

were excluded (7177 patients were included). Significant reductions in stent thrombosis with continued thienopyridine, as compared with placebo, were observed within 3 months after randomization (0% vs. 0.23%, $P=0.01$), and the difference increased over the 12-to-30-month treatment period (0.23% vs. 0.72%; hazard ratio, 0.33; 95% CI, 0.15 to 0.72; $P=0.004$). Furthermore, in this subgroup analysis, as in the primary analysis, continued thienopyridine was associated with a larger absolute risk reduction for myocardial infarction that was not related to stent thrombosis (absolute difference, 0.81 percentage points), as compared with the risk reduction for the end point of stent thrombosis. These findings highlight the relevance of the study results to current coronary procedures and secondary prevention of myocardial infarction.

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Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc1501195

Multiple-System Atrophy

TO THE EDITOR: Fanciulli and Wenning's review (Jan. 15 issue)¹ on multiple-system atrophy is comprehensive and up to date. In it, the authors state that the open-label administration of gabapentin could ameliorate cerebellar symptoms in single cases of this disease. However, the cited reference describes a noticeable improvement in gait in one patient who received a diagnosis of olivopontocerebellar atrophy (OPCA) after a single dose of 400 mg of gabapentin and alleviation of dysarthria and oscillopsia in another patient with OPCA during long-term therapy with gabapentin.² These patients could not have received a diagnosis of multiple-system atrophy, since neither had features of autonomic dysfunction.³ In contrast, gabapentin was found to cause generalized weakness and to worsen gait and dysarthria in three patients with multiple-system atrophy, forcing withdrawal of the drug.⁴

The reasons for the differing effectiveness of gabapentin in patients with multiple-system atrophy (a primary oligodendroglial α -synucleinopathy) and OPCA (a neuronopathy of the cerebellar cortex, inferior olive, and pontine nuclei)⁵ could depend on differences in pathophysiology or neurochemistry between these diseases, although the precise cause remains undetermined.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1501657

TO THE EDITOR: In their review, Fanciulli and Wenning point out that urinary dysfunction is a key feature of multiple-system atrophy, with urgency, daytime frequency, and nocturia being the most common urinary symptoms. However, it

should be noted that although overactive bladder is a common feature in Parkinson's disease, multiple-system atrophy is far more frequently characterized by detrusor underactivity, dyssynergic urethral function, and incomplete bladder emptying alone or in association with storage symptoms.¹ This could be related in part to cell loss affecting the Onuf nucleus, which is usually spared in Parkinson's disease.² α -Adrenergic blockers can be prescribed to improve bladder emptying, as advocated in the review, but they should be used with extreme caution because of the autonomic failure with orthostatic hypotension present in most patients and the inherent risk of syncope with α -adrenergic antagonist medication.³ Clean, intermittent self-catheterization is the mainstay of management of bladder-emptying problems if allowed by the patient's motor impairment; the safety profile is excellent, and the problems of urethral ulceration described in the article are rare.⁴

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DOI: 10.1056/NEJMc1501657

TO THE EDITOR: I read with interest Fanciulli and Wenning's review but was dismayed by the statement that placement of a percutaneous endoscopic gastrostomy tube lowers the risk of aspiration pneumonia. This widely held idea has never been proved to be true. As Marik pointed out,¹ feeding tubes cannot protect against contaminated oral secretions, a major risk factor for

the development of pneumonia. In addition, patients with percutaneous endoscopic gastrostomy tubes have frequent gastroesophageal reflux, more commonly in those with neurologic versus mechanical dysphagia.² One study involving patients in nursing homes showed that tube feeding was an independent risk factor for the development of aspiration pneumonia, with an odds ratio of 3.0.³

In a review of tube feeding in patients with advanced dementia, Finucane et al.⁴ found no data to support this intervention, a conclusion that is likely to be applicable in the setting of progressive neurodegenerative disease. For patients with multiple-system atrophy, tube feeding is unlikely to be helpful and could potentially be harmful.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1501657

THE AUTHORS REPLY: In response to Gazulla and Berciano: to date, there is no symptomatic treatment available for cerebellar ataxia associated with multiple-system atrophy. Gazulla and colleagues previously found class IV evidence for the efficacy of gabapentin in OPCA, a nosologic entity that may evolve into multiple-system atrophy of the cerebellar subtype. Gazulla and colleagues subsequently found side effects of open-label gabapentin or pregabalin administration in three patients with multiple-system atrophy (class IV evidence). We conclude that the currently available evidence regarding the safety and efficacy of gabapentin in multiple-system atrophy is insufficient.

Urge incontinence was reported more frequently than incomplete bladder emptying in two

epidemiologic cohorts of patients with multiple-system atrophy, with simultaneous occurrence in one third of cases.^{1,2} Clean, intermittent self-catheterization is the first-line therapy for urinary retention of more than 100 ml, and α_1 -adrenoreceptor blockers have been proposed as add-on therapy.³ We agree with Peyronnet and colleagues that α_1 -adrenoreceptor blockers should be used cautiously in patients with multiple-system atrophy owing to exacerbation of orthostatic hypotension. Tamsulosin may be preferred to other α_1 -adrenoreceptor blockers, given a higher selectivity for prostatic α_1 -adrenoreceptors.⁴ Evening scheduling of α_1 -adrenoreceptor blockers is preferred in order to minimize hypotensive side effects and to manage nocturnal hypertension in affected patients. Nocturnal use of urine condoms can represent an additional safety measure to prevent orthostatic syncope in patients with nocturia and orthostatic hypotension.

In response to Babu: aspiration pneumonia is the most common cause of death in multiple-system atrophy. In patients with severe dysphagia, tube feeding may be necessary to prevent choking, provide adequate caloric intake, and reduce the amount of aspirated oropharyngeal

material. It cannot, however, prevent the aspiration of oral secretion. To this end, strategies aimed at reducing saliva production could be implemented (e.g., botulinum-toxin injection into salivary glands or scopolamine transdermal patch), but evidence for the safety and efficacy of such approaches is limited in multiple-system atrophy.

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Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc1501657

Severe Ebola Virus Infection Complicated by Gram-Negative Septicemia

TO THE EDITOR: The World Health Organization (WHO) recently published its first global report on antimicrobial resistance surveillance.¹ For countries in the WHO African region, the proportions of invasive *Escherichia coli* isolates that were antimicrobial-resistant ranged from 0 to 36% for third-generation cephalosporins and from 0 to 53% for fluoroquinolones. In the past few years, studies from Europe and Canada have consistently shown that fecal colonization by multidrug-resistant Enterobacteriaceae is common in returning international travelers (with rates of 22 to 53% among travelers returning from Africa).²⁻⁴ These generally were *E. coli* isolates that produced an extended-spectrum beta-lactamase and were resistant to third-generation cephalosporins as well as to several other classes of antibiotic agents including fluoroquinolones. As suggested by Kreuels et al. (Dec. 18 issue),⁵

sepsis that is likely to be due to bacterial translocation may complicate Ebola virus disease (EVD) and contribute to mortality. While treating clinicians await the results of blood cultures, empirical antimicrobial treatment of sepsis should take into account the consideration of fecal colonization by multidrug-resistant Enterobacteriaceae in patients with EVD who were treated in or medically evacuated from Africa.

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No potential conflict of interest relevant to this letter was reported.

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