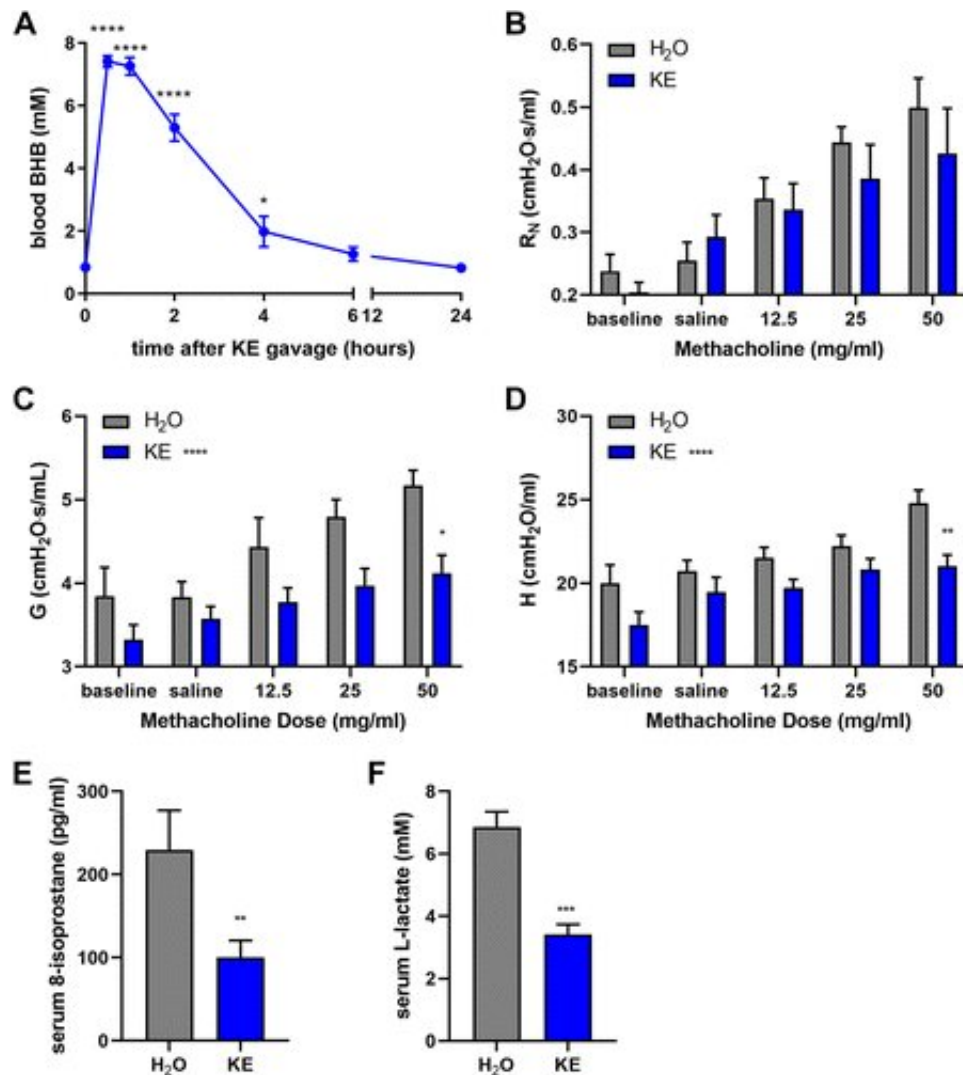


Ketone bodies reduce markers of asthma in obese mice

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Ketone ester administration acutely decreases methacholine responsiveness. Mice were administered 200 μ L of water (H₂O) or ketone ester (KE; ~4 g/kg) by oral gavage. Blood β -hydroxybutyrate (BHB) (A) was measured before or at several time points following KE administration; n = 5 mice/group. Airway

resistance (R_N) (B), tissue damping (G) (C), and tissue elastance (H) (C) were measured 1 h following water or ketone ester gavage. Serum 8-isoprostane (E) and lactate (F) were measured; $n = 6$ mice/group. * $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$, **** $P \leq 0.0001$, compared with time 0 by ANOVA (A) or the water group by t test (E and F). * $P \leq 0.05$, ** $P \leq 0.01$, compared with water group at the same dose of methacholine (B–D). Credit: DOI: 10.1152/ajplung.00309.2021

More than half of people with asthma are obese. These individuals do not respond well to standard therapies, but new research out of the Vermont Lung Center holds promise for improving asthma treatments for this population. The study is published in the *American Journal of Physiology-Lung Cellular and Molecular Physiology*. It was chosen as an APSselect article for February.

"Our results provide innovative first steps toward a safe, efficacious and cost-[effective strategy](#) that may uniquely target obese asthma," the researchers wrote.

In addition to responding poorly to [standard therapies](#), people with obesity and asthma are hospitalized at higher rates. Weight loss is a typical recommendation to ameliorate the effects of obesity on asthma. However, short of [surgical intervention](#), only about 15% of people can sustain 10% [weight loss](#) for an entire year through diet changes. Even fewer can sustain weight loss for five years.

The research team set out to explore if ketone bodies, which are products of fat metabolism generated by the liver during weight loss, could provide relief from asthma symptoms. They used both genetic and diet-induced mouse models of obesity. In these, along with normal-weight controls, they tested a variety of methods of applying ketone bodies. They induced the natural generation of ketone bodies through a

[ketogenic diet](#) in some mice and, in others, through rapid weight loss from a low-fat diet. Other cohorts were given supplementary ketone esters either long term in their food or in acute doses immediately before testing.

In all these models and methods of intervention, the mice with [ketone bodies](#) in their system showed less sensitivity to a trigger of airway constriction commonly used in the diagnosis of asthma. The authors note that ketone ester supplementation is considered safe and is already used in some human populations.

"This ketone ester supplementation strategy could be optimized as an approach to promote a state of 'therapeutic ketosis' similar to that achieved through the feeding of a ketogenic diet or fasting, without any caloric deficit or the need for substantial lifestyle modification," the authors wrote.

More information: Madeleine M. Mank et al, Therapeutic ketosis decreases methacholine hyperresponsiveness in mouse models of inherent obese asthma, *American Journal of Physiology-Lung Cellular and Molecular Physiology* (2021). [DOI: 10.1152/ajplung.00309.2021](https://doi.org/10.1152/ajplung.00309.2021)

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