

Guidelines for the Evaluation of Impairment/Disability in Patients with Asthma

BACKGROUND

The 1982 and 1986 American Thoracic Society (ATS) statements (1, 2) on the evaluation of impairment and disability caused by respiratory disorders were primarily of relevance for patients with respiratory disorders associated with irreversible damage. Asthma was dealt with only as a modifying condition. Patients with asthma have features that differ from other respiratory disorders, including: (1) The condition is characterized by variable airflow obstruction and the individual's clinical status varies from time to time; (2) the airflow limitation is partially or completely reversible with appropriate therapy; (3) the condition is associated with airway hyperresponsiveness to irritants such as dusts, fumes, gases, or smoke; (4) in many cases, environmental or occupational exposure to specific sensitizers provokes airway inflammation, which, on repeated exposure may become chronic and irreversible. Specific guidelines for patients with asthma are necessary because of these features.

PURPOSE

The purpose of this statement is to provide specific guidelines for the determination of impairment and disability in subjects with asthma for use by health professionals and disability boards. It takes into consideration not only impairment related to reduced lung function but other parameters, such as the degree of airway hyperresponsiveness and the type and amount of medication required to control symptoms, which are important reflections of the severity of asthma (3). This statement does not address the methods of identification of the cause of asthma.

DEFINITIONS

The definitions used by the previous ATS statement (2) will be used here.

Impairment is defined as a functional abnormality resulting from a medical condition. It may or may not be stable at the time the evaluation is made, and may be temporary or permanent. Impairment that persists after appropriate therapy, with no prospect of future improvement, is permanent. Some impairments are not dependent on lung function, but are related to the prognosis (e.g., unresectable lung cancer) or to public health considerations (e.g., tuberculosis) or inability to work in the same environment that causes asthma (e.g., occupational asthma).

Disability is a term used to indicate the total effect of impairment on the patient's life. It is affected by diverse factors such as age, sex, education, economic and social environment, and the energy requirement of the occupation.

Two people with identical impairment may be differently affected in their life situations. The rating of health impairment is within the jurisdiction of a physician's expertise to quantitate. However, the determination of disability also requires consideration of many

nonmedical variables. Physicians, however, generally have considerable knowledge about how impairment affects their patients' lives. Therefore it is important for physicians to identify all the individual factors modifying the impact of impairment on their patients' lives for administrators who determine disability compensation.

DIAGNOSIS OF ASTHMA

Asthma should be suspected in the presence of a compatible history of cough, sputum, wheeze, chest tightness, or breathlessness, particularly when the symptoms are episodic and worse at night (4). The diagnosis of asthma requires both relevant symptoms (currently or by history) and the presence of airflow limitation that is partially or completely reversible either spontaneously or after treatment, or the presence of airway hyperresponsiveness to methacholine or histamine in the absence of airflow limitation.

In the presence of severe airflow limitation, it may not be possible to distinguish between asthma and other types of obstructive lung disease. Additional diagnostic criteria should be considered such as the presence of blood or sputum eosinophilia.

METHODS

Measurement of Spirometry

Spirometric measurements should be carried out using equipment, methods of calibration, and techniques that meet the criteria outlined in the most recent revision (5) of the ATS official statement on standardization of spirometry (6), or subsequent revisions of that statement, whichever is most current. The measurement of height, prediction equations, and corrections for racial differences should follow those outlined in the ATS official statement on "Lung Function Testing: Selection of Reference Values and Interpretational Strategies" (7).

Spirometric measurements should be made, if possible, after withholding inhaled bronchodilators for 6 h and long-acting bronchodilators (e.g., long-acting theophylline preparations) for 24 h. However, if it is not possible to withhold bronchodilators for this period of time, they can be used, but the time these medications are taken before the test should be noted. Antiinflammatory preparations such as cromolyn, inhaled or systemic corticosteroid should not be withheld.

FEV₁, FVC, and FEV₁/FVC should be determined from spirometry. When airflow limitation is present, i.e., FEV₁/FVC is less than the lower limit of normal, which is defined as the lowest 5% of the reference population (7), spirometry should be repeated after the administration of an inhaled β -adrenergic agonist. An improvement in FEV₁ of 12% or greater, with an absolute change of at least 200 ml, from the baseline level, confirms that there is significant reversibility, and together with the appropriate history, the diagnosis of asthma (7). When the improvement in FEV₁ is < 12%, a steroid trial should be given. This can be given as high-dose inhaled steroid (> 800 mcg beclomethasone or equivalent/day) although prednisone 30 to 40 mg for a period of 1 to 2 wk may

- tients with severe COPD. *Chest* 1990; 97:322-7.
31. Zibrak JD, Hill NS, Federman ED, Kwa SL, O'Donnell C. Evaluation of intermittent long-term negative pressure ventilation in patients with severe chronic pulmonary disease. *Am Rev Respir Dis* 1988; 138:1515-28.
 32. Celli B, Lee H, Criner G, Bermudez M, Rassulo J, Gilmartin M, Miller G, Make B. Controlled trial of external negative pressure ventilation in patients with severe airflow limitation. *Am Rev Respir Dis* 1989; 140:1251-6.
 33. Shapiro SH, Ernst P, Gray-Donald K, Martin JG, Wood-Dauphinee S, Beaupré A, Spitzer WO, Macklem PT. Effect of negative pressure ventilation in severe pulmonary disease. *Lancet* 1992; 340:1425-29.
 34. Elliott MW, Mulvey DA, Moxham J, Green M, Branthwaite MA. Domiciliary nocturnal nasal intermittent positive pressure ventilation in COPD: Mechanisms underlying changes in arterial blood gas tensions. *Eur Respir J* 1991; 4:1044-52.
 35. Piper AJ, Parker S, Torzillo PJ, Sullivan CE, Bye PTP. Nocturnal nasal IPPV stabilized patients with cystic fibrosis and hypercapnic respiratory failure. *Chest* 1992; 102:846-50.
 36. Elliott M, Carroll M., Wedzicha J, Branthwaite M. Nasal positive pressure ventilation can be used successfully at home to control nocturnal hypoventilation in COPD (abstract). *Am Rev Respir Dis* 1990; 141:322.
 37. Roussos C. Function and fatigue of respiratory muscles. *Chest* 1985; 88:1245-315.
 38. Rochester DF, Braun NMT, Lane S. Diaphragmatic energy expenditure in chronic respiratory failure. *Am J Med* 1977; 63:223-32.
 39. Carrey Z, Gottfried SB, Levy RD. Ventilatory muscle support in respiratory failure with nasal positive pressure ventilation. *Chest* 1990; 97:150-8.
 40. Hoepfner VH, Cockcroft DW, Dosman JA, Cotton DJ. Nighttime ventilation improves respiratory failure in secondary kyphoscoliosis. *Am Rev Respir Dis* 1984; 129:240-3.
 41. Bergofsky EH. Respiratory failure in disorders of the thoracic cage. *Am Rev Respir Dis* 1979; 119:643-69.
 42. Hill NS, Eveloff SE, Carlisle CC, Goff SG. Efficacy of nocturnal nasal ventilation in patients with restrictive thoracic disease. *Am Rev Respir Dis* 1992; 145:365-71.
 43. McClement JH, Christianson LC, Hubayton RT, Simpson DG. The body-type respirator in the treatment of chronic obstructive pulmonary disease. *Ann NY Acad Sci* 1965; 121:746-50.
 44. Fraimow W, Cathcart RT, Goodman E. The use of intermittent positive pressure breathing in the prevention of the carbon dioxide narcosis associated with oxygen therapy. *Am Rev Respir Dis* 1960; 81:815-22.
 45. Sauret JM, Guitart AC, Rodriguez-Frojan G, Cornudella R. Intermittent short-term negative pressure ventilation and increased oxygenation in COPD patients with severe hypercapnic respiratory failure. *Chest* 1991; 100:455-9.
 46. Meduri GU, Conoscenti CC, Menashe P, Nair S. Noninvasive face mask ventilation in patients with acute respiratory failure. *Chest* 1989; 95:865-70.
 47. Brochard L, Isabey D, Piquet J, et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med* 1990; 323:1523-30.
 48. Marino W. Intermittent volume cycled mechanical ventilation via nasal mask in patients with respiratory failure due to COPD. *Chest* 1991; 99:681-4.
 49. Pennock BE, Kaplan PD, Carlin BW, Sabangan JS, Magovern JA. Pressure support ventilation with a simplified ventilatory support system administered with a nasal mask in patients with respiratory failure. *Chest* 1991; 100:1371-6.
 50. Chevrolet JC, Jolliet P, Abajo B, Toussi A, Louis M. Nasal positive pressure ventilation in patients with acute respiratory failure. *Chest* 1991; 100:775-82.
 51. Benhamou D, Girault C, Faure C, Portier F, Muir JF. Nasal mask ventilation in acute respiratory failure. *Chest* 1992; 102:912-7.
 52. Udawadia ZF, Santis GK, Stevan MH, Simonds AK. Nasal ventilation to facilitate weaning in patients with chronic respiratory insufficiency. *Thorax* 1992; 47:715-8.
 53. Foglio C, Vitacca M, Quadrio A, Scalvini S, Marangoni S, Ambrosino N. Acute exacerbations in severe COLD patients. Treatment using positive pressure ventilation by nasal mask. *Chest* 1992; 101:1533-8.

be required in some patients. An improvement in FEV₁ of 20% with steroid trial also confirms the presence of asthma. When airflow limitation is absent, i.e., FEV₁/FVC is above the lower limit of normal (7), the level of airway responsiveness should be determined.

Measurement of Airway Responsiveness

Measurement of airway responsiveness is needed for the diagnosis of asthma and for impairment rating when the subject has no current objective evidence of airflow limitation. When the baseline FEV₁ is below 70% of predicted, response to the inhaled β -adrenergic agonist and not the measurement of airway responsiveness is the appropriate test to establish the diagnosis of asthma (8).

Measurement of airway responsiveness should be made by methacholine or histamine inhalation test using standardized

methods (9–11). It is imperative that standardized methods be used in order to adequately interpret the results. The test should be done after withholding inhaled short-acting β -adrenergic agonist or ipratropium for 6 h and long-acting β -adrenergic agonist or theophylline for 24 h; in the case of histamine tests, short-acting antihistamines should be withheld for 48 h and astemizole for 1 or 2 months. Antiinflammatory preparations should not be withheld because withdrawal of these for a few hours does not influence measurement of airway responsiveness to histamine or methacholine, whereas prolonged withdrawal of these drugs can lead to an exacerbation of asthma. The subjects should be asked to refrain from smoking and exposure to cold air for two hours before the test.

The results should be expressed as the provocation concentration to cause a fall in FEV₁ of 20% (PC₂₀ or PD₂₀) (9). Airway hyperresponsiveness is considered to be present when the PC₂₀

SEQUENCE OF TESTING

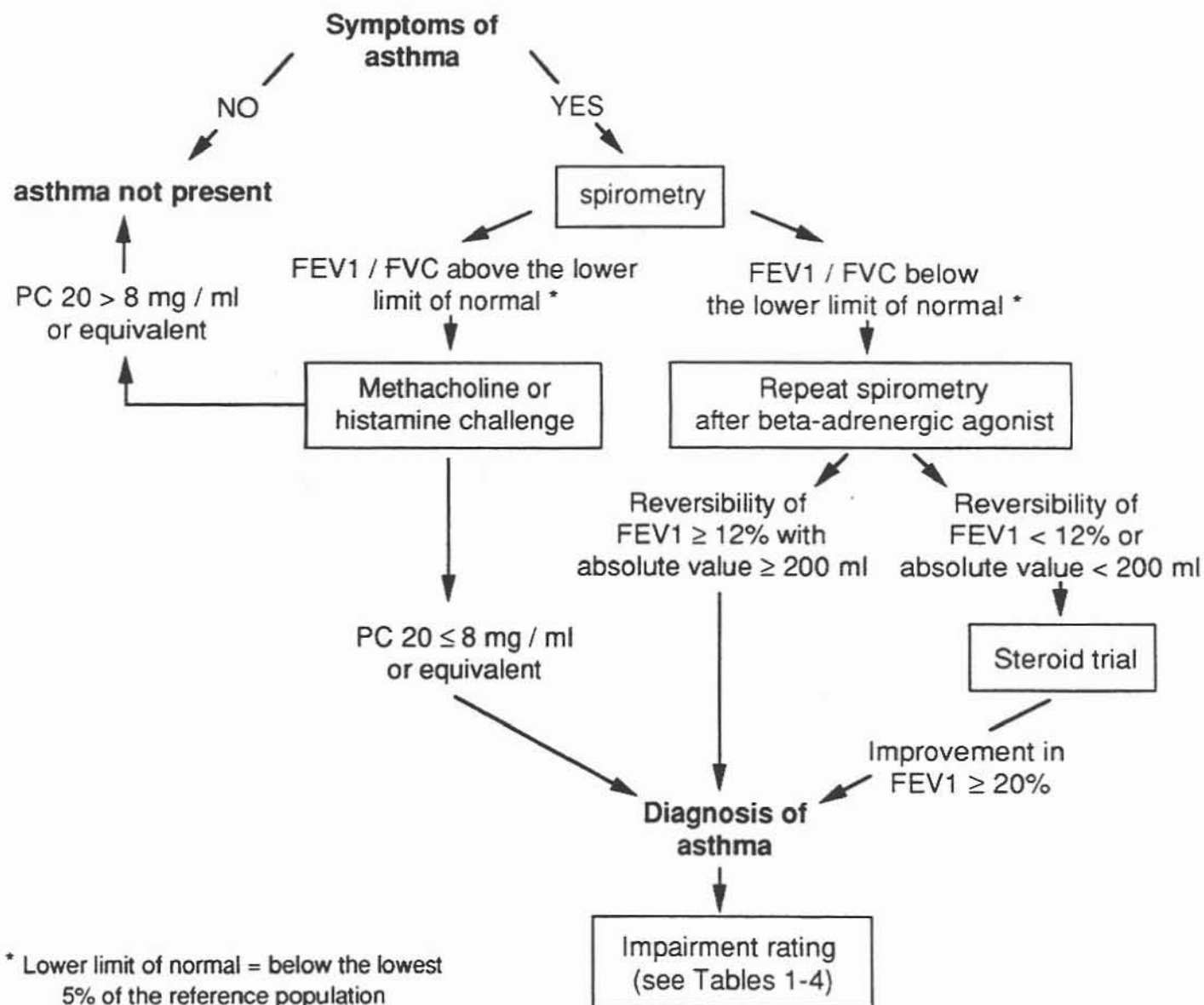


Figure 1. Sequence of testing.

is ≤ 8 mg/ml methacholine or histamine using the tidal breathing method or its equivalent when other standard methods are used (10-12).

Exercise Test

Exercise testing should not be done routinely in the investigation of asthma. However, many physicians perform spirometry before and after exercise testing in the investigation of dyspnea. If a subject has been shown to have a 15% or more decline in FEV₁ from the baseline level after exercise, this information will be useful in the assessment of impairment, particularly if the level of effort is similar to their usual work or daily activities.

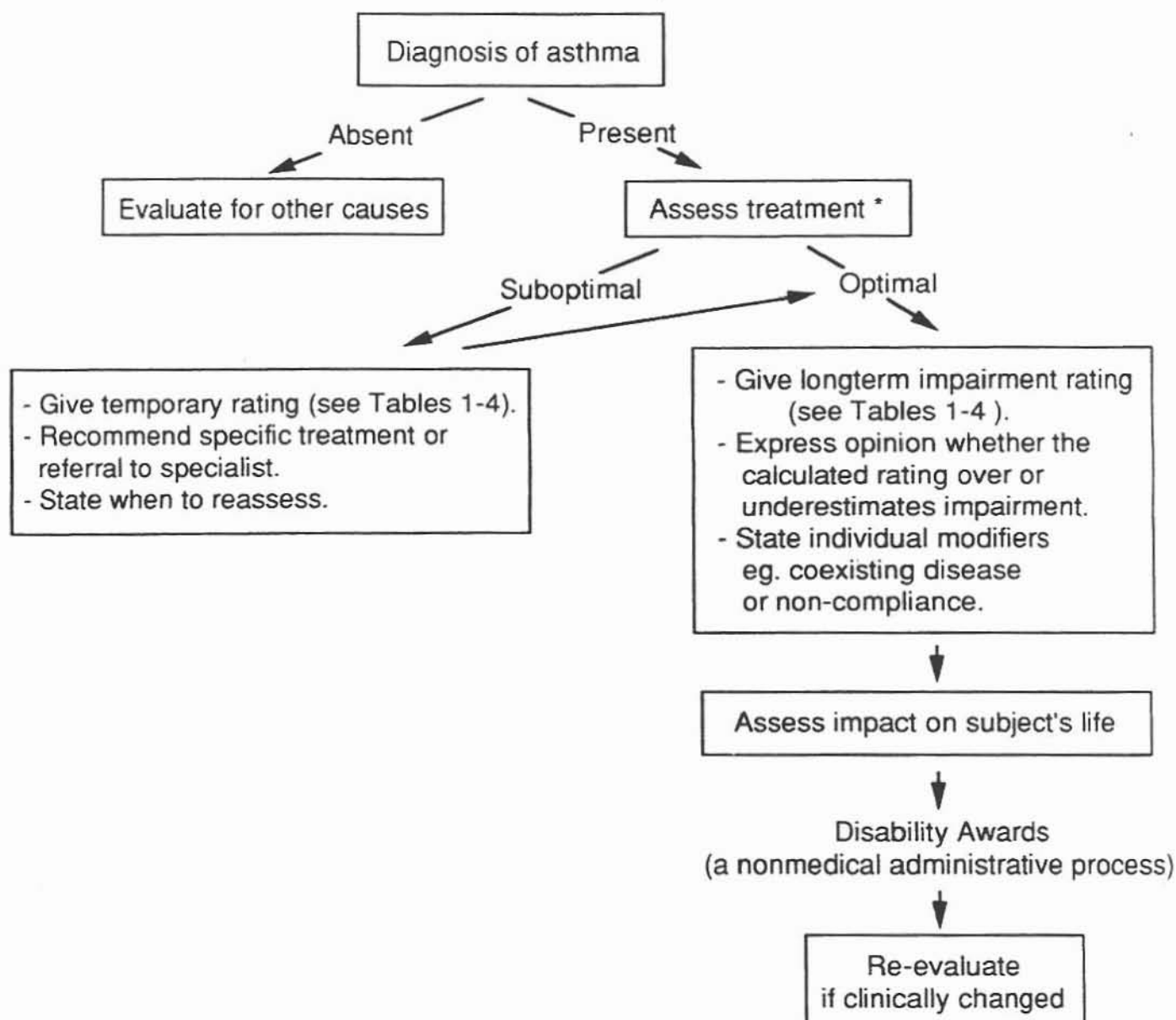
Measurement of Diffusing Capacity and Lung Volumes

These measurements are necessary only to distinguish asthma from other conditions. They are not required for impairment evaluation in patients with asthma.

PROCESS OF EVALUATION

The sequence of testing to be performed is defined in figure 1, while figure 2 shows the process of evaluation. There are two types of impairment/disability, temporary and permanent. Temporary impairment/disability refers to a situation that is likely to change. For example, the individual may be expected to improve so that the

PROCESS OF IMPAIRMENT EVALUATION



* See text for objectives of optimal treatment of asthma

current functional status does not describe the anticipated future status. Temporary impairment/disability can be evaluated from the results of tests used to establish the diagnosis of asthma. Permanent impairment/disability refers to a situation when the individual has reached maximal medical improvement and is receiving optimal therapy. Evaluation for permanent impairment/disability should be done after the objectives of optimal treatment of asthma have been attained.

The objectives of treatment include the following (4):

1. To achieve control or the best overall results (least symptoms, least need for β -adrenergic agonist when taken only if required, best expiratory flow rates, least diurnal variation of flow rates and least side-effects from medication).
2. To use the minimum medication to maintain control or the best overall results.
3. To treat exacerbations early to prevent them from becoming severe.

Physicians involved in the evaluation of impairment should assess whether the objectives of treatment of asthma have been achieved. They should therefore be familiar with the recent published guidelines for treatment of asthma by the National Asthma Expert Panel in the United States (4). In addition to the American Expert Panel's guidelines, other countries such as the United Kingdom (13), Australia (14), New Zealand (14), and Canada (15) have their own published guidelines. Effective management of asthma depends on both pharmacologic and nonpharmacologic measures. Nonpharmacologic measures include environmental control, patient and family education, and regular supervision. In some subjects it may take several months to achieve the objectives of treatment.

If the objectives of treatment are not achieved, the following should be done:

1. Give rating for temporary impairment (see tables 1 through 4).
2. Recommend specific treatment, or give referral to a specialist experienced in the management of asthma (e.g., pulmonary physician or allergist).
3. State when to reevaluate (when the objectives of treatment have been achieved or in 6 months, whichever is shorter).

RE-EVALUATION

Because asthma may improve or worsen with time, it is necessary to re-evaluate the subject if the clinical status changes even after long-term impairment/disability evaluation has been completed.

PARAMETERS TO BE CONSIDERED FOR RATING OF IMPAIRMENT

Tables 1 through 4 include the parameters used for classifying the extent of impairment. This is done based on both physiologic and clinical parameters.

TABLE 1
POSTBRONCHODILATOR FEV₁

Score	FEV ₁ , % predicted
0	> lower limit of normal
1	70-lower limit of normal
2	60-69
3	50-59
4	< 50

TABLE 2
REVERSIBILITY OF FEV₁ OR DEGREE OF AIRWAY HYPERRESPONSIVENESS*

Score	% FEV ₁ change	or	PC ₂₀ mg/ml or equivalent
0	< 10		> 8
1	10-19		8 - > 0.5
2	20-29		0.5 - > 0.125
3	≥ 30		≤ 0.125
4	-		-

* When FEV₁ is above the lower limit of normal, PC₂₀ should be determined and used for rating of impairment; when FEV₁ is < 70% predicted, the degree of reversibility should be used; when FEV₁ is between 70% predicted and the lower limit of normal either reversibility or PC₂₀ can be used.

Reversibility with bronchodilator is calculated as,

$$\frac{\text{FEV}_1 \text{ post-bronchodilator} - \text{FEV}_1 \text{ pre-bronchodilator}}{\text{FEV}_1 \text{ pre-bronchodilator}} \times 100\%$$

Airway responsiveness is expressed as that concentration of agent that will provoke a fall in FEV₁ of 20% from the lowest post saline value. Plot the concentration of methacholine/histamine against the fall in FEV₁ using a logarithm scale for the doubling concentrations. The PC₂₀ is obtained by interpolation between the last two points. The formula for linear interpolation of the PC₂₀ from the log dose response curve is as follows:

$$PC_{20} = \text{antilog } C1 + \frac{(\log C2 - \log C1)(20 - R1)}{(R2 - R1)}$$

Where C1 = second last concentration (< 20% FEV₁ fall)
 C2 = last concentration (> 20% FEV₁ fall)
 R1 = % fall FEV₁ after C1
 R2 = % fall FEV₁ after C2

Physiologic Parameters

The level of airflow limitation and either its reversibility or the level of airway responsiveness should be used in the impairment rating as shown in tables 1 through 4.

The postbronchodilator FEV₁ should be used in determining the level of airflow limitation. When there is no evidence of airflow limitation as defined above, the score is zero; when there is a severe degree of airflow limitation (FEV₁ < 50% predicted), the score is 4.

Whether the reversibility of airflow limitation or the degree of airway hyperresponsiveness should be used in impairment rating is dependent on the prebronchodilator FEV₁. When the prebronchodilator FEV₁ is above the lower limit of normal, the degree of airway hyperresponsiveness should be used; when the prebronchodilator FEV₁ is between 70% predicted and the lower limit of normal, either the degree of airway hyperresponsiveness or the degree of reversibility can be used; when the prebronchodilator FEV₁ is < 70% predicted, the degree of reversibility should be used.

TABLE 3
MINIMUM MEDICATION NEED*

Score	Medication
0	No medication
1	Occasional bronchodilator, not daily and/or occasional cromolyn, not daily
2	Daily bronchodilator and/or daily cromolyn and/or daily low-dose inhaled steroid (< 800 μ g beclomethasone or equivalent)
3	Bronchodilator on demand and daily high-dose inhaled steroid (> 800 μ g beclomethasone or equivalent) or occasional course (1-3/yr) systemic steroid
4	Bronchodilator on demand and daily high-dose inhaled steroid (> 1000 μ g beclomethasone or equivalent) and daily systemic steroid

* The need for minimum medication should be demonstrated by the treating physician, e.g., previous records of exacerbation when medications have been reduced.

TABLE 4
SUMMARY IMPAIRMENT RATING CLASSES*

Impairment Class	Total Score
0	0
I	1-3
II	4-6
III	7-9
IV	10-11
V	Asthma not controlled despite maximal treatment; i.e. FEV ₁ remaining < 50% despite use of \geq 20 mg prednisone/day.

* The impairment rating is calculated as the sum of the patient's scores from tables 1, 2, and 3.

The degree of reversibility and airway hyperresponsiveness are given less weight compared with the other parameters, with a maximum score of 3.

Clinical Parameters

Although symptoms are a critical component of asthma because of their subjective nature, they should not be the only criterion for impairment rating. The frequency of acute exacerbations requiring emergency room treatment or hospitalization has been used in previous attempts to rate impairment (2). Given the efficacy of currently recommended antiinflammatory preparations in the treatment of asthma, frequent emergency room visits or hospitalizations generally reflect inadequate treatment and failure to achieve the objectives of treatment. The nature and frequency of medications required to maintain asthma under control (or the best results) give a better reflection of the severity of the disease and are more useful for the purpose of impairment assessment. The use of medication requirement as an important component in the rating scheme will be enhanced if the treating physicians follow published treatment guidelines (12-15).

The minimum medication required to maintain control of asthma (or the best results) can be used to rate severity (16), as indicated in table 3. A subject requiring occasional use (not daily) of bronchodilator (inhaled β -adrenergic agonist or oral theophylline) and/or cromolyn can be considered to have very mild asthma (or a severity score of 1). The need for inhaled β -adrenergic agonist or oral theophylline on a daily basis and additional daily low-dose inhaled steroid or cromolyn reflects an increase in severity of asthma. The need for daily high-dose inhaled steroid ($>$ 800 mcg of beclomethasone or equivalent doses of other agents) and systemic steroid is given the highest severity score of 4. It is important that the rating physician be confident that these medications are the minimum required to maintain control (or the best results) in a subject and that reduction in medications leads to exacerbation of symptoms and reduced lung function.

IMPAIRMENT RATING

Impairment rating can be determined using the scheme shown in tables 1 through 4. This rating scheme attempts to standardize a method to quantify the effect of the illness on the subject's life, similar to earlier ATS guidelines on evaluation of impairment/disability (1, 2), rather than to quantify the severity of the disease itself. For the description of the clinical disease severity per se, the clinical severity scale of the National Asthma Expert Panel (4) should be used. The degree of impairment is calculated as the sum of the scores for postbronchodilator FEV₁, reversibility of FEV₁, or PC₂₀, and medication need. The class of impairment is

expressed as Class 0, I, II, III, IV or V. Total impairment/disability (Class V) in a subject with asthma is defined as asthma that cannot be controlled adequately; despite maximal treatment, including \geq 20 mg oral prednisone per day, the FEV₁ remains below 50% of predicted.

The evaluating physician may also express an opinion as to whether the impairment rating obtained overestimates or underestimates impairment due to unusual circumstances of individual subjects. These circumstances should be described in detail. Individual modifying factors, such as barriers to compliance in treatment, limitations to environmental control measures, and coexisting disease that might influence the impact of asthma on the subject's life should be clearly stated. In addition, the evaluating physician should indicate the effects asthma has on the subject's quality of life, including the impact on the subject's ability to perform his or her normal job.

SPECIAL CONSIDERATIONS FOR SUBJECTS WITH OCCUPATIONAL ASTHMA

General Comments

Occupational asthma is a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes or conditions that are attributable to a particular occupational environment and not to stimuli encountered outside the workplace. Occupational asthma may encompass both immunologic and nonimmunologic causes: (1) immunologic occupational asthma occurs upon reexposure to an agent after a latent period of immune sensitization; (2) nonimmunologic occupational asthma that does not induce immune sensitization as determined by currently available technology. An irritant and potentially toxic agent may trigger new asthma as an aftermath of an acute inhalation injury in some patients. Such individuals have nonspecific airway hyperresponsiveness and should be evaluated for impairment as for other general forms of asthma.

There are many follow-up studies of subjects with documented occupational asthma showing that the majority (60 to 90%) of subjects failed to recover several years after leaving exposure (17). Early diagnosis and cessation of exposure are documented prognostic factors that increase the likelihood of a favorable outcome (17). It has been shown that continuous exposure to the offending agent leads to deterioration of symptoms and even fatalities (17). It is therefore important to diagnose occupational asthma early and for the worker to avoid further exposure to the offending agent.

General Approach

Assessment of individuals with occupational asthma should be done by physicians with expertise in this area. Assessment for impairment/disability should take place at least on two occasions.

1. *Temporary impairment/disability.* Once the diagnosis of occupational asthma is made, the proper treatment is to remove the worker from exposure. These patients should be considered 100% impaired on a permanent basis for the job that caused the illness and for other jobs with exposure to the same causative agent. Because the individual cannot return to the previous job, plans for vocational rehabilitation should be instituted as soon as the diagnosis of occupational asthma is made. It is not necessary to wait for a permanent disability rating to initiate vocational planning. Several alternatives should be considered in the management of subjects with occupational asthma:

- Relocation to a new job either in the same plant or in a different plant where there is no exposure.
- Rehabilitation into a new job or early retirement. Financial compensation should be offered in every instance in which there

is loss of earnings. The amount and duration of compensation should be made known to the worker so that the worker can make rational decisions about the changes.

- In some special situations, modification of the job such as improved ventilation, process change, or product substitution may enable the worker to remain. It is important to remember that when the agent acts by sensitization, the worker may react to levels of exposure well below those considered safe for individuals without prior sensitization. The ability of a respirator to provide adequate protection against the low levels that might trigger an attack and the ability of the asthmatic individual to work safely and effectively with the respirator must be carefully assessed before relying on these devices.

2. *Long-term impairment/disability.* Assessment for long-term impairment/disability should be carried out 2 yr after the removal from exposure when improvement has been shown to plateau (18). Evaluation should be done after the above objectives of treatment have been achieved and using the scaling system as for subjects with nonoccupational asthma.

List of participants: This statement was prepared by the ATS Ad Hoc Committee on Impairment/Disability Evaluation in Subjects with Asthma. The members of the Committee are as follows: Moira Chan-Yeung, M.B., (Chair); Philip Harber, M.D., (Co-Chair); William Bailey, M.D.; John Balmes, M.D.; Scott Barnhart, M.D.; Frederick E. Hargreave, M.D.; Jean-Luc Malo, M.D.; Charles Reed, M.D.; and Hal Richerson, M.D.

References

1. Evaluation of impairment/disability secondary to respiratory disease. A statement of the American Thoracic Society. *Am Rev Respir Dis* 1982; 126:945-51.
2. Evaluation of impairment/disability secondary to respiratory disorders. A statement of the American Thoracic Society. *Am Rev Respir Dis* 1986; 133:1205-9.
3. Chan-Yeung M. Pulmonary perspective—evaluation of impairment/disability in patients with occupational asthma. *Am Rev Respir Dis* 1987; 135:950-1.
4. Guidelines for the diagnosis and management of asthma. Expert panel report. National Asthma Education Program. Bethesda, MD: National Heart, Lung and Blood Institute. National Institute of Health Publication No. 91-3042A, 1991.
5. American Thoracic Society. Standardization of spirometry—1987 Update. *Am Rev Respir Dis* 1987; 136:1285-8.
6. Gardner RM, Chairman. Report of Snowbird Workshop on standardization of spirometry. *Am Rev Respir Dis* 1979; 119:831-8.
7. Lung function testing: selection of reference values and interpretational strategies. A statement of the American Thoracic Society. *Am Rev Respir Dis* 1991; 144:1202-18.
8. Ramsdale EH, Morris MM, Roberts RS, Hargreave FE. Bronchial responsiveness to methacholine in chronic bronchitis: relationship to airflow obstruction and cold air responsiveness. *Thorax* 1984; 39:912-8.
9. Juniper EF, Cockcroft DW, Hargreave FE. Histamine and methacholine inhalation tests: tidal breathing method. Laboratory procedure and standardization. Canadian Thoracic Society Statement. AB Draco: Lund, Sweden, 1991.
10. Yan K, Salome C, Woolcock AJ. Rapid method for measurement of bronchial responsiveness. *Thorax* 1983; 38:55-61.
11. Fabbri LM, Mapp CE, Hardrick DJ. Standardization of the dosimeter method for the measurement of airway responsiveness in man. In: Airway responsiveness, measurement and interpretation. Hargreave FE, Woolcock AJ, eds. Astra Pharmaceuticals Canada Ltd: Mississauga, Ontario, 1985; 29-34.
12. Ryan G, Dolovich MB, Roberts RS, Frith PA, Juniper EF, Hargreave FE, Newhouse MT. Standardization of inhalation provocation tests: two techniques of aerosol generation and inhalation compared. *Am Rev Respir Dis* 1981; 123:195-9.
13. British Thoracic Society. Guidelines for management of asthma in adults: I - Chronic persistent asthma. *BMJ* 1990; 301:651-3.
14. Woolcock A, Rubinfeld AR, Seale JP, Landau LL, Antic R, Mitchell C, Rea H, Zimmerman P. Asthma management plan, 1989. *Med J Aust* 1989; 151:650-3.
15. Hargreave FE, Dolovich J, Newhouse M. The assessment and treatment of asthma: a conference report. *J Allergy Clin Immunol* 1990; 85:1097-111.
16. Report of the Working Groups. Workshop on environmental and occupational asthma. *Chest* 1990; 98:240S-50S.
17. Chan-Yeung M. State of the art—occupational asthma. *Chest* 1990; 98:148S-61S.
18. Malo J-L, Cartier A, Ghezzi H, Lafrance M, Mccants M, Lehrer S. Patterns of improvement on spirometry, bronchial hyperresponsiveness, and specific IgE antibody levels after cessation of exposure in occupational asthma caused by Snow crab processing. *Am Rev Respir Dis* 1988; 138:807-12.