SCIENCE

11 April 1975

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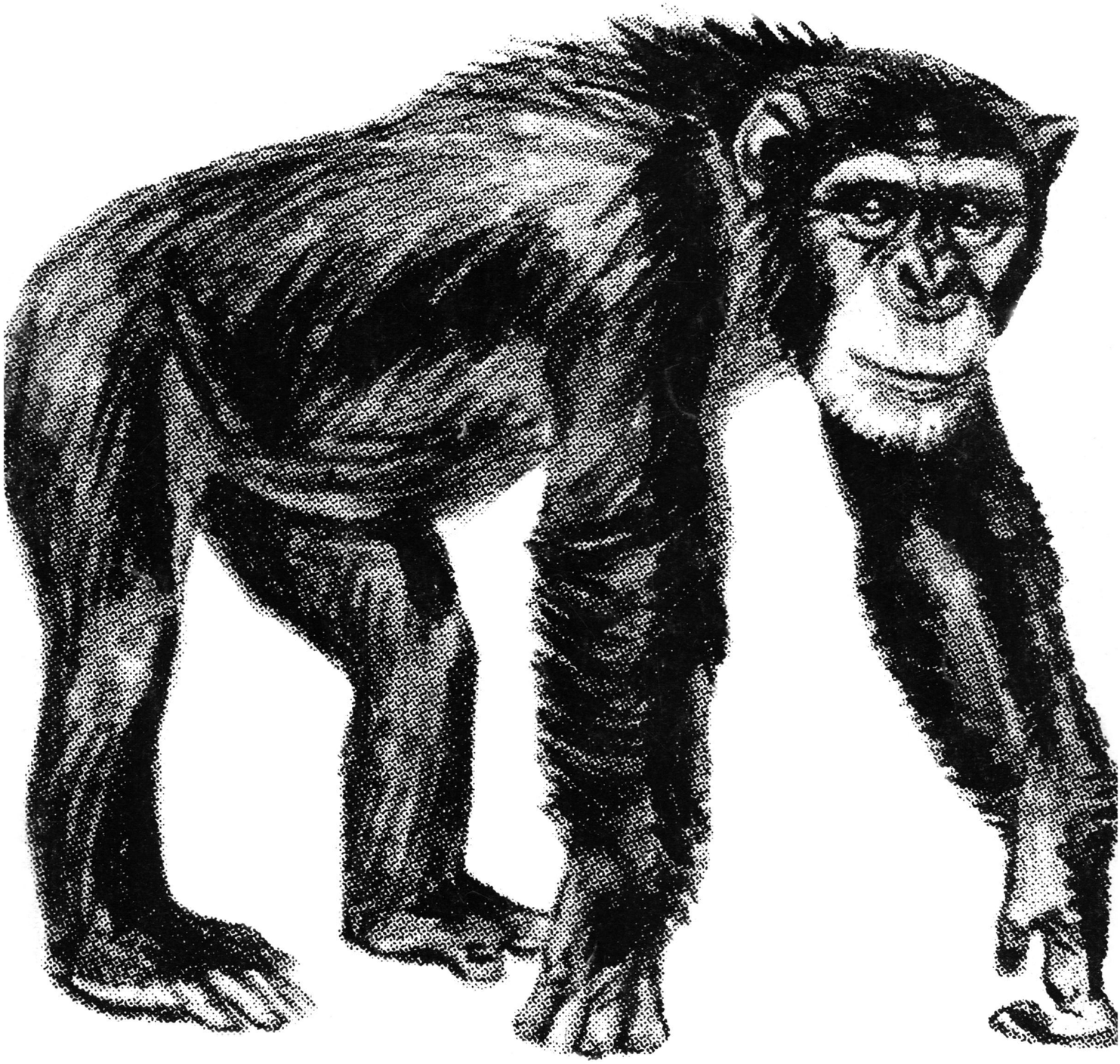
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



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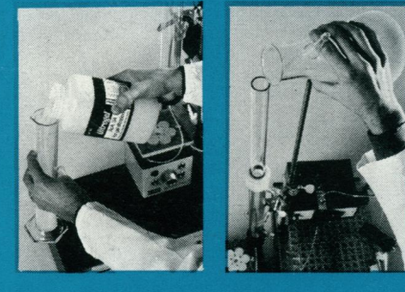

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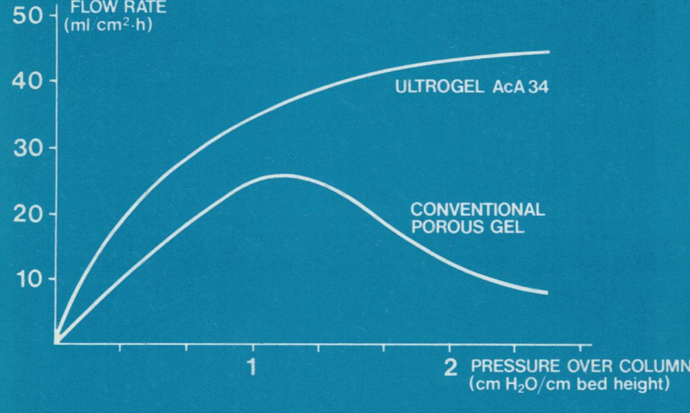

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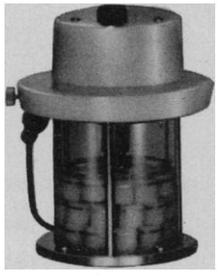

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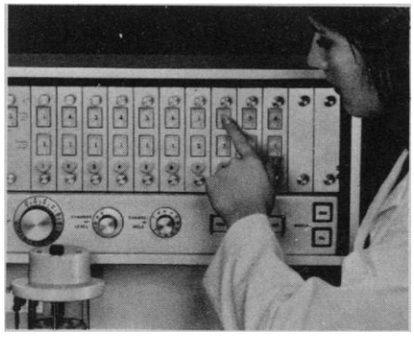

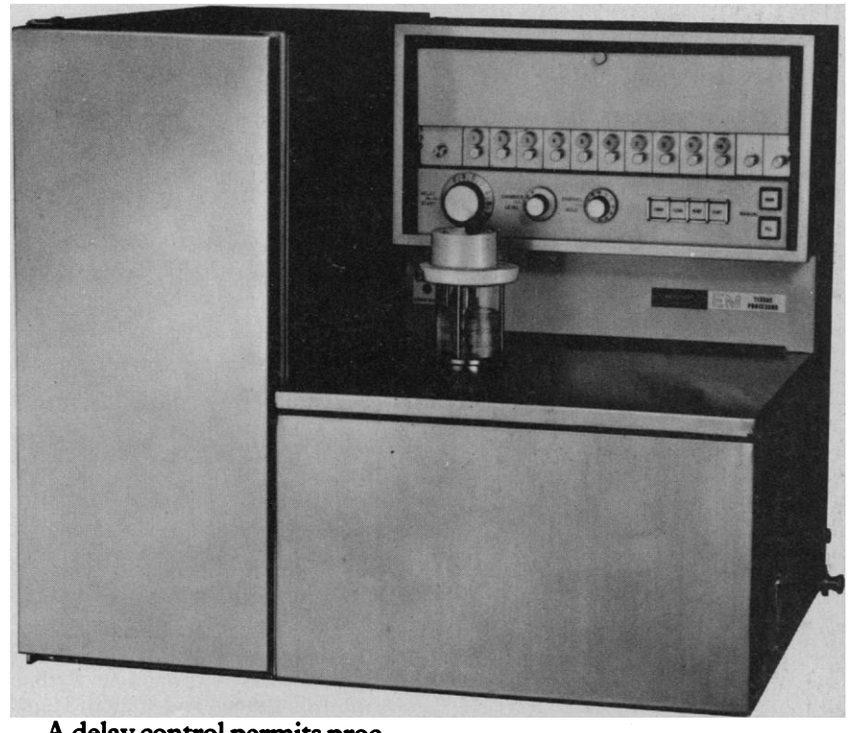

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COVER

Chimpanzee (*Pan troglodytes troglodytes*). Although chimpanzees differ substantially from humans in anatomy and way of life, the proteins and DNA of the two species differ no more than do those of sibling species. See page 107 [Part 1a of plate II by Pierre Dandelot, Paris Museum of Natural History; from *A Field Guide to the Larger Mammals of Africa* by Jean Dorst, Houghton Mifflin Company, 1970]

Finnigan GC/MS
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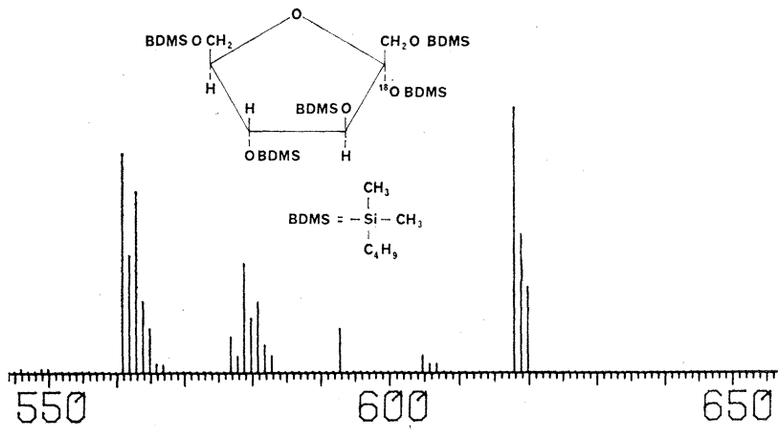
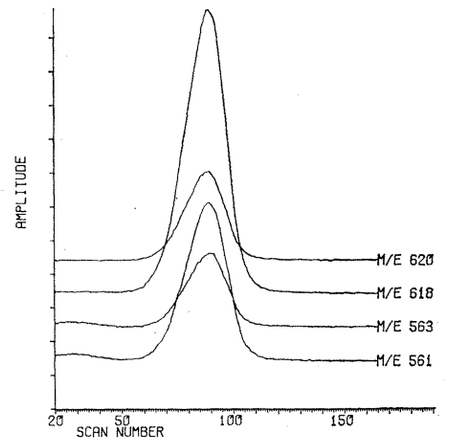


Partial mass spectrum of (2-^{18}0)-pentakis-(butyldimethylsilyl)fructofuranose



Mass fragmentogram of four ions of interest.

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An Example

The (2-^{18}O)-pentakis-(butyldimethylsilyl) fructofuranose is being used in isotope labeling studies of intact cells. This analysis was performed to verify the position of the ^{18}O isotope and to measure its enrichment at that position. The isotope ratios were obtained by comparing the integrated areas of the specific ion chromatograms of the (2-^{18}O) fructose. These specific mass ions are chosen because they are the diagnostic ions of the (2-^{18}O) fructose. The ion at m/e 561 (M^+–189) contains 31.3 atom % excess ^{18}O measured at 0.36% precision. Combustion techniques were used to show that this was the total amount of ^{18}O in the (2-^{18}O) fructose. Thus, the ion at m/e 561 contains all of the C-2 oxygen atom and measurement of the m/e 563/561 ratio can be used to calculate the ^{18}O enrichment in this oxygen atom. This provides meaningful data in the metabolism studies of fructose in intact cells. The 0.36% figure is typical of the precision and accuracy obtainable by mass fragmentography.

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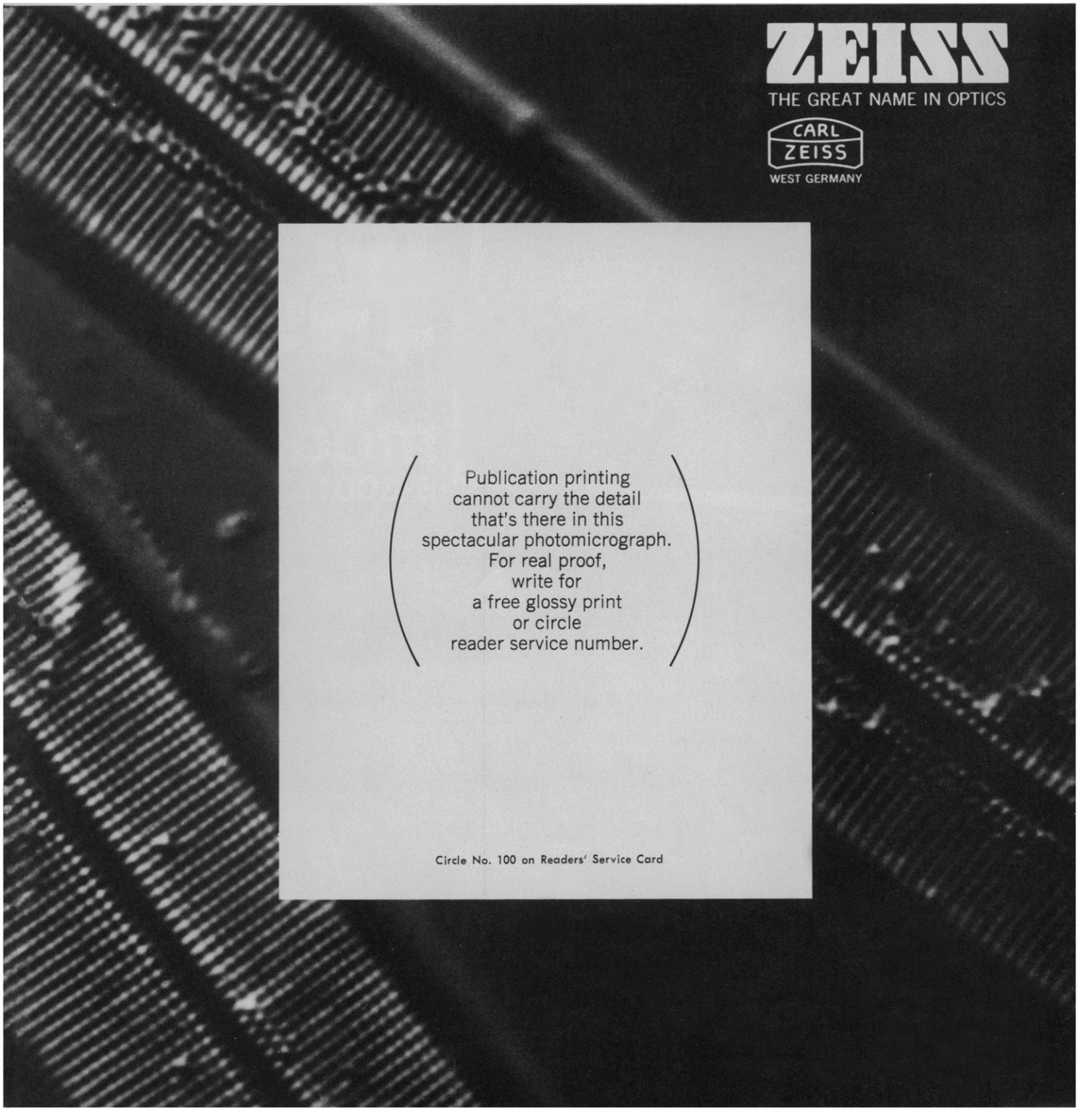

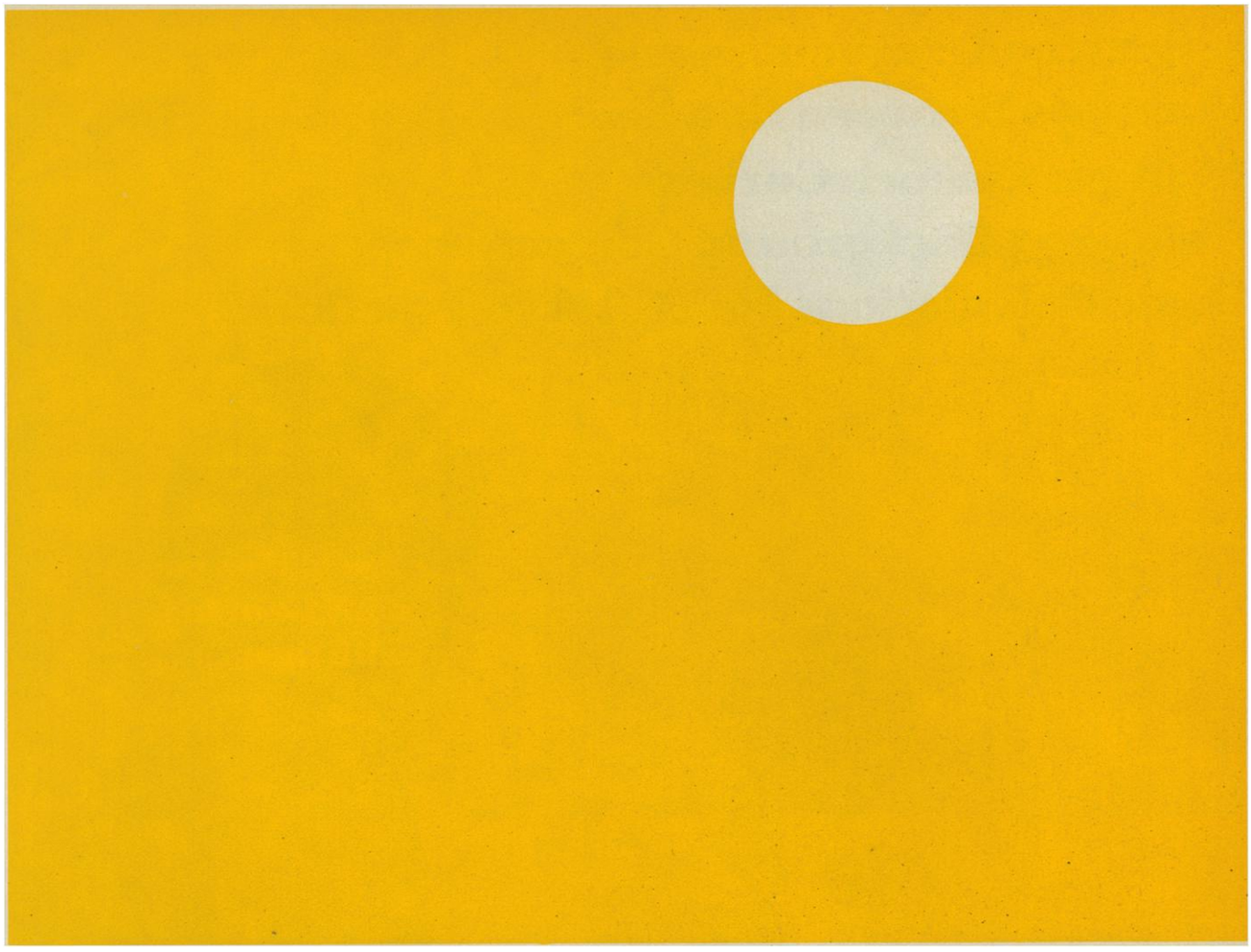

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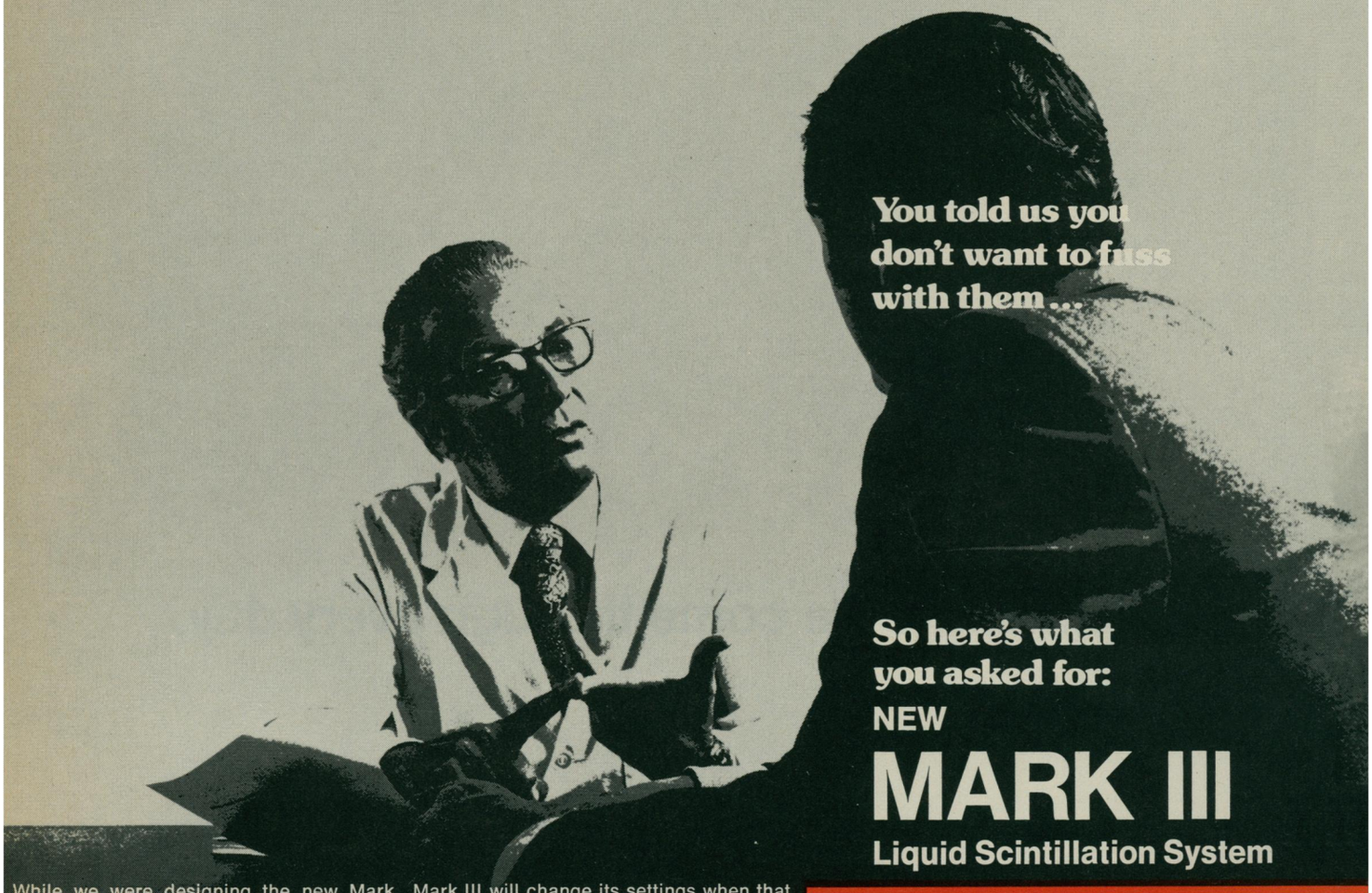

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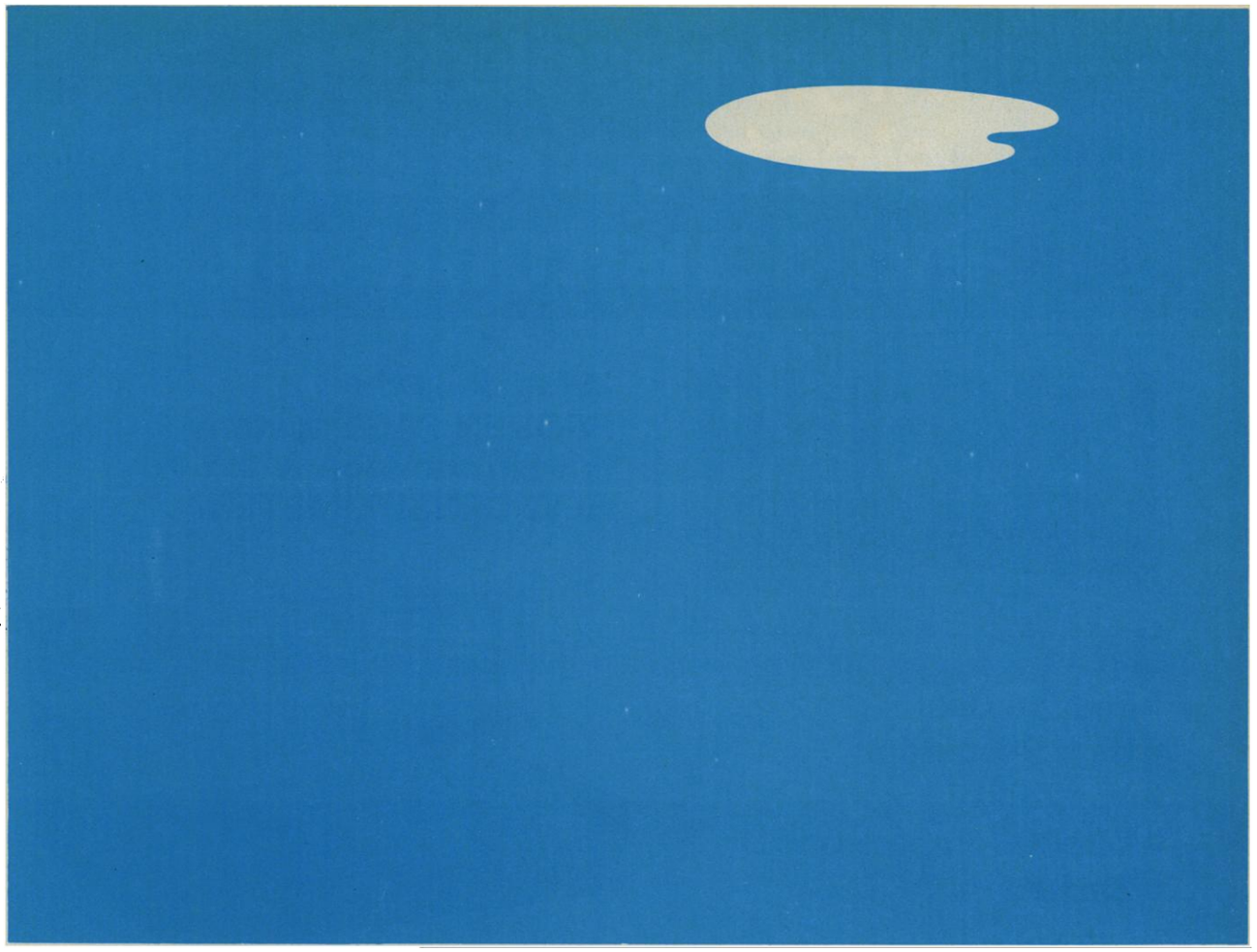

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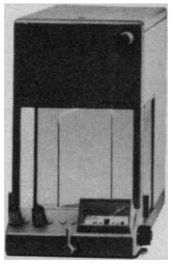

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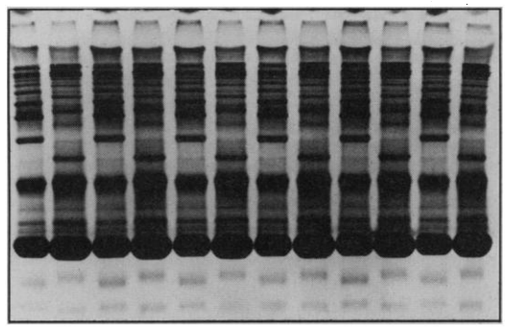

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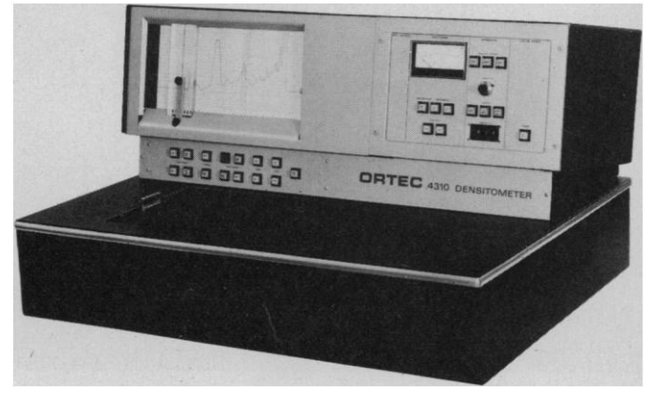

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LETTERS

The Ethics of Experimentation

The ethics of biomedical research have been a matter of concern to the public and to the profession for some time. Jewish Chronic Disease Hospital, Willowbrook State Hospital, Vacaville, and Tuskegee are familiar names in the litany of "horror stories" which the press has publicized since the early 1950's. Federal regulations governing research, which mandated peer review, have existed since 1967. Revisions of these regulations proposed in 1974 elicited considerable comment in professional literature and in the research community. In 1974, Congress established a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The commission has a 2-year mandate to review a range of problems and to recommend policy to the Secretary of the Department of Health, Education, and Welfare and to Congress.

Yet, despite wide publicity and frequent discussion, the nature of the problem remains ill-defined. A forum convened by the National Academy of Sciences (NAS) in Washington, D.C., on 18–19 February included a pantheon of distinguished researchers. They were summoned to discuss "Experimentation using human subjects: Values in conflict." Experimentation they did discuss; value conflict they barely noticed. The sessions manifested, among those presenting papers, an apparent lack of perception about the ethical issues.

The dominant note was the benefit brought by human experimentation to modern medical care. Indeed, while this thesis could scarcely be doubted, the abundant benefits add up to only half an argument in favor of experimental medicine. They constitute only the major premise. Another premise is needed to draw any conclusion. That premise must read, "but these benefits are sufficient ethical justification for doing x, y, and z, where x, y, and z stand for such activities as the use of children, prisoners, and the poor as research subjects." The planners of the conference clearly intended the second premise to be addressed, for they scheduled sessions on children, the poor, and the institutionalized. But again and again, even in these sessions, the circular argument emerged: "We would not have made the progress we have without these subjects; therefore, it is ethical to use these subjects."

I believe that it is possible to carefully frame the premises necessary to justify ethically certain research. Unfortunately, that was not done and those who have given most thought to doing it were either missing from, or given only minor roles in, the Academy forum.

Admittedly, doubts were occasionally expressed and sharp dissent was several times entered. But, as one commentator —a philosopher—remarked, the panelists almost to a man seemed to miss the public perception of the problem: research appears to involve a threat to the integrity and dignity of significant populations. Repeatedly, that concern was voiced by persons speaking from the audience. But on the stage, the participants either ignored, denied, or excused, with affirmations of peer review and informed consent, the "public perception of the problem."

Three reflections are stimulated by this event. First, it is imperative to point out the necessity and the utility of biomedical research. But every eulogy must be tempered with a confession, either of abuses (which may not be frequent, but when they occur, are flagrant) or of serious problems about selection of subjects, assessment of risks, and adequacy of consent. These matters still need to be studied, pondered, and improved by careful and innovative techniques. Awareness that a great portion of research is done among vulnerable and captive populations urges us to consider a fairer distribution of both the burdens and the benefits of modern medicine.

Second, the total absence of ethicists on the platform of the forum was remarkable. Certain professional theologians and philosophers of considerable ability have devoted attention to these problems. They are not scientists nor physicians, but they understand what an ethical issue is. They are generally able to define these issues in terms suitable for public debate. Also, those who practice the academic trade of ethics seldom advocate particular moral views. They may be deeply committed to certain positions, but their professional skills are directed principally to the analysis of moral arguments of all colors. They expose presuppositions and explore the logic of debate in order to render the issues more obvious for public discussion. One suspects that the absence of ethicists from the platform and their relegation to the audience was dictated by the fear that they would "take sides." Ironically, their

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presence may have prevented just that from happening.

Finally, the forum did make evident how necessary it is to educate the profession and the public on these issues. The National Commission for the Protection of Human Subjects has been given certain definite tasks by Congress. Its work will consist of making many recommendations about legislation, regulation, structures or review, reporting, and surveillance. But these practical tasks must not overwhelm its basic responsibility: "To determine the ethical principles underlying research." This responsibility would be poorly discharged if the commission issued a list of moral precepts. It must also find ways to instruct the profession and the public in the serious moral choices posed to our society by experimental medicine.

These reflections are prompted by my own triple role. As member of a medical faculty, I participate in the biomedical research community. There one sees vividly the values of research and the integrity of researchers. As a teacher of bioethics, I am engaged in the attempt to render moral problems more intelligible and suitable for reasonable public discussion. As a member of the National Commission for the Protection of Human Subjects, I recognize the unique educational opportunities of such a body. Its policy recommendations will be meaningful only if the research community and the public comprehend the issues.

Peculiarly enough, the proper task of the forum was enunciated at its end rather than at its beginning. In his closing remarks, NAS president Philip Handler stated that, although some might consider it trivial to discuss experimentation when worldwide problems of starvation, poverty, and pollution press upon us, "It is never trivial to seek to determine what is human and appropriate to human dignity." A sustained and refined concentration on "what is human and appropriate to human dignity" would have made the forum an exercise in ethics rather than an exposure of partisan enthusiasm.

ALBERT R. JONSEN

Health Policy Program,
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San Francisco 94143

The Secretary of the Department of Health, Education, and Welfare has requested statements regarding the use of prisoners as experimental subjects. The Medical Committee for Human Rights holds that prisoners cannot be considered "normal volunteers" in experiments.

The fundamental requirement of "free and informed consent" in inevitably compromised within the prison's closed and coercive system. Such "consent" by a prisoner is not truly "free" or adequately "informed," nor is it "consent" in the sense of an agreement freely entered into by equals under conditions of trust. It is not "informed" because sources of information are lacking in prisons. These considerations cannot properly be set aside simply because his status as a member of a captive population has made the prisoner a convenient and inexpensive experimental subject.

The major considerations motivating prisoners to "volunteer" are material inducements which promise to make their incarceration more tolerable and the hope or promise that participation will bring an earlier release. An unequivocal elimination of such factors would sharply reduce this reservoir of human subjects.

Prisoners cannot be considered "normal" subjects because their response to experimental activities may be distorted by the fact that they are not in a "normal" environment; also, covert drug abuse is rampant in prisons; finally, prisoners may consciously or unconsciously distort experimental results if this will, in their view, aid in their release or ameliorate the conditions of their confinement.

Efforts to protect subjects of experimentation by the establishment of committees with representation by fellow prisoners is no solution: such prisoner representatives are more or less subject to the same constraints as their fellows and cannot, therefore, serve them as free agents.

In view of the foregoing considerations, concern for the human rights of the subject and for the scientific validity of experimental results compels us to oppose in toto the use of prisoners as experimental subjects and to insist that the Nuremberg Code prohibiting such use be stringently applied. Other countries have demonstrated that they are able to carry out necessary research involving human subjects without resort to the prison population; we can and must do likewise.

PAUL LOWINGER

Medical Committee for Human Rights,
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(Continued on page 174)

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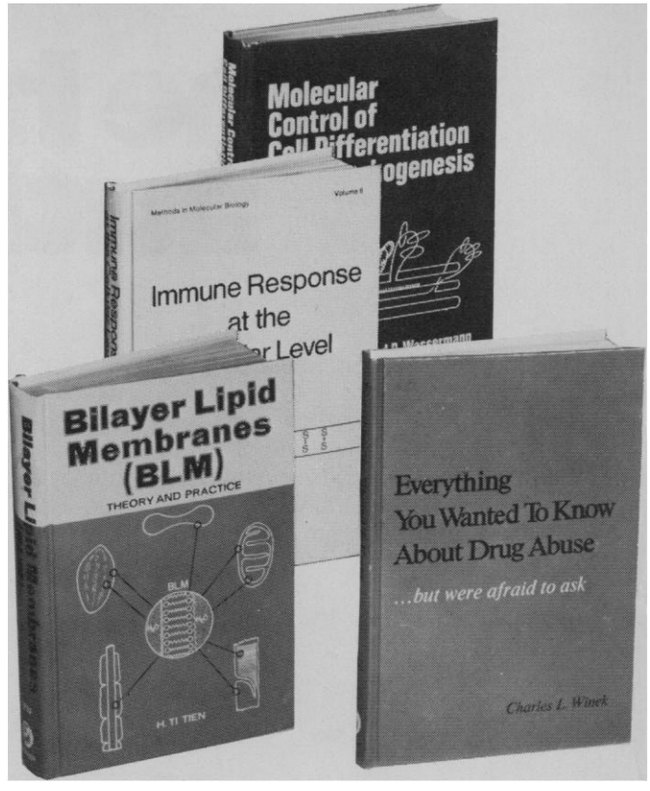

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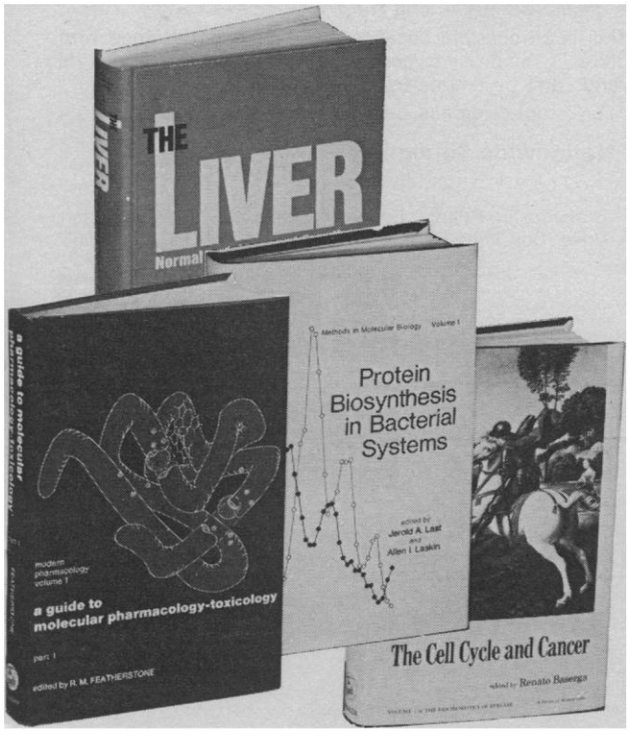

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11 April 1975, Volume 188, Number 4184

SCIENCE

Coercive Power of the Federal Purse

Use of the leverage of the government dollar to accomplish objectives which have nothing to do with the purposes for which the dollar is given has become dangerously fashionable, and there is no obvious constitutional basis on which to resist this encroachment.

The difficulty of obtaining review of a denial of a grant or a contract makes the allocation or withholding of funds easy to manipulate for vindictive or political purposes. This was precisely what was proposed in order to get back at Jerome Wiesner for his opposition to the antiballistic missile program.

There have been other less flagrant, but equally pernicious, efforts to use the leverage of the spending power to "discipline" educational institutions. The most notorious was Congressman Hebert's persistent effort to deny all Department of Defense grants to any institution which discontinued its Reserve Officers Training program.

Another example of use of the leverage of the government dollar is the proposed health manpower legislation. With laudable motive and seeming plausibility, this legislation seeks to remedy the shortage of primary care physicians and the obvious uneven availability of medical care throughout the country. It does not use the device of special assistance for the training of primary physicians, or special bounties for graduates who commit themselves to practice where they are most needed. It proceeds, rather, by telling the medical schools that all general support for medical education, the so-called capitation grants, will be withdrawn unless a school increases its general practice training and requires some proportion of its graduates to enter practice where there is a shortage of doctors. Were it not for the federal financial support it would be hard to find warrant in the Constitution for federal regulation of medical school curricula or for drafting graduates to serve in places not of their choice.

This same leverage is carried to far greater extremes in other federal legislation already on the books. It might be called the "now that I have bought the button, I have a right to design the coat" approach. Thus if we are to receive support for physics, let's say, we must conform to federal policies in the admission of women to the art school, in the provision of women's athletic facilities, and in the recruitment of women and minorities, not just in the federally supported field, but throughout the university. Even in the name of a good cause such as "affirmative action," this is constitutionally objectionable.

The farthest outreach of federal regulation under the banner of the spending power is the Family Educational Rights and Privacy Act, the so-called Buckley Amendment to the Education Act. Again, the purpose is laudable. Schools should not be able to build up prejudicial files on students against which the student has no redress if he has no way of knowing what is in them. But the end does not justify the means in this case either.

We all remember the warning of former President Eisenhower against the dangers of the military-industrial complex, but hardly anyone remembers that he went on to say, "The prospect of domination of the nation's scholars by federal government, project allocation, and the power of money, is ever present, and is gravely to be regarded."

High on the agenda of the legal profession, especially its scholarly branch, should be to see to it that, in terms of both limits on authority and redress against its abuse, the coercive power of the federal purse is made subject to a rule of law.

It is high time that we learn once again to ask not only "Is your objective worthy?" but also "Are the means you would use consistent with the values of the Constitution?"—KINGMAN BREWSTER, *President, Yale University, New Haven, Connecticut 06520*

Excerpted from a speech delivered to the Fellows of the American Bar Foundation on 22 February 1975.

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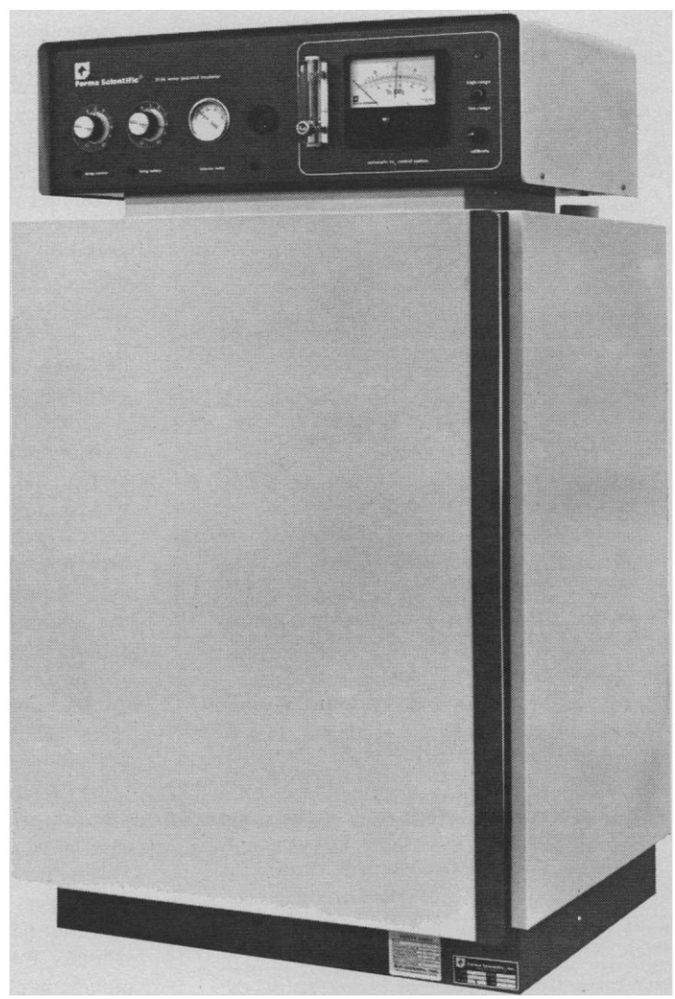

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Fig. 2. Colordip has a tungsten light source in the probe head which with eight filters and a fiber optic light system enables the operator to dispense with cuvettes, sample preparation, and problems caused by stray light.

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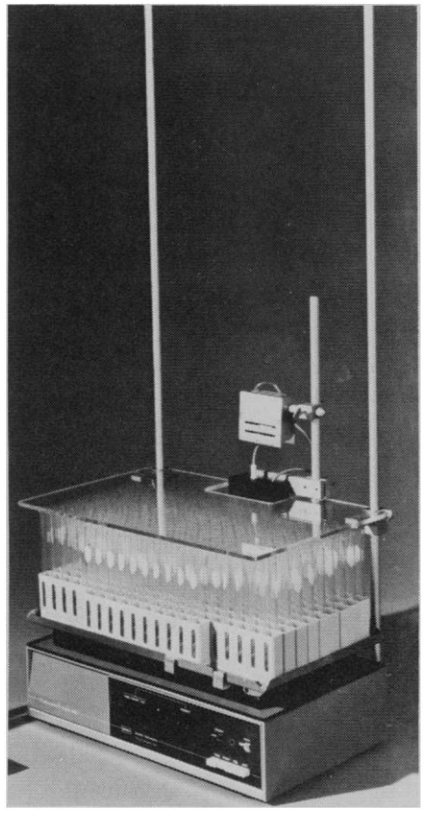

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LETTERS

(Continued from page 100)

Inefficient Medical Care

The computers at Yale–New Haven and New York hospitals have not looked in the right place if, as Deborah Shapley reports (News and Comment, 28 Feb., p. 30), they have found no evidence of waste and inefficiency.

The place to start looking is in the information flow of daily medical care. Every doctor in practice wastes hours looking for information that ought to be handed to him as he needs it. Patients sit around in waiting rooms while someone tries to find their medical records. Medical care suffers, not in the glamor fields like open heart surgery, but in the thousands of times information is passed from one person to another.

In the clinical laboratory alone, which accounts for nearly one-quarter of the nation's hospital bill, 50 percent of laboratory results are unused medically (*1*); 40 percent of patients' records are incomplete (*2*); 30 percent of test requests are not properly processed (*3*); 20 percent of laboratory reports are lost (*2*); and 10 percent of laboratory specimens are never received (*2*).

SAMUEL RAYMOND
William Pepper Laboratory, University of Pennsylvania Medical School, Philadelphia 19104

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Honeybee Controversy

Regarding the correspondence (Letters, 6 Sept. 1974, p. 814; 13 Dec. 1974, p. 975) about the von Frisch versus Wenner controversy over the language of bees, it has been suggested that von Frisch's hypothesis alone applies (*1*); that Wenner's hypothesis alone applies (*2, 3*); and that they are not mutually exclusive and may peacefully coexist (*4*). Now Davenport (Letters, 13 Dec. 1974, p. 975) offers us the vision of a compromise.

As a firm supporter of Wenner's hypothesis, I believe, however, that the controversy will not be resolved until it is generally understood that it reflects a much wider, basic, theoretical controversy between Lorenz's school of animal behavior and Schneirla's school (*5*).

The behavior suggested by Wenner's hypothesis will only make sense when viewed as a detail within the context of the continuous, dynamic process of the ontogenetic development of foraging behavior in the honeybee. It is exactly the need for this kind of study, while bearing in mind the low psychic level of insects in general, which is urged by Schneirla's theory.

Davenport might have explained to his students that the problem is somewhat more complicated than he seems to suggest. Firm supporters of von Frisch's hypothesis are well aware, for instance, that one of the Wenner groups' major experiments (*3, 6*), is based by the group on the assumption that the accumulation of odor in the hive facilitates recruitment of new bees to an outside food source scented with this odor, on the following day (*3*). This assumption has, however, been summarily disproven by Lindauer (*7*). No wonder supporters of von Frisch refuse to budge.

Wenner's group made a major breakthrough when they found that the mere introduction of odor into the hive will cause foragers, at the phase in which they cease to forage at an outside food source scented with this odor (after depletion of the source), to resume flights to the source (*3, 8*). However, the mere accumulation of odor in the hive does not have the effect Wenner's group believes it has. The effective factor in that case is the accumulation in the hive of bees who have experienced the exchange of tactual stimuli with a dancing forager carrying this particular odor, and have received food from her that is scented with this odor. This situation involves bees at a very different phase, that is, one of the dance-attending phases. One can dispense with dances, or even with the mediation of a returning forager carrying the odor into the hive, in the first situation, but not in the second (unless, of course, one uses a very sophisticated dummy which will not only dance, but also distribute food).

This small example accentuates the need for a detailed study of the ontogenetic development of foraging behavior in the honeybee, similar to the one carried out by Schneirla for the army ants (*9*). Such a study would remove all sort of hurdles which Wenner's hypothesis constantly runs into. Wenner has mainly extended his studies

over space (justifiably demanding that the behavior of the whole population during a certain incident be taken into account), but as far as the individual development of the behavior of bees over time is concerned, he has barely touched some isolated incidents in a dynamic continuum.

R. ROSIN*

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Political Decision

Recent history suggests that, rationalism and "objectivity" notwithstanding, scientists are at least as politically gullible as anyone else. In 1931 Sir Julian Huxley visited the Soviet Union and returned to England to publish *A Scientist among the Soviets* (*1*), praising "the elevation of science and scientific method to its proper place in the affairs" of that country. In 1949 he felt obliged to recant in *Soviet Genetics and World Science* (*2*), a book written in defense of "that freedom of the intellect which we fondly imagined had been laboriously won during the past three or four centuries." A reading of Medvedev's *Rise and Fall of T. D. Lysenko* (*3*) makes it very plain that there was no fundamental change in Soviet society during this period; the crushing of intellectual freedom was an inevitable consequence of ideological totalitarianism. One hopes the sad saga of H. J. Muller's sojourn in the Soviet wilderness has not been forgotten, nor J. B. S. Haldane's ultimate resignation from his beloved Communist Party in protest of Lysenkoism. Yet, human nature being what it is, scientists continue to seek utopias in improbable places. I have not been to Cuba, but on reading the letter from Ellis, Levitt, and Fausto-Sterling (27 Dec. 1974, p. 1159) I felt an overwhelming sense of déjà-vu: once again the United States, and the United States alone, is hindering the realization of paradise on Earth in a revolutionary Socialist state.

We may all praise the Cuban revolution if it has indeed stimulated science there, but that is not all that it has done, and at any rate mere numbers are no indication of intellectual climate, as Russia's record shows. The price of the revolution is being paid, most immediately by the prisoners behind barbed wire on the Isle of Pines and elsewhere (are there any scientists among them?), but ultimately, perhaps, by all the Cuban people under a regime which subordinates human freedoms to the state ideology. I hope readers of *Science* will keep this in mind while pondering the appeal for support from the scientific community for an end to the blockade. This is a political decision with many consequences, of which improvement in scientific communication may be one of the least important. I hope readers who are impressed by the figures concerning women and minorities in Cuban science will balance them against the ruthless persecution of homosexuals reported even by observers favorably disposed toward the new Cuban society (*4*). As for the ideal of international cooperation embodied in the charters of the United Nations and Unesco, I will take Ellis *et al.* more seriously when they publicly denounce the Castro regime's complicity in the unprecedented subversion of those ideals by the Third World when it read Israel out of Unesco in 1974.

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