and then adds to that natural immunity by vaccinating girls as they approach child-bearing age. Long-range computer simulations find the UK strategy is more effective if less than 80% of the target group is vaccinated, while the USA strategy is superior if the inoculation rate is higher.

Although it is relatively simple to predict the long-term effects of a vaccination program, short-term effects can depend sensitively on how the program is carried out. For instance, several years after the United States began its rubella vaccination program there was actually a sharp jump in birth defects due to CRS.

Schwartz and Aron have shown the timing of a vaccination program can be crucial in determining its results. One of the most striking results comes from Aron, who investigated the effects of vaccinating against a disease with a 2-year high/low pattern of epidemics. She found the timing of a program inoculating one-third of all newborns dramatically affects the resulting pattern of infection. If the vaccinations are given as a mild winter approaches, the epidemics gradually settle down to a 1-year cycle with relatively mild winter peaks. If, however, the vaccinations are performed before a severe winter, the result is a 3-year cycle with very severe epidemics every third winter and mild outbreaks the other two.

Although Aron's work avoids chaotic solutions, it is indicative of chaos's influence on epidemiology. Until recently, researchers restricted themselves to simple solutions of their models, assuming the complicated ones both were too difficult to deal with and had no application to the real world. The work on chaos has lifted a psychological barrier, showing that even the complicated behavior of epidemiological patterns may yield to analysis by uncomplicated mathematical models. ■ ROBERT POOL

ADDITIONAL READING

J. L. Aron, "Simple versus complex epidemiological models," to appear in *Applied Mathematical Ecology* (Springer-Verlag, New York, in press).

J. L. Aron and I. B. Schwartz, "Seasonality and period-doubling bifurcations in an epidemic model," *J. Theor. Biol.* **110**, 665 (1984).

L. F. Olsen, "Poliomyelitis epidemics in Denmark over the period 1928–1958 were chaotic," *Math. Comput. Model.* **10**, 155 (1988).

L. F. Olsen, G. L. Truty, W. M. Schaffer, "Oscillations and chaos in epidemics: A nonlinear dynamic study of six childhood diseases in Copenhagen, Denmark," *Theor. Pop. Biol.* **33**, 344 (1988).

W. M. Schaffer and M. Kot, "Nearly one dimensional dynamics in an epidemic," *J. Theor. Biol.* **112**, 403 (1985).

W. M. Schaffer, S. Ellner, M. Kot, "Effects of noise on some dynamical models in ecology," *J. Math. Biol.* **24**, 479 (1986).

I. B. Schwartz, "Multiple stable recurrent outbreaks and predictability in seasonally forced nonlinear epidemic models," *ibid.* **21**, 347 (1985).

How to Fix the Clouds in Greenhouse Models

Climate models are moving toward the realistic simulation of clouds needed to calculate the size of the greenhouse warming

CLIMATE RESEARCHERS are convinced that increasing amounts of carbon dioxide and other greenhouse gases will eventually warm Earth noticeably, but they are equally certain that their current computer models cannot be trusted to predict the precise magnitude of that warming. The models are still too unrealistic.

In this issue of *Science* (p. 57), V. Ramanathan of the University of Chicago and his colleagues report a first step toward fixing the weakest part of current models, their clouds. These researchers report that observations by two satellites in the Earth Radiation Budget Experiment (ERBE) show for the first time that the clouds of today's climate cool Earth below the temperature it would be without any clouds. The next step will be the improvement of the models so that their clouds behave the way these and other new observations show clouds do under the present climate. Only then might modelers have some confidence in predictions of cloud behavior and thus climate behavior under the coming greenhouse.

Until ERBE, not enough observations had been taken around the globe for researchers to even be sure whether today's clouds cooled or heated Earth. Clouds cover about half of Earth, doubling the proportion of sunlight reflected back into space to 30%. This reflection by clouds surely tends to cool Earth. But clouds not only can block incoming, shortwave radiation but also the longwave, infrared radiation emitted by the warmed air and surface beneath them. Thus, by trapping longwave radiation, clouds can have a greenhouse effect that tends to counteract the effect of their reflectivity.

The initial ERBE results, including final ones for 1 month and preliminary ones for three other months, show that reflection by clouds wins out by a modest margin. Clouds around the globe in April 1985 reduced absorption of incoming solar radiation (340 watts per square meter) by 44.5 watts per square meter while reducing infrared losses to space by 31.3 watts per square meter. That produces a net reduction in radiative heating of Earth of 13.2 watts per square meter. This gives clouds a major role in the present climate. By contrast, current climate models predict that a doubling of carbon dioxide will warm Earth 2.8° to 5.2°C through an increase in net radiative heating of only 4 watts per square meter.

Working with such small changes to the climate system's energy input is a problem, but a bigger challenge for modelers is that as greenhouse gases change the climate, the clouds will presumably change, in turn altering the climate. Cloud areas, altitudes, proportions by type, and water contents could all change, in the process altering the radiative fluxes in and out of the climate system. Clouds that change with changing climate, thus creating feedbacks affecting climate, have begun to be included in models only in the past few years.

"You have every right to be very, very skeptical of the results" of today's models. "But this is the best that we're doing."

A recent study points up how far the models have to go before they get a handle on these cloud feedbacks. An unprecedented intercomparison of 11 greenhouse models, which was conducted by the models' creators and is headed by Robert Cess of the State University of New York at Stony Brook, shows that although the sensitivity of current models to climate forcing such as greenhouse gases varies by a factor of 3, the same models without clouds are in excellent agreement. "The models aren't bad except for the clouds," says Cess.

When judged by the ERBE data from the present climate, five models taken for illustrative purposes have varying success in reproducing the observed net cloud cooling. They all have a cloud cooling rather than a warming, but the model that comes closest to the observed cooling does so by having its clouds reflect too much solar radiation and trap too much longwave radiation. That does not encourage confidence in the model's response to increasing greenhouse gases, nor, for that matter, in any model-based claims that the greenhouse warming is here.

Most current models have a positive cloud feedback, that is, changes in clouds under a strengthening greenhouse amplify the warming. The inclusion of this positive cloud feedback seems largely responsible for the doubling in recent years of model sensitivity to greenhouse gas increases. The feedback can be traced to a decrease in the model of low and middle cloud cover and an increase in high, cirrus-type cloud cover, which produces a proportionately greater trapping of infrared emissions.

Whether that is the way real clouds will react is unclear. Researchers are not even sure whether the real world cloud feedback will be positive or negative, much less what size it will be. "You have every right to be very, very skeptical of the results" of today's models, says Michael Schlesinger of Oregon State University, himself one of the leading American modelers. "But this is the best that we're doing."

While the state of the art of climate modeling is not what anyone would like, there are signs that, for whatever reason, the current estimates of the warming for a carbon dioxide doubling may not be all that bad. Michael MacCracken of Lawrence Livermore National Laboratory recently compared model and real world responses to various climate forcings. Models reproduce the cycle of the seasons, in which regional energy inputs vary by 100 watts per square meter, as well as the climate of the most recent glacial maximum, in which latitudinal and seasonal variations differ by 20 to 40 watts per square meter. The models also generate the greenhouse warming that has kept Earth from freezing over during the past few billion years.

Other comparisons can be made. The sensitivity of the models is consistent with the small to negligible climate effect of a veil of volcanic aerosol in the stratosphere. Given a number of uncertainties, the model responses, or at least those toward the lower end of the range, are consistent with the 0.5°C global warming of the past century.

MacCracken concludes that the global average temperature increase under a carbon dioxide doubling would be a few degrees Celsius plus or minus 50%. It would not be 10° nor a few tenths of a degree. For policy-makers, MacCracken suggested, perhaps that is all they need to know about the magnitude of the global warming. That and that feedbacks can only amplify or damp a forced climate change, not negate it. Consistent forecasts of regional changes of any kind will likely be out of reach for many years. ■ RICHARD A. KERR

Neurotoxicity Creates Regulatory Dilemma

New, more sensitive tests that detect damage to brain neurons in animals are leading researchers to reexamine the potential toxicity of some drugs already on the market

WHEN SHOULD A COMPOUND be classified as a neurotoxin and a health hazard? The answer is not always clear and fenfluramine, an appetite-suppressing prescription drug, is a continuing case in point. The current dilemma is this: people have been taking fenfluramine for nearly 20 years without any observable toxic effects, but new studies show that, in rats, fenfluramine selectively damages the fine endings or terminals of nerve cells in the brain that release serotonin as a transmitter.

The issue of fenfluramine toxicity is not new. Ten years ago the Food and Drug Administration (FDA) investigated reports that it killed groups of nerve cells in the brain, but the results could not be confirmed. Today, however, new tests are available that can detect more subtle damage to specific brain regions and neurotransmitter pathways. It is these new tests that point to fenfluramine toxicity in rats given five or more times the daily human dose.

Fenfluramine belongs to a class of amphetamine-related drugs that also includes ecstasy (3,4-methylenedioxymethamphetamine or MDMA), which is designated as an illegal drug (see *Science*, 19 February 1988, p. 864), and Ritalin, which is used to treat children who are hyperactive. Using similar criteria for determining neurotoxicity, researchers have preliminary data indicating that in rats fenfluramine is more neurotoxic than ecstasy and that Ritalin is not toxic, even at very high doses. The FDA has a new program to reevaluate this class of drugs for potential toxicity and is not targeting fenfluramine or any other drug in particular.

Nevertheless, the seemingly conflicting data about the safety of fenfluramine in humans and its toxicity in rats leave FDA officials in something of a quandary. "When we talk about the neurotoxicity of drugs, what exactly do we mean?" asks Joseph Contrera of the FDA. "What are the appropriate criteria? Is it long-lasting depletion of a neurotransmitter, selective damage to a particular population of neurons, or a visible lesion in the brain?" Until recently when new techniques became available, FDA used the latter criterion, which indicated that a large number of nerve cells in the brain had died.

Despite extensive studies on fenfluramine, scientific opinion on the drug is currently divided. Many clinical researchers are strong proponents of its continued use for patients who need to lose weight, citing the drug's effectiveness and the lack of clinical data showing evidence of toxicity. For example, Michael Weintraub of the University of Rochester in New York and his colleagues

"When we ask about the neurotoxicity of drugs, what exactly do we mean? What are the appropriate criteria?"

have just completed a 4-year study of people taking fenfluramine in combination with another diet drug. "The drugs were far superior to a combination of diet, behavioral modification, and exercise in producing weight loss," says Weintraub, adding that no one reported toxic side effects. But most clinical studies, including this one, were not designed to assess neurotoxicity.

At least part of the reason is that damage to serotonin neurons in the brain is difficult to measure in people. Early studies of fenfluramine showed that it causes a decrease in overall brain levels of serotonin and its metabolite (5-HIAA) in cerebrospinal fluid, but these decreases were thought to be transient and an indication of the drug's efficacy, not its potential toxicity. Furthermore, behavioral tests of serotonin depletion in people simply do not exist. "Serotonin helps to regulate sleep, sexual behavior, mood, and the perception of pain," says Lewis Seiden of the University of Chicago in Illinois. "These factors are very subtle and hard to test for." Precisely how fenfluramine curbs the appetite and how this effect may be related to its actions on serotonin neurons in the brain is also not fully resolved.