

theophylline acutely or chronically it is wise to reduce risk by aiming for a serum concentration of 5–10 mg/L in many patients. The National Institutes of Health expert panel report similarly recommends aiming for 5–15 mg/L. Should we discard “an old friend”? Theophylline still has a role in asthma management, but on the basis of present research and the availability of agents that are safer and more effective, it is a very small role. On the other hand, in the long-term management of chronic obstructive pulmonary disease, some patients receive definite benefit in relief of dyspnoea, and its role seems more secure.⁵

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SIR—In his commentary, Banner raises several issues. The therapeutic range for theophylline was decided on the basis of the acute bronchodilatory effect of intravenous aminophylline in asthmatics.¹ Theophylline increased the forced expiration volume (FEV₁) throughout the plasma range of 55–110 µmol/L (10–20 mg/L). The upper range of the dose-response was not explored because of the likelihood of toxicity. At this time it was judged that theophylline exerted its beneficial effect via inhibition of phosphodiesterase. Doubt has been cast on the importance of this mechanism of action because the inhibitory constant for inhibition of phosphodiesterase by theophylline was shown to be well above the therapeutic range in vitro.² There is a large, heterogeneous family of phosphodiesterases, and a phosphodiesterase has been identified in guineapig trachea with an inhibitory constant for theophylline of 57 µmol/L.³ Because about 50% of theophylline in plasma is protein bound, this would equate to a plasma concentration of 104 µmol/L. If a similar phosphodiesterase were present in man it could readily account for theophylline-induced bronchodilation.

Theophylline has many other actions. In-vitro studies have shown adenosine antagonism by theophylline even below the accepted therapeutic range,⁴ and this has been shown to occur in man. Adenosine causes vasodilation when infused directly into the brachial artery. Two groups of patients with essential hypertension were compared (off medication). Vasodilation by adenosine was significantly blunted in the group in which aminophylline was co-infused with adenosine, with a dose of aminophylline insufficient to cause vasodilation. To investigate whether phosphodiesterase inhibition might in some way account for this effect, papaverine (a phosphodiesterase inhibitor with no adenosine antagonist properties) was substituted for aminophylline. It had no effect on adenosine-induced vasodilation both at a non-vasodilating dose and at a higher, vasodilating dose.⁵

A careful evaluation is needed of the possible beneficial mechanisms of action of theophylline in the treatment of acute and chronic airflow limitation. This examination should reveal avenues for development of newer, more

effective, less toxic agents for treatment of these conditions. If it turns out that acute bronchodilation is not the main beneficial effect, then a lower therapeutic range may be indicated.

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Treatment of long-standing Lyme disease with ceftriaxone

SIR—It is well known that spirochaetal infections can persist for many years. However, reports on long-standing Lyme borreliosis are scant.^{1,2} Here we report on a case of Lyme borreliosis that had persisted for 53 years.

An 89-year-old female patient contracted *Borrelia burgdorferi* infection in 1938. At that time, she exhibited the salient characteristics of Lyme disease: erythema migrans and 'flu-like symptoms for a week followed by neurological symptoms, especially paraesthesias, headaches, and neck stiffness. Her memory of the tick bite, erythema migrans, and the following symptoms was very clear. Later she had recurrent episodes of arthralgia, myalgia, dizziness, headaches, recurrent paraesthesias, and occasionally an irregular heart beat. These symptoms have persisted with changing intensity for the past 53 years. Upon physical examination, she exhibited characteristic acrodermatitis chronica atrophicans (ACA) on her hands and legs. IgG and western blot were positive for *B burgdorferi* infection.

The patient then was treated with intravenous ceftriaxone 2 g daily for 14 days. After an episode of increasing intensity of symptoms, which lasted for a day, symptoms gradually diminished. A week after the end of treatment, she was symptom free. She has been seen twice during the following year and has remained without symptoms. The ACA has improved despite her age. Blood samples showed decreasing IgG against *B burgdorferi*.

We conclude that *B burgdorferi* infection may persist for many years without necessarily causing permanent damage. Thus, even in very long-standing cases of Lyme disease, antimicrobial treatment can prove beneficial and it should not be withheld.

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