Anti-inflammatory drugs may quell asthma

Asthmatic children treated with anti-inflammatory drugs fare better than their peers who receive standard therapy with bronchodilator drugs, Dutch scientists report. Their finding offers the hope that anti-inflammatory drugs will help some youngsters outgrow the debilitating respiratory illness.

Scientists know that exercise, cold air, or exposure to allergens can set off an asthma attack. Such triggers cause the muscles surrounding the airways to contract, leading to an inability to catch one's breath. But muscle contraction is just part of the asthma story. The other key component of this chronic disease is ongoing inflammation of the airways.

A team of Dutch scientists led by Elisabeth E. van Essen-Zandvliet of the Sophia Children's Hospital in Rotterdam decided to examine two pediatric asthma treatments, one designed around an anti-inflammatory drug and the other aimed at relaxing tightened airways with a bronchodilator.

They began by recruiting 116 youngsters age 7 to 16 with moderate to severe asthma. Next, the Dutch team randomly assigned each young person to one of two treatment groups. One group received treatment with an inhaled bronchodilator and a placebo three times a day. The remaining participants used a bronchodilator and an aerosol version of a steroid drug called budesonide.

On average, the children in the bronchodilator-placebo group got worse, the researchers report in the September AMERICAN REVIEW OF RESPIRATORY DISEASE, a journal published by the American Lung Association. They found that such youngsters showed declining lung function and suffered more asthma attacks than did children assigned to the other treatment regimen.

Indeed, about half the youngsters relying on the bronchodilator drug alone experienced such a decline that they were forced to drop out of the study by the 22nd week. At that time, an independent review panel stopped the trial and recommended that all the children receive treatment with inhaled steroids.

"This study suggests that anti-inflammatories can actually affect the disease process," comments H. William Kelly, an asthma expert at the University of New Mexico in Albuquerque who wrote an editorial to accompany the Dutch report. It's the first long-term pediatric study of this size, he told SCIENCE NEWS.

The new findings add to the growing unease about relying on bronchodilators as standard treatment. Many asthma experts now believe that an overuse of these drugs may cause asthma to progress. While bronchodilators do open constricted airways, they do not halt the inflammation that can ultimately cause scarring and a permanent narrowing of the bronchial tubes, Kelly notes.

The Dutch study underscores a recommendation made last year by a panel of experts appointed by the National Heart, Lung, and Blood Institute. That group advised physicians to rely on anti-inflammatory drugs as the mainstay of asthma treatment (SN: 2/9/91, p.86).

Physicians remain reluctant to prescribe inhaled steroids for their pediatric asthma patients, however, perhaps because previous studies have linked these drugs to growth abnormalities, Kelly says. While the Dutch study found no sign of impaired growth in the children taking inhaled steroids, further safety studies are needed, van Essen-Zandvliet concedes.

For now, Kelly suggests that physicians first try cromolyn sodium, an anti-inflammatory drug that is nearly free of side effects. For youngsters who continue to get worse, Kelly recommends an inhaled steroid. He believes the benefits of such therapy far outweigh the potential hazards. *—K.A. Fackelmann*

Model finds clusters for new materials

Chemists typically create new materials by joining atoms together. But scientists are now turning their attention to a different kind of building block: clusters of atoms or molecules. Toward that end, two physicists have derived a recipe for clusters most likely to form a stable solid.

By fiddling with the numbers and types of atoms in a cluster, researchers can ensure that the cluster's atoms will hang together even when they move close to another cluster to form a new material, says Purusottam Jena of Virginia Commonwealth University in Richmond.

Jena and Virginia Commonwealth colleague Shiv N. Khanna modeled clusters containing 13 aluminum atoms or 12 aluminum atoms plus a carbon or silicon atom at the cluster's core. That single-atom substitution makes the cluster much more stable and therefore amenable to staying intact, they report in the Sept. 14 PHYSICAL REVIEW LETTERS.

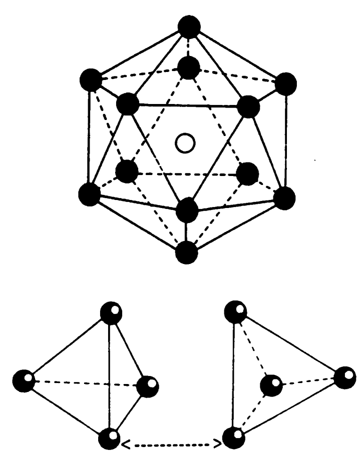
A cluster acts like a giant atom, Jena explains. In both single atoms and clusters, electrons settle into specific energy levels. An atom becomes most stable when electrons fill up a level, so atoms tend to borrow or lend leftover electrons to empty or fill incomplete levels. When an atom joins a cluster, its excess electrons become the cluster's electrons. And, like an atom, the cluster becomes most stable with its energy levels filled, Jena says.

Thus, clusters work best when the leftover, or "valence," electrons total two, eight, 20, or 40 — numbers that fill energy levels. In addition, atoms in the ideal cluster building block pack together tightly, the scientists say.

In the 13-aluminum-atom cluster studied by Khanna and Jena, the atoms form a compact, 20-sided configuration. But the aluminum contributes only 39 electrons to the cluster's levels.

Carbon and silicon both donate an extra electron, so when either stands in for one aluminum, the electrons total 40 and the cluster's atoms bind more strongly, say Jena and Khanna. The researchers also determined that these substitutions do not disrupt the close packing of atoms in the cluster.

Jena and Khanna went on to model the interaction between two aluminum-silicon clusters. Their computers were not powerful enough to deal with the energies of all 26 atoms, so the researchers simulated two four-atom magnesium clusters instead. These stable clusters contain eight valence electrons. The team tested whether the magnesium clusters shrink, swell, or twist when pushed together.



Khanna & Jena/PHYSICAL REVIEW LETTERS

Top: Aluminum cluster with silicon atom at the center. Bottom: Two close magnesium clusters.

"All they do is rotate; they don't fall apart," Jena says.

Those results bode well for the potential of aluminum-silicon clusters as building blocks, the scientists suggest. "When I pack them together, they will remain intact," says Jena. He hopes other researchers will try to make a solid using this cluster, but he notes that scientists must first develop better ways to make large quantities of clusters in specific sizes. *—E. Pennisi*