Breathing freely threatens seeing clearly

People with asthma breathed a sigh of relief with the advent of inhaled steroids in the early 1990s. These widely used, synthetic hormones relieve inflammation where it counts—in the lungs and bronchial passages—without the severe side effects of oral steroids.

So effective are inhaled steroids at staving off asthma attacks that doctors now regard them as a mainstay of therapy. Thousands of people take high doses daily in regimens that may last a lifetime.

New research indicates, however, that inhaled steroids may have an unsuspected dark side.

A study of nearly 50,000 elderly people in the Canadian province of Quebec found that prolonged, high-dose use markedly increases a person's risk of glaucoma, the leading cause of blindness.

"This was a surprise," reports Samy Suissa of McGill University Health Centre in Montreal. "We've been told inhaled steroids are safe because they act on the lungs and are not diffused through the body."

Before inhaled steroids arrived in drug stores, doctors often prescribed potent oral versions of the drug, which have severe drawbacks. Among other things, they can suppress the adrenal gland and throw the body's hormone balance out of whack. In older people, oral versions cause osteoporosis, which weakens bones.

Many studies of inhaled steroids found them to be relatively free of such side effects. Researchers attribute this safety profile to the body's ability to clear most inhaled steroids from the bloodstream.

Eighty percent of each inhalation collects in the mouth and throat; swallowing carries it to the liver, where it is metabolized. About 20 percent of each dose enters the lungs. Oxygen ushered from the lungs into the blood carries some of the inhaled asthma medicine along with it. "Steroids are apt to be disseminated throughout the body," Suissa asserts. "We wondered whether taking steroids directly into the lungs would carry them into the eyes."

Suissa and his colleagues began their study after seeing reports of two cases of glaucoma in people using inhaled steroids. Other researchers had previously reported that steroid eye drops can cause the disease.

Although no one understands precisely why glaucoma occurs, doctors have learned how the disease progresses. The eye fills with excess fluid, which puts pressure on the optic nerve, the lens, and other structures, dislodging them.

The McGill team looked for an association between inhaled steroids and glaucoma in people age 66 and older whose records appear in Quebec's centralized medical records database.

Between 1988 and 1994, 9,793 people in this group had been diagnosed as having glaucoma. For comparison, the researchers selected at random 38,325 people from the same database who did not have the disease. They found that those who had used high doses of inhaled corticosteroids for at least 3 months were 44 percent more likely to have developed glaucoma. The researchers report their findings in the March 5 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

In the United States, where about 100,000 older people use high-dose inhaled steroids, this elevated risk translates into an estimated one-third of the 3,000 cases of glaucoma among people over 65, Suissa says.

"It's an interesting finding," says Lea Davies of Georgetown University Medical Center in Washington, D.C. She adds that it would be interesting to find out whether inhaled steroids pose a similar risk to children.

Suissa, whose study did not address this issue, agrees that young people, who could take inhaled steroids for decades, may face an increased risk.

He cautioned against abandoning inhaled steroids, however, because they remain the best way to prevent sometimes fatal asthma attacks. People who use the inhalers should talk to their doctor about the risk of glaucoma and get their eyes checked at regular intervals, he advises. —*S. Sternberg*

Winging it: An unusual approach to flight

Ever desperate to leave the ground, humans will strap just about anything to their bodies and leap into the air. Hence the sports of hang gliding, skydiving, and bungee jumping, to name but a few extreme rites of flight.

Animals make do with just a few alterations of their basic skeleton. For instance, birds have a modified arm and hand, while bats rely on skin stretched over greatly elongated fingers.

A reptile from Earth's distant past developed a unique flying apparatus. Instead of fashioning a wing from its existing skeleton, this ancient creature evolved completely new bones to spread wings made of skin, according to a study of a newly discovered fossil.

"This is really without parallel in any other gliding or actively flying animal—the fact that they actually developed new skeletal elements to support the wing," says Hans-Dieter Sues of the Royal Ontario Museum in Toronto. Sues collaborated with Eberhard Frey and Wolfgang Munk of the State Museum for Natural History in Karlsruhe, Germany. They describe their work in the March 7 SCIENCE.

The animal, called *Coelurosauravus*, lived during the late Permian period, more than 250 million years ago, making it the oldest known flying vertebrate. About as long as a small squirrel, this reptile had at least 22 slender bones extending outward and back from each side of its chest. The bones supported a foldable wing, much like a Japanese fan.

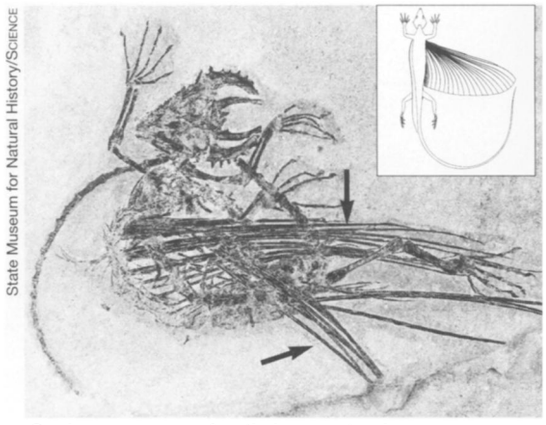
Scientists initially discovered fossils of *Coelurosauravus* in the early 1900s but until now had failed to decipher the creature's secret. The first paleontologists to study *Coelurosauravus* discovered the thin wing bones but removed them, thinking they were fish structures that had somehow been superimposed, says Robert L. Carroll of McGill University in Montreal. Later, a different paleontologist misidentified it as a dinosaur.

Carroll made his own mistakes while studying a *Coelurosauravus* fossil from Madagascar in the 1970s. He surmised that the wing bones were elongated ribs, sticking out perpendicular to the backbone in a design reminiscent of the modern gliding lizard *Draco*.

A recently discovered *Coelurosauravus* fossil from Germany, however, reveals that the wing bones were not part of the ribs, report Sues and his colleagues. Much more complete than previous specimens, the new fossil shows that the wing rods were bony structures growing out of the skin; they did not attach to the rest of the skeleton, the researchers say.

"They corrected a lot of mistakes I made and others made," says Carroll. "It's really a startlingly different kind of flying animal."

Unlike birds and bats, *Coelurosauravus* could not truly fly because it lacked muscles to flap its wings. Nonetheless, it may have covered long distances by gliding from trees. *Draco* can sail 30 meters in one leap. —*R. Monastersky*



State Museum for Natural History/SCIENCE

Coelurosauravus *fossil shows wing bones (arrows). Sketch of animal (inset) depicts one wing folded and the other spread out.*