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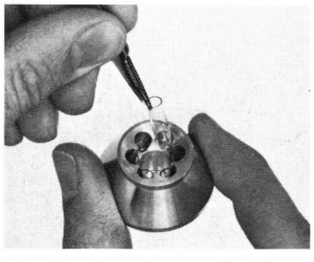

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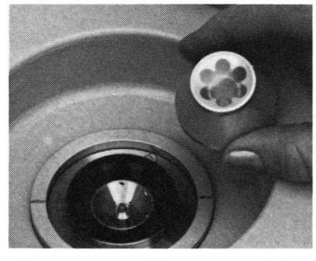

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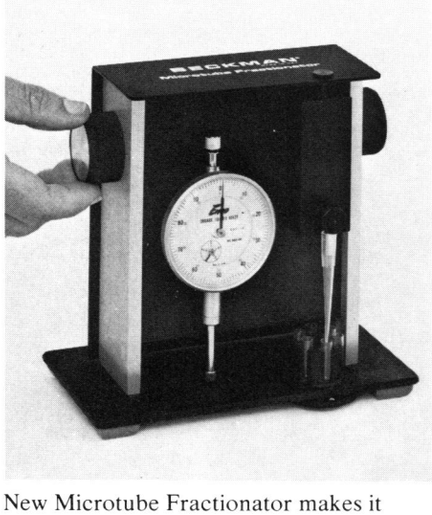

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COVER

Polyoma virus protein coat model as seen in a false color x-ray radiograph. The icosahedrally symmetric capsid structure is viewed along a twofold axis. The negative was exposed successively through a red and blue filter to produce a shamrock green combination of cyan and yellow in the print. See page 1117. [William Saunders and D. L. D. Caspar, Rosenstiel Center, Brandeis University, Waltham, Mass.]

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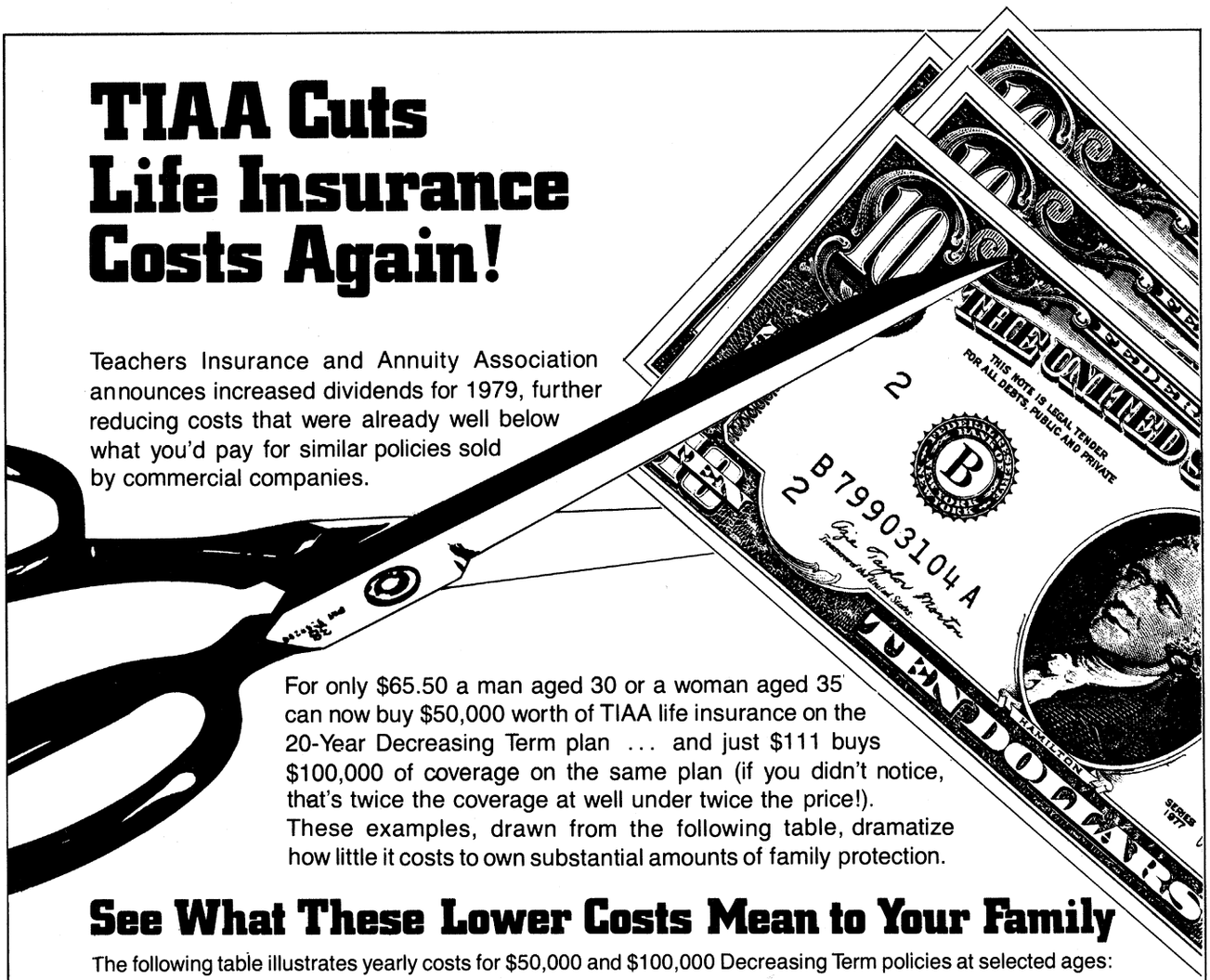

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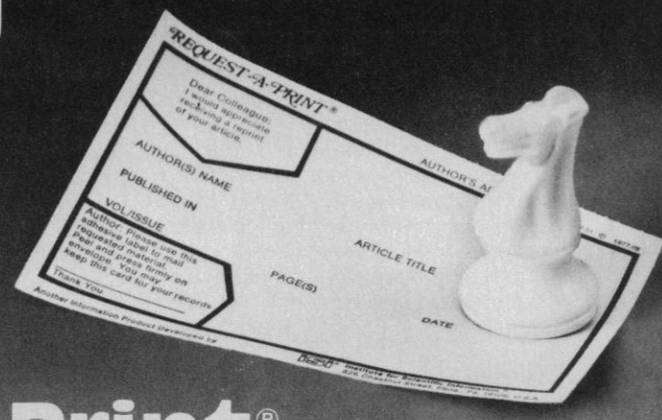

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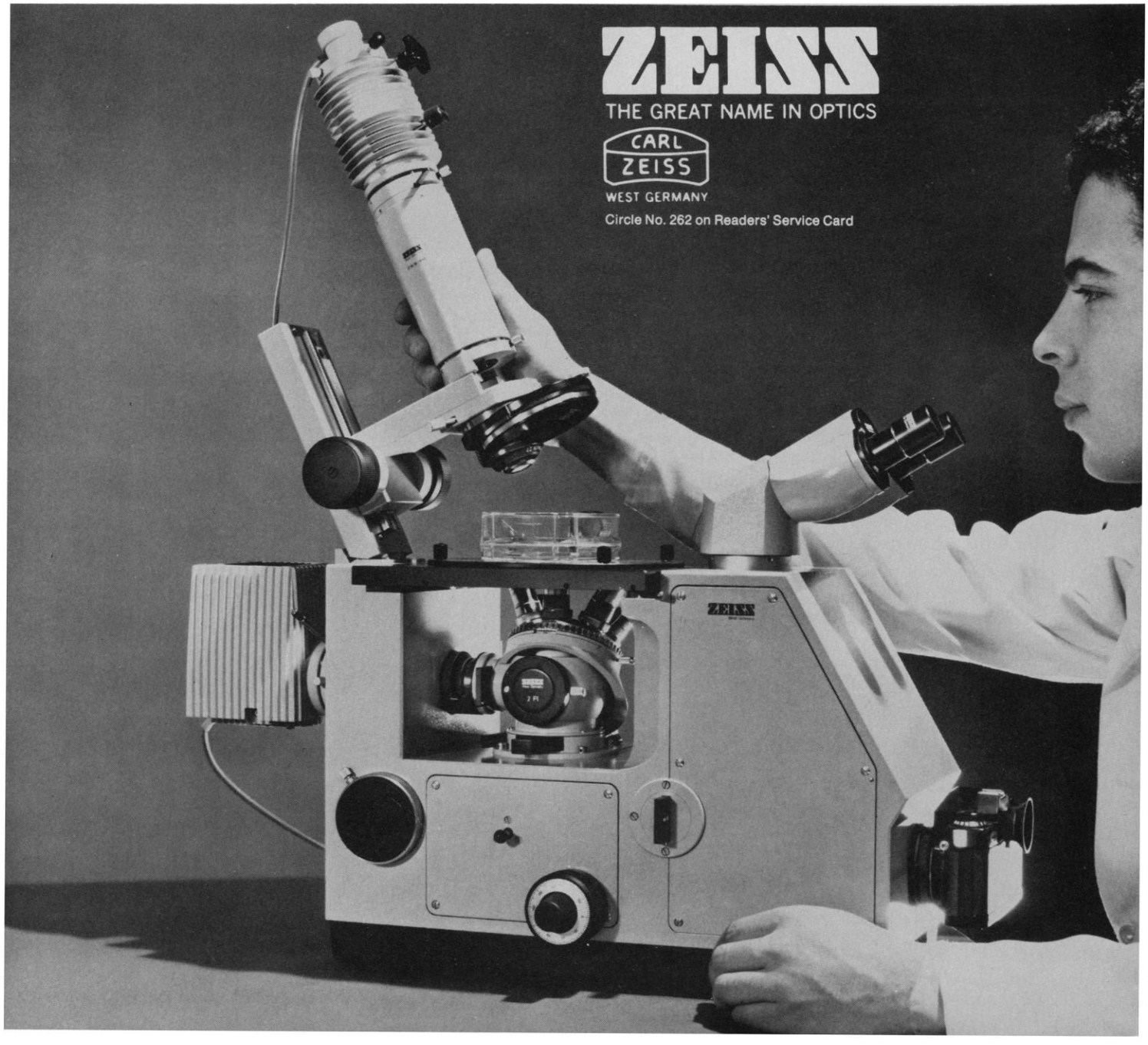

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In his article, "Carter attempt to limit doctor supply faces tough going in Congress" (News and Comment, 16 Feb., p. 630), R. Jeffrey Smith discusses the history of capitation grants, in particular a misconception that has been fostered by the Carter Administration. By linking the proposed elimination of capitation grants to a perceived need for reducing the output of physicians, the Administration would have us believe that the cut serves public purposes other than a reduction in government expenditures. Since, however, the link is specious, discussion of the proposed elimination of capitation support is directed to the wrong issues.

Capitation grants to schools of medicine were originally intended to defray a substantial part of medical education costs. To quote from a recent letter from Kenneth M. Endicott, formerly director of the Bureau of Health Manpower:

> By 1969, when I took charge of the Bureau, nearly half of the medical schools were receiving financial distress grants. In effect, when a school encountered financial difficulties, the federal government stepped in with the "last dollar" and rescued the school. This seemed to me to be a policy which encouraged over-spending and penalized prudent management. As an alternative, I proposed a "first dollar" approach in the form of capitation grants at a level calculated to put most of the schools on a sound financial base. The idea was accepted by the Administration and was incorporated in the Administration's legislative proposal. There were to be no strings attached other than maintenance of effort. In the course of the legislative process, the House added a requirement that each school increase enrollment. . . . In conference, the House prevailed and, as a result, the 1971 Act mandated an increased enrollment as a condition for receiving capitation grants.

Thus capitation grants, although conditional upon, were not intended as a reward for or the financing of expansion. More important, the expansion that occurred as a result of this condition is not a very significant factor in the need of schools for the flexible funds that capitation grants provide. Schools of medicine with the number of students; the need for faculty, by far the largest item in educational costs, varies only slightly with moderate changes in class size. Thus the 20 students per class that most schools added as a consequence of the federal health manpower program may have required some capital investment in facilities but had little effect on faculty size and cost. Because these additional students, at least currently in privately supported schools, add more in income (in

the form of tuition) than they do in cost, the last thing these schools are likely to do in the interests of financial stability is to decrease their enrollment. Merlin DuVal is quite right in saying that if the Administration wants schools to reduce their enrollment they will have to provide funds specifically for that purpose and the amount needed would have to be significantly greater than that which would be lost in tuition. That amount would be a substantial part of the current capitation support and would largely negate the primary purpose of the Administration, which is a reduction in expenditures.

Rather than concentrating on the fancied effects on medical school enrollment that would be entailed by elimination of capitation grants, and debating the desirability of an increase or decrease in the future number of physicians, we should be examining the more readily predictable consequences. Schools of medicine would lose a substantial fraction of their flexible funds, and since most would find it difficult to make up the loss by reducing expenditures, a major increase in tuition would be necessary, at least in private schools. Since the increased need for student financial aid eats up about half of any increment in tuition, it would be necessary to raise tuition by roughly twice the lost per capita amount in order to generate an equal net income. Those low- and middle-income students not discouraged by the cost from undertaking a medical education would have to borrow the additional money, increasing further the already substantial debts with which most of our students already graduate, or apply for scholarship support through the Health Service Corps, which could accommodate few of them because it is already oversubscribed. While the earning power of physicians is such that they should be able to repay their debts from future income, many of us are concerned about the bias toward careers that lead rapidly to high incomes that is inevitably induced by such substantial debts. I am particularly concerned that talented people who might make substantial contributions to the future of medicine will be diverted from academic careers by the relatively low income that such careers promise.

These are the issues that we should be addressing when we consider the President's budget proposals, not the imponderables of the supply of physicians.

ROBERT W. BERLINER
Office of the Dean, School of Medicine, Yale University, New Haven, Connecticut 06510

Chemical Carcinogenesis: Dose-Response Extrapolation

Marvin A. Schneiderman (Letters, 16 Feb., p. 603) implies that if you can devise an appropriate biological model for chemical carcinogenesis, you can devise a theoretical dose-response curve that will enable a meaningful extrapolation to be made to very low carcinogen doses. This may be good theory, but practically it is grossly error-prone.) My figure, used by Thomas H. Maugh II (Research News, 6 Oct. 1978, p. 37) is meant to illustrate the point that the further you extrapolate from the data base, the greater the level of uncertainty in the predictions. Significant tumor yields in animal experiments usually range from 5 to 100 percent. Vast numbers of animals have to be used to establish a 1 percent tumor yield, and much below this level adequate facilities are not available even on a worldwide basis. Therefore extrapolation to dose levels including one tumor in a population of 10^6 or 10^8 cannot be confirmed experimentally. In cancer induction the uncertainties in extrapolation are compounded by the complexity of the process and the vase number of factors, such as promoting agents, which may drastically affect tumor yield.

Schneiderman draws attention to the fact that the figure does not show the incidence of tumors occurring in a population not exposed to the carcinogen. As a logarithmic scale was, in fact, used, this incidence would not appear in the figure if the spontaneous tumor incidence was zero. More realistically, most spontaneous tumor incidences range from a fraction of 1 percent to several percent both in humans and in rodents. The uncertainty of establishing an *induced* tumor incidence at a level of one tumor in a population of 10^6 or 10^8 against a background incidence of, say, 1 percent is very considerable, especially if you realize that the actual human population (the real objective) is genetically heterozygous and diverse in its habits, so that spontaneous incidence will vary from one subset of the control population to another. The real or theoretical shape of the dose-response curve is quite irrelevant to my argument.

It is becoming clear that many chemical carcinogens must remain in low levels in our environment, despite the best efforts of regulatory agencies. Let us not pretend at this time that efforts at dose-response extrapolation for carcinogens is any better than pragmatic level-setting. Only a more complete understanding of the many factors involved in carcinogen-

esis can lead to a rational appreciation of the effects of low levels of specific chemical carcinogens.

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Chimpanzee Task Force Report

The Interagency Primate Steering Committee (IPSC) of the National Institutes of Health has recently published a report (*1*) on the current and future needs for chimpanzees in biomedical programs in the United States. The report contains a number of errors, which is surprising when one considers the source of the publication and the expertise represented by the many primatologists consulted. In addition, there are apparently no detailed position papers supporting the statements and claims made in the report that are available for public scrutiny. It is therefore impossible to check the source of and justification for some of the questionable statements.

The report states that 200 chimpanzees are currently being used in toxicology and pharmacology programs and that future demands will require about 100 animals per year. However, there are few, if any, good reasons for using chimpanzees in terminal toxicological studies. It is also stated that 150 animals are currently being used in the field of hematology, immunology, and immunogenetics and that approximately 50 additional animals will be required every year. However, the World Health Organization Collaborating Center on Hematology in Primate Animals estimates that the actual figures are considerably lower than this (*2*). This raises the possibility that some of the other figures in the report are also inflated. Certainly the draft of the National Primate Plan published in 1977 gave a much lower estimate than the task-force report for the total number of chimpanzees currently being used in research and testing. It is estimated in the section on "Other research areas" that about 80 animals a year will be required, including ten for molecular biology projects. Presumably, the animals for this program will be passed on from other research projects involving necropsies, since it is inconceivable that these animals will be killed (or maintained) solely as a source of material for studies on the molecular biology of chimpanzee macromolecules.

The report suffers from a number of other shortcomings. First, the task force states that its evaluation has "clearly shown that [the chimpanzee] is absolutely essential for research on several important human diseases." While it is true that the chimpanzee is an important research model in some areas, the report does not substantiate the above quotation. In addition, the task force does little to demonstrate concern for conservation issues and does not emphasize the need to develop other research models that might eliminate the demand for chimpanzees in particular fields. For example, there may well be other satisfactory models in hepatitis research.

Second, the task force does not adequately consider the implications of its projected demand of 300 to 350 chimpanzees per year. Current U.S. breeding programs produce only about 40 to 50 animals a year (the major chimpanzee facilities contain about 750 animals altogether), leaving an annual import demand of 250 to 300 animals. In the 5 years up to 1977, the West African dealers were exporting between 200 and 250 animals every year to the whole world (not just the United States) (*3*). Because of increased restrictions on this trade as a result of the threat posed to wild chimpanzee populations, the numbers exported have fallen considerably in the last year or two, and apparently the main traders have now stopped operations altogether. Presumably, some attempt may be made to tap the Central African chimpanzee population, but this is likely to run into the same problems that have developed in the West African trade.

Third, the bibliography is most unsatisfactory. Only a few references are provided, many of which are not particularly current. Fourth, the report should have considered some of the ethical aspects of chimpanzee use and caging.

The IPSC has the prestige of the National Institutes of Health backing its publications, but that is no excuse for the production of this document. The chimpanzee, and those who are concerned about its use in biomedical laboratories, deserve detailed arguments and justifications as to why this animal in particular is required for *specific* research needs.

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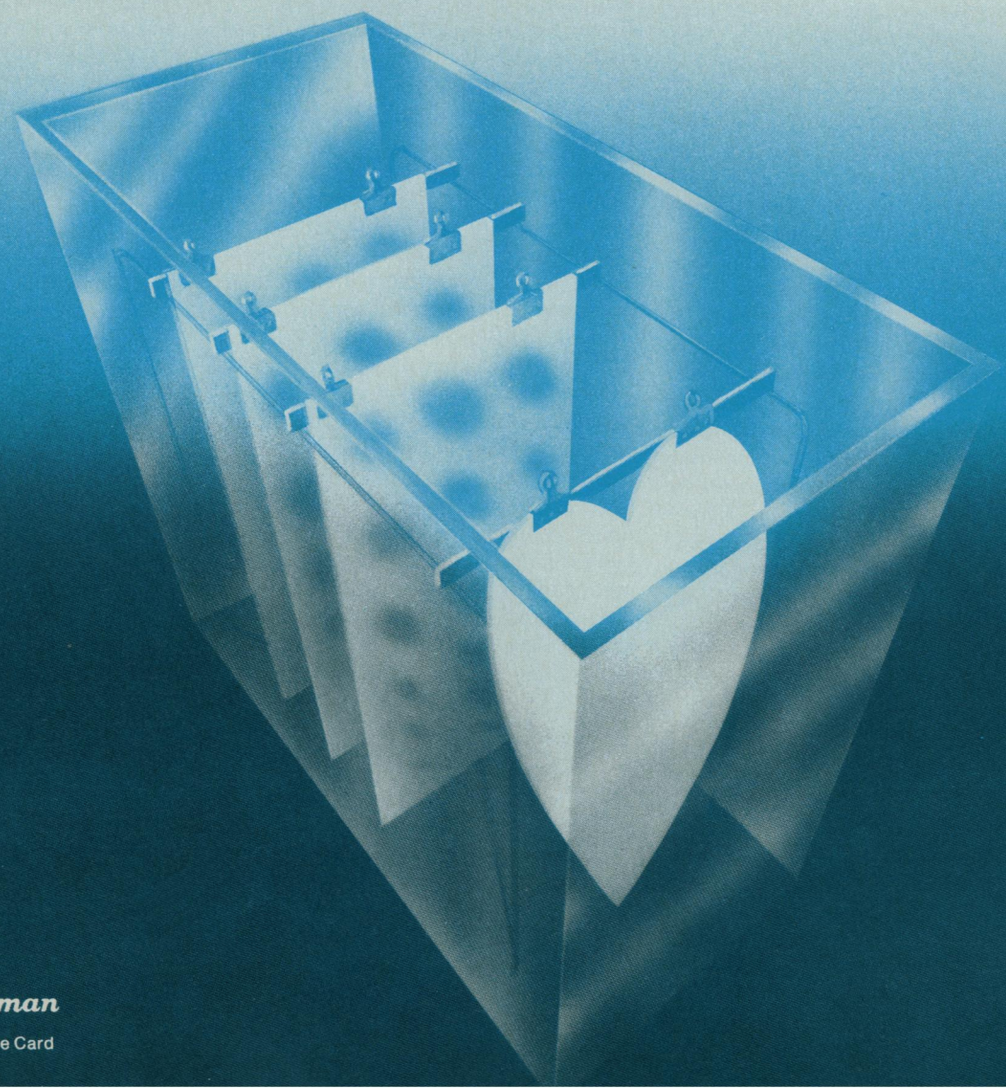

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16 March 1979, Volume 203, Number 4385 SCIENCE

International Cooperation in Earth Sciences

Prospects are excellent that research in the earth sciences will continue to be exciting and productive. Progress in the past two decades was fostered by the use of equipment such as the deep-sea drilling ship, by the emergence of the concept of plate tectonics, and by growing international cooperation among various branches of the earth sciences. New equipment is being developed, and the quality of older forms is being improved. The concept of plate tectonics has been stimulating and fruitful, but it does not readily explain, for example, earthquakes in supposedly stable places. Thus the extent of the applicability of plate tectonics is being questioned, and the questions create research opportunities.

International cooperation in earth sciences is being facilitated by major programs sponsored by the International Scientific Unions and United Nations agencies. The International Scientific Unions generally have fostered cooperation since their founding. However, those in the earth sciences have been particularly active. Geologists have conducted great quadrennial geological congresses at far-flung sites since 1880. Carefully prepared field trips associated with the congresses have enabled visiting scientists to examine important outcrops in many lands. This tradition will be continued when the next congress is held in Paris in July 1980 and field trips are conducted in western Europe.

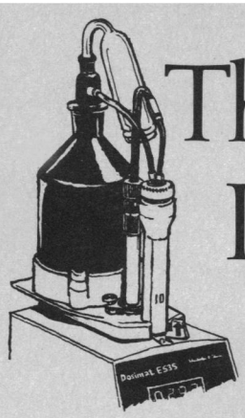
Another, more intense form of cooperation in science was initiated with the International Geophysical Year (IGY) during 1957 and 1958. Major cooperative programs dealing with many phases of the solid earth and its envelope were conducted. Participants from various nations found stimulus and satisfaction in joint efforts. The success of the IGY led to further programs in the earth sciences, including an Upper Mantle Project (1962 to 1970) initiated by the International Union of Geodesy and Geophysics (IUGG).

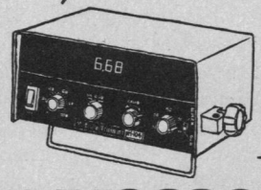
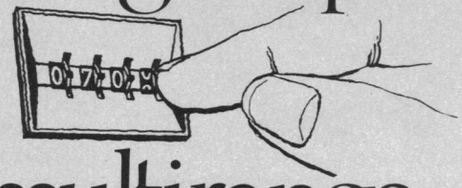
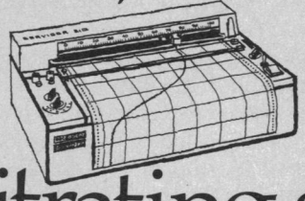
The International Union of Geological Sciences (IUGS) joined with Unesco to initiate in 1973 an International Geological Correlation Program, which now involves about 1000 geologists, 62 projects, and a total of 115 countries. The program is designed to encourage international research on geological problems related to the identification and assessment of natural resources and the improvement of the environment.

During the 1970's IUGS also collaborated with IUGG in the International Geodynamics Project. This interdisciplinary program emphasized study of tectonic plates and phenomena attending their collisions. Attention was focused on the ocean basins, island arcs, and continental margins. Since the ocean basins are comparatively young, the program dealt essentially with events of the past 200 million years. But 200 million years is only about 5 percent of the earth's age, and it is study of the continents that will reveal ancient events. At present, about 20 percent of the heat generated within the earth reaches the surface by conduction. The remainder is available for other processes such as mechanical work. During the past 200 million years sufficient energy was available in the earth to move continents thousands of miles. In an earlier day, when still more energy was present, motions probably occurred more rapidly and the energy might have been manifested in ways other than horizontal motion.

To understand the workings of the great heat engine known as the earth, observations from many places must be correlated. The present state must be examined, and evidence must be assembled about events that occurred in earlier times. The phenomena involved are complex; crucial data are difficult to obtain; potential sources of data everywhere must be tapped. Without comprehensive planning and good exchange of information and ideas, progress would be slow.

Thus the opportunities of the next decade call for further international cooperation among geologists, geochemists, geodesists, and geophysicists. Negotiations between IUGS and IUGG are proceeding. Prospects are good that a new joint program will be formulated.—PHILIP H. ABELSON



The Metrohm pH Stat Titrator. It gives you self-refilling burets, a removable digital pH Meter,  quick-release  titration vessels, finger tip setting of stat point  or end point, and a multirange recorder,  all in the same pH stat titrating system.

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