

9 November 1979 • Vol. 206 • No. 4419

\$1.50

SCIENCE

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



A photograph of a Beckman Model TJ-6 centrifuge. The machine is a boxy, blue-colored unit with a large circular lid on top that is propped open. Inside the lid, a black rotor is visible, holding four sample tubes in a cross pattern. The tubes contain liquids of different colors: yellow, blue, green, and red. The front panel of the centrifuge features several controls: a large white knob on the right for speed, a smaller knob for time, a switch for start/stop, and a power switch. The brand name 'BECKMAN' and model 'Model TJ-6 Centrifuge' are printed on the front. The background is a light, textured surface.

No Wonder the Beckman TJ-6 is the Most Popular Centrifuge Ever Introduced!

Users appreciate how quiet it is. They like the removable bowl that makes cleaning a snap. They like the colorful adapters which bring a new practicality and ease of handling to table-top centrifuges.

Owners are delighted with the TJ-6's excellent reliability. And if there is a problem, they know there

Send for Brochure SB-490 for a full description of this superior table-top centrifuge. Write to:

BECKMAN

Receptor Site Studies



α -Adrenergic

Clonidine hydrochloride, [4-³H]-
Desmethylinipramine hydrochloride,
[2,4,6,8-³H]-
Dihydro- α -ergocryptine, 9,10-[9,10-³H(N)]-
WB-4101 (2,6-Dimethoxyphenoxyethyl)
aminomethyl-1, 4-benzodioxane,
2-[*phenoxy*-3-³H(N)]-
Epinephrine, *levo*-[*methyl*-³H]-
Norepinephrine, *levo*-[7,8-³H(N)]-

β -Adrenergic

Carazolol, DL-[3,6-³H(N)]-
Dihydroalprenolol hydrochloride, *levo*-
[*propyl*-2,3-³H]-
Epinephrine, *levo*-[*N-methyl*-³H]-
Hydroxybenzylisoproterenol, *p*-[7-³H]-
Iodoxybenzylpindolol, [¹²⁵I]-
Isoproterenol, DL-[7-³H(N)]-
Norepinephrine, *levo*-[7,8-³H(N)]-
Propranolol, L-[4-³H]-

Aspartate

Aspartic acid, D-[2,3-³H]-
Aspartic acid, L-[2,3-³H]-
Methyl-D-aspartic acid, *N*-[*methyl*-³H]-

Benzodiazepine

Diazepam, [*methyl*-³H]-
Flunitrazepam, [*methyl*-³H]-

Cholinergic

Muscarinic

Acetylcholine chloride, [*N-methyl*-³H]-
Choline chloride, [*methyl*-³H]-
Pilocarpine, [³H(G)]-
Quinuclidinyl benzilate,
DL-[*benzyl*-4,4'-³H(N)]-
Scopolamine methyl chloride,
[*N-methyl*-³H]-

Nicotinic

Acetylcholine chloride, [*N-methyl*-³H]-
 α -Bungarotoxin, [¹²⁵I]-
Choline chloride, [*methyl*-³H]-
Tubocurarine chloride, *dextro*-[13'-³H(N)]-

Dopaminergic

ADTN Amino-6,7-dihydroxy-
1,2,3,4-tetrahydronaphthalene,
2-[5,8-³H]-
Amphetamine sulfate, D-[³H(G)]-
Apomorphine, [8,9-³H]-
Chlorpromazine, [³H]-
Dihydroxyphenylethylamine,
3,4-[*ethyl*-1-³H(N)]- or [*ethyl*-2-³H(N)]-
Haloperidol, [³H(G)]-
Propylnorapomorphine, *N*-[*propyl*-³H(N)]-
Spiroperidol, [1-*phenyl*-4-³H]-

GABA

Alanine, β -[3-³H(N)]-
Aminobutyric acid, γ -[2,3-³H(N)]-
Dihydropicrotoxinin, α -[8,10-³H]-
Isoguvacine hydrochloride, [³H]-
Muscimol, [*methylene*-³H(N)]- or [4-³H]-
Nipecotinic acid, [*ring*-³H]-

Glutamate

Glutamic acid, L-[3,4-³H]-

Glycine

Glycine, [2-³H]-

Histamine

H₁

Histamine, [³H(G)]-
Pyrilamine, [*pyridinyl*-5-³H]- (Mepyramine)

H₂

Histamine, [³H(G)]-

Opiate

Dihydromorphine, [7,8-³H(N)]-
Enkephalin (5-L-leucine), [*tyrosyl*-3,5-³H(N)]-
Enkephalin (5-L-methionine),
[*tyrosyl*-3,5-³H(N)]-
Enkephalinamide
(2-D-alanine-5-L-methionine),
[*tyrosyl-ring*-2,6-³H]-
Ethylketocyclazocine, [9-³H]-
Morphine, [6-³H(N)]-

Serotonin

Hydroxytryptamine binoxalate, 5-[1,2-³H(N)]-
Hydroxytryptamine creatinine sulfate,
5-[1,2-³H(N)]-

Steroid

Androgen

Dihydrotestosterone,
[1,2,4,5,6,7,16,17-³H(N)]-
Methyltrienolone, [17 α -*methyl*-³H]- (R1881)*
Testosterone, [1,2,6,7,16,17-³H(N)]-

Estrogen

Estradiol, [2,4,6,7,16,17-³H(N)]-
Iodo-3, 17 β -estradiol, 16 α -[¹²⁵I]-
Moxestrol, [11 β -*methoxy*-³H]- (R2858)*

Glucocorticoid

Dexamethasone, [6,7-³H(N)]-
Prednisolone, [6,7-³H(N)]-
Triamcinolone acetone, [6,7-³H(N)]-

Mineralocorticoid

Aldosterone, D-[1,2,6,7-³H(N)]-

Progesterone

Dihydroprogesterone, [1,2-³H(N)]-
Nor-17 α -ethynyltestosterone, 19-[6,7-³H(N)]-
Progesterone, [1,2,6,7-³H(N)]-
Promegestone, [17 α -*methyl*-³H]- (R5020)*

*Manufactured by NEN under licensed agreement of
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Miscellaneous

Dihydroxyvitamin D₃, 1 α , 25-[26,27-³H]-
Hydroxyvitamin D₃, 25-[26,27-³H]-
Imipramine hydrochloride, [2,4,6,8-³H]-
Melanocyte stimulating hormone inhibiting
factor, [*proline*-2,3,4,5-³H]- (MIF)
Phencyclidine, [*piperidyl*-3,4-³H(N)]-
Reserpine, [*benzoyl*-³H(G)]-

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SCIENCE

LETTERS	Max Born: Another Impression: <i>G. V. R. Born</i> ; Two-Career Job Hunting: <i>C. T. Walbridge</i> ; Nuclear Accident: <i>W. A. Lochstet</i> ; Phenacetin Studies: <i>J. B. Vaught</i> and <i>C. M. King</i>	636
EDITORIAL	New Magazine: Opportunity for the Membership: <i>K. E. Boulding</i>	641
ARTICLES	The 46° Halo and Its Arcs: <i>R. G. Greenler</i> et al.	643
	Endothermy and Activity in Vertebrates: <i>A. F. Bennett</i> and <i>J. A. Ruben</i>	649
	Coal Conversion Technologies: Some Health and Environmental Effects: <i>S. C. Morris</i> et al.	654
NEWS AND COMMENT	Recombinant DNA: Warming Up for Big Payoff	663
	Supreme Court to Say if Life Is Patentable	664
	New Strength in the Diet-Disease Link?	666
	Crick Looks Back on DNA	667
	<i>Briefing</i> : RFF Back on Its Feet; Nevada Closes Low-Level Radioactive Waste Dump; Helms and Colby Clash on Sharing CIA Data; Harvard Medicine Takes a Lesson from Dalai Lama.	668
RESEARCH NEWS	Is a Diamond Really Forever?	670
	What Is Unified in Unified Field Theories.	672
BOOK REVIEWS	The Visible College, <i>reviewed by A. Thackray</i> ; Disturbing the Universe, <i>G. B. Field</i> ; Dynamics of the Solar System, <i>J. D. Mulholland</i> ; Aspects of Diagenesis, <i>D. L. Graf</i> ; Asbestos and Disease, <i>D. H. Wegman</i> ; Books Received.	674
REPORTS	Solar Availability for Winter Space Heating: An Analysis of SOLMET Data, 1953 to 1975: <i>J. G. Asbury</i> , <i>C. Maslowski</i> , <i>R. O. Mueller</i>	679

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SCIENCE is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1515 Massachusetts Avenue, NW, Washington, D.C. 20005. Second-class postage (publication No. 484460) paid at Washington, D.C., and at an additional entry. Now combined with *The Scientific Monthly*. Copyright © 1979 by the American Association for the Advancement of Science. Domestic individual membership and subscription (51 issues): \$34. Domestic institutional subscription (51 issues): \$70. Foreign postage extra: Canada \$12, other (surface mail) \$15, air-surface via Amsterdam \$40. First class, airmail, school-year, and student rates on request. Single copies \$1.50 (\$2 by mail); back issues \$2.50 (\$3 by mail); classroom rates on request. **Change of address:** allow 6 weeks, giving old and new addresses and seven-digit account number. **Postmaster:** Send Form 3579 to *Science*, 1515 Massachusetts Avenue, NW, Washington, D.C. 20005. *Science* is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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Experimental Coarsening of Antiphase Domains in a Silicate Mineral: <i>M. A. Carpenter</i>	681
Carbon-14 Dating of Small Samples by Proportional Counting: <i>G. Harbottle, E. V. Sayre, R. W. Stoenner</i>	683
Chrysotile Asbestos in a California Recreational Area: <i>W. C. Cooper et al.</i>	685
Fossil Counterparts of Giant Penguins from the North Pacific: <i>S. L. Olson and Y. Hasegawa</i>	688
Angular Invariants in Developing Human Mandibles: <i>R. L. Webber and H. Blum</i> . .	689
A New Mineralized Layer in the Hinge of the Oyster: <i>M. R. Carriker and R. E. Palmer</i>	691
<i>Xenopus</i> Liver: Ontogeny of Estrogen Responsiveness: <i>J. K. Skipper and T. H. Hamilton</i>	693
Phase Resetting and Annihilation of Pacemaker Activity in Cardiac Tissue: <i>J. Jalife and C. Antzelevitch</i>	695
Lectin-Induced Mucus Release in the Urn Cell Complex of the Marine Invertebrate <i>Sipunculus nudus</i> (Linnaeus): <i>S. V. Nicosia</i>	698
Calcium Dependence of Toxic Cell Death: A Final Common Pathway: <i>F. A. X. Schanne et al.</i>	700
Rapid Killing of Single Neurons by Irradiation of Intracellularly Injected Dye: <i>J. P. Miller and A. I. Selverston</i>	702
Monocular Light Exclusion for a Period of Days Reduces Directional Sensitivity of the Human Retina: <i>J. M. Enoch, D. G. Birch, E. E. Birch.</i>	705
Microsecond Sensitivity of the Human Visual System to Irregular Flicker: <i>A. L. Diamond</i>	708
Phase Advance of the Circadian Sleep-Wake Cycle as an Antidepressant: <i>T. A. Wehr et al.</i>	710
Functional Organization of Lateral Geniculate Cells Following Removal of Visual Cortex in the Newborn Kitten: <i>E. H. Murphy and R. Kalil</i>	713
Molecular Microanalysis of Pathological Specimens in situ with a Laser-Raman Microprobe: <i>J. L. Abraham and E. S. Etz</i>	716
PRODUCTS AND MATERIALS	
HPLC Column Packer; Densitometer and Spotter for Thin-Layer Chromatography; Scanning Electron Microscope; Ventilator for Small Animals; Gel Electrophoresis System; Immunoreagents; Automated HPLC; Literature . . .	720

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GEOLOGY AND GEOGRAPHY (E)
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COVER

Reconstruction of the largest species in the fossil family Plotopteridae, shown to scale with the outline of the largest living penguin. These giant seabirds inhabited the North Pacific about 30 million years ago. They were flightless and had paddle-like wings similar to penguins, but belong to the unrelated order Pelecaniformes. See page 688. [B. Daltzell, Rockville, Maryland]

The American Association for the Advancement of Science was founded in 1848 and incorporated in 1874. Its objects are to further the work of scientists, to facilitate cooperation among them, to foster scientific freedom and responsibility, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

Laboratory animal bedding: is it an uncontrolled variable that can jeopardize your work?

As research becomes more sophisticated, and the analytical systems that track it get more sensitive, one begins to focus on those elements previously viewed as having little real significance. Be it the air our animals breathe, or the noise that disturbs them, or the photoperiod... we *now* know that these environmental factors can indeed be consequential. But how about animal bedding? Consider, for example, this authoritative comment:

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taminants into animal colonies, breeders and users of laboratory animals should exercise caution in the purchase, transportation, and the handling of these products."

"Guide for the Care and Use of Laboratory Animals." ILAR (NIH, DHEW Pub. no. 78-23).

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(Comment: significantly lower than other beddings tested.)		
<u>Coliform</u>		
Presumptive	neg.	neg.
Confirmed	neg.	neg.
Pseudomonads	neg.	neg.
Yeasts & molds	0	0
<u>Irritant Properties</u>		
24 hr intact skin	0.0	0.0
abraded skin	0.0	0.0
72 hr intact skin	0.0	0.0
abraded skin	0.0	0.0
Conclusion:	non-primary irritant	non-primary irritant
<u>Pesticide Residues</u>		
<u>Chlorinated hydrocarbons</u>		
BHC	<0.01	<0.01
Lindane	<0.01	<0.01
Iteptachlor	<0.01	<0.01
Aldrin	<0.01	<0.01
Heptachlor Epoxide	<0.01	<0.01
DDE	<0.01	<0.01
Dieldrin	<0.01	<0.01

	Ab-Sorb-Dri™ (Hardwood)	Pine-Dri™ (Pine)
Endrin	<0.01	<0.01
DDD	<0.01	<0.01
DDT	<0.01	<0.01
<u>Organophosphates</u>		
Diazinon	<0.01	<0.01
Methyl Parathion	<0.01	<0.01
Malathion	<0.01	<0.01
Ethyl Parathion	<0.01	<0.01
Ethion	<0.01	<0.01
<u>Polychlorinated</u>		
<u>Biphenyls (PCB)</u>	0.03	0.02
<u>Detergent Residues</u>		
	0.0	0.0
<u>Heavy Metals</u>		
	<10.0 PPM	<10.0 PPM

So if a consistent, "defined" bedding sounds like worthwhile insurance, let us tell you more.

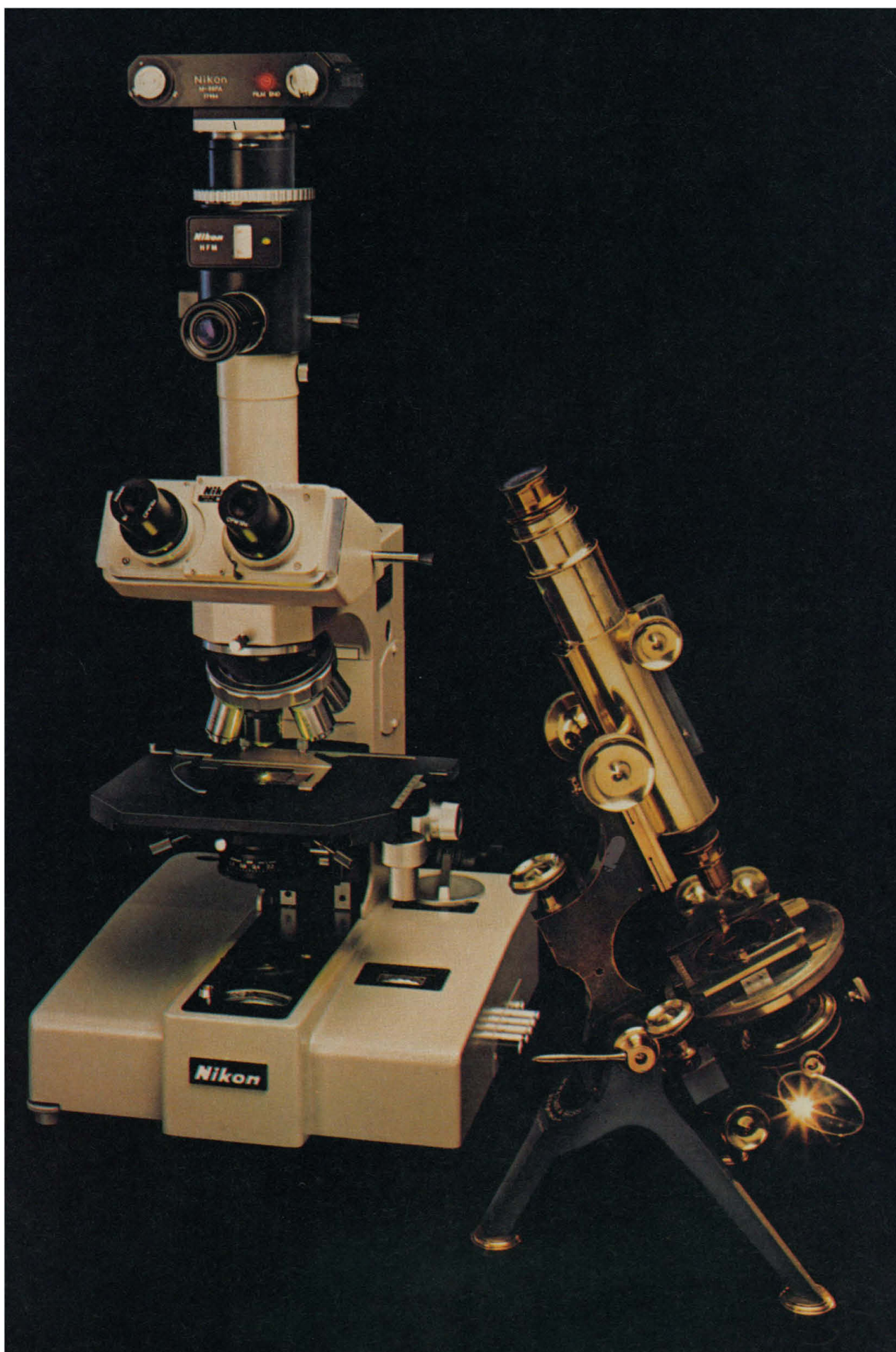
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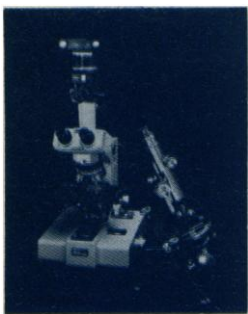
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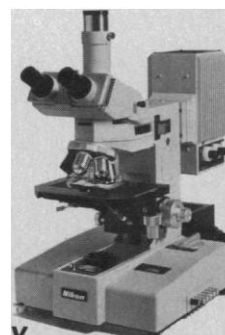
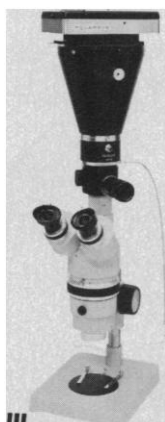
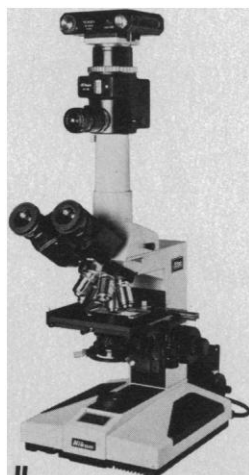
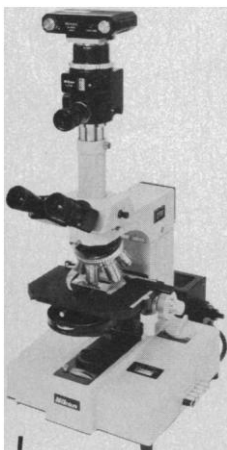
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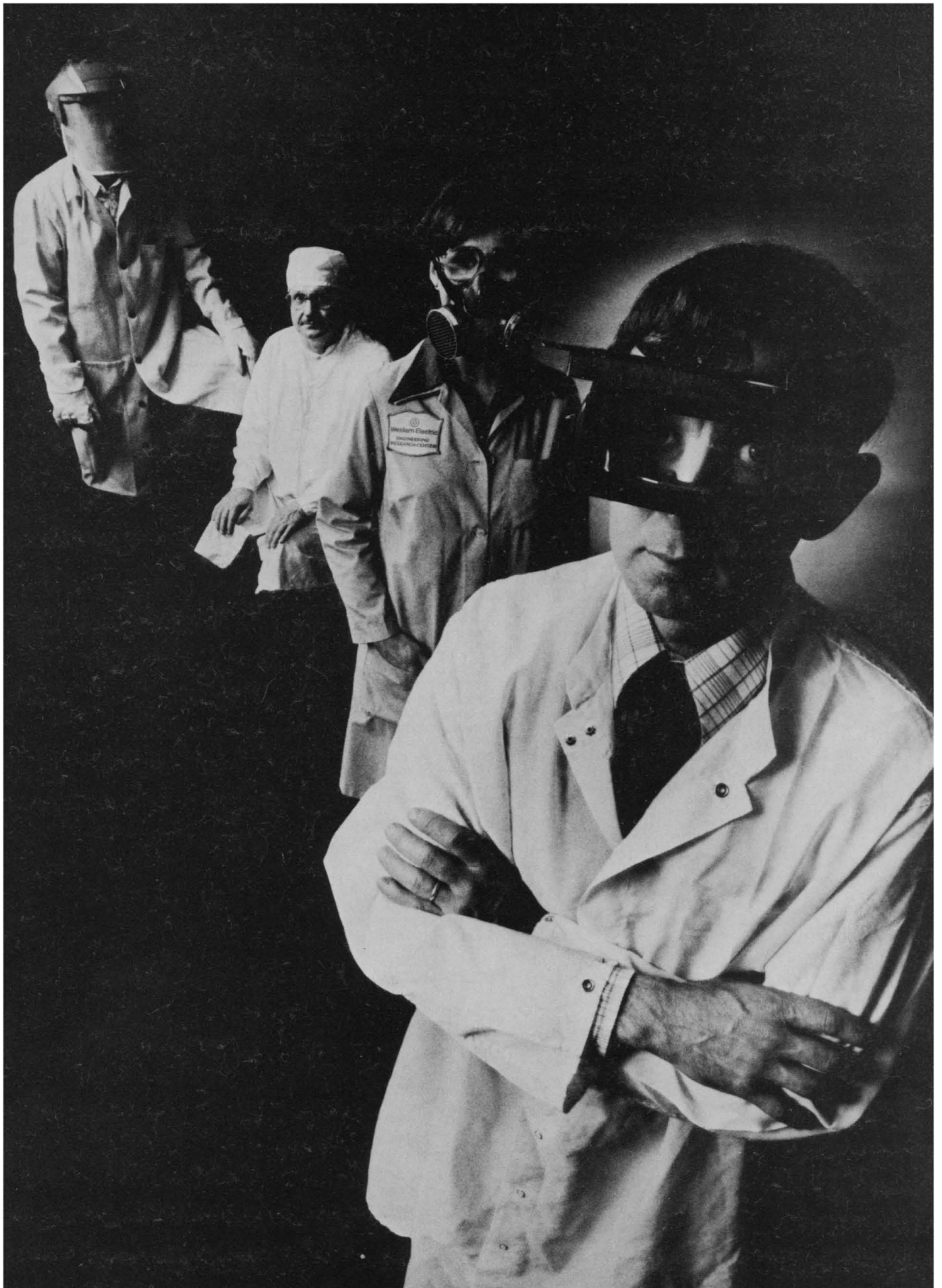
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They are a vital part of Western Electric's commitment to helping the Bell System keep the cost of communications service down, while keeping the quality up.

The Factory's Laboratory

The people at our Engineering Research Center work full time on manufacturing research. Over 50% of them are PhD's.

At home in the factory as well as the lab, they turn theoretical

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Much of the work of the Engineering Research Center is designed to keep Western Electric ahead of technology, by anticipating what new processes will be needed for tomorrow's products.

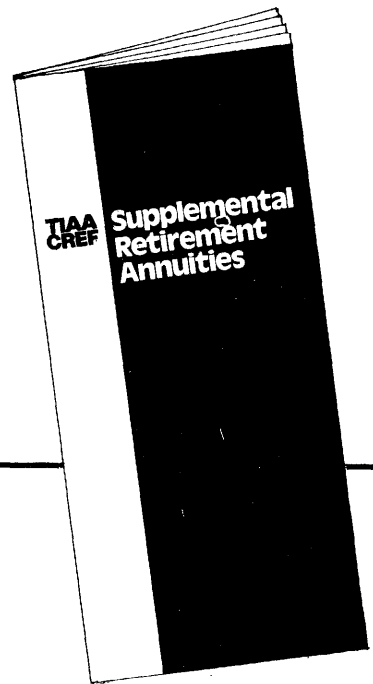
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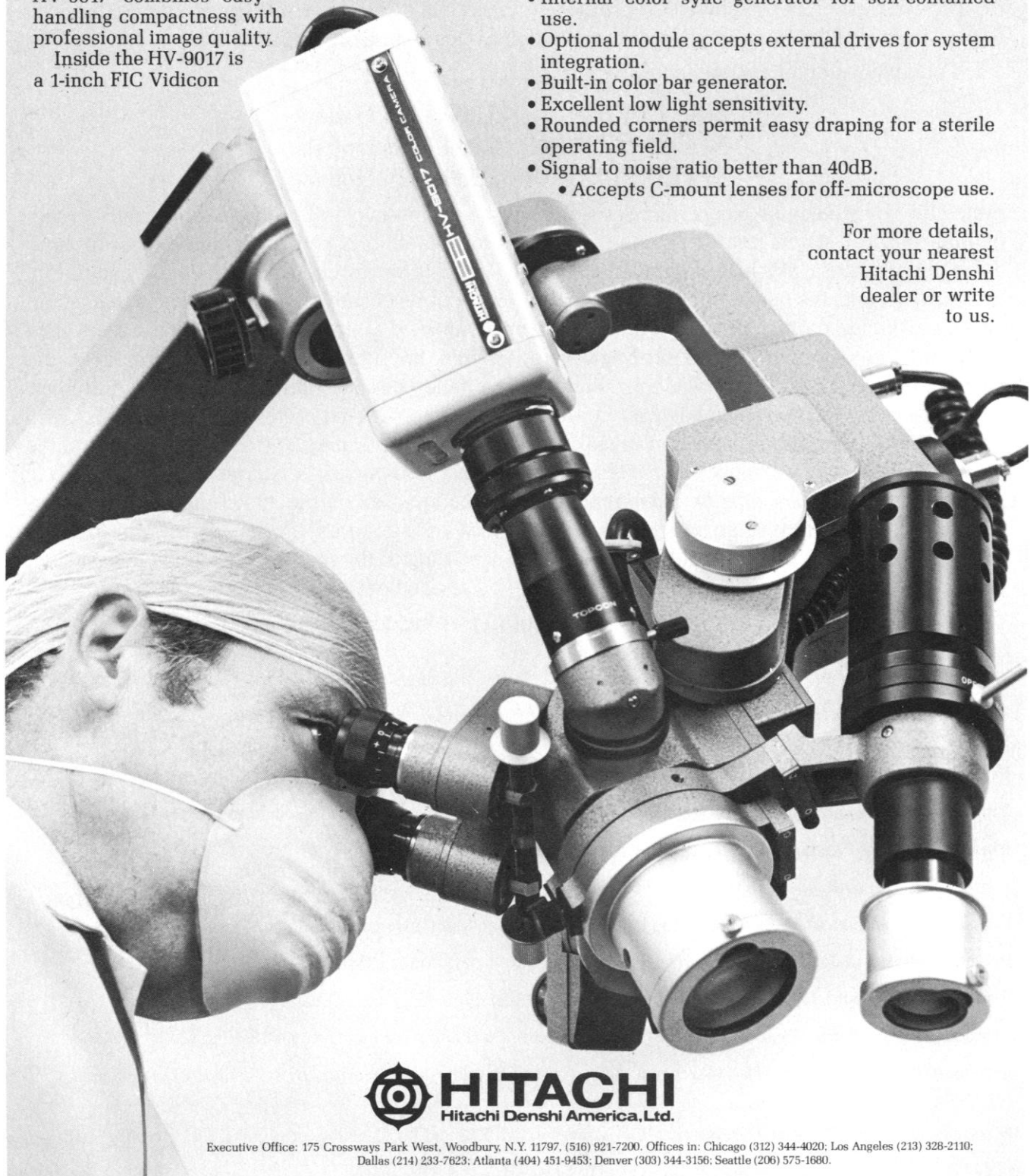
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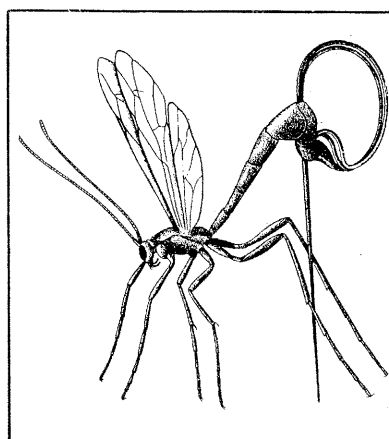
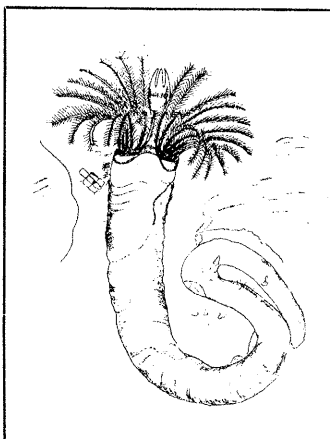
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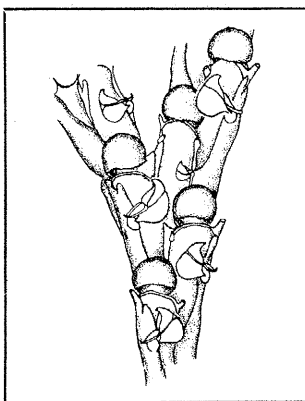
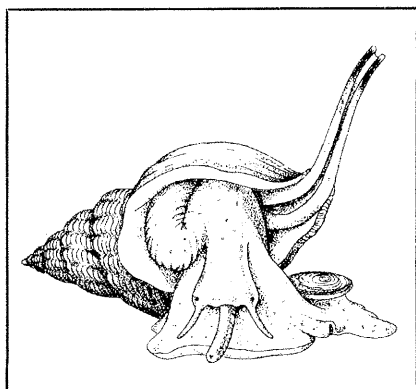
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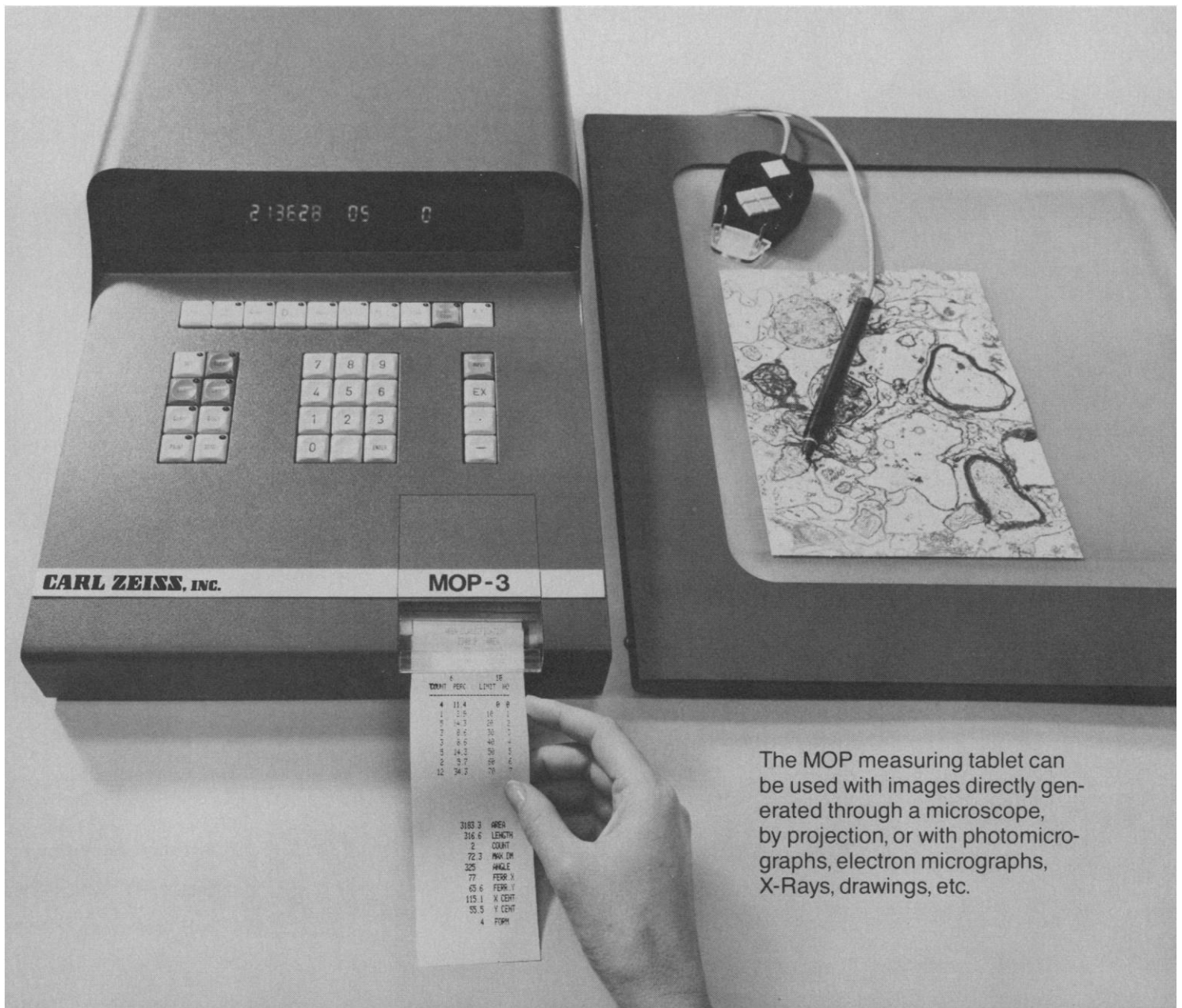
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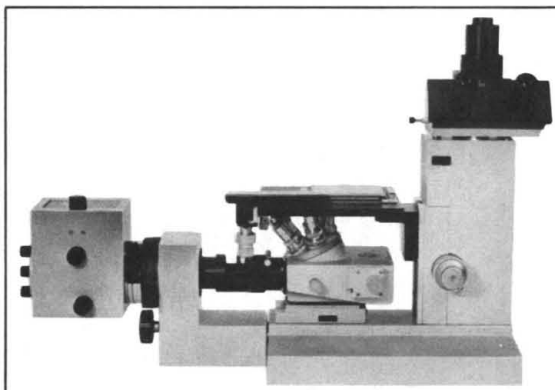
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LETTERS

Max Born: Another Impression

The review by J. L. Heilbron of the published "Recollections" (1) of my late father Max Born (17 Aug., p. 740) gives an inadequate impression of his character. As it was his character as much as his scientific imagination that provided the basis of the world center for theoretical physics in Göttingen, that impression should not be left uncorrected.

What Heilbron describes as my father's continuous self-deprecation was the marvelous, unconscious humility which is a hallmark of the greatest men. He was quite well aware of his mental powers but clearly felt strongly that they gave him no rights over others. He was anything but humorless; he loved fun and laughed a great deal. To describe him as merely decent is a masterpiece of understatement; he was one of the innately best people anyone could hope to meet.

His sparks of genius were by no means limited to physics. Heilbron leaves out vast areas of achievement which were on the highest level: his music, his philosophy, his political activities, his work for others, and his many close friendships with outstanding contemporaries in science and the arts.

Those who read the book will realize that Max Born was rightly appreciated for many wonderful qualities, quite apart from those he displayed as a scientist.

G. V. R. BORN

Department of Pharmacology,
King's College, University of London,
Strand, London WC2R 2LS, England

References

1. M. Born, *My Life: Recollections of a Nobel Laureate* (Scribner, New York, 1979).

Two-Career Job Hunting

Since we recognize that many women in academia are penalized by being part of two-career households (21 Sept., p. 1125), the question becomes, How do we deal with the problem?

The right kind of data retrieval system may help. It is possible for employment services to index available jobs by geographical proximity for retrieval by pairs. For example, a professor of physics may be sharing a household with an associate professor of political science, and both are looking for jobs; a computer program can be set up to seek out suitable jobs within reasonable physical proximity one of another. Defining the

terms "suitable" and "proximity" would be done with the help of the couple involved.

To get enough job openings into such a system (or to interconnect the existing systems) is likely to be a substantial effort, but the expense conceivably could be borne by affirmative action programs in public and private institutions.

This kind of help for couples in academia could be extended to other kinds of two-career households. One could simply list the locations of the jobs not by institution and institutional proximity but by zip code.

CHARLES T. WALBRIDGE
*Environmental Research Laboratory-
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Nuclear Accident

Peter A. Morris (Letters, 13 July, p. 148) discusses the "eminently safe nuclear operations in the United States" accomplished during the development and application of high-powered nuclear reactors. No mention is made of the SL-1 accident which occurred at the National Reactor Test Station in Idaho on 3 January 1961 (1). At the time, the reactor in question was managed by Combustion Engineering, Inc. This accident is notable in that the entire crew of three persons who were on duty died within hours of the event as a result of their injuries. It is important to note that the development of high-powered reactors in this country was not totally free of safety errors, as Morris' letter might suggest.

WILLIAM A. LOCHSTET
*Department of Physics, University of
Pennsylvania, University Park 16802*

References

1. W. B. Cottrell, *Nucl. Saf.* 3, 64 (1962).

Phenacetin Studies

Macklin *et al.* (Letters, 13 July, p. 144) write that phenacetin is not as harmful as the many reports concerning its carcinogenicity would indicate. We are concerned that their letter and the previous one by Cuatrecasas (5 Jan., p. 6) may introduce a number of misconceptions into the literature if left unanswered.

The case reports concerning the carcinogenicity of analgesics containing phenacetin cannot be considered insignificant. Attention was drawn to the carcinogenic properties of phenacetin by

the association of the abuse of this drug with the development of a relatively uncommon type of tumor, that of the renal pelvis. More than 140 cases of kidney and bladder tumors have now been reported in the literature (1) among abusers of phenacetin-containing analgesics, that is, those taking more than 1 gram per day—the maximum recommended dose of some products that are currently available in this country without a prescription. Phenacetin-containing analgesics are usually of two types: those containing antipyrine (phenazone), phenacetin, and caffeine and those containing aspirin, phenacetin, and caffeine. The mutagenicity of aminopyrine is irrelevant, since the patients in the Swedish studies were known to have taken primarily antipyrine-containing analgesics. Phenacetin and caffeine are the ingredients common to all the analgesic mixtures implicated in the above reports of tumor induction in Sweden, Australia, and the United States. There is no reason to believe caffeine is the causative agent.

In studies (2) that show evidence of phenacetin carcinogenicity, doses of 500 milligrams per kilogram or higher were administered. Human abusers of the analgesic mixtures often take 20 milligrams per kilogram per day for 20 years or more before kidney failure or tumor formation occurs. Given the fiscal and statistical limitations of experimental carcinogenesis studies, it appears reasonable to administer 500 milligrams per kilogram per day for 2 years to the relatively small numbers of animals usually employed in such tests.

Unlike the studies cited above, the Burroughs Wellcome study of phenacetin effects on C57BL/6 mice has not been published or made available to the scientific community. A single negative experiment with one inbred strain is not definitive, since the animals may have a genetically restricted capacity to carry out the metabolic events crucial to the carcinogenic process. The metabolic events responsible for the carcinogenic activity of a compound are not necessarily those that contribute to its acute toxicity.

The Data Evaluation/Risk Assessment Subgroup of the National Cancer Institute's (NCI's) Clearinghouse on Environmental Carcinogens considered the NCI bioassay (3) of an aspirin, phenacetin, and caffeine (APC) mixture to be inconclusive rather than negative. It was unanimously recommended by this committee that APC be considered for retesting in the bioassay program. Urinary tract and endocrine tumors were found that were considered important, al-

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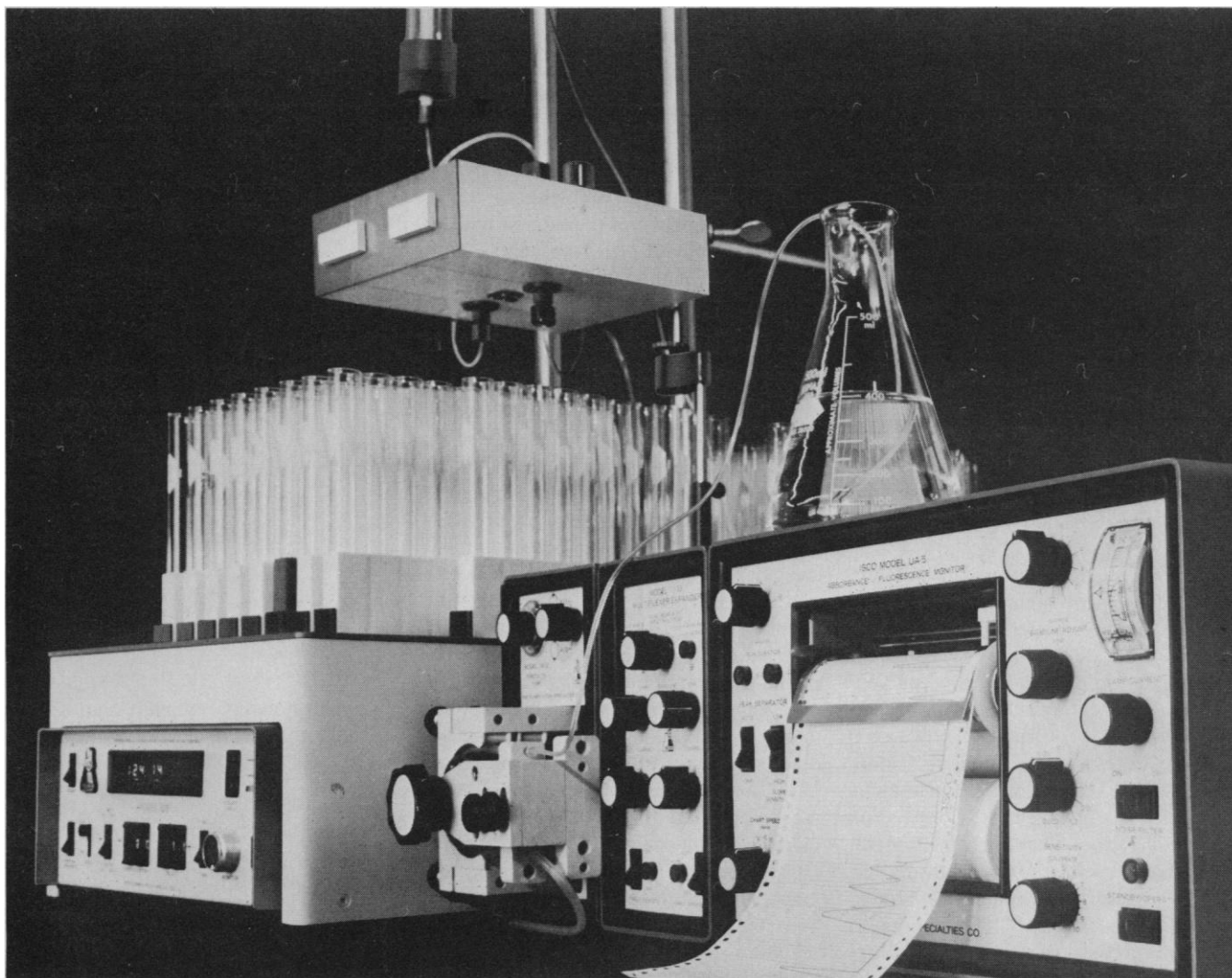
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though their incidence was statistically insignificant. The use of Fischer rats in these studies may have resulted in an underestimate of the carcinogenic effects of phenacetin, since Fischer rats are known to be relatively resistant to the induction of extrahepatic tumors by aromatic amines (4). In contrast, aromatic amines may induce high incidences of mammary and ear duct tumors in Sprague-Dawley rats (5). Such tumors were found by Johansson and Angervall in their 1976 phenacetin study (2).

The claims made by Macklin *et al.* concerning the use of pelleted diets are speculative. Much of their argument is based on the premise that the melting point of phenacetin is exceeded in the pelleting process. The melting point (mp) of phenacetin given in their letter is incorrect; phenacetin melts at 134° to 135°C (6) (273° to 275°F), not at 134° to 135°F. Even if the melting point were reached, they present no evidence that significant degradation would occur or that *N*-oxidation would occur spontaneously.

The argument that the Charles River Formula diet used by Isaka *et al.* (2) contains *N*-nitroso derivatives which might be responsible for tumorigenicity overlooks the fact that control animals fed the same formula developed only a small number of tumors. Whether there may be synergistic effects between nitrosamines in commercial feed and test compounds is a matter of some concern (News and Comment, 13 Oct. 1978, p. 192; Letters, 8 Dec. 1978, p. 1034; Letters, 5 Jan., p. 7) that has not been resolved. While there is no evidence that this phenomenon occurred in this instance, phenacetin can act synergistically with at least one carcinogenic nitrosamine in the induction of urinary bladder tumors (7). To minimize this carcinogenic effect of phenacetin would ignore the cumulative effects of the exposure of humans to a multiplicity of carcinogens over their lifetime.

Although the structure of phenacetin allows for a number of metabolic reactions that are not possible with 2-acetylaminofluorene, *N*-hydroxylation of phenacetin does occur, and there is reason to believe that this is a vitally important step in the metabolic activation of phenacetin, as it is for 2-acetylaminofluorene (8). *N*-Hydroxyphenacetin is both a carcinogen (9) and, when enzymatically activated, a mutagen (10). The possibility that phenacetin may be nitrosated has received little attention (11).

In contrast to the claim by Macklin *et al.*, both phenacetin and *N*-hydroxyphenacetin have been demonstrated to

be mutagenic to *Salmonella typhimurium* TA 100, with the supernatant (9000g) from hamster liver homogenate as the activating system (12).

Although phenacetin is not as potent a carcinogen as some others to which we are exposed daily, we believe that its use in nonprescription analgesics should be banned. The ever-increasing body of data from animal and human studies concerning the metabolism, mutagenicity, and carcinogenicity of phenacetin, is impossible to ignore. Swedish and Australian authorities have long since taken action to minimize exposure to phenacetin. The documented cumulative effects of carcinogens argues strongly for the reduction of exposure to phenacetin. Alternative analgesics are available.

J. B. VAUGHT

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Erratum: In the report by M. E. Trulson and B. L. Jacobs, "Long-term amphetamine treatment decreases brain serotonin metabolism: Implications for theories of schizophrenia" (21 Sept., p. 1295), the column headings "Norepinephrine" and "Tryptophan" in Table 1 (p. 1296) are transposed. The data under "Norepinephrine" should have been listed under "Tryptophan," and vice versa.

Erratum: A News and Comment briefing, "Carcinogens in Scotch" (24 Aug., p. 769), incorrectly reported that carrot and beet juice contain relatively high levels of nitrosamines. So far as is known, they do not. They do contain nitrates and nitrites, the precursors of nitrosamines.

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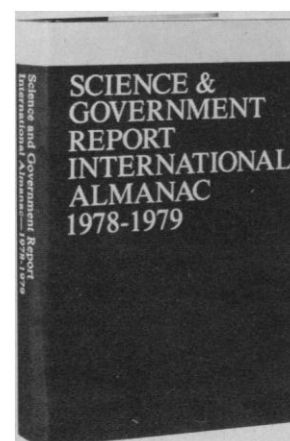
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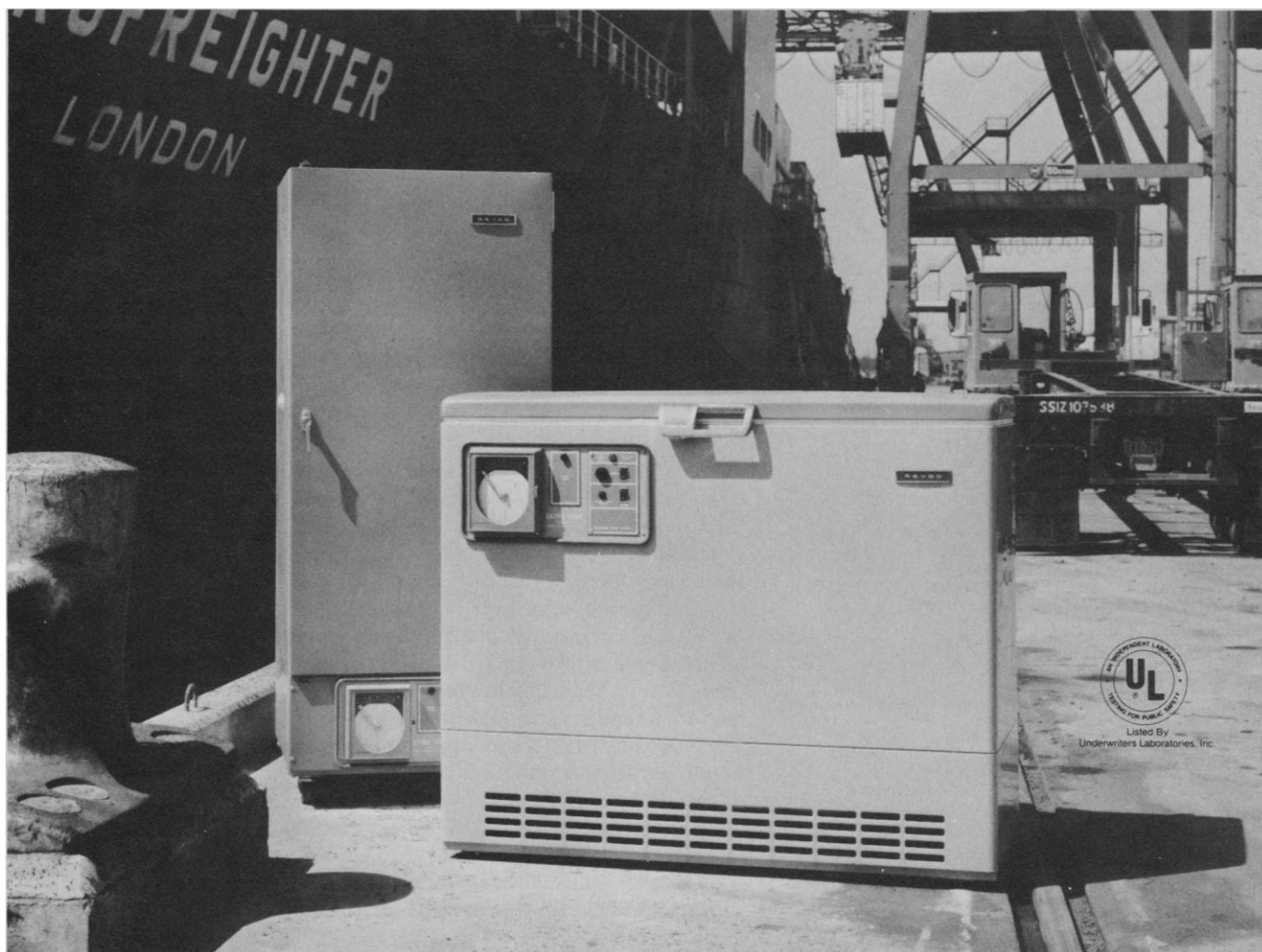
The Board of directors of the AAAS, meeting in Washington on 20 and 21 April, unanimously made the important decision that the Association should publish a new magazine, to be called *Science 80*, *Science 81*, *Science 82*, and so on. It is in no sense a substitute for the present *Science* magazine, which will continue as before to serve the membership and to present AAAS to the world. The object of the new magazine is to bring the findings, the methods, the spirit, and the ethic of science to a larger audience of perhaps a half-million to a million people. It will be colorful, and written to a considerable extent by professional science writers. It will be less technical than *Scientific American*, more rigorous than *Smithsonian*, and more theoretical than *Popular Mechanics*. A careful study of the market has suggested that there is a niche for such a magazine.

If that were all, however, why should AAAS do it? Why not leave it to one of the commercial publishers who have also shown interest in this niche? There are two major answers to this question. One is that AAAS from its very beginning has regarded the education of the general public in matters scientific to be one of its major functions. The second is that the new magazine provides an opportunity for the membership of the Association to participate in this educational enterprise in a variety of ways. Much of the strength of AAAS is that it symbolizes the existence of a scientific community, interested in the pursuit of evidence about a real world and inspired by curiosity and a love of veracity. Scientists are also human beings and share the faults of the species, but we should never forget that they are a subspecies of human beings with a peculiar culture of their own. If the new magazine does not reflect this culture, it will fail in its purpose of presenting science, which is a product of the scientific community, to the public at large.

Since the new magazine must fill felt public needs, the editors will set up mechanisms for identifying urgent public wishes for authentic information. However, at the same time, members should regard this new magazine not merely as a consumer good, but as an opportunity to express their own concerns and interests in the presentation of science to a larger public. I suggest that each of the AAAS sections appoint one or two correspondents to read the magazine carefully and send brief reports to the Association with criticisms and suggestions for further articles, to be transmitted to the editor and the editorial board. Members should write letters to the editor and should submit suggestions for articles themselves.

In the start-up phases of the new magazine, virtually all the content will be prepared by professional science news writers. Too few practicing scientists are good science writers at a popular level. After the style and level of the magazine are fully established, members of the Association should try to practice the art of science writing for the general public. There is no guarantee, of course, that unsolicited articles would be accepted, but this is true also of *Science* or any other reputable journal. Nevertheless, such articles would be welcomed with a clear understanding about the audience to which they are addressed.

Once the magazine is established, one would like to link it with an extensive research project in how the images of science in the minds of the general public change in regard to content and credibility. The scientific community may be facing a deepening crisis of credibility. We have pretended to know more than we do. Science is a treasure chest, but every treasure chest is also a Pandora's box and we cannot escape responsibility as a scientific community for the evil consequences as well as the good arising from increased knowledge. A new magazine should give us an opportunity to work out some of these problems and to break down some of the walls, both of language and of pride, that separate scientists from our fellow human beings.—KENNETH E. BOULDING



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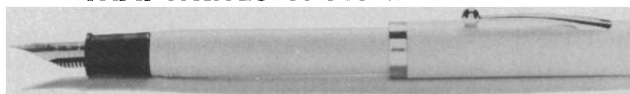
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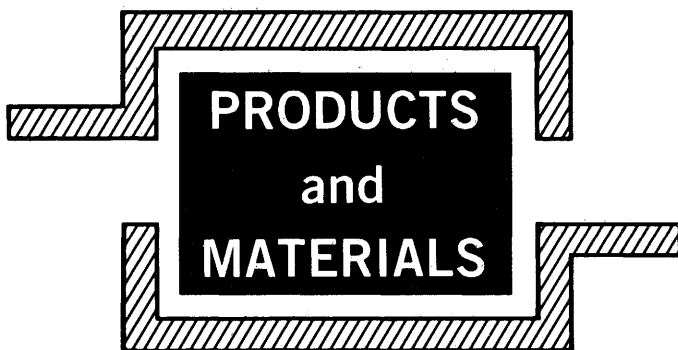
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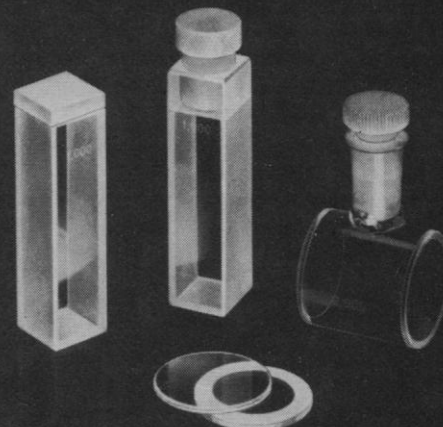
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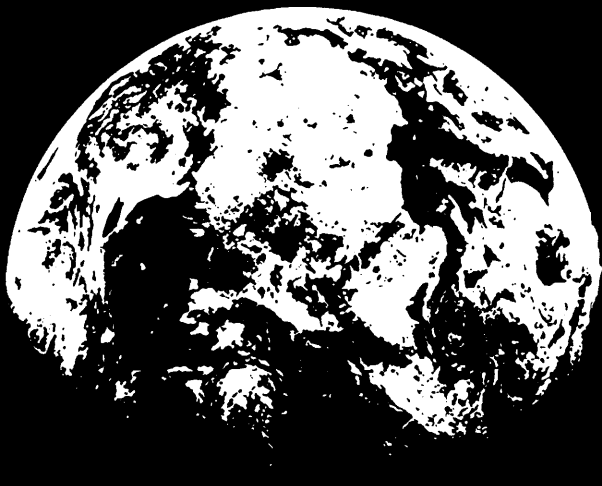
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