Taking Shots at Ozone Hole Theories

The word from atmospheric chemists monitoring the spring thinning of the ozone layer over Antarctica is that two leading theories are as good as dead, but they won't lie down

RESEARCHERS keeping an eye on the temporary thinning of the ozone layer over Antarctica this austral spring could take some comfort. This spring's hole, as the thinning is popularly known, is no larger in extent than any other since the ozone holes began intensifying in 1977. There is no reason to think that this hole is about to engulf the globe. And the progressively larger ozone loss each October has at least paused this year.

The problem is that an intensive effort in Antarctica to monitor the chemistry of the hole has so far failed to provide any simple explanations for the hole or its deepening. Whether the hole is a harbinger of a catastrophic global ozone depletion remains unknown. The atmospheric chemists in Antarctica do argue that they have strong evidence against nonchemical theories, but proponents of those theories are as yet not giving an inch.

The broadest view of the situation comes from the total ozone mapping spectrometer (TOMS) aboard the Nimbus-7 satellite. Arlin Krueger of the Goddard Space Flight Center in Greenbelt, Maryland, reports that by 16 October, ozone concentrations within the hole had not decreased as much as they had by the same date in 1985, when they fell by almost 50% from August values, but they were slightly lower than at the same time in 1984. Such a pause in the steep downward trend of October concentrations since 1977 has been common, says Krueger. Given more time, notes Krueger, it may be the 1985 hole that will appear to have been anomalously intense.

TOMS satellite measurements have also been used to monitor the less well-known band of higher than normal ozone concentrations that rings the hole each October. The downward trend in the ring also paused this year or even recovered, roughly equaling the concentrations that were recorded during 1984.

Richard Stolarski and Mark Schoeberl at Goddard have recently quantified the behavior of this ozone doughnut and found that during any one year not much happens to the total amount of ozone poleward of 44°S while the hole appears and disintegrates over the pole. While polar values are plummeting 40% or more in September and into October, ring values rise, roughly compensating for the losses over Antarctica. In November winds blow the entire doughnut away, leaving the total amount of ozone slightly greater than before.

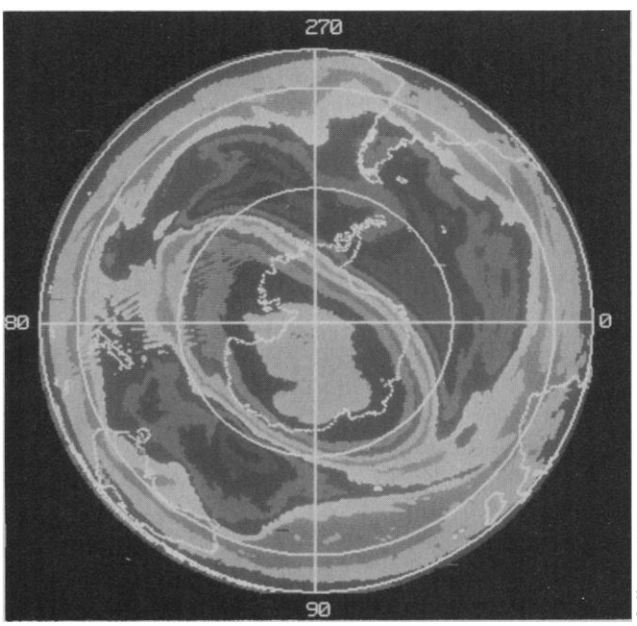
Stolarski and Schoeberl see the most straightforward explanation of the doughnut's formation to be winds that carry ozone away from the pole and into the ring, which is centered at about 50°S. They consider it less likely that winds from north of the area might blow ozone into the ring while chlorine from man-made compounds, including chlorofluorocarbons, simultaneously catalyzes the destruction of an equal amount of ozone over the pole. "The year-to-year deepening of the hole," says Schoeberl, "definitely has some dynamical component."

The atmospheric chemists of the National Ozone Expedition disagree. Speaking via satellite on 20 October to a press conference, they noted that from their site at McMurdo Station under the edge of the hole they had not found the nitrous oxide and aerosol particles that they would expect to be carried into the hole by ozone-depleted air from below. Uplift of ozone-depleted air was the one dynamic mechanism in print at the time of the press conference.

The expedition members said that they also have strong evidence against the solar cycle theory proposed by Linwood Callis of the Langley Research Center and Murali Natarajan of SASC Technologies, Inc., both located in Hampton, Virginia. Although commended for its detail and thoroughness, many researchers consider the solar cycle theory, which postulates a buildup of nitrogen compounds destructive to ozone, a poor bet for a variety of reasons. One strike against the theory, according to expedition members, is their discovery that the ozone loss is confined to altitudes between 12 and 20 kilometers. The solar cycle theory predicts significant losses well above 20 kilometers. Another problem is that the expedition's measurement of nitrogen dioxide concentrations within the hole are the lowest "we have observed anywhere in the world." The solar cycle theory predicts high abundances of that gas. Although the rapid declines in ozone at relatively low altitudes are bothersome, Callis says, "we still see many pieces of evidence [from outside the hole

The Antarctic ozone hole near its 1986 peak

On 16 October the TOMS instrument aboard the Nimbus-7 satellite caught the extreme low in ozone concentration near the south pole (central areas), the ring of high concentrations outside the hole (upper right, lower left), and more typical background concentrations of the rest of the southern hemisphere. The hole and ring rotate about the pole in about a week.



A. Krueger/NASA

itself] that tend to confirm the solar cycle hypothesis."

Almost by default, the expedition members came down on the side of a chemical explanation for the formation of the hole. Catalytic destruction by man-made compounds has been a leading contender if only because the hole has been deepening in proportion to the increase of chlorine-containing compounds in the atmosphere. Those chemical analyses made by the expedition that were complete or in preliminary form by mid-October were at best consistent with catalysis of ozone destruction by chlorine, but no particular chemical theory could be proved or disproved. "We believe that a chemical mechanism is fundamentally responsible for the formation of the hole," said expedition leader Susan Solomon of the National Oceanic and Atmospheric Administration's Aeronomy Laboratory in Boulder, "but what's happening is more complicated than what has been proposed so far." One complication may be chemical reactions on stratospheric cloud particles, the products of the reactions not being released until the particles evaporate when sunlight hits them in the spring.

Things will certainly get more complicated before the mystery is solved, as suggested by the size of the November special issue of *Geophysical Research Letters*. It contains 46 papers that bring together a variety of observations and theories bearing on the hole. Already some of the papers are being cited in support of one view or another. Schoeberl notes that several papers report evidence of a small climate change in the stratosphere since 1979. And ozone decreases seem to be correlated with temperature decreases. Thus, the temperature change might have led to the progressive strengthening of winds into the polar stratosphere and the intensification of the hole, says Schoeberl. In that case, a dynamic mechanism could both create a hole each October and intensify it from year to year.

Everyone agrees that the atmospheric circulation over Antarctica makes the stratosphere there special. Atmospheric circulation may be solely responsible for the hole and its intensification, in which case the hole could become merely a scientific curiosity. Or the circulation may be creating special conditions under which particularly voracious chemical reactions occur. If those reactions can occur elsewhere in the future when chlorine concentrations are still higher, the entire global ozone layer could be in greater danger than previously thought. With such a crucial distinction to be made, researchers will probably be taking at least the next 2 or 3 years to come to a decision. ■

RICHARD A. KERR

Drug Resistance of Cancer Cells Probed

A better understanding of cancer cells' defenses against chemotherapeutic drugs is beginning to point the way to improved therapies

ALTHOUGH some cancers, especially certain blood cell cancers, can be cured by drug therapy, many of the more common malignancies respond poorly to chemotherapy. For some malignancies, of which colon cancer is a notable example, the drug resistance appears to be an inherent property of the tumor cells. For other cancers, the resistance develops in response to treatment with chemotherapeutic drugs. But however the resistance arises, the all too common result is treatment failure and death for the patient. "Drug resistance is the most important and challenging topic in cancer treatment research today," says Bruce Chabner, who heads the Division of Cancer Treatment at the National Cancer Institute (NCI).

The recent Bristol-Myers Symposium* had as its topic the current progress toward understanding the biochemical causes of drug resistance. "We can now focus on a spectrum of mechanisms—at the membrane level, at the cytoplasmic level with the glutathione system, and at the level of DNA repair and gene amplification," notes symposium co-organizer Paul Woolley of Georgetown University School of Medicine.

Perhaps not surprisingly, the defenses that help cancer cells to survive treatment with chemotherapeutic drugs often reflect the innate ability of cells to protect themselves against damage by foreign chemicals. These defense systems may already be strong in the cells that give rise to inherently resistant cancers. However, drug-susceptible tumors have shown a remarkable ability to adapt to exposure to chemotherapeutic agents by increasing the activity of the defenses.

The past year has seen a great deal of progress toward understanding the origins of multidrug resistance, a common occurrence with current chemotherapeutic regimens. Clinicians frequently find that a patient's tumor will initially shrink in response to treatment with a particular drug or drug combination, but after some period of time will begin growing again. The tumor will then prove to be resistant not just to the drugs with which the patient was treated, but to additional, unrelated drugs as well.

Enhancement of a membrane-level defense produces at least some cases of this type of multidrug resistance. Researchers have known for several years that one of the hallmarks of multidrug resistance is an enhanced ability of the cells to expel or pump out chemotherapeutic drugs. Now several groups have cloned genes for the pump molecule, a membrane glycoprotein, called the P-glycoprotein (where the P stands for "permeability") that is present in higher than normal amounts in the membranes of multidrug-resistant cells.

The groups approached the cloning from different directions. Victor Ling and his colleagues at the Ontario Cancer Institute in Toronto, who originally linked the P-glycoprotein to multidrug resistance in 1976, began with the glycoprotein itself.

Meanwhile, Michael Gottesman and Ira Pastan of NCI, in collaboration with Igor Roninson of the University of Illinois College of Medicine in Chicago and David Housman of the Massachusetts Institute of Technology in Cambridge, had found that cells that display multidrug resistance have increased copy numbers of a gene that they designated *mdr*. Gene amplifications occur frequently in drug-resistant tumor cells and may directly produce the resistance. The classic example of this is resistance to the drug methotrexate, which kills cells by inhibiting an enzyme needed for making the purine building blocks of DNA. Robert Schimke and his colleagues at Stanford University School of Medicine have shown that tumor cells can overcome the inhibition by amplifying the number of genes for the enzyme, which is called dihydrofolate reductase, and making more of the enzyme.

In any event, Gottesman, Pastan, and Roninson obtained circumstantial evidence indicating that the gene encodes the P-glycoprotein. Overproduction of the glycoprotein as a result of the gene amplification might therefore account for the cells' drug resistance. The investigators then went on to

*The Ninth Annual Bristol-Myers Symposium on Cancer Research was organized by the Vincent T. Lombardi Cancer Research Center of Georgetown University School of Medicine and held in Washington, D.C., on 15 and 16 October.