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Allergy drugs linked to tumour growth

Results of laboratory tests arouse concern among reseachers

BY PAUL TAYLOR
Medical Reporter

A variety of widely used allergy medications appear to speed the growth of cancerous tumours in laboratory mice, according to a study by Canadian scientists.

The researchers found that three anti- histamines – Claritin, Hismanal and Atarax – acted as "tumour promoters." This means that although the drugs did not cause the cancers they did accelerate the growth of existing tumours in the mice.

"We don't want to cause panic," said Dr. Lorne Brandes, who headed the research team at the Manitoba Cancer Treatment and Research Foundation in Winnipeg.

But he added that further studies should be carried out to determine whether these drugs, which are used for relief of hay fever, allergies or itching, also promote cancer growth in humans.

"Some people take these medications for the entire [allergy] season. If there are risks .....I think we should at least try to understand what they might be."

A representative for Schering-Plough Corp., which makes Claritin, insisted that the medication has been extensively tested for safety.

"In 1.5 billion patient-days of use, no drug-related carcinomas have ever been reported," Dr. Francis Cuss, vice-president of the biological research, said yesterday from his office in Kenilworth, N.J.

"One would have expected, if this was a major issue, to have seen some evidence of the growth promotion before now."

The Canadian study is being published today in the *Journal of the National Cancer Institute*, based in Bethesda, Maryland. But an editorial in the same issue of the journal warns against drawing hasty conclusions from a single study involving rodents.

"It is our belief that human data, when available, should be the primary bases upon which decisions about medical and public health practices are made," writes Douglas Weed, an official with the U.S. National Cancer Institute in Bethesda. "At this time, we recommend no changes in current practice."

As part of the study, the researchers tested five different antihistamines, of which three seemed to promote cancer and two did not.

The mice were first injected with either melanoma (a skin cancer) or fibrosarcoma (a soft tissue cancer) cells. Some of the mice were set aside and did not receive any drugs.

The other mice were divided into treatment groups and received human-equivalent doses of one of the five antihistamines for 18 to 21 days.

At the end of the experiment, all the tumours were surgically removed, weighed and compared among treatment groups.

The rodents that received Claritin (also known by the generic name loratadine), Hismanal (astemizole) or Atarax (hydroxyzine) had tumours that were 1.5 to 3 times larger than those in the mice that did not receive the medications, Dr. Brandes said.

Hismanal is made by Janssen Pharmaceutica of Piscataway, N.J., while Atarax is made by Roerig, a division of Pfizer Pharmaceuticals, of New York, N.Y.

Two other antihistamines, Nyquil (also known by generic name of doxylamine) and Reactine (cetirizine), did not seem to speed up cancer growth in the mice that received them.

Dr. Brandes noted that all the drugs are equally effective antihistamine agents. Why then would some antihistamines appear to promote cancer growth while others don't?

One of the researchers, Dr. Frank LaBella, a professor of pharmacology at the University of Manitoba, speculated that the apparent cancer promoters may be more effective in penetrating the cell and disruping regular activities that regulate growth. He said that antihistamines normally bind to receptors on the surfaces of cells, but that certain antihistamines may be also binding to enzymes within cells, and preventing them from doing their normal work.

"So what may be happening is that whatever substances that are normally regulated and maintained [by the enzymes] are disrupted."

Both Dr. Brandes and Dr. LaBella are concerned that a wide range of drugs, with similar properties, may be promoting cancer growth. In a separate study published two years ago, Dr. Brandes and fellow researchers found that Prozac, a popular antidepressant medication, also appeared to speed the development of cerain cancers in mice. Eli Lilly & Co., the maker of Prozac, insists the drug is safe.

With so much at stake, the study by the Canadian researchers is bound to come under close scrutiny from pharmaceutical companies and regulatory authorities.

"Obviously, we are taking this seriously. And we will be discussing it with our experts," said Dr. Cuss of Schering-Plough.

A statement issued yesterday by Pfizer Inc. said the company has conducted three studies and found "no evidence of tumourogenic activity in the 2,517 patients taking hydroxyzine [Atarax]."

Even so, Dr. Brandes noted, drugs are usually scrutinized for their ability to cause cancer, and are not necessarily examined for their ability to speed its growth.

"We should certainly not ignore the findings. Even though [the drugs] may not cause cancer, they can accelerate it."

Meanwhile, Canadian officials, like their U.S. counterparts, believe it's premature to change existing regulations regarding the drugs.

"This is one study by one research group," said Dr. Brian Gillespie, chief of the drug evaluation division of Health Canada in Ottawa.

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The 1992 study refered to in the third paragraph of the right-hand column and referenced below is the first reference in the NCI journal article referenced above.

Brandes, L.J., Arron, R.J., Bogdanovic, R.P., Tong, J., Zaborniak, C.L.F., Hogg, G.R., Warrington, R.C., Fang, W., and F.S. LaBella: Stimulation of malignant growth in rodents by antidepressant drugs at clinically relevant doses. *Cancer Research* **52**(#13): 3,796-3,800 (1992). [DC Library call number: PER RC261.A274]

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