
Guidelines for the Diagnosis and Treatment of COPD (Chronic Obstructive Pulmonary Disease) 3rd edition

Pocket Guide

Edition

**Committee for the Third Edition of the COPD Guidelines
of The Japanese Respiratory Society**

「Guidelines for the Diagnosis and Treatment of COPD (Chronic Obstructive Pulmonary Disease)」 3rd. ed., Pocket Guide

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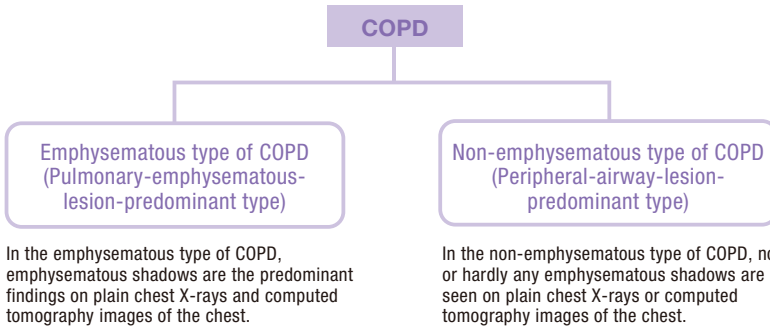
*The page number printed after each title indicates the corresponding page of the “Guidelines for the Diagnosis and Treatment of COPD (Chronic Obstructive Pulmonary Disease) 3rd edition”.

What is COPD?

A. Definition

p5

COPD (chronic obstructive pulmonary disease) is an inflammatory disease of the lungs that is caused by long-term inhalation exposure to noxious substances such as tobacco smoke. COPD is characterized by irreversible airflow obstruction as demonstrated by pulmonary function tests. The airflow obstruction is progressive and attributable to the complex effects of the peripheral airway lesions and emphysematous lesions that contribute to the pathology in various ratios. Clinically, COPD is characterized by exertional dyspnea and chronic cough and sputum production whose onset and progression are gradual.



It has been suggested that analysis of COPD by subtypes based on the clinical pictures or respiratory function level is important in addition to the above classification based on the diagnostic imaging findings.

B. Epidemiology

p6

- Surveys on COPD prevalence carried out in various countries have reported rates of around 10%.
- According to the WHO survey conducted in 2001, COPD was ranked as the 5th highest cause of death in high-income nations, and the 6th highest cause of death in low- and middle-income nations.
- The Nippon COPD Epidemiology (NICE) study reported a prevalence of COPD in Japan of 8.6%. Based on the results of the study it was estimated that about 5.3 million Japanese 40 years of age and older, and about 2.1 million Japanese 70 years of age and older, are afflicted by COPD.

- COPD is ranked as the 10th highest cause of death in Japan. However, the ratios of men and women 65 years of age or older and 75 years of age or older who have COPD have been increasing.

C. Risk factors

:p10:

	Greatest risk factors	Important risk factors	Possible risk factors
Exogenous factors	Tobacco smoke	Air pollution Passive smoking Exposure to occupational dusts and chemical substances	Respiratory infection Socioeconomic factors
Endogenous factors	α_1 -AT deficiency		Gene mutations Airway hypersensitivity Autoimmune responses Aging

α_1 -AT : α_1 -antitrypsin

- The greatest risk factor for COPD is tobacco smoke, but because COPD develops in only some smokers, the presence of a genetic predisposition to sensitivity to tobacco smoke has been suggested.
- α_1 -AT deficiency is well known as to be a genetic risk factor for predisposition to COPD, but it is extremely rare among Japanese. Mutations in inflammation-related genes, antioxidant genes, protease genes, and antiprotease genes have been pointed to as other genetic risk factors for predisposition to COPD.

D. Pathology

:p16:

- COPD patients exhibit specific changes in the architecture of their central airways, peripheral airways, alveoli, and pulmonary vessels, probably secondary to inflammation caused by inhalation of noxious substances such as tobacco smoke.
- The inflammation is severer than in healthy smokers, and it persists for a long time even after smoking cessation.
- Airflow obstruction occurs as a result of the complex effects of peripheral airway lesions and emphysematous lesions.
- The inflammation affects the whole body and leads to systemic comorbidities.

■ Pathological changes in the lungs in COPD and bronchial asthma

		COPD	Bronchial asthma
Airways	Epithelial detachment	—	+++
	Squamous metaplasia	+++	—
	Thickening of the basal membrane	+ / —	+++
	Angiogenesis	+ / —	+++
	Fibrosis	+++ (in peripheral airways)	+ (in severe cases)
	Smooth muscle hyperplasia	+ (in peripheral airways)	+++
	Goblet cell and bronchial gland hyperplasia	+++	++
	Loss of alveolar attachments	+++	+ / —
Alveolar region	Alveolar destruction/ enlargement	+++	—
Pulmonary vessels	Intimal/smooth muscle hyperplasia	++	—
	Fibrosis of the vessel wall		

E. Etiology

p20

- COPD is characterized by increased inflammatory responses by the airways and lungs caused by noxious substances such as tobacco smoke.
- The increased inflammatory response leads to a protease/antiprotease imbalance and oxidant/antioxidant imbalance, and, in turn, damage to the airways and lungs.
- New hypotheses regarding its pathogenesis of COPD, including an apoptosis hypothesis, have also been proposed.

F. Pathophysiology

p23

- The basic pathologic conditions that lead to exertional dyspnea in COPD are airflow obstruction and dynamic pulmonary hyperinflation.
- Hypersecretion of airway mucus causes chronic cough and sputum production, but does not occur in all COPD patients.
- Uneven distribution of ventilation-perfusion ratios leads to hypoxemia. In severe cases, hypercapnia due to alveolar hypoventilation is also observed.
- Severe cases are complicated by pulmonary hypertension, whose progression leads to cor pulmonale. The major cause of pulmonary hypertension is hypoxic pulmonary vasoconstriction.
- In some cases, it is difficult to differentiate COPD from refractory asthma with little reversibility.

- COPD is characterized by the presence of systemic comorbidities. COPD should be considered a systemic disorder that requires comprehensive severity assessment and treatment. It is also important to pay attention to pulmonary complications such as lung cancer and pneumothorax.

■ Differentiation of COPD from asthma

		COPD	Asthma
Age at onset		Middle and advanced age groups	All age groups
Causative factors		Smoking Air pollution	Allergy Infection
Allergy history Family history		—	— ~ +
Cells involved in airway inflammation		Neutrophils CD8+T-lymphocytes Macrophages	Neutrophils CD4+T-lymphocytes
Symptoms	Continuousness	Progressive	Circadian
	Form of onset	Exertional	Paroxysmal
Reversibility of airflow obstruction		— (~ +)	+
Airway hypersensitivity		— (~ +)	+

■ Systemic effects of COPD

- Systemic inflammation characterized by increased inflammatory cytokine and C-reactive protein levels.
- Nutritional disorders leading to decreased fat mass and lean-body mass
- Musculoskeletal disorders associated with decreased muscle mass and muscle strength
- Cardiovascular diseases, including myocardial infarction, angina pectoris, and cerebrovascular accidents
- Osteoporosis leading to vertebral compression fractures
- Depression
- Diabetes mellitus
- Sleep disorders
- Anemia

Diagnosis of COPD

A. Diagnosis (Diagnostic criteria)

p32

1. FEV₁/FVC <70% on spirometry after bronchodilator administration
2. Rule out the possibility of other diseases that cause airflow obstruction

- COPD must always be suspected when symptoms such as cough, sputum, or exertional dyspnea are present.
- To make a definitive diagnosis, other diseases that cause airflow obstruction must be ruled out by radiography, pulmonary function tests, and electrocardiography. Differential diagnosis from bronchial asthma is difficult in cases of COPD with high airway reversibility, cases of refractory asthma with low reversibility, and cases of COPD complicated by asthma.

■ Diseases to be differentiated from COPD

- | | |
|--------------------------------------|-----------------------------------|
| 1. Bronchial asthma | 7. Pneumoconiosis |
| 2. Diffuse panbronchiolitis | 8. Pulmonary lymphangiomyomatosis |
| 3. Congenital sinobronchial syndrome | 9. Congestive heart failure |
| 4. Obstructive bronchiolitis | 10. Interstitial lung disease |
| 5. Bronchiectasis | 11. Lung cancer |
| 6. Pulmonary tuberculosis | |

B. Diagnosis (Diagnostic criteria)

p33

The stage classification of COPD is based on the degree of airflow obstruction (%FEV₁), not on the severity of the COPD.

Differences from the 2nd edition:

1. “Stage 0: group at risk” has been omitted.
 2. The phrases “mild COPD”, “moderate COPD”, “severe COPD”, and “very severe COPD” have been omitted.
 3. The statement on concurrent right heart failure has been omitted from the characteristic features of “stage IV”.
- The ratio of forced expiratory volume in one second to forced vital capacity (FEV₁/FVC) is used to diagnose COPD, whereas FEV₁ as a percentage of predicted FEV₁ (%FEV₁) is used to determine the stage of the disease.
 - COPD is classified into four stages: stage I, mild airflow obstruction (%FEV₁ ≥ 80%); stage II, moderate airflow obstruction (50% ≤ FEV₁ < 80%); stage III, severe airflow obstruction (30% ≤ FEV₁ < 50%); and stage IV, very severe airflow obstruction (%FEV₁ < 30% or %FEV₁ < 50%, and accompanied by chronic respiratory failure).

FEV₁/FVC for diagnosis vs %FEV₁ for stage classification

p33

FEV₁ is used to determine the stage of COPD, because FVC decreases as COPD progresses, and thus the FEV₁/FVC value does not always reflect the progression in stage of the disease.

Since FEV₁ varies with age, physical status, and sex, the ratio of the actually measured FEV₁ to the predicted FEV₁ (FEV₁%predicted or %FEV₁) is used for stage classification.

Since the predicted FEV₁ may vary with race, it is desirable to use the values calculated by using the following formula provided by the Japanese Respiratory Society to predict the results of spirometry for healthy Japanese subjects.

■ Males	VC (L) = 0.045 × height (cm) - 0.023 × age (yr) - 2.258
	FVC (L) = 0.042 × height (cm) - 0.024 × age (yr) - 1.785
	FEV ₁ (L) = 0.036 × height (cm) - 0.028 × age (yr) - 1.178
■ Females	VC (L) = 0.032 × height (cm) - 0.018 × age (yr) - 1.178
	FVC (L) = 0.031 × height (cm) - 0.019 × age (yr) - 1.105
	FEV ₁ (L) = 0.022 × height (cm) - 0.022 × age (yr) - 0.005

C. Phenotype classification

p35

- The prognosis of COPD patients cannot be made on the basis of %FEV₁ alone.
- In addition to %FEV₁, the prognosis depends on such factors as the degree of exertional dyspnea, exercise tolerance, and nutritional status.
- From the standpoint of treatment and management, symptoms such as chronic cough and sputum, airway reversibility, frequency of exacerbations, and presence of systemic comorbidities are also important factors to consider.
- The pathogenesis of the airflow obstruction associated with COPD is attributable to emphysematous lesions and peripheral airway lesions. Accordingly, COPD can be classified into two types, an emphysematous type and a non-emphysematous type.

D. Clinical findings

p37

- Major symptoms of COPD are chronic cough, sputum production, and exertional dyspnea.
- Symptoms should be assessed as objectively as possible by using questionnaires such as the MRC, CCQ, or IPAG*.
- Since the typical physical findings in COPD usually do not appear until the disease has become severe, the absence of abnormal findings does not rule out the possibility of COPD.

* MRC (Medical Research Council Dyspnoea Scale): a questionnaire designed by the British Medical Research Council to measure the influence of dyspnea on daily life
CCQ (Clinical Chronic Obstructive Pulmonary Disease Questionnaire): a questionnaire that enables scoring of COPD-related symptoms, functional status, and mental health status.
IPAG (International Primary Care Airways Group questionnaire): a questionnaire designed by the International Primary Care Airways Group to score COPD-related symptoms and risk factors.

■ Functional dyspnoea can be assessed by the Medical Research Council dyspnoea scale.

Grade 0	Not troubled with breathlessness except with strenuous exercise.
Grade 1	Troubled by shortness of breath when hurrying or walking up a slight hill.
Grade 2	Walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on the level.
Grade 3	Stops for breath after walking ~100 m or after a few minutes on the level.
Grade 4	Too breathless to leave the house or breathless when dressing or undressing.

Note) The breathlessness scale presented above is based on the ATS/ERS (the American Thoracic Society and the European Respiratory Society) 2004 disease staging system. The breathlessness scale used in the assessment of the eligibility for insurance-covered pulmonary rehabilitation grades the condition using the numbers 1-5 instead of 0-4. The equivalent grades are obtained by adding +1 to those defined in the above system.

E. Tests

p41

E-1. Diagnostic imaging

p41

- A plain chest X-ray is a useful means of excluding other diseases or diagnosing advanced emphysematous lesions and airway lesions, but it is not suitable for detecting early stage lesions.
- High-resolution computed tomography (HRCT) can be effective as a means of early detection of emphysematous lesions.
- Emphysematous lesions appear as ill-defined low attenuation areas (LAA) on HRCT images, and thus can be distinguished from normal lung.
- HRCT is capable of detecting airway wall thickening.
- Assessment of emphysematous lesions and airway lesions based on HRCT images is also useful in phenotype classification of COPD.

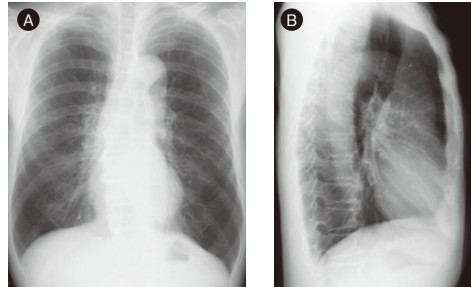
■ Plain chest x-rays of COPD patients

A : P-A view

Findings include increased radiolucency of the lung fields, diminished peripheral blood vessel shadows in the lung fields, flattening of the diaphragm, decrease in the cardiothoracic ratio due to a teardrop heart, and widening of the intercostal spaces.

B : Lateral view

Findings include flattening of the diaphragm, widening of the intercostal spaces, and increase in the retrocardiac space.



E-2. Pulmonary function tests

p47

- The diagnosis of COPD requires detection of an obstructive ventilation disorder by spirometry.
- A post-bronchodilator FEV₁/FVC less than 70% is considered evidence of the presence of an obstructive ventilation disorder.
- Decreased gas exchange in COPD patients can be demonstrated by measuring pulmonary carbon monoxide diffusing capacity (D_{LCO}).

E-3. Arterial blood gas analysis and pulse oximetry

p51

- Arterial blood gas analysis is a useful means of assessing ventilation status, oxygenation capacity, and acid-base balance in a patient.
- Other indices in addition to arterial oxygen pressure (PaO₂), such as degree of anemia or cardiac output, should be taken into account when assessing tissue oxygenation.
- Arterial blood gas analysis is a useful means of assessing the severity of the disease during exacerbations as well as during stable periods.
- A pulse oximeter allows continuous non-invasive measurement of oxygen saturation by pulse oximetry (SpO₂).

E-4. Exercise tests, respiratory muscle function tests, sleep studies p54

- Exercise tests are useful as a means of evaluating exercise tolerance, identifying factors that limit exercise, assessing severity and outcome, and assessing the effectiveness of treatment.
- Most COPD patients exhibit decreased exercise tolerance. The primary cause of decreased exercise tolerance is the limited mobility imposed by the ventilation disorder. In addition, hypoxemia during exercise, impaired pulmonary blood flow, decreased oxygen transport capacity, or muscle weakness can also cause decreased exercise tolerance.
- The results of respiratory muscle function tests in most COPD cases show decreases in both inspiratory and expiratory muscle strength.
- Hypoxemia associated with hypercapnia develops in some patients due to hypoventilation during sleep.

E-5. Evaluation of pulmonary hypertension and cor pulmonale p59

- The mean resting pulmonary arterial pressure of healthy adults should be no more than 15 mmHg, but some COPD patients exhibit pulmonary hypertension with values exceeding 20 mmHg.
- Chronic pulmonary hypertension results in right ventricular hypertrophy and enlargement, a condition called cor pulmonale.
- Cardiac output is normal or above normal in most patients with pulmonary hypertension secondary to COPD.
- Most COPD patients with PaO₂ of 60 Torr or less have pulmonary hypertension as a complication, and evaluation of pulmonary hypertension based on the physical findings, chest X-rays, and results of electrocardiography, cardiac ultrasonography, and biomarker tests is essential in such cases.

E-6. Assessment of QOL p62

- Improvement in quality of life (QOL) is the goal of COPD treatment from the patient's point of view.
- QOL can be assessed quantitatively by using two varieties of questionnaires, i.e., questionnaires based on generic scales and questionnaires based on disease-specific scales.

E-7. Sputum examination, breath tests, blood tests p65

- Sputum, expired gas, and expired breath condensate examinations are used to evaluate airway inflammation in COPD patients.
- Increases in markers of inflammation, such as C-reactive protein (CRP), are observed in the peripheral blood of COPD patients.

Treatment and management of COPD

A. Goals and methods of COPD management

p70

Goals of COPD management

- Improvement of symptoms and exercise tolerance
- Improvement of QOL
- Prevention and treatment of exacerbations
- Prevention of disease progression
- Prevention and treatment of systemic comorbidities and pulmonary complications
- Improvement of survival prognosis

Methods of COPD management

- Smoking cessation guidance
- Pharmacologic therapy
- Pulmonary rehabilitation (patient education, exercise therapy, nutrition therapy)
- Oxygen therapy
- Ventilatory support
- Surgical treatment

- To achieve the goals of management, it is important to establish a plan for symptom evaluation, follow-up, avoidance of risk factors, management during the stable period, and management during exacerbations.

B. Smoking cessation

p71

- Smoking accelerates the progression of respiratory dysfunction. Smoking cessation slows the progression of respiratory dysfunction and reduces mortality.
- Smoking cessation is the single most important, efficacious, and cost-effective method of intervention to reduce the risk of developing COPD and slow its progression.
- Smoking is essentially a form of drug addiction, i.e., nicotine addiction.
- Even a brief 3-minute period of smoking cessation advice from clinicians has been reported to increase the smoking cessation rate.
- Smoking cessation therapy is facilitated by using a combination of behavioral therapy and pharmacologic therapy.
- Outpatients with nicotine addiction who meet the eligibility criteria can receive Japanese-National-Health-Insurance-covered smoking cessation therapy.

Strategies to help a patient quit smoking

Ask	Systematically identify all tobacco users at every visit.
Advise	Strongly urge all tobacco users to quit.
Assess	Determine willingness to make a quit attempt.
Assist	Aid the patient in quitting.
Arrange	Schedule follow-up contact.

C. Management of stable COPD

p76

The stage classification of COPD is not necessarily informative in regard to the severity of the disease.

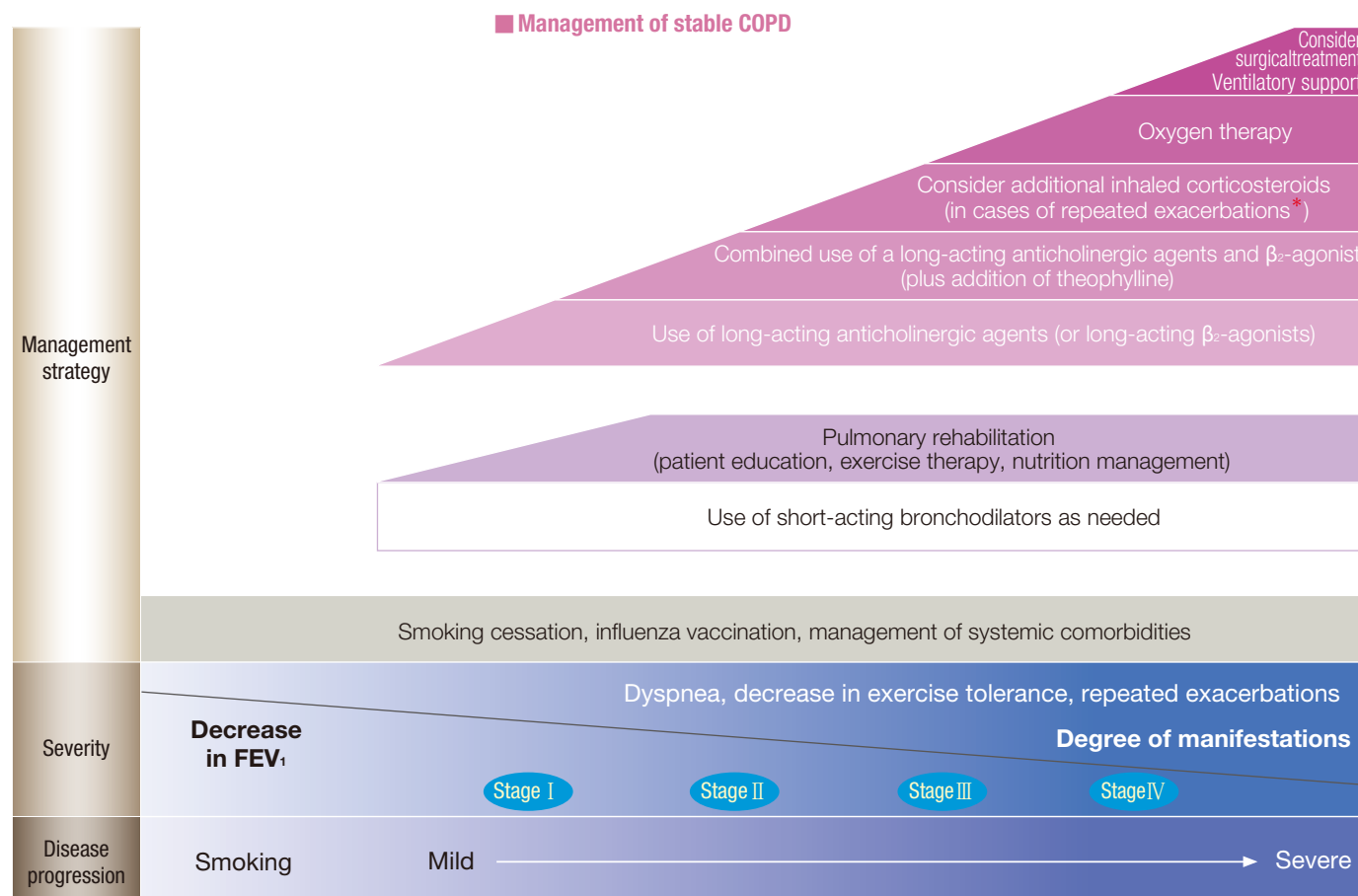
- Detailed evaluation of the patient's condition is essential to treatment and management -

- Avoiding exposure to tobacco smoke is the most important part of the strategy to prevent the onset and slow the progression of COPD.
- Management of stable COPD involves gradual enhancement of treatment based on comprehensive evaluation of severity. The evaluation of severity should take into account the degrees of other manifestations in addition to the progression of disease stage based on the degree of airflow obstruction (i.e., decrease in FEV₁).
- Preventing exacerbations of COPD is essential, because exacerbations cause progression of airflow obstruction and increase mortality.
- It is important to determine the management policy for each COPD patient based on a comprehensive evaluation of the patient's condition*, taking into account the stage, type, and severity of the disease as well as responsiveness to treatment. It is also important to manage systemic comorbidities and pulmonary complications.

* In addition to dyspnea, such symptoms as cough and sputum production are also important targets of treatment and management to improve QOL and prevent exacerbations.

Drugs that prevent exacerbations of COPD

Drugs	Remarks
Long-acting anticholinergic agents Long-acting β_2 -agonists Long-acting β_2 -agonists combined with inhaled corticosteroids	—
Inhaled corticosteroids	Recommended for patients with a %FEV ₁ below 50%
Theophylline Carbocisteine N-acetylcysteine Ambroxol Macrolides	Whether these drugs have an additive effect with the above four drugs and combination is unknown.



- The treatment strategy should be selected based on a comprehensive evaluation of severity, taking into account the degree of manifestations in addition to the degree of decrease in FEV₁.
- In cases of repeated exacerbations, introduction of inhaled corticosteroids* or mucus-regulating drugs in addition to long-acting bronchodilators should be considered (see the left table).

C-1. Vaccination

p78

- Since immunization with influenza vaccines has been reported to reduce mortality due to exacerbations of COPD by 50%, all COPD patients should be vaccinated against influenza.
- Pneumococcal vaccine is recommended in COPD patients 65 years of age and older and those under 65 years whose %FEV₁ is less than 40%.

C-2. Pharmacologic therapy

p79

- Pharmacologic therapy can reduce symptoms, prevent exacerbations, and improve QOL and exercise tolerance.
- Bronchodilator medications constitute the core of pharmacologic therapy. The most appropriate medications should be selected for each patient based on their responsiveness to treatments, prescribed in dosages according to severity, and continued with sufficient attention to adverse drug reactions.
- Bronchodilators comprise anticholinergic agents, β_2 -agonists, and methylxanthines. The most recommended route of administration is inhalation. It is preferable to use multiple agents rather than to increase the dose of a single drug when the patient does not respond well.
- Inhaled corticosteroids can reduce the frequency of exacerbations and prevent deterioration of QOL in patients who experience repeated exacerbations and whose %FEV₁ is less than 50%.
- The combined use of an inhaled glucocorticoid and a long-acting β_2 -agonist is more effective in improving respiratory function, preventing exacerbations, and improving QOL than treatment with a single drug.
- The use of long-acting anticholinergic agents or long-acting β_2 -agonists combined with inhaled glucocorticoids may slow the progression of airflow obstruction and reduce mortality.

■ Drugs and their formulations used for the management of COPD in the stable stage

Drug	Metered dose inhaler (μg)	Dry powder inhaler (μg)	Nebulizer (mg/mL)	Oral (mg)	Injection (mg)	Patch (mg)	Duration of action (hours)
1. Bronchodilators							
Anticholinergics							
● Short-acting type Ipratropium bromide Oxipropium bromide	20 100						6-8 7-9
● Long-acting type Tiotropium		18					≥24
β₂-agonists							
● Short-acting type Salbutamol Terbutaline Hexoprenaline Procaterol Tulobuterol Fenoterol Clenbuterol Mabuterol	100 5-10 100		5 0.1	2 2 0.5 25-50μg 1 2.5 10μg 25-50μg	0.2		4-6 4-6 4-6 8-10 8 8 10-12 8-10
● Long-acting type Salmeterol Formoterol* Tulobuterol (Patch)		25-50 4.5-12				0.5-2	≥12 ≥12 24
Methylxanthines							
Aminophylline Theophylline (Slow release)				50-400	250		~24 ~24
2. Corticosteroids							
Topical administration (inhalation)							
Beclomethasone Fluticasone Budesonide Ciclesonide	50-100 50-100 50-200	50-200 100-200					
Systemic administration (oral, injection)							
Prednisolone Methylprednisolone				5 2-4	40-125		
3. Long-acting β₂-agonist/inhaled corticosteroid							
Salmeterol/Fluticasone Formoterol/Budesonide*		50/100, 250 4.5/160					
4. Mucousregulatory drugs							
Bromhexine Carbocisteine Fudosteine Ambroxol Acetylcysteine			2 200	4 250-500 200 15	4		

* Medicine not marketed in Japan as of June, 2009

C-3. Non-pharmacologic therapy

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a. Pulmonary rehabilitation

(p86)

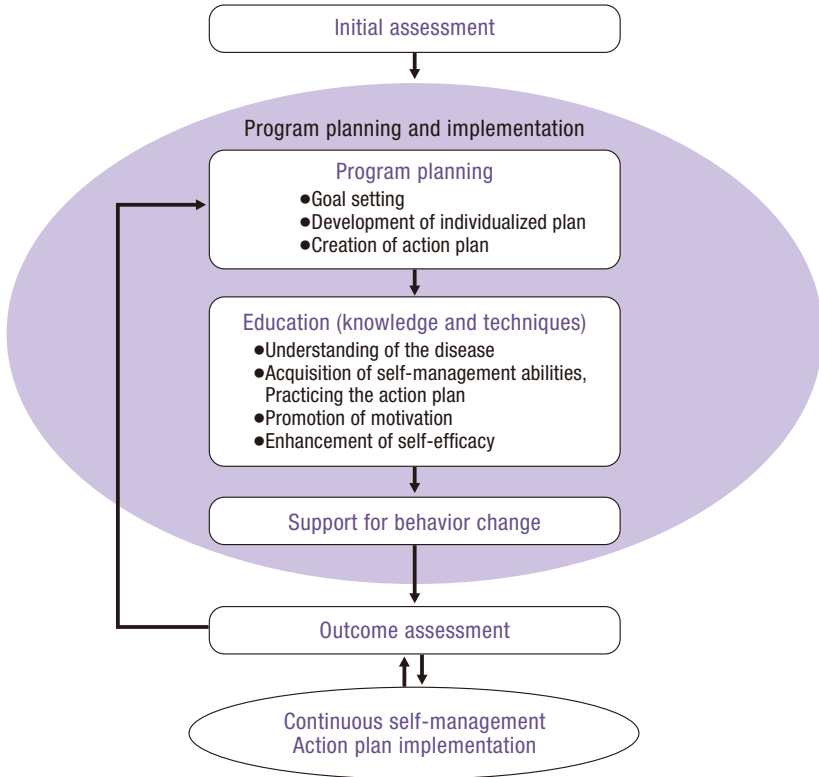
- Pulmonary rehabilitation can help maintain COPD patients in good mental and physical condition and improve the quality of their daily life. The effects of pulmonary rehabilitation are additive to those of pharmacologic therapy.
- Exercise therapy is the core of pulmonary rehabilitation. When instituting exercise training, it is desirable to adjust patients' breathing patterns and provide them with flexibility training.
- An even greater positive effect can be anticipated by having a multidisciplinary team working on comprehensive program.
- Concomitant nutrition therapy is desirable in order to prevent weight loss as a result of exercise training and enhance its therapeutic effects.
- Exercise training should be performed continuously and regularly. The maintenance phase of the program mainly comprises endurance and muscle strength training. By that time patients should have made exercise a habit and incorporated it into their lifestyle.

b. Patient education

(p93)

- Patient education is intended to help patients deepen their understanding of the disease and gain the skills they will need for self-management during the stable period and exacerbations. It is also intended to inspire them to tackle the disease with medical professionals. Patient education may improve the patients' health status by enhancing their ability to manage their disease.
- Patient education is based on guiding principles supported by behavioral science or behavioral psychology research. Action plans can help patients improve their self-management abilities.

■ Patient education process



(Pulmonary Rehabilitation Manual, 2007)

■ Structure of the education program for COPD patient

- | | |
|---|---|
| 1. Self-management of the disease | 9. Importance of exercise |
| 2. Structure of the lung, lung diseases, and tests | 10. Nutrition and diet therapy |
| 3. Smoking cessation | 11. Nutritional supplementation therapy |
| 4. Environmental factors | 12. Home oxygen therapy |
| 5. Pharmacologic therapy | 13. Home mechanical ventilation therapy |
| 6. Vaccination | 14. Access to welfare services |
| 7. Prevention of exacerbations, early management of exacerbations | 15. Psychological support |
| 8. Tips for daily life and management of dyspnea | 16. Ethical issues |

(Pulmonary Rehabilitation Manual, 2007)

c. Nutrition management

(p96)

- About 70% of Japanese COPD patients experience weight loss, indicating that the incidence of nutrition disorders in Japan is higher than in Western countries.
- Mild weight loss is mainly attributable to the decrease in fat mass (FM), whereas moderate or severe weight loss represents marasmic protein-energy malnutrition accompanied by a decrease in muscle protein mass.
- The incidence of progression to respiratory failure and the risk of death are high in patients with weight loss. Weight loss is a prognostic factor that is independent of airflow obstruction.
- Patients whose %IBW is less than 90% are suspected of having a nutrition disorders, and nutrition therapy is indicated. Since most patients whose %IBW is less than 80% have lean body mass (LBM), aggressive nutritional supplementation therapy should be considered.
- Nutritionists, physicians, and nurses should form a team to provide behavioral therapy as part of nutritional guidance.

IBW : $80 \leq \%IBW < 90$: mild decrease; $70 \leq \%IBW < 80$: moderate decrease; $\%IBW < 70$: marked decrease

BMI : low body weight < 18.5 , standard body weight 18.5 - 24.9, excess body weight > 25.0

d. Oxygen therapy

(p101)

- In Japan, COPD patients account for 48% of all patients who receive long-term oxygen therapy (LTOT) or home oxygen therapy (HOT).
- LTOT for more than 15 h/day improves the survival prognosis of COPD patients with severe chronic respiratory failure.
- LTOT is indicated for chronic respiratory failure in patients whose PaO_2 is 55 Torr or less, and in patients whose PaO_2 is 60 Torr or less who exhibit marked hypoxemia during sleep or during exercise and for whom the physician has concluded that HOT is necessary. The PaO_2 value estimated based on the SpO_2 can be used as the basis for determining whether oxygen therapy is indicated, but maximum effort to perform arterial blood gas analysis should be made before instituting oxygen therapy.
- To achieve better understanding of oxygen therapy it is important to educate patients' families as well as the patients themselves.
- Airplane travel can result in an exacerbation of hypoxemia in patients whose resting PaO_2 is 70 Torr or less.

It should be noted that the criteria provided by academic societies are "indication criteria" based on medical judgments, whereas those used in the social insurance system are "eligibility criteria" based on public health policy judgments.

■ Eligibility criteria for Japanese-National-Health Insurance-covered HOT

● Diseases covered by Japanese National Health Insurance

1. Severe chronic respiratory failure
2. Pulmonary hypertension
3. Chronic heart failure
4. Cyanotic congenital heart defects

● Eligible patients with severe chronic respiratory failure

Patients whose PaO_2 is 55 Torr or less, and patients whose PaO_2 is 60 Torr or less who exhibit marked hypoxemia during sleep or exercise and for whom the physician has concluded that HOT is necessary. The PaO_2 value estimated based on SaO_2 can be used to determine whether HOT is indicated.

(Interpretation of the revision of medical fees in fiscal year 2006)

e. Ventilatory support

(p106)

- Introduction of home mechanical ventilation therapy (HMV) should be considered only when other treatments such as pharmacologic therapy, pulmonary rehabilitation, and nutrition therapy are provided at their maximum levels.
- Noninvasive intermittent positive-pressure ventilation (NPPV) should be the method of ventilatory support of first choice because of its ease of institution and low invasiveness.
- Institution of NPPV should be considered in the following patients: patients with hypercapnia ($\text{PaCO}_2 \geq 55$ Torr) or sleep-disordered breathing such as nocturnal hypoventilation, and such symptoms as dyspnea, morning headaches, and hypersomnolence, or such signs as cor pulmonale; and patients with a history of repeated exacerbations.
- Institution of HMV requires sufficient preparation and training, and it is preferable to have the support of a multidisciplinary medical team to obtain satisfactory outcomes.

f. Surgical treatments, endoscopic treatments

(p109)

- Surgical treatment should be considered for patients in whom only limited therapeutic efficacy has been obtained despite fully adequate medical treatment.
- Lung volume reduction surgery (LVRS) is indicated for patients with reduced exercise tolerance in whom emphysematous lesions are unevenly distributed and predominantly present in the upper lobes. The positive effect of the surgery on FEV_1 values lasts for about three years postoperatively.
- Bronchoscopic volume reduction (BVR), a less invasive procedure, is in the development stage.
- COPD is the most frequent indication for lung transplantation in Western countries, but there have only been few cases of lung transplantation for COPD in Japan. Juvenile COPD (pulmonary emphysema) is an indication for bilateral lung transplantation.
- Predicted postoperative %FEV and %DLCO, and preoperative $\text{V}_{O_2\text{max}}$ are useful as predictors of postoperative complications and mortality in patients with lung cancer complicated by COPD.

C-4. Treatment of COPD complicated by asthma

p116

- Concurrent asthma is suspected in COPD patients with such symptoms as paroxysmal dyspnea, wheezing, and cough occurring predominantly during the night and in the early morning.
- Findings such as the presence of an atopic predisposition and increase eosinophil count in sputum and peripheral blood suggest complication by asthma.
- Corticoid inhalation therapy should be used in cases of COPD complicated by asthma, regardless of the severity of the COPD.
- Either an anticholinergic agent or β_2 -agonist can be used as a long-acting bronchodilator in combination with an inhaled corticosteroid. Both of an anticholinergic agent and a β_2 -agonist should be used concomitantly when combination treatment with a single bronchodilator is ineffective.
- Combined use of a leukotriene receptor antagonist is also effective.

■ Diagnostic indices for concurrent asthma

1. Paroxysmal dyspnea
2. Wheezing and cough, especially when they occur during the night and in the early morning
3. Presence of atopic predisposition (IgE antibodies to environmental allergens)
4. Increased eosinophil count in sputum and peripheral blood

■ Diseases to include in the differential diagnosis

1. Upper airway diseases
Laryngitis, epiglottitis, vocal cord dysfunction (VCD)
2. Central airway diseases
Tracheal tumor, tracheal foreign body, tracheomalacia, bronchial tuberculosis, sarcoidosis
3. Diseases of the bronchi and pulmonary alveoli
Diffuse panbronchiolitis, pulmonary fibrosis, hypersensitivity pneumonitis
4. Cardiovascular diseases
Congestive heart failure, pulmonary thromboembolism
5. Cough caused by angiotensin-converting enzyme inhibitors or other drugs
6. Other diseases
Spontaneous pneumothorax, vagus nerve stimulation symptoms, hyperventilation syndrome, psychogenic cough
7. Allergic respiratory diseases
Allergic bronchopulmonary aspergillosis, allergic granulomatous angiitis (Churg-Strauss syndrome), eosinophilic pneumonia

(Modified in part from the Guidelines for Asthma Management and Prevention, 2006)

C-5. Systemic comorbidities and pulmonary complications

p118

- Prevention and treatment of systemic comorbidities and pulmonary complications are an integral part of the treatment of COPD, because they are important factors affecting the severity of the patient's condition, QOL, and survival prognosis.
- Systemic comorbidities associated with COPD include osteoporosis, cardiovascular diseases, gastrointestinal diseases, and depression. Pulmonary complications include pulmonary hypertension, pneumonia, pneumothorax, and lung cancer.
- Countermeasures against cardiovascular diseases and lung cancer are particularly important because they can cause death along with respiratory failure.

C-6. Home management

p121

- Home management is based out of respect for the wishes and hopes of the patient, and is intended to increase the level of the patient's and the family's QOL by minimizing the need for hospitalization and providing them with support for a more independent lifestyle by improving the treatment environment in the home.
- The success of home management lies in the use of the liaison critical path involving acute phase hospitals, recovery phase hospitals, primary care physicians, and home-visiting nursing stations in the local healthcare network.
- Social resources such as provided by the social welfare law of disabled persons (disability certification) and nursing care insurance should be used to reduce the burden on the patient and family.
- Self-management education has proven to be effective in the home management of COPD. It is desirable to establish a comprehensive home management system including home rehabilitation, home-visit nursing, and telemedicine.

■ Disability ratings based on the levels of respiratory dysfunction

Class	Classification criteria	Comments
Class 1	Daily self-care activities are extremely restricted by respiratory dysfunction	So breathless that the patient can hardly walk. FEV ₁ /predicted VC is impossible to measure because of respiratory dysfunction. FEV ₁ /predicted VC < 20 or PaO ₂ ≤ 50 Torr
Class 3	Daily domestic activities are markedly restricted by respiratory dysfunction	FEV ₁ /predicted VC > 20 - 30 or PaO ₂ ≥ 50 - 60 Torr or equivalent conditions
Class 4	Daily social activities are markedly restricted by respiratory dysfunction	FEV ₁ /predicted VC ≥ 30 - 40 or PaO ₂ ≥ 60 - 70 Torr or equivalent conditions

D. Management during exacerbations

p125

D-1. Definition, frequency, and causes of exacerbations

p125

- Exacerbation of COPD means sudden worsening of symptoms such as dyspnea, cough, and sputum, that differs from ordinary physiological fluctuations and requires changes from the treatment during the stable period. “Exacerbation” does not refer to aggravations of symptoms that are attributable to concurrent diseases such as heart failure, pneumothorax, or pulmonary thromboembolism.
- The most common causes of exacerbations are respiratory infection and air pollution. However, in about 30% of the cases the cause is unknown.

D-2. Severity assessment, tests, indications for hospitalization

p127

- The severity classification based on aggravation of dyspnea, increased sputum volume, and purulence of sputum is useful in deciding whether to treat with antibiotics.
- Tests are necessary to decide on a plan of treatment, to decide whether hospitalization is indicated, and to make the differential diagnosis of other diseases.
- Inpatient treatment is recommended for patients in respiratory failure, patients classified as being in stage III (severe airflow obstruction), and patients classified as being in stage IV during the stable period.

■ Classification of the severity of exacerbations of COPD

Mild exacerbation	At least one of the three indices: aggravation of dyspnea, increase in sputum volume, purulent sputum is positive, and at least one of the following is present: upper respiratory tract infection within 5 days, pyrexia that cannot be attributed to other causes, increased wheezing, increased cough, more than 20% increase in respiration rate or heart rate.
Moderate exacerbation	Two of the three indices are positive.
Severe exacerbation	All the three indices are positive.

■ Indications for hospitalization

- Sudden aggravation of dyspnea
- Development of cyanosis or edema
- Lack of response to the initial treatment for the exacerbation
- A serious comorbidity
- Frequent exacerbations
- Onset of arrhythmia
- Uncertain diagnosis requiring differential diagnosis
- Elderly patients
- Insufficient home support

D-3. Pharmacologic therapy for exacerbations

p129

- Prior patient education is important for early detection and adequate management of exacerbations.
- The principles of pharmacologic therapy during exacerbations is summed up in the acronym ABC: antibiotics, bronchodilators, and corticosteroids.
- First-line drugs for the treatment of exacerbations of dyspnea are inhaled short-acting β_2 agonists.
- Systemic corticosteroid therapy is recommended for exacerbations in patients whose disease stage was assessed as stage III (severe airflow obstruction) or IV (very severe airflow obstruction) during the stable period, in patients who require inpatient management, and in patients under outpatient management who have severe dyspnea. In general, prednisolone is administered in doses of 30 - 40 mg/day for 7 - 10 days.
- Use of antibiotics is recommended for patients with purulent sputum and patients who require ventilatory support.

D-4. Removal of airway secretions

p133

- When an exacerbation is due to bacterial infection, purulent sputum is observed.
- Bronchodilators, corticosteroids, and antibiotics that are used to treat exacerbations are effective in removing airway secretions.
- Non-pharmacologic methods of removing airway secretions include airway humidification with a nebulizer, tapping, squeezing, postural drainage, and use of sputum removal equipment.

D-5. Oxygen therapy

p135

- Oxygen therapy is indicated for patients whose PaO_2 is less than 60 Torr or SpO_2 is less than 90%.
- The goal of oxygen therapy is the recovery of PaO_2 to 60 Torr or over, or SpO_2 to 90% or over.
- Excessively high PaO_2 increases the risk of CO_2 narcosis. Oxygen administration should be started at low flow rates, especially in cases of type II respiratory failure ($\text{PaO}_2 \leq 60$ Torr and $\text{PaCO}_2 > 45$ Torr).
- Ventilatory support should be considered for patients with $\text{PaCO}_2 > 45$ Torr and $\text{pH} < 7.35$.

D-6. Ventilatory support

p137

- Ventilatory support is indicated when respiratory status fails to improve despite fully adequate pharmacologic therapy and oxygen therapy.
- NPPV should be the first choice for ventilatory support in exacerbations of COPD.
- Invasive positive-pressure ventilation (IPPV) is indicated in patients who require some kind of airway maintenance.
- Adequate informed consent must be obtained before implementation of ventilatory support.

■ Criteria for institution of NPPV

Presence of at least two of the following conditions:

1. Use of accessory respiratory muscles and dyspnea associated with paradoxical respiration
2. Respiratory acidosis with $\text{pH} < 7.35$ and $\text{PaCO}_2 > 45$ Torr.
3. Respiration rate exceeding 25/min.

D-7. Ventilatory support

p140

- It is important to educate patients in the stable stage about how to prevent exacerbations and how to deal with exacerbations when they occur.
- Smoking cessation, vaccination, inhaled corticosteroids, and long-acting bronchodilators are effective in preventing exacerbations.

E. Prognosis

p142

- The progression of COPD results in a poorer survival prognosis. However, an improvement in prognosis can be expected with adequate management.
- Prognostic factors include age, sex, smoking, level of dyspnea, FEV₁, airway hypersensitivity, pulmonary hyperinflation, hypoxemia, pulmonary hypertension, exercise tolerance, exacerbations, systemic comorbidities, and pulmonary complications.
- Smoking cessation, influenza vaccination, and LTOT/HOT can improve the survival prognosis of COPD patients. Furthermore, combined use of a long-acting β_2 -agonist and inhaled corticosteroid as well as inhalation of a long-acting anticholinergic agent may improve the survival prognosis.

Ethical issues

p146

- Informed consent must be obtained before treatment. Information based on scientific evidence must be provided to the patient and family from their point of view to inform them of all treatment options and that they may change their choice of options during the course of treatment.
- Advance directives include a wide range of instructions regarding a living will and “do not resuscitate” directives. Patients are invited to express their will and wishes regarding terminal care and intensive care during future exacerbations, as well as regarding the use of a mechanical ventilator.
- The privacy of the patient must be given primary consideration. Patients must also be fully informed of their right to protection of their privacy.

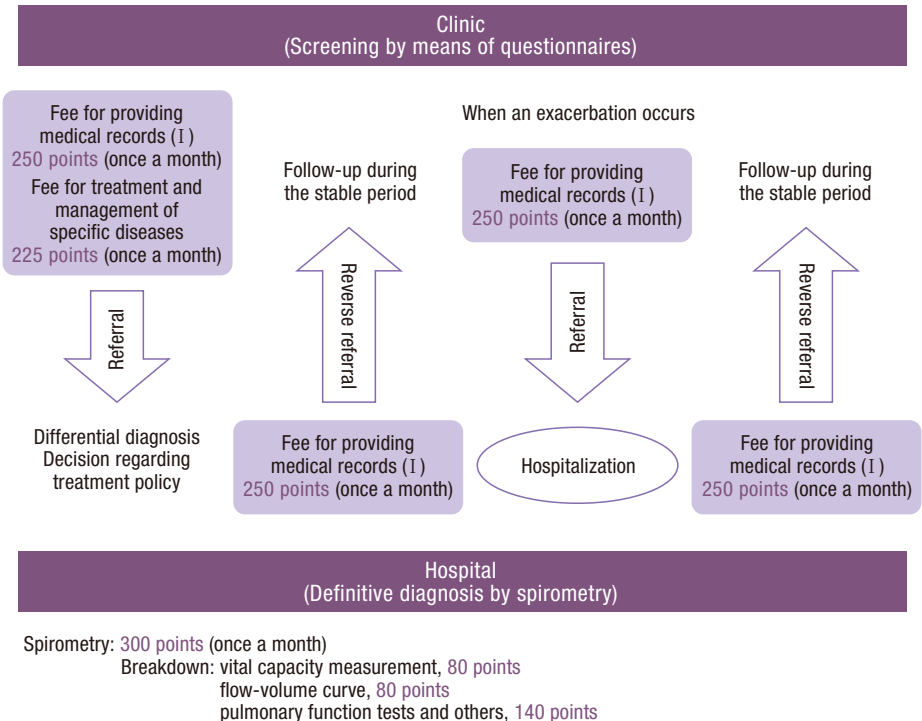
COPD in primary care

p156

- Since many patients who actually have COPD are attending primary care clinics, COPD should be suspected and diagnosed aggressively in patients attending clinics for other diseases.
- The “IPAG handbook”, a set of guidelines for the diagnosis and management of COPD intended for primary care physicians, is provided by the International Primary Care Airways Group. A Japanese-language version of the handbook is available for free download at the homepage of the Japanese Respiratory Society.
- The following procedure should be followed in patients with symptoms suggestive of airway diseases, such as cough, wheezing, breathlessness (dyspnea), tightness in the chest, watery nasal discharge, and nasal itching, 1) confirm chronicity, 2) rule out non-respiratory diseases, 3) rule out infection. If a chronic airway disease is suspected, questionnaires and diagnostic guides should be used to proceed in making the diagnosis.
- A “COPD questionnaire” can be used for patients suspected of having COPD. A “differential diagnosis questionnaire” is available for use in cases requiring differential diagnosis from asthma.
- Diagnostic treatment is emphasized in primary care. If spirometry is not available or a diagnosis cannot be made based on the physical findings, it is recommended that diagnostic treatment be started and the diagnosis be made according to the response. However, at some point pulmonary function tests become necessary to make a definitive diagnosis and to accurately evaluate the patient’s condition.
- When differential diagnosis between COPD and asthma is difficult, treatment for asthma should be given priority. The clinical course should be assessed after sufficient treatment for asthma with a combination of an inhaled corticosteroid plus long-acting β_2 -agonist (plus leukotriene receptor antagonist and theophylline). If there is no response, the conditions can be diagnosed as COPD. If there is a partial response, a diagnosis of COPD complicated by asthma can be made.
- In principle, the severity assessment should be based on respiratory function and manifestations. However, if spirometry is not available, severity can be estimated on the basis of the degree of the manifestations.
- Since COPD is a chronic disease accompanied by many comorbidities, it is more beneficial for patients to receive care related to daily management at primary care clinics. Therefore, it is recommended that primary care physicians be in charge of daily practice and refer patients to specialists when exacerbations or complications develop.

- Referral to a specialist is necessary in the following situations: when it is difficult to make a definitive diagnosis; when it is difficult to diagnose complications or assess the severity; when there is no response to the initial treatment; when previously effective treatment becomes ineffective; when the primary care physician believes the case is too difficult to handle for any reason.
- Patients whose PaO₂ is less than 60 Torr or whose SpO₂ is less than 90%, or patients assessed as stage III (severe airflow obstruction) or IV (very severe airflow obstruction) in a stable period who experience an exacerbation must be referred to specialized hospitals to receive inpatient care.

■ Cooperation between medical institutions in Japan in regard to the treatment of COPD



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