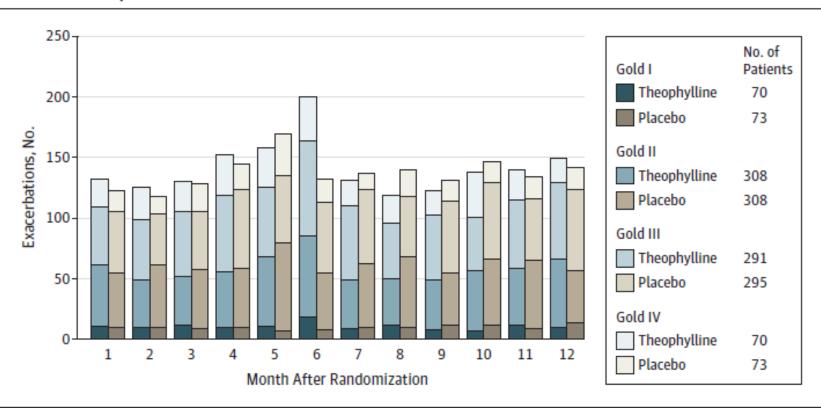
Figure 2. Exacerbations for Each Treatment Month by Baseline GOLD Stage^a for Low-Dose Theophylline and Placebo Groups^b



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Chronic COPD

- <u>Theophylline</u> may favorably affect the major factors associated with functional impairment in chronic obstructive pulmonary disease (COPD), such as dyspnea, exercise capacity, respiratory mechanics, and respiratory muscle strength. (See <u>'Effects on functional impairment'</u> above.)
- <u>Theophylline</u> is generally considered a third-line bronchodilator drug in chronic COPD, after inhaled anticholinergics and beta-2 agonists. (See <u>"Management of refractory chronic obstructive pulmonary disease"</u>, <u>section on 'Theophylline'</u>.)
- For patients with persistent functional impairment despite both smoking cessation and the use of inhaled bronchodilators, <u>theophylline</u> may reduce functional impairment and exacerbation frequency, although the effect in individual patients is variable. (See <u>'Effects on functional impairment'</u> above.)
- In general, patients with COPD can be adequately treated with serum levels in the 8 to 12 mcg/mL range. Once an
 appropriate serum level has been achieved, subsequent measurements can be made at 6 to 12 month intervals or
 if the patient's clinical status or concomitant medications change. (See <u>'Dosing'</u> above.)
- When compared to acute intoxication, chronic <u>theophylline</u> overmedication is associated with a greater frequency of major toxicity, occurs at relatively lower theophylline levels, and cannot be predicted by the peak serum theophylline concentration. (See <u>"Theophylline poisoning"</u> and <u>'Toxicity'</u> above.)

Acute COPD exacerbation

 Methylxanthines are NOT recommended for routine management of acute exacerbations of COPD. In addition to a lack of efficacy in this setting, methylxanthines increase the likelihood of side effects (eg, nausea, vomiting). (See <u>'Acute exacerbation'</u> above.)

COPDの急性増悪の治療

- A table to assist with emergency management of severe exacerbations of COPD is provided (table 1).
- An exacerbation of COPD is characterized by an acute increase in symptoms beyond normal day-to-day variation that leads to a change in medication. (See <u>'Introduction'</u> above.).
- We recommend that all patients having a COPD exacerbation receive inhaled short-acting bronchodilator therapy (<u>Grade 1B</u>). Short-acting beta-adrenergic agonists (SABA, eg, <u>albuterol</u>, <u>levalbuterol</u>) are the mainstay of therapy; a short-acting anticholinergic agent (eg, <u>ipratropium</u>) may be used as an alternative, or in combination with the SABA. For more severe exacerbations, the combination is usually preferred. (See <u>'Beta adrenergic agonists'</u> above and <u>'Anticholinergic agents'</u> above.)
- We recommend that all patients having a COPD exacerbation receive systemic glucocorticoids (<u>Grade 1A</u>). A
 reasonable dose for patients not requiring intensive care unit admission is <u>prednisone</u> 40 to 60 mg orally once
 daily, or the equivalent, for 5 to 14 days. (See <u>'Systemic glucocorticoids'</u> above.)
- Antibiotics are indicated for many patients having a COPD exacerbation. (See "Management of infection in exacerbations of chronic obstructive pulmonary disease", section on 'Summary and recommendations' and "Evaluation for infection in exacerbations of chronic obstructive pulmonary disease", section on 'Summary and recommendations'.)

 「テオフィリンの事
- Mucoactive agents, methylxanthines, and mechanical techniques to augment sputum clearance have not been shown to confer benefit for COPD exacerbations. (See 'Treatments without documented benefit' above.)
- Patients with hypoxemia due to an exacerbation of COPD should receive supplemental oxygen. We suggest that supplemental oxygen be titrated to a target of 88 to 92 percent pulse oxygen saturation, rather than using highflow, untitrated oxygen (<u>Grade 2B</u>). (See 'Oxygen therapy' above.)
- Noninvasive ventilation (NIV) improves numerous clinical outcomes and is the preferred method of ventilatory
 support in many patients with an acute exacerbation of COPD. Invasive mechanical ventilation is required in
 patients with respiratory failure who fail NIV, do not tolerate NIV, or who have contraindications to NIV. Both NIV
 and invasive mechanical ventilation for patients with an exacerbation of COPD are discussed separately. (See
 "Noninvasive ventilation in acute respiratory failure in adults" and "Invasive mechanical ventilation in acute
 respiratory failure complicating chronic obstructive pulmonary disease".)
- Several measures have been shown to reduce COPD exacerbations, including smoking cessation, pulmonary rehabilitation, proper use of medications (including metered dose inhaler technique), and vaccination against seasonal influenza and pneumococcus. (See <u>'Prevention'</u> above.)

COPDの急性増悪にはテオフィリンは元来効果はありません。 役割分担が違うのではと思うのですが?

SUMMARY AND RECOMMENDATIONS

- <u>Theophylline</u> has bronchodilatory, anti-inflammatory, immunomodulating, and bronchoprotective effects. (See <u>'Therapeutic actions'</u> above.)
- <u>Theophylline</u> remains a potentially useful and inexpensive medication for patients with chronic asthma whose symptoms are not controlled with conventional doses of inhaled glucocorticoids, and patients who cannot take or are poorly compliant with inhaled medications. (See <u>'Indications'</u> above.)
- The addition of <u>theophylline</u> to inhaled glucocorticoids is more effective than increasing the dose of inhaled glucocorticoids. (See <u>'Additive maintenance therapy'</u> above.)

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- <u>Salmeterol</u> is more effective than <u>theophylline</u> when added to inhaled glucocorticoids, although the differences are
 not large. More studies are needed to evaluate the relative efficacy of therapeutic concentrations of theophylline
 and anti-leukotriene agents as add-on therapies. In patients in whom the addition of a long-acting beta agonist
 (LABA) to high dose inhaled glucocorticoid does not seem effective, a trial of substituting theophylline for the
 LABA may be worthwhile. (See <u>'Compared to other additive therapies'</u> above.)
- <u>Theophylline</u> is not routinely indicated for the treatment of acute severe asthma in the intensive care unit.
 Intravenous theophylline (as theophylline or <u>aminophylline</u>) may be added when patients with severe acute asthma fail to respond to vigorous use of inhaled <u>albuterol</u> and <u>ipratropium</u> with systemic glucocorticoids, although evidence for this is lacking. (See <u>'Additive acute therapy for hospitalized patients'</u> above.)
- Safe use of oral <u>theophylline</u> as a maintenance therapy requires initiating treatment at a low dose, measuring a serum concentration to adjust the dose, and reducing the dose in the presence of physiologic states or medications that impair theophylline metabolism. (See 'Safe use of theophylline' above.)
- The absorption characteristics of specific formulations vary considerably, particularly with regards to the effects of food. Familiarity with these details is important. (See 'Selection of product and dosing interval' above.)

喘息におけるテオフィリンの効果です