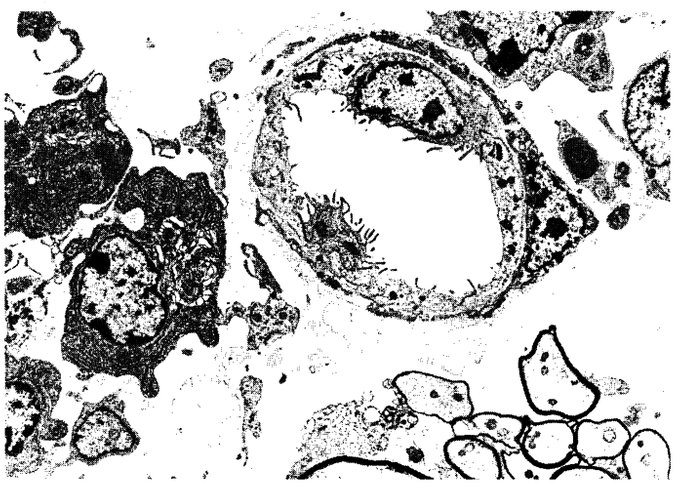
other identical guinea pig, the second animal became paralyzed within 10 days and later died. These animals had large numbers of lymphocytes that had migrated into the nervous system."

Today, the techniques for inducing EAE are more sophisticated. Dale McFarlin, also at NINCDS, and Cedric Raine, at Albert Einstein College of Medicine, collaborated to develop a recent model for MS in mice. Damage to the central nervous system in these mice becomes permanent, and the disease becomes progressive by expanding into larger and larger regions of the spinal cord and brain as it does in MS.



Electron micrograph of grafted quail spinal cord from a chimera that had both wing and leg paralysis. Plasmocytes (left and top right) are around the blood vessel (top center), and several nerve fibers (lower right) have less myelin than normal. ×3670

Fallis works with a mouse model very similar to one developed by McFarlin. He takes lymph node cells from a mouse that already has experimental allergic encephalomyelitis and injects the lymphocytes and macrophages into a second mouse. The second mouse develops a form of experimental allergic encephalomyelitis that resembles the early stage of MS in which symptoms come and go. To transfer EAE from the first mouse to the second, a subset of helper T cells must be present in the lymph node preparation. "If this subset of T cells is removed, the naïve mouse doesn't get sick," says Fallis.

Fallis and his colleagues follow the course of EAE in the second mouse by looking for lymphocytes that react to the original antigen, myelin basic protein. "These reactive cells appear to be T cells and are in the periphery, even though experimental allergic encephalomyelitis is a central nervous system disease. EAE may be a systemic disease that is manifested in the central nervous system," says Fallis.

There are major unanswered questions concerning MS. T lymphocytes are present in the brains and spinal cords of MS patients, but how do they get there? "Some people think that T cells have the capacity to break down the blood-brain barrier. Others think that T cells squeeze through it, perhaps because of a local inflammation at the level of the barrier," says Fallis.

And what stimulates T cells to attack central nervous system myelin after they get through the blood-brain barrier? In order to mount the abnormal immune response, T lymphocytes must simultaneously "see" both brain antigens and antigens made by the major histocompatibility complex (MHC) genes. This means that some cell type in the central nervous system has to present both kinds of antigens to the T cells. "There are two candidates for this, endothelial cells that line brain capillaries and astrocytes," says McFarland.

Traugott has demonstrated that, in a mouse EAE model and in MS tissue, astrocytes and endothelial cells have a common ability to express class II antigens coded for by MHC genes and to present brain antigens to T lymphocytes. After T cells are stimulated in this manner, they secrete factors that signal macrophages to invade brain tissue, and demyelination results.

What McFarland finds intriguing about Le Douarin's bird chimera model for MS is that "it may provide a suggestion about the mechanism for the disease. That is, you may not need myelin or its basic protein as an antigen." It may be enough to trigger T cells and macrophages to migrate into central nervous system tissue and cause demyelination. ■ **DEBORAH M. BARNES**

ADDITIONAL READING

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Briefing:

Cancer Progress Data Challenged

For several years, statistician John Bailar of the Harvard School of Public Health has been a thorn in the side of the National Cancer Institute. The NCI has said its goal is to reduce age-adjusted cancer mortality by 50% by the year 2000. That goal is "unlikely," Bailar says because "overall cancer mortality is going up." The problem, according to Bailar, is not that cancer treatments are ineffective but that they are not getting better. Now Bailar and his colleague Elaine M. Smith of the University of Iowa Medical Center in Iowa City make their argument in the 8 May issue of the *New England Journal of Medicine*.

Bailar and Smith's data are not in dispute. They come from the National Center for Health Statistics and they indicate that, from 1962 to 1982, age-adjusted cancer mortality rates in the United States increased from 170.2 to 185.1 per 100,000. Yet no one denies that there has been remarkable progress in treating some cancers. Childhood cancers and Hodgkins disease, for example, are remarkable success stories. But these successes are almost washed out in the statistics because they represent such a small proportion of cancers. According to Vincent DeVita, director of the NCI, "50% of all cures through chemotherapy occur in 10% of all cancer patients." Most cancer deaths are from just a few kinds of cancer, particularly lung cancer, which dominates the bleak cancer statistics. Early detection programs for lung cancer have not been successful and the cancer continues to have a grim prognosis.

Yet even if the lung cancer data are removed from the cancer mortality rates, there is no dramatic difference in the overall picture, Bailar and Smith argue. They deleted the lung data and report that the age-adjusted cancer mortality rate since 1950 shifts from an 8% increase to a 13% decrease. But it is only fair, they suggest, to also delete cancers of the stomach and cervix from the data because these cancer survival rates also changed, but for the better, for reasons having nothing to do with treatment advances. (Stomach cancer incidence has been declining for unknown reasons and cervical cancer incidence has declined largely because, it is suspected, of widespread Pap smear screening.) If these two cancers are also excluded from the total picture, the cancer mortality rates stay essentially the same from 1950 until 1982.

Statisticians caution, however, that care

must be taken in interpreting the statistics. Although he basically agrees with Bailar and Smith, Marvin Zelen of Harvard University offers a few cautionary notes. For example, Zelen says, "if you really cure people, you only know about it if they live a long time. The vital statistics of today might reflect the therapies of 10 to 15 years ago."

There also is the problem of interpreting mortality data. These data are usually taken from death certificates. But, Zelen notes, "there are many patients who die of cancer but do not have cancer listed as the cause of death on their death certificates."

Still another caveat is that the data on cancer may be skewed by the changes in heart disease mortality. "Mortality associated with cardiovascular diseases is going down and so more people are at risk for other diseases. They may then die of cancer," Zelen remarks.

A final difficulty, according to Zelen, is in the very age-adjusted rate concept itself. Eleven to 12% of the population is older than age 65, but 60% of those who die from cancer are older than age 65. "When you quote age-adjusted figures, all the action is in those over age 65. If anything is going on [in the mortality data], it gets modulated." In other words, to make a big difference in the age-adjusted rates, you have to concentrate on the very oldest members of the population, who may be least likely to live significantly longer with better treatments.

Yet despite the difficulties in interpreting data, analyses such as Bailar and Smith's do raise important policy questions. Where should the emphasis be in combatting cancer? Bailar and Smith argue that there should be more emphasis on prevention, specifically on smoking cessation. "The major conclusion we draw is that some 35 years of intense effort focused largely on improving treatments must be judged a qualified failure," they write in their *New England Journal* article.

Others, while not denying that cancer prevention is a major goal, are not yet ready to throw in the towel on treatments. Edward Sondik, who is chief of surveillance and operations research at the NCI, notes that in order to assess current treatments, researchers must predict how recent apparent advances will affect survival statistics and how long it will take for the effect to show up in mortality data. Then they must look for their predicted effect. Sondik and his colleagues are doing such analyses now.

With all these complications in interpreting the data, there is no simple answer to the question of whether the war on cancer is being won. "It gets very political," says Zelen. "Unfortunately, people have all sorts of axes to grind." ■ GINA KOLATA

The Continental Plates Are Getting Thicker

Petrologists and seismologists now agree that the old cores of the continents have deep roots extending well below the thickest ocean plates

A continent and an ocean basin, so different that one is usually high and dry and the other is forever filled with water, were assumed to be structured much the same beneath the surface. Each seemed to be composed of slabs of rigid rock as much as 100 kilometers thick, the tectonic plates that together cover the globe and drift about it on a layer of viscous rock.

There is now a consensus among earth scientists that continental and ocean plates differ in more than their height with respect to sea level. To judge from the rock recovered from beneath the oldest crust of at least one continent, long-lived continental roots extend downward as much as 190 kilometers into the 650-kilometer-deep upper mantle. But to judge from the way seismic waves pass beneath the continents, the roots extend 250 or even 400 kilometers beneath the surface. Reconciling this difference is the next task for seismologists and petrologists, but it is clear that somehow, perhaps through the collisions of plate tectonics, continents have stabilized part of the mobile mantle rock beneath them to form deep roots.

The first telling evidence of the existence of continental roots came from observations of the waves passing beneath continents from large earthquakes. In the mid 1970's, Stuart Sipkin, now at the U.S. Geological Survey in Golden, Colorado, and Thomas Jordan, now at the Massachusetts Institute of Technology (MIT), found that seismic waves passing beneath continents traveled faster than those passing beneath ocean basins.

They probed these two types of regions by comparing the speed of waves reflected off the core directly to a seismometer with those that bounced between the core and the surface twice rather than once. The primary difference between the two paths is the passage of the waves through the upper mantle near the surface reflection of the longer path. When the surface reflection occurred in an ocean basin, the difference in the time required to traverse each path was considerably greater than when the reflection point was in a continent. Thus, the waves traveled much faster than expected through the upper mantle and crust beneath the continent than beneath the ocean basin.

Sipkin and Jordan attributed the differences among the pairs of mantlewide paths to differences in the rock that extend at least 200 and perhaps more than 400 kilometers below the surface. Jordan took these and other seismic observations, combined them with geochemical, petrological, and geophysical data supporting such deep-seated differences, and proposed that the drifting continents carry with them at least several hundred kilometers of chemically distinctive mantle rock.

In the last few years, several seismological studies based on the use of different analytical techniques and different kinds of seismic waves that follow various paths through the mantle have supported Jordan's contention that the first few hundred kilometers of mantle beneath continents are somehow different. In 1984, John Woodhouse and Adam Dziewonski of Harvard University mathematically combined observations of waves that travel near the surface and within the upper mantle. They used the same type of analysis developed for the medical x-ray technique called computerized axial tomography or CAT scanning. The resulting three-dimensional map showed zones of relatively high seismic velocity extending 250 to 350 kilometers beneath the continents. New analyses including more than three times the number of initial observations produce similar results, says Woodhouse.

Arthur Lerner-Lam of Lamont-Doherty Geological Observatory and Jordan have recently used surface seismic waves particularly suited to mapping changes in seismic properties with depth to probe the western Pacific and the Eurasian continent. By building mathematical models of the mantle to reproduce the seismic wave shapes that they found, Lerner-Lam and Jordan tried to find some structure of the mantle that could reproduce their results while keeping differences in mantle structure at minimal depths. Confining the differences to depths shallower than 220 kilometers does not work,