterize four stages of disease. Stages I and II include only node-negative tumors. Stage I is subdivided into Ia and Ib based on the difference in T status between T1a and T1b. Stage II includes only T2N0 tumors. Stage III includes any T3, any N1, or any N2,M0 tumors. Stage IV includes any T4, N3, or M1 tumors.

Discussion

Until 30 years ago, MPM was thought to be a rare and idiopathic tumor. The link between asbestos exposure and the subsequent development of MPM was first established in 1960 by Wagner et al.[12] Because of the histologic similarities between the epithelial form of MPM and adenocarcinoma, accurate pathologic diagnosis of MPM was initially challenging. It only became routine with the advent of electron microscopy and the increasing use of immunohistochemistry.[13,14] The importance of CT scanning and MRI in the noninvasive staging of MPM, their marked superiority to plain chest radiography, but their significant inaccuracy relative to surgical and pathologic staging have only recently been documented.[15,16] Aside from a few small surgical series, including a seminal report by Butchart et al[2] in 1976, little effort was made to stage MPM precisely. It was largely viewed as a tumor that presented with involvement of all pleural surfaces and encasement of the lung, and that inevitably led to death within 2 years of diagnosis because of cardiopulmonary failure from locally progressive disease.[17-25] Yet a wide and seemingly inexplicable range of median survival rates from 6 to 18

months were reported in various series (Table 7). Infrequent cases of survival beyond 4 years, with or without treatment are well recognized. A lack of understanding of the natural history and of the biology of MPM and its apparently capricious behavior have engendered a sense of nihilism and a disorganized approach to the study of this disease.

The critical importance of an accurate staging system and of identifying significant prognostic factors is well accepted in the study and treatment of all other solid tumors. For instance, the management of non-small cell lung cancer evolved dramatically during the past 20 years as a result of intensive study of its natural history. This led to a new international staging system in 1986[10] which in turn facilitated the selection of patients for surgical resection and the investigation of novel treatment strategies such as neoadjuvant therapy for stage IIIA(N2) disease. Meticulous staging of tumors of patients with non-small cell lung cancer now allows identification of homogeneous groups of patients according to prognosis. It would be impossible to determine whether a specific form of therapy was beneficial if patients with T1N0 tumors were grouped together with patients with M1 tumors. To improve the dismal prognosis of MPM, systematic staging and classification of patients by known prognostic factors must be applied in prospective multi-institutional clinical trials.

At least five staging systems for MPM have been proposed previously. Three of these utilize a simple stage I through IV classification without specific TNM descriptors (Tables 1-3). Two of them are TNM based (Tables 4 and 5). None of them has been uniformly used for survival analyses in reported series, although the Butchart et al[2] system (Table 1) is cited most frequently. All five systems are to some extent imprecise and incompletely validated.

The staging system presented herein builds on the previous staging systems but incorporates very specific TNM descriptors based on emerging information about the natural history of MPM. Because of these more recent survival data, the stage groupings represent a departure from previous staging systems. This new staging system separates out subsets of patients with early tumors. Previously, these categories were grouped together. The rationale for placing T1aN0 tumors in stage I, T3 tumors and N1-2 tumors in stage III, and T4 tumors, N3, and M1 disease in stage IV is now solid. A more difficult issue is where to place T1b and T2N0 tumors. Given the data of Boutin et al,[7] it is possible that both belong in stage II. Additional data in large numbers of patients with tumors staged at thoracotomy and not just by thoracoscopy are needed to clarify this. Some individuals may object to the concept of recognizing the T1 and T2N0 subsets by separating them into stages I and II, because historically, the number of patients diagnosed with such early tumors has been small. However, the rising incidence of MPM and the increasing use of thoracoscopy for its early diagnosis[26] and the apparently better prognosis of these tumor subsets justify this stage grouping.

This staging system presumes that most patients with early tumors are evaluated surgically and pathologically by thoracoscopy, thoracotomy, and possibly, mediastinoscopy. Discrepancies between radiographic staging by CT or MRI and surgical staging are well recognized, particularly with respect to chest wall, diaphragmatic, mediastinal, and nodal involvement. In many respects, these discrepancies are similar to those seen in the radiographic staging of lung cancer.[15,16] However, the TNM descriptors used in this system are potentially applicable to CT or MRI interpretation. Were CT or MRI routinely coupled with thoracoscopy, mediastinoscopy, and directed biopsies of other sites, it is possible that this staging system could stratify patients in clinical trials that do not include thoracotomy and surgical resection.

No TNM staging system fully recognizes the pathologic and biologic variables that influence survival. Many factors are reported to be prognostic in MPM, including histology, age, gender, performance status, type of symptoms, weight loss, history of asbestos exposure, and platelet count (A. P. Chahinian, personal communication).[11,22,25,27-31] Of these, only histologic condition appears to be universal across all reported series. Epithelial histologic condition is always associated with a significantly better outcome than other cell types. The sarcomatous and desmoplastic histologic features appear to have an even worse prognosis than do tumors of mixed histologic features. While the TNM staging system presented herein can accurately describe the anatomic extent of disease, clinical trials should stratify for histologic features for the purposes of survival analysis. Moreover, little is currently known about the molecular biology of MPM. A staging system can separate patients into relatively homogeneous groups but does not account for variations in behavior within a given TN subset that can be explained only by differences in tumor biology. Future investigation may detect important biologic abnormalities that affect the clinical staging of tumors of patients with MPM.

The fund of knowledge about the behavior and treatment of MPM is still rudimentary and can be equated with our understanding of lung cancer 40 years ago. This proposed system is not intended to be definitive or to justify certain types of treatment such as surgical resection. It merely forms an internationally agreed on basis for future prospective studies that will allow refinements in the staging system and will permit accurate assessment of new treatment regimens. Only systematic study of the natural history of this cancer combined with earlier diagnosis by thoracos-

copy and careful investigation of novel treatment strategies in properly selected patients will ultimately alter the dismal outcome of this disease. The new international staging system presented herein provides a framework in which these studies can be performed.

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APPENDIX 1

The following members of the International Mesothelioma Interest Group were the major contributors to the development of this new staging system: Dr. Joseph Aisner, Newark, NJ; Dr. Christian Boutin, Marseille, France; Dr. Eric G. Butchart, Cardiff, Wales, UK; Dr. Philippe Chahinian, New York; Dr. L. Penfield Faber; Chicago; Dr. Robert Heelan, New York; Dr. Karin Mattson, Helsinki, Finland; Dr. Harvey I. Pass, Bethesda, Md; Dr. Edward F. Patz, Jr, Durham, NC; Dr. Bruce Robinson, Perth, Australia; Dr. Valerie W. Rusch, New York; Dr. Lauri Tammilehto, Helsinki, Finland; and Dr. Nicholas J. Vogelzang, Chicago.

APPENDIX 2

Dr. Seena Aisner, Newark, NJ; Dr. Karen H. Antman, New York; Dr. Chandra P. Belani, Pittsburgh; Dr. Jean Bignon, Créteil, France; Dr. Ola Brodin, Uppsala, Sweden; Dr. Richard Feins, Rochester, NY; Dr. Robert Ginsberg, New York; Dr. Samuel Hammar, Bremerton, Wash; Dr. James Herndon, Durham, NC; Dr. Gunna Hillardel, Stockholm, Sweden; Dr. David Ilson, New York; Dr. Steven Keller, New York; Dr. David Kelsen, New York; Dr. Mark Krasna, Baltimore; Dr. Paula Maasilta, Helsinki, Finland; Dr. Isabelle Monnet, Créteil, France; Dr. Victor L. Roggli, Durham, NC; Dr. Pierre Ruffié, Villejuif, France; Dr. Ullastina Salminen, Helsinki, Finland; Dr. Leonard Saltz, New York; Dr. Gary Strauss, Boston; Dr. Jean-Regis Viallat, Marseille, France; and Dr. Friedrich von Bültzingslöwen, Donaustauf, Germany.

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