Arctic ozone succumbs to chemical assault

When a huge research expedition returned a year ago from studying the Arctic stratosphere, participants reported spotting an atmospheric murder weapon but no clear sign of a murder. They had measured very high levels of ozone-destroying chlorine chemicals, but without further analysis they couldn't say whether the chlorine had actually depleted the Arctic's ozone levels (SN: 2/25/89, p.116).

Since then, however, scrutiny of the expedition data has revealed that chemicals did indeed destroy stratospheric ozone in some Arctic regions, according to a series of reports in a special issue of GEOPHYSICAL RESEARCH LETTERS released last week. And all the evidence points to chlorine as the culprit.

For six weeks in January and February of 1989, scientists probed the dark Arctic stratosphere with instrument-laden aircraft. The expedition followed an Antarctic project two years earlier that helped scientists identify how chlorine — which comes largely from manufactured compounds called chlorofluorocarbons — creates the dramatic ozone hole there each September.

When the Antarctic hole develops, ozone can disappear almost completely from some altitudes, so it's relatively easy to spot the loss. But Arctic depletions are more subtle. Mark R. Schoeberl of the NASA Goddard Space Flight Center in Greenbelt, Md., and his colleagues report that altitudes near 20 kilometers suffered an average loss of about 15 percent over a 35-day period during the Arctic mission. Using a different detection technique, Edward V. Browell from the NASA Langley Research Center in Hampton, Va., and his co-workers identified regions with losses of up to 17 percent.

Preliminary analyses suggested the Arctic stratosphere held the potential to destroy significant amounts of ozone. In the new reports, researchers describe finding chlorine monoxide at levels 100 times higher than those over the United States. Moreover, they say, the Arctic stratosphere lost much of its active nitrogen; at sufficient levels, active nitrogen prevents ozone destruction.

But several factors in the Arctic inhibit the development of a real ozone hole. Wind patterns isolate the Antarctic from the rest of the globe's stratosphere into mid-spring, giving activated chlorine plenty of time to eat up ozone with the help of sunlight. The Arctic stratosphere, however, gets invaded by warmer air during late winter, before significant sunlight reappears and energizes the destructive chemical reactions. When the fresh air breaks into the Arctic stratosphere during late February, it deactivates the chlorine molecules and shuts down the ozone depletion cycle. In addition, the Arctic stratosphere does not get cold enough to allow sufficiently widespread formation of the cloud particles that help activate chlorine molecules. Such factors currently prohibit massive ozone loss in the Arctic, but researchers warn that conditions could change.

While scientists came away from the expedition with a better understanding of the ozone destruction process, the mission also highlighted some important knowledge gaps. In particular, investigators still need to identify the process that pulls active nitrogen out the polar stratosphere.

In the Antarctic, researchers had found the atmosphere lacked both active nitrogen and water vapor. They reasoned that frozen water in polar regions coats small cloud particles made of frozen nitric acid, forming ice particles that fall out of the stratosphere after a few days. But the Arctic measurements refute this idea, because intense nitrogen loss occurred there without intense dehydration, reports David W. Fahey of the National Oceanic and Atmospheric Administration in Boulder, Colo., in the March 22 NATURE. This suggests that polar nitrogen gets bound into a large frozen particle through some other process that does not require much of the water to fall out of the stratosphere. — *R. Monastersky*

Anticancer drugs: In vivo la différence!

When tumors develop resistance to anticancer drugs, chemotherapy becomes a toxic exercise in futility. For decades, scientists have assumed that lab-cultured tumor cells and tumors in the body develop drug resistance in much the same way — a belief that has formed the basis for *in vitro* studies of tumor cells to pinpoint the genetic, metabolic and molecular changes accompanying drug resistance *in vivo*. "We've thought all along that *in vivo* and *in vitro* drug resistance were pretty much the same," says Beverly Teicher of the Dana-Farber Cancer Institute in Boston.

Now, Teicher and her colleagues have discovered striking differences between chemotherapy resistance *in vivo* and *in vitro*. To survive the toxic onslaught, resistant tumor cells in the body appear to rely in part on interactions with noncancerous tissues — an assist unavailable to cells growing in culture.

The group found that the drug resistance displayed by breast-cancer cells in mice vanished when those cells were removed and cultured — only to reappear when the resulting cell lines were reinjected into other mice. Moreover, the body's distribution and processing of anticancer drugs differed between mice with resistant tumors and control mice with drug-sensitive tumors, the team reports in the March 23 SCIENCE.

The researchers began by injecting breast-cancer cells into four groups of healthy mice and allowing the tumors to grow. Each group of mice then received a different anticancer drug. Twenty-four hours later, the team excised the tumors and transplanted the cells into four new groups of mice, again allowing each cell line to proliferate and exposing it to the same drug as before. They repeated the process 10 times in all, using new host mice each time to ensure that the tumor — and not the liver or kidney — was the site of drug resistance, Teicher says.

Next, they removed some resistant tumor cells from each of the mouse groups and grew them *in vitro*. After exposing these cells to the corresponding anticancer drug for one hour on three different occasions, the team observed "virtually no resistance," Teicher says. They left the cells untreated for the next four to six weeks, then injected them into yet another set of host mice. Drug resistance returned almost immediately.

The researchers continued passing the tumor cells into fresh hosts and leaving them drug-free. Three to five months after the last drug exposure, tests showed that three of the cell lines had lost their *in vivo* drug resistance. Teicher says this suggests that drug resistance in the body is reversible, most likely via a modification in the transcription of DNA to RNA and the translation of RNA into proteins. One cell line, however, continued to resist chemotherapy. These cells may have used a separate mechanism of resistance, Teicher speculates.

The team also looked at the distribution of two of the anticancer drugs in the animals' bodies. Compared with drug-sensitive tumors, resistant tumors absorbed the drugs more slowly and at lower levels, with the overflow excreted more rapidly from the body.

Some tumors secrete hormones capable of influencing normal tissue in yet-undetermined ways, Teicher notes. It's possible, she told SCIENCE NEWS, that these secretions play an indirect role in *in vivo* drug resistance.

If researchers can duplicate the new results with other tumor cells, physicians might consider waiting longer between chemotherapy treatments to allow drug resistance to fade from surviving tumor cells, Teicher suggests.

The study may also have implications for *in vitro* research into the mechanisms of chemotherapy resistance. If the findings are confirmed, says Kurt Kohn of the National Cancer Institute in Bethesda, Md., scientists will have to interpret results from tissue culture studies more carefully. — *C. Decker*