with fractalkine, and articles such as that of Balabanian and colleagues provide an essential test of the durability of such putative mechanisms in the context of disease.

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I am sure this article will stimulate discussions, but it does not provide us with the information we yet need. Rigid studies are needed that are of the same scientific quality as the study by Culpitt and coworkers in a larger number of patients and definitely over a longer period of time to provide solid advice to physicians on the role of theophylline for COPD, as they undoubtedly will not measure inflammatory markers in sputum. For longer term studies in patients with COPD and significant comorbidity, compliance and side-effects will be of great importance. In this context, I was definitely surprised that 20% of subjects complained of nausea with low-dose theophylline. We should remember that chemotaxis of neutrophils to the very same stimulus N-formyl-methionyl-leucyl-phenylalanine can be inhibited by other remedies, including chicken soup (9), which undoubtedly has potential for fewer adverse events, although in this case, long-term trials and health economic assessments are also still outstanding.

The article of Culpitt and associates undoubtedly adds to the current literature and addresses the urgent clinical question of how to deal with inflammation in COPD. What the article cannot do is provide evidence that low-dose theophylline is of any clinical benefit for patients with COPD. The only way to prove that this form of treatment is clinically superior to other remedies, including chicken soup, is performing a long-term clinical trial with theophylline in COPD, something Albrecht Kossel has not yet witnessed in the 114 years since his Berlin presentation in 1888.

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