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11 November 1977

Volume 198, No. 4317

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COVER

A right-handed scribe enumerates cattle circa 1350 B.C. See page 631. [Stanley Coren, University of British Columbia, Vancouver, Canada]

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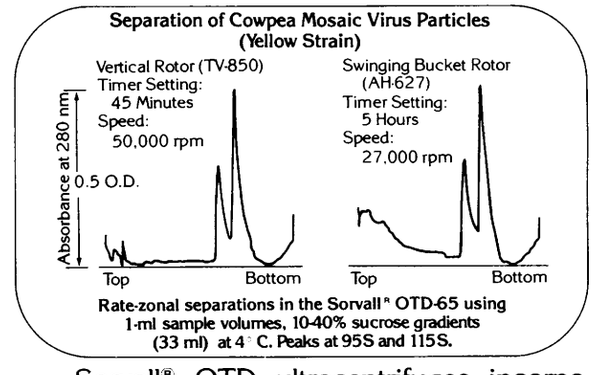

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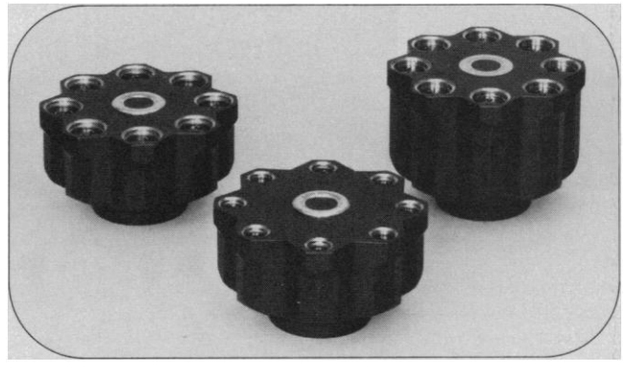

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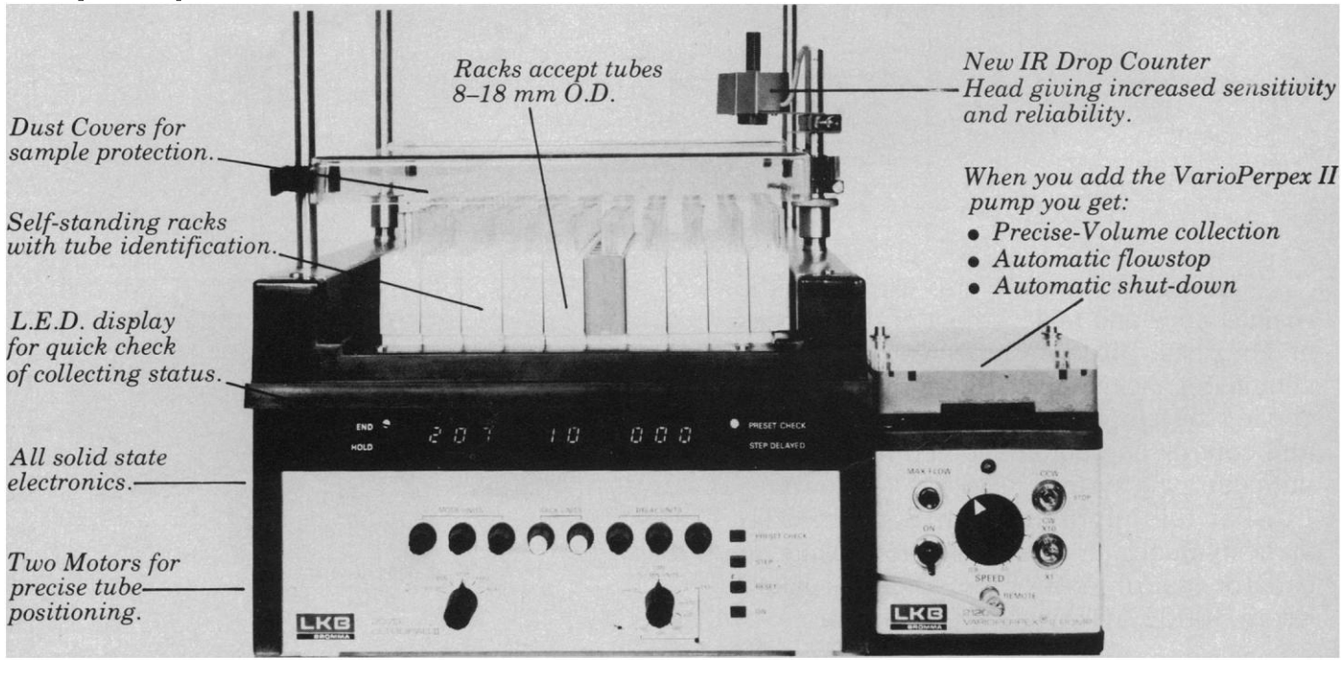

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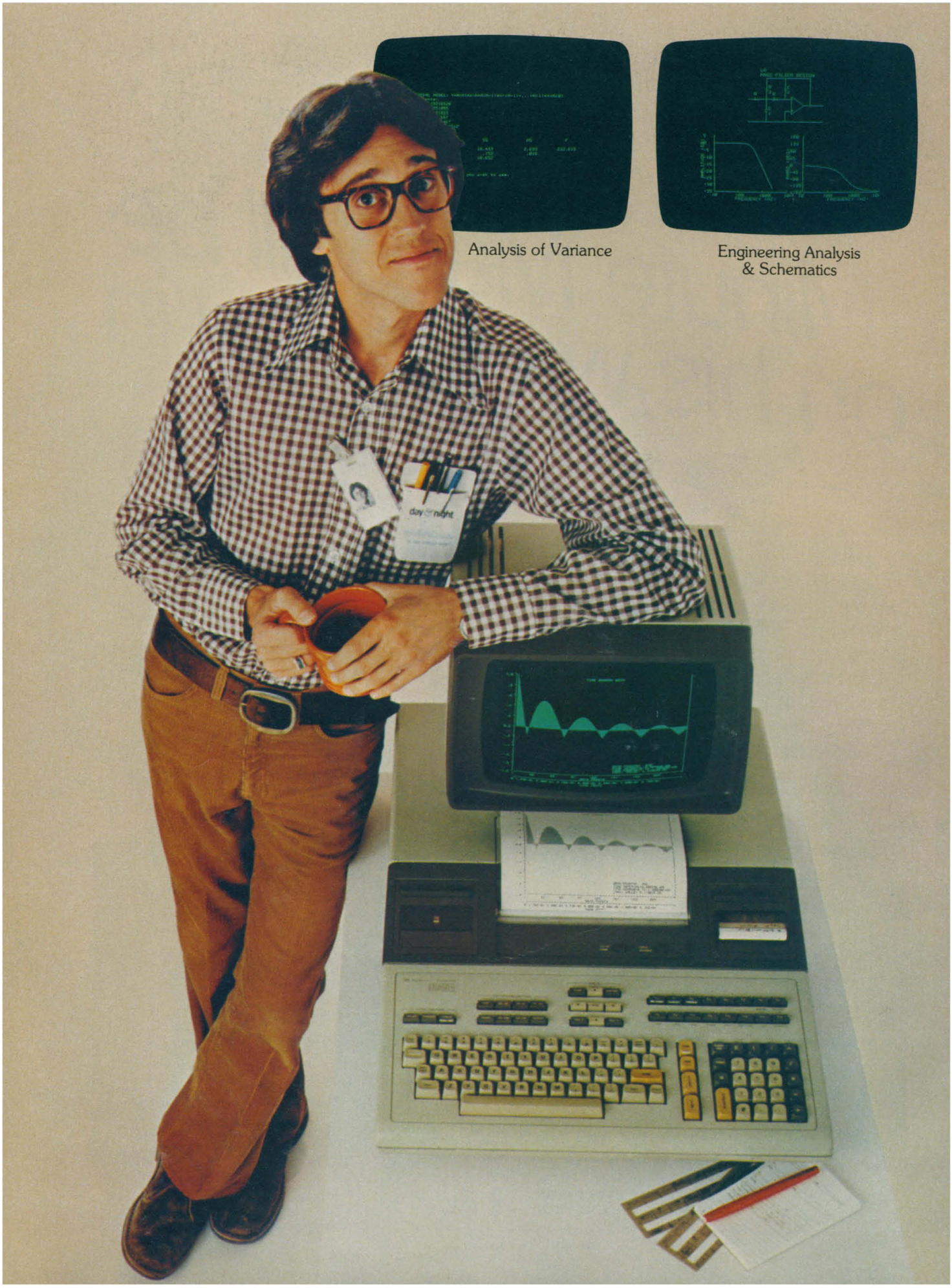
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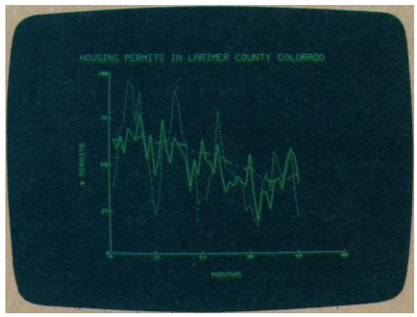

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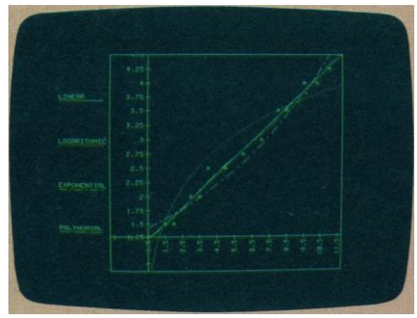

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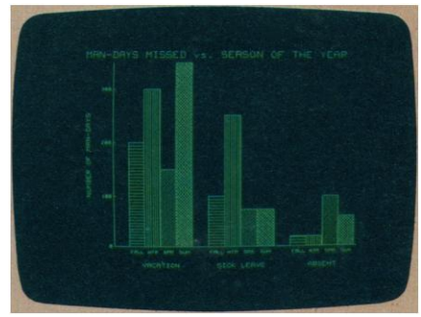

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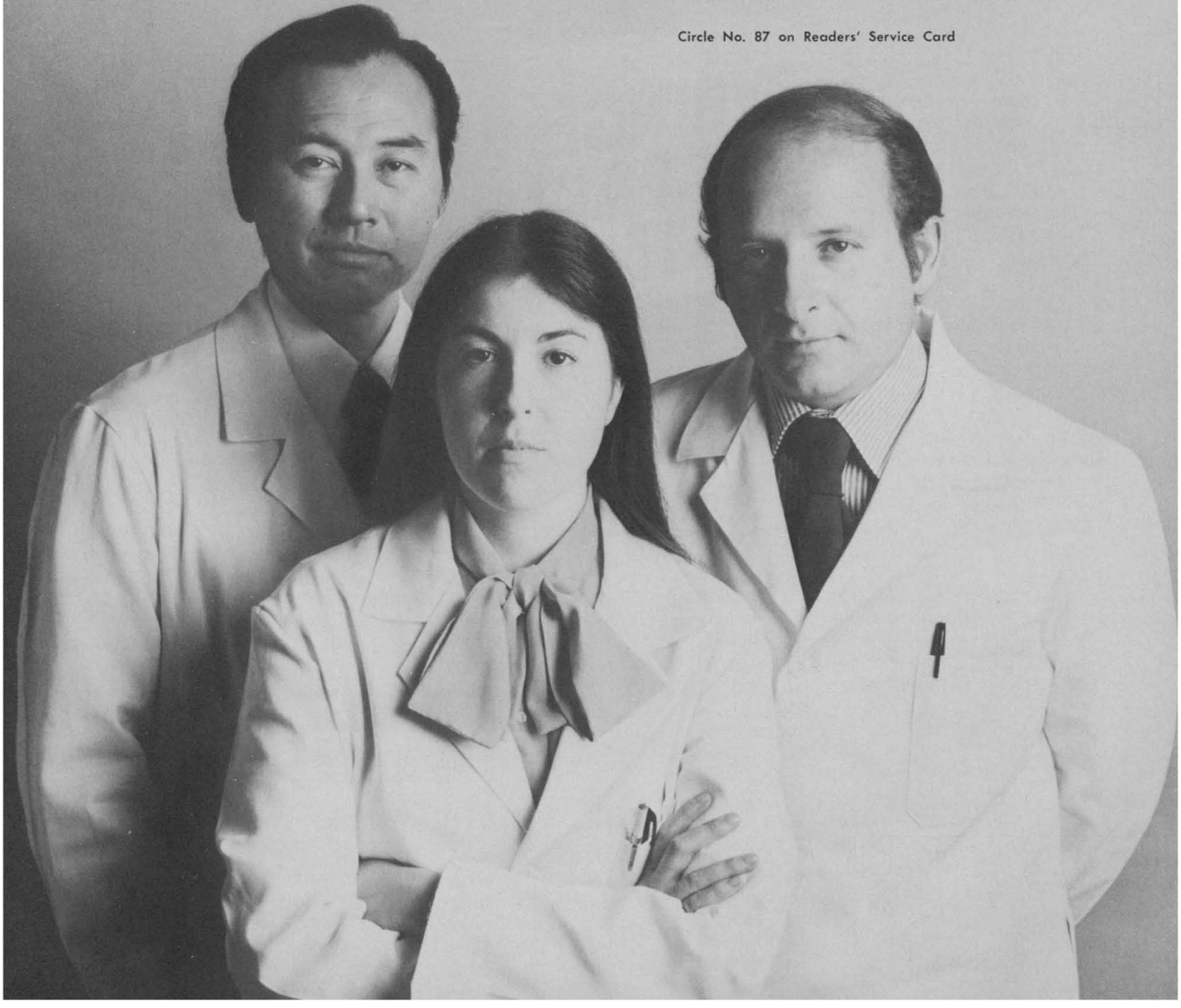

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- mRNA (from chick embryo)
  Neufang, O., & Tiedemann, H. (1975) Hoppe-Seyler's Z. Physiol. Chem. **356,** 1445-50.
- localization of synthesizing polysomes (in rat lung)
  Cutroneo, K.R., Newman, R.A., Prichard, P.M., Guzman, N.A., & Sharawy, M.M. (1977) Int. J. Biochem. **8,** 421-6.
- localization of lysine hydroxylation (in rat lung)
  Guzman, N.A., Rojas, F.J., & Cutroneo, K.R. (1976) Arch. Biochem. Biophys. **172,** 449-54.
- lysine hydroxylase (from chick embryo)
  Murray, J.C., Lindberg, K.A., & Pinnell, S.R. (1977) J. Clin. Invest. **59,** 1071-9.
- proline hydroxylase (from guinea pig granuloma)
  Miller, R.L., & Udenfriend, S. (1970) Arch. Biochem. Biophys. **139,** 104-13.

Collagenase ABC has been used in tissue culture to study:

- collagen synthesis by human lung explant)
  Bradley, K., McConnell-Breul, S., & Crystal, R.G. (1975) J. Clin. Invest. **55,** 543-50.
- collagen synthesis and hydroxylation (by 3T6 mouse fibroblasts)
  Bates, C.J., Prynne, C.J., & Levene, C.I., (1972) Biochim. Biophys. Acta **263,** 397-405.
- preparation of collagen precursors (from rat skin and bone)
  Smith, B.D., McKenney, K.H., & Lustberg, T.J. (1977) Biochemistry **16,** 2980-5.
- isolation of tissue collagen (from rat aorta)
  Newman, R.A., & Langner, R.O. (1975) Anal. Biochem. **66,** 175-84.
- studies of wound healing (in rat skin)
  Diegelmann, R.F., Rothkopf, L.C., & Cohen, I.K. (1975) J. Surg. Res. **19,** 239-43.

A few other collagenase uses:

- studies on elastin synthesis after eliminating collagen (in primate muscle cell culture)
  Narayanan, A.S., Sandberg, L.B., Ross, R., & Layman, D.L. (1976) J. Cell Biol. **68,** 411-9.
- modification of acetylcholinesterases (in the electric organ of *Electrophorus electricus*)
  Johnson, C.D., Smith, S.P., & Russell, R.L. (1977) J. Neurochem. **28,** 617-24.

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"The collagenase used for these assays did not release any radioactivity when incubated with [^{3}H]tryptophan-labeled proteins from *Escherichia coli*." Guzman *et al.* (1976) Arch. Biochem. Biophys. **172,** 450; also in Cutroneo *et al.* (1977) Int. J. Biochem. **8,** 422.

"A more critical criterion of the specificity of the purified collagenase in this system is that it did not digest tryptophan-^{14}C-containing proteins isolated from guinea pig granuloma (collagen does not contain this amino acid)." Miller & Udenfriend (1970) Arch. Biochem. Biophys. **139,** 106.

"However when chick globin mRNA. . . . was added to wheat germ extract, about 15% of the newly synthesized, [^{3}H] proline labelled protein was degraded by rechomatographed Worthington collagenase, but only 0.5% by the Advance Biofactors collagenase." Neufang & Tiedemann (1975) Hoppe-Seyler's Z. Physiol. Chem. **356,** 1446.

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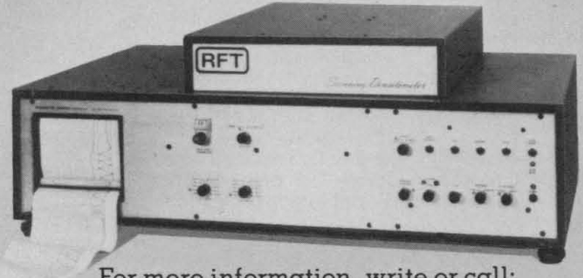

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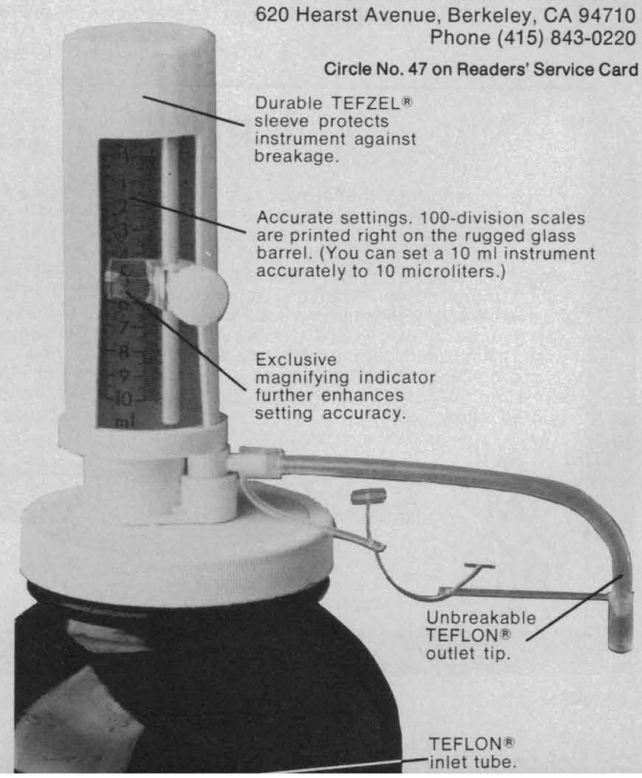

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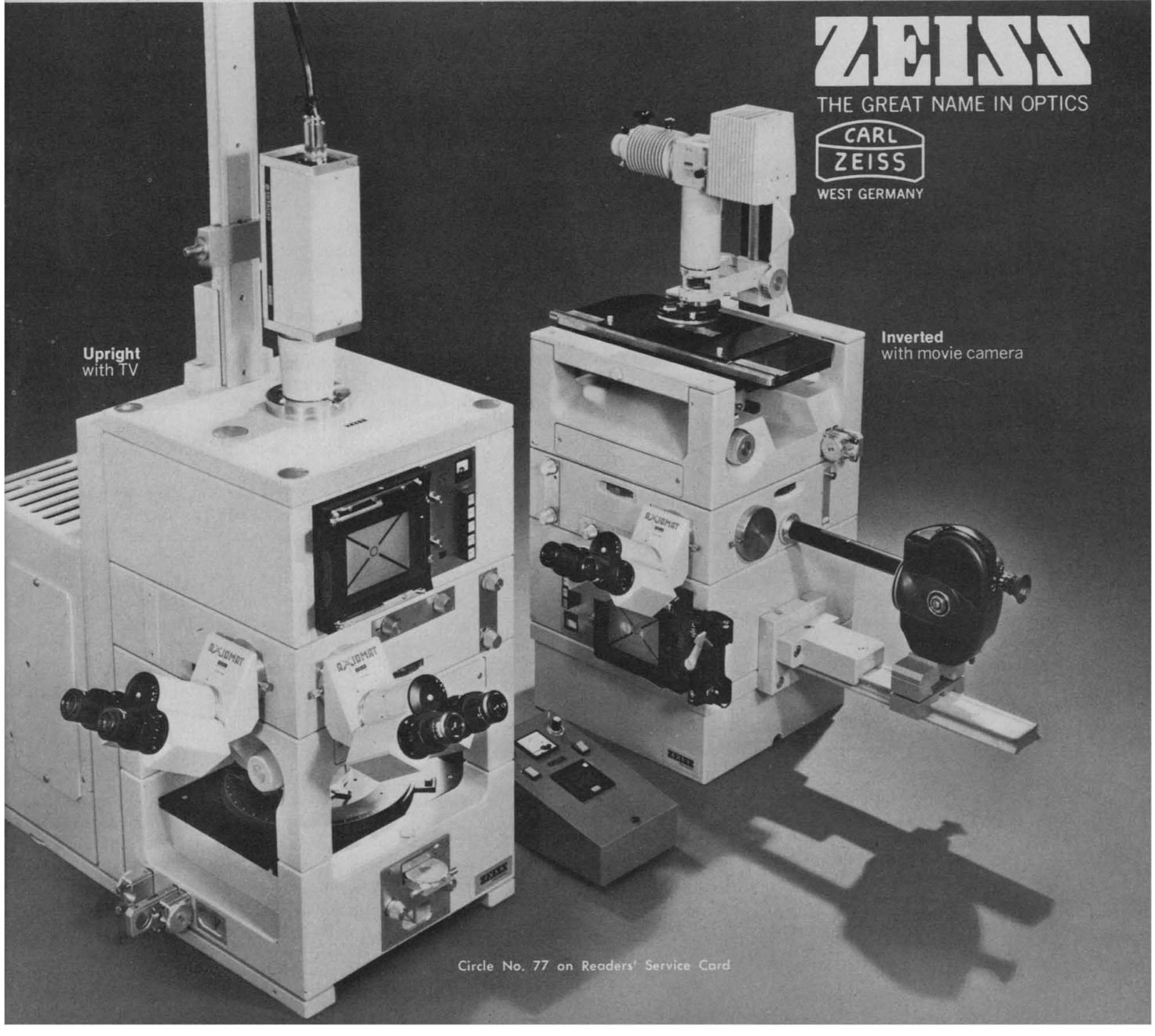

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LETTERS

NBS: State of Health

The article by Gina Bari Kolata, "National Bureau of Standards: A fall from grace" (News and Comment, 2 Sept., p. 968) and the following response by F. Karl Willenbrock and Ruth M. Davis (Letters, 7 Oct., p. 8) occasion this rejoinder. I write as an individual NBS staff member who has served as chairman of committees concerned with research at the bureau.

Clearly the title of Kolata's article is ambiguous, as a "fall from grace" can be (i) a descent from a state of felicity or (ii) a loss of place in the pleasure of another. The content of the article appears to be consistent with meaning (i), while the letter from Willenbrock and Davis (correctly) denies the applicability of meaning (ii), as evidenced by the (undisputed) assignment of 15 new tasks by Congress to NBS in the past 10 years. The nature of these assignments (whose value is not questioned) has been such that the associated work has been concentrated in the NBS institutes headed, until recently, by Willenbrock and Davis. This has quite naturally led to a measure of vigor in those institutes.

Unfortunately the new (and urgent) congressional assignments were made during a period of essentially static funding and severe personnel constraints at NBS. Response to these mandates was made at significant cost to the health of some of the long-term efforts already under way. Much of this discipline-oriented (but also urgent) long-term work is centered in the two other NBS institutes, whose programs, as a result, have been weakened and, in some cases, terminated.

That such a condition bodes ill for the eventual health of NBS has been widely recognized. The quotes Kolata obtained from the senior NBS managers indicate that they perceive the problem in rather stark terms. For obvious reasons, their statements are more circumspect than, but entirely consistent with, those of the Statutory Visiting Committee, which has the duty of reporting to the Secretary of Commerce on the adequacy of the bureau's efforts and programs. (The members of the visiting committee are identified in Kolata's article.)

This year's report by the chairman of the Statutory Visiting Committee states: "NBS has critical problems"; is on the "brink of serious trouble"; and "persistent retrenchment that has taken place threatens to bring NBS to a mediocrity that is unacceptable." The committee

sees the additional assignments as having "forced NBS leadership into defensive management, whereby long-range programs are sacrificed to salvage short-term objectives." The predominant source of information for the members of the visiting committee is NBS management itself. It therefore appears that the pessimistic view of the present state of NBS conveyed by Kolata's article is more in accord with reality than the optimistic picture one might derive from the letter of Willenbrock and Davis.

In truth, those areas of NBS which are best known to the community of science have suffered considerable damage over the past several years. [The thoughtful letter from Michael N. Alexander (7 Oct., p. 8) rightly emphasizes that this has happened in other government (and industrial) laboratories.] Recent events, including the proposal of a radical reorganization of NBS, offer hope that an opportunity is at hand to reverse or at least mitigate some of the more devastating trends of the last decade. My sense of the institution is that this comes none too soon but not yet too late. There remains at NBS a cadre of scientific workers who have an appreciable culture in their disciplines, residual commitment to the institution, and even a measure of hope for its future.

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Recombinant DNA Guidelines: Scientific and Political Questions

An article in the News and Comment section of the 22 July issue of *Science* (p. 348) includes a summary of the spring meetings of the National Institutes of Health Recombinant DNA Advisory Committee. An observer is quoted as writing that the committee members "often mocked their own restrictions," and three statements by committee members are cited in support of this interpretation: "These high levels are political, not scientific"; "P4 was designed to prevent research"; and "P1 is a laboratory plus a bureaucrat." As a member of the committee, I would like to comment.

While perhaps mocking in tone, these are profound statements about some of the problems faced by the committee. In the proper sense of the word "political," meaning the setting of policy, the guidelines are indeed political, and not scientific. This is a most crucial point. The scientific question is, What is the estimated

probability that various types of recombinant DNA research could produce a dangerous or undesirable microorganism? The political (policy) question is, What measures, if any, should be taken in response to this estimate? In contrast to the scientific question, the latter question is answered by considering the political climate, sociological factors, and one's own value judgments.

The committee's answer to the scientific question was in essence:

1) The only experiments for which there was clearly a finite probability of harm were among those cited in the original warnings about possible dangers of recombinant DNA research and which were placed under voluntary moratorium.

2) For the rest of the experiments the possibility that there could be a real danger could only be assessed on an intuitive basis until there were more data and broader scientific input.

In the view of the committee, the appropriate response, that is, the policy decision, was to ban the experiments in the first category above and to place a graded series of restrictions on the other experiments sufficient to allay the most serious of the intuitive concerns. It should be noted that these restrictions in effect *instituted* a partial moratorium on much recombinant DNA research and in no way represented *ending* a moratorium. Thus, the decision to specify containment levels for particular experiments was primarily one of policy, being based on value judgments as to how to respond to a problem for which there was an inadequate data base, and not based on a rational estimate of the probability of risk.

The failure of the guidelines to be clearly perceived as being a policy statement rather than a scientific document has been responsible for much of the excessive concern about possible public health problems from recombinant DNA research. Particularly, classification of an experiment as a "P4 experiment" is seen by many as prima facie evidence of serious biohazard, rather than as a supercautious recommendation on dealing with an unknown area of research.

The committee quite consciously recognized that its recommendation that P4 facilities be used for certain experiments served a twofold purpose—to ensure maximum containment and to severely limit the number of experiments in those categories that at the time were considered to be the most conjectural of the permitted experiments. In that sense, the statement "P4 was designed to prevent research" is quite true. The fact that, as of this writing, there is still no certified P4 facility in this country bears this out.

The third comment, "P1 is a laboratory plus a bureaucrat," also carries an extremely important message. This statement was made during discussion of what administrative procedures to recommend for laboratory work involving physical and chemical characterization of recombinant molecules free of host or vector microorganisms. The committee agreed that this type of work was free of any conceivable risk, and the suggestion was made, "Why not put it in P1?" The reply was, "No, because P1 is a laboratory plus a bureaucrat," expressing the idea that laboratories doing unquestionably safe research must be assiduously protected from encumbrances such as the multiple levels of administrative review inherent in being under the guidelines.

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Medical School Transfers

In discussing Philip H. Abelson's editorial "Coercion of medical schools" (16 Sept., p. 1137) Theron A. Ebel states (Letters, 21 Oct., p. 250) that 69 percent [actually, the figure should be 64 percent, from the quoted data (*1*)] of the U.S. citizens seeking to transfer from foreign medical schools through COTRANS (the Association of American Medical Colleges' Coordinated Transfer Application System) were from three states. While not taking any position on the desirability of such transfers, one might point out that the three states in question (New York, New Jersey, and California) represent more than 22 percent of the country's population, a figure perhaps more pertinent than the 6 percent of the states they constitute. There is still a discrepancy, but one not quite so shocking as that quoted by Ebel.

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References

1. W. F. Dube, *Characteristics of U.S. Citizens Seeking Transfer from Foreign to U.S. Medical Schools in 1975 via COTRANS* (Association of American Medical Colleges, Washington, D.C., 1977), p. xi; available from ERIC Reproduction Service, Arlington, Va.

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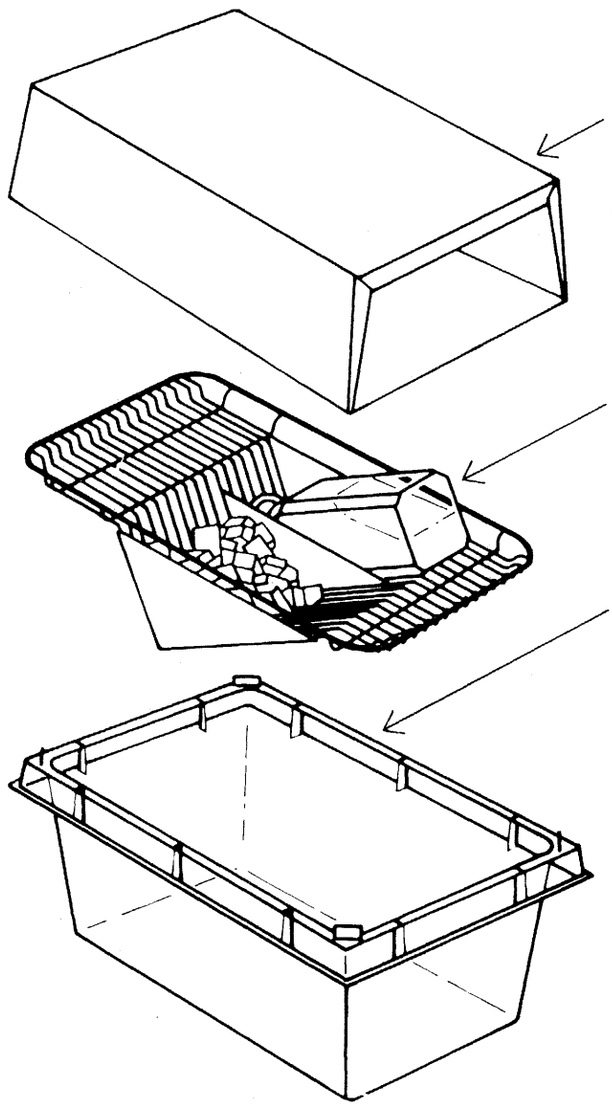

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11 November 1977, Volume 198, Number 4317 **SCIENCE**

Environmental Assessment: A Pragmatic View

Population growth and supporting technology create the potential for tremendous environmental problems. The major question is how to control human activities so as to maximize societal and individual well-being while minimizing harmful effects on health and the environment. Two kinds of effort are required as a basis for decision-making. One is estimation of the actual risks or effects associated with technological options: this is difficult because of the diversity of potentially harmful anthropogenic agents, the large number of organisms and ecosystems that may be affected, and the complexity of exposure pathways and action mechanisms. The other effort is equally difficult because it involves a value judgment: namely, the judgment of what level of risk is acceptable.

The required action is obvious if gross effects are produced (such as those from thalidomide) or if an agent or process that is of very little real benefit (for instance, cyclamates in soft drinks) is even suspect. A dilemma arises when a highly beneficial activity results in low levels of pollutant exposure which, theoretically, could produce harmful effects that are not detectable epidemiologically or cannot be attributed to the pollutant should they occur in individuals. Exposure to ionizing radiation from diagnostic X-rays or nuclear power is one example; use of saccharin is another. A dilemma also arises if the activity is intertwined with societal habits or the economy. Obvious examples are the health effects that can be related to smoking and to the use of automobiles.

In such dilemmas, the course of action must fall between two extremes. One is to take immediate action when a potentially harmful agent is recognized, disregarding any benefits from its use, the availability of substitutes, or the socioeconomic effects of the action. But such precipitous action often does more harm than good. The other is to defer action until its net effect has been determined. Such deferred action often would not be in time to protect the public.

There are other difficulties, many largely unappreciated by researchers, policy-makers, or the public. One major problem is that the present research effort is inadequate. For example, although $2 billion and 30 years have been spent studying the biological effects of ionizing radiation, acceptable exposure levels are still debated. Chemical pollutants are much more complex and many carry the same potential hazards, such as persistence and delayed carcinogenic effects. Another problem is that once a pollutant has been identified and publicized there is a tendency to reduce its risk to zero before acquiring biological and biomedical knowledge; this can lead to increased or prohibitive costs without commensurate benefits. And there is the problem of deciding which pollutants should receive attention first. To clarify decision-making and deepen public understanding, the following principles are proposed:

1) In every environmental and health assessment, the risk or effect (biological and economic) of a given action should be weighed against the risk or effect of not taking that action.

2) All risks or effects should be expressed in terms of the changes that would be produced in our existing state of well-being.

3) In all estimates of risks or effects, there should be a clear statement of the uncertainties that pertain to the assessment to be used in decision-making.

If these principles are adopted, it should be easier to effectively allocate our national research and engineering resources, to avoid making small risks even smaller while larger risks remain unattended, and to give society time for whatever planned and orderly socioeconomic changes are necessary to meet future conditions.—CYRIL COMAR, *Professor Emeritus, Cornell University, and Director, Environmental Assessment Department, Electric Power Research Institute, Palo Alto, California 94303*

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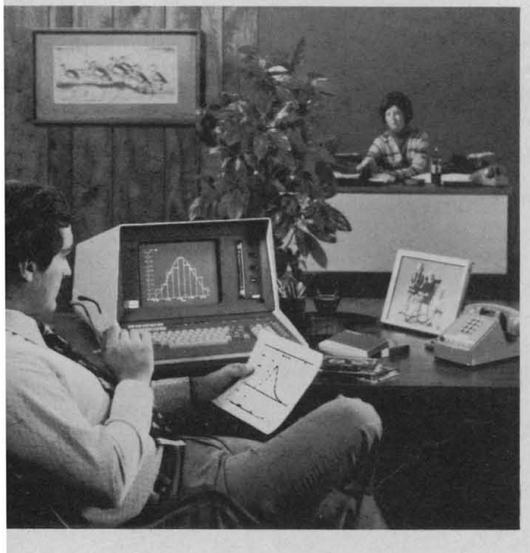

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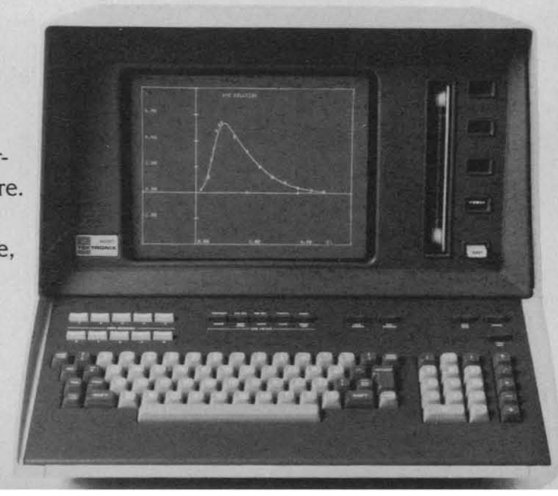

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Literature

Centria describes an automated system for radioimmunoassay. Union Carbide Clinical Diagnostics. Circle 694.

Digital Dosimetry is devoted to the model 192 exposure/exposure-rate meter for gamma- and x-irradiation. Capintec. Circle 696.

Amino Acid Analyzer features the model 119CL for analysis of protein hydrolyzates in less than 2 hours. Beckman Instruments. Circle 697.

Noninvasive Carboxyhemoglobin Analyzer describes the Ecolyzer Carboximeter for clinical and research applications. Iadec. Circle 698.

Chromatography Products is a 36-page catalog that also reviews techniques. ICN Pharmaceuticals. Circle 703.

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(Continued from page 602)

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