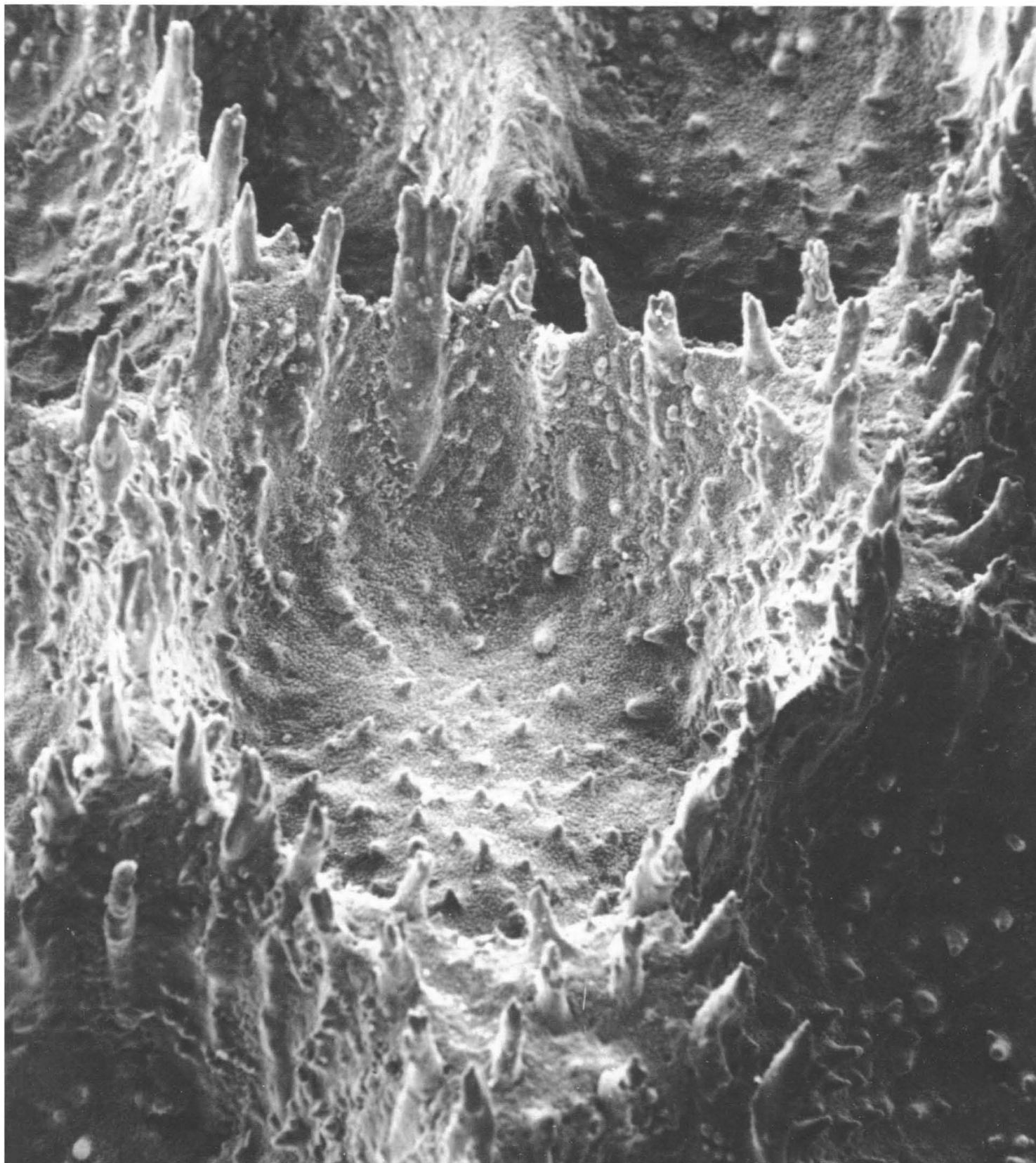


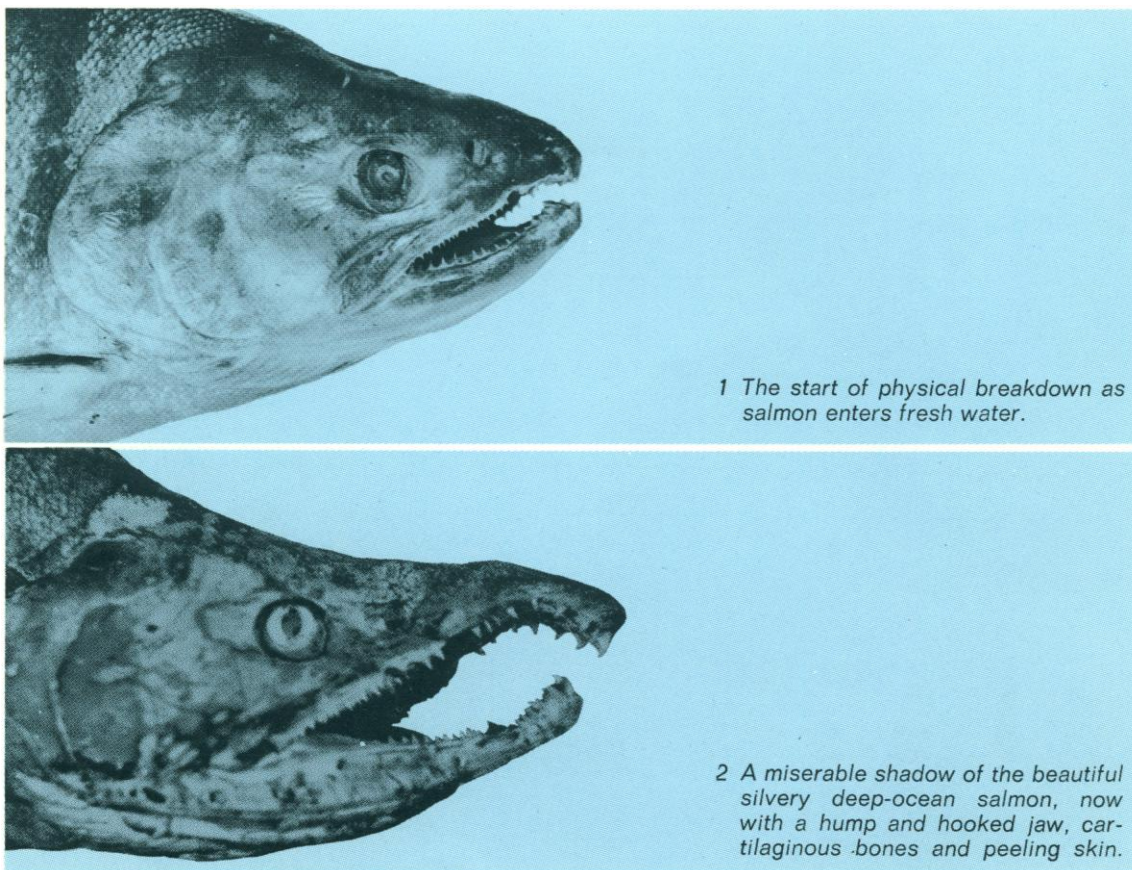
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4 September 1970

Vol. 169, No. 3949

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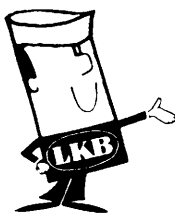




1 The start of physical breakdown as salmon enters fresh water.

2 A miserable shadow of the beautiful silvery deep-ocean salmon, now with a hump and hooked jaw, cartilaginous bones and peeling skin.

Kind permission of Oceans Magazine



The Ultratome at Sea

LKB have taken part in another "first", this time at sea, aboard the "Alpha Helix".

The "Alpha Helix" investigations concerned the rapid aging of salmon, illustrated in the photos above, which occurs when the salmon enter fresh waters on their spawning run.

During the autumn of 1968 the first electron-micrograph made aboard a ship, was produced on this physiological research vessel belonging to the University of California, San Diego's Scripps Institution of Oceanography. A standard LKB Ultratome cut the sections.

Excellent results were achieved, even when the ship was under way, in the open sea. There could hardly be a more convincing demonstration of the versatility of the LKB Ultratome.


Some of the answers found by the research team could have a direct application to man, and ultimately help to reduce the physical and mental deterioration associated with human aging.



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COVER

Exoskeleton of the colonial stony coral *Pocillopora damicornis* showing several cup-shaped corallites, each of which contained, in life, a single coral polyp (about $\times 120$). See page 978. [Sherwood W. Wise, Jr., Swiss Federal Institute of Technology, Zurich, Switzerland]

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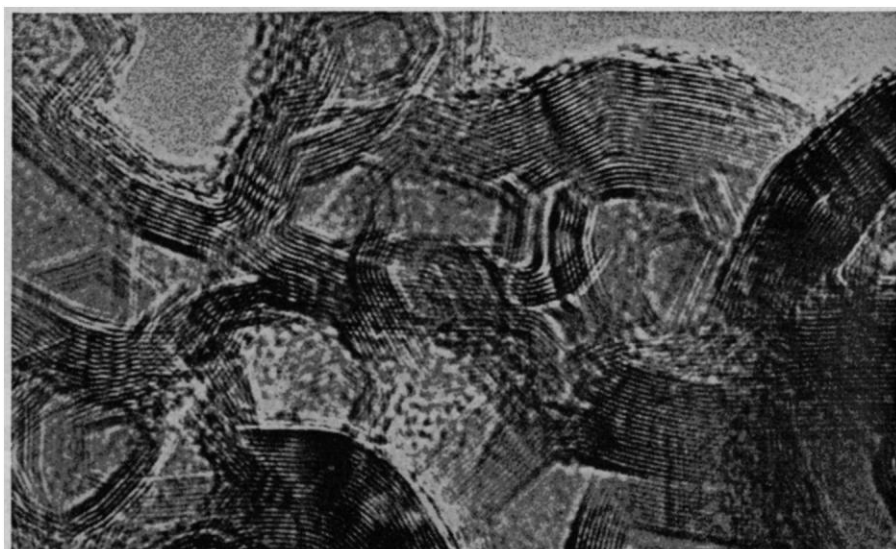
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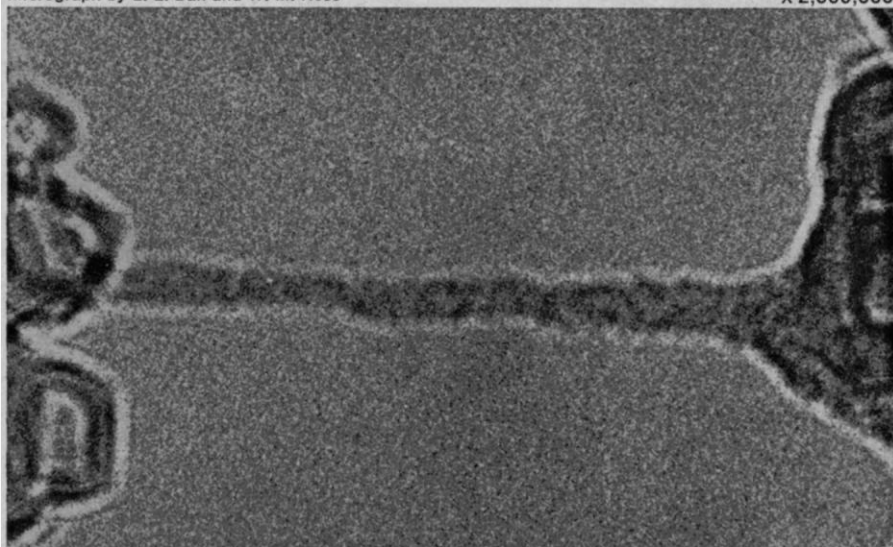
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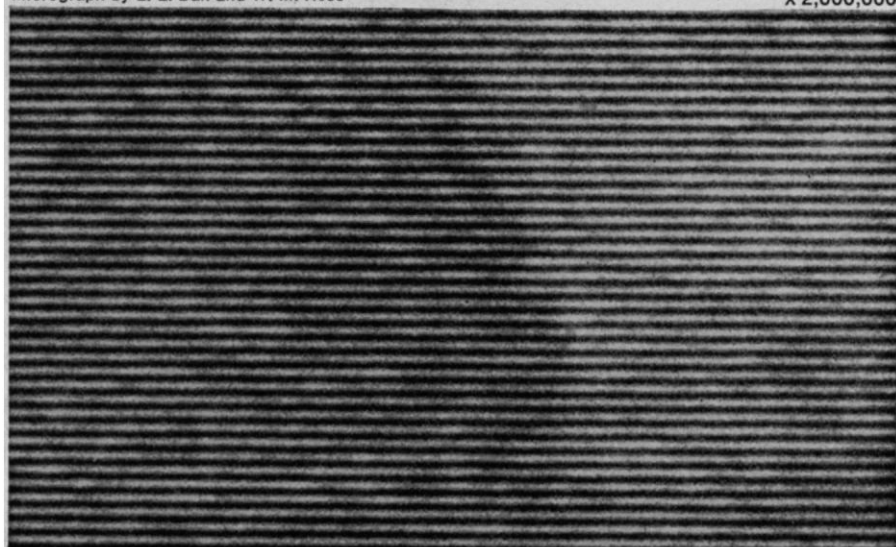
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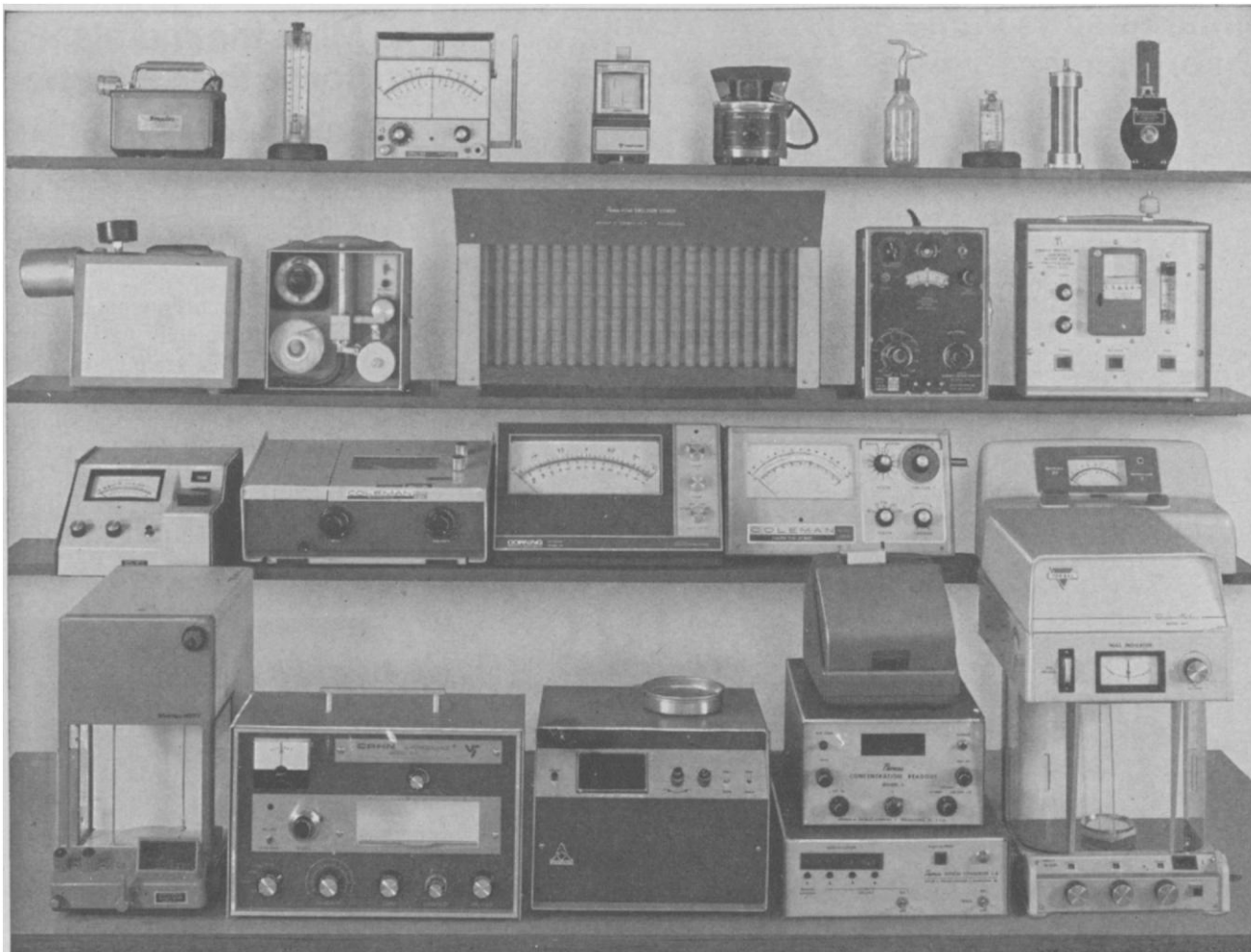
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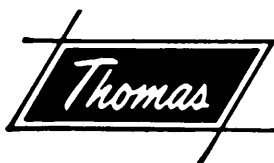
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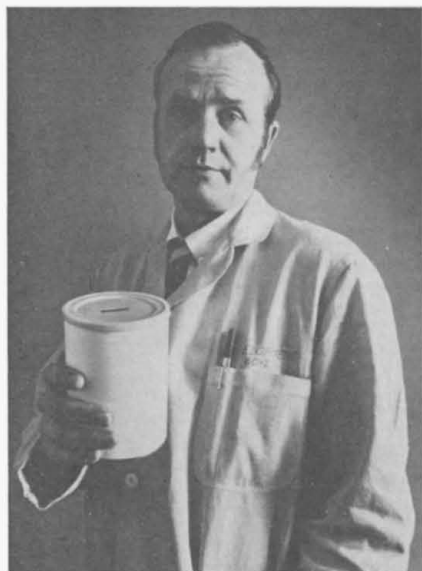
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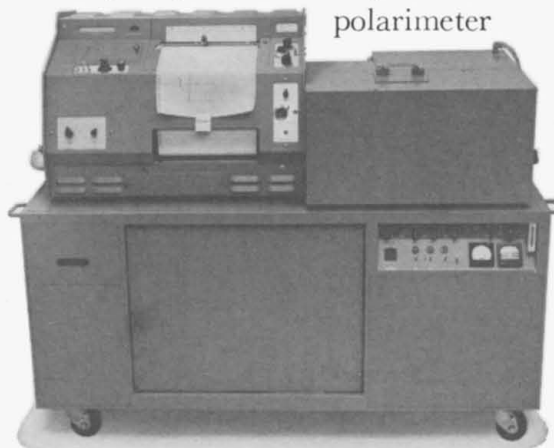
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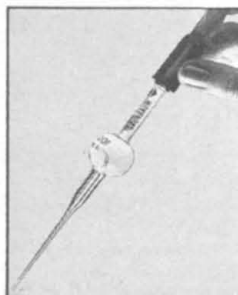
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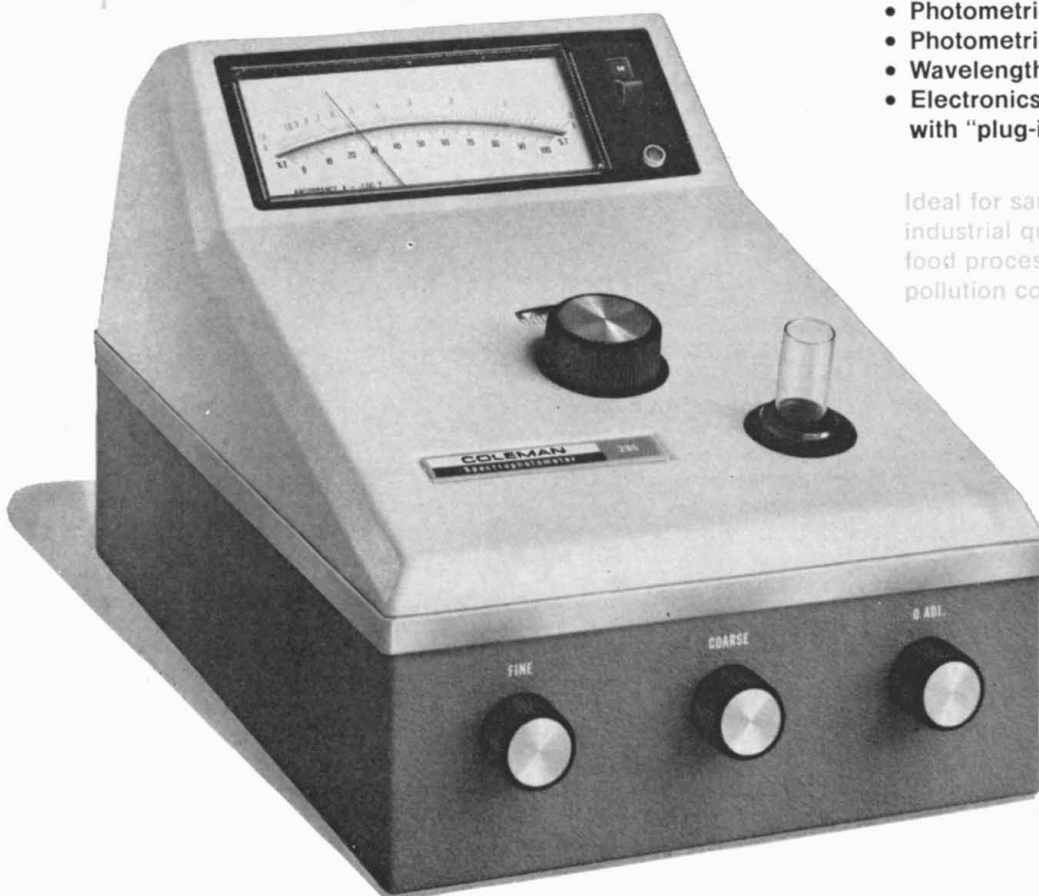
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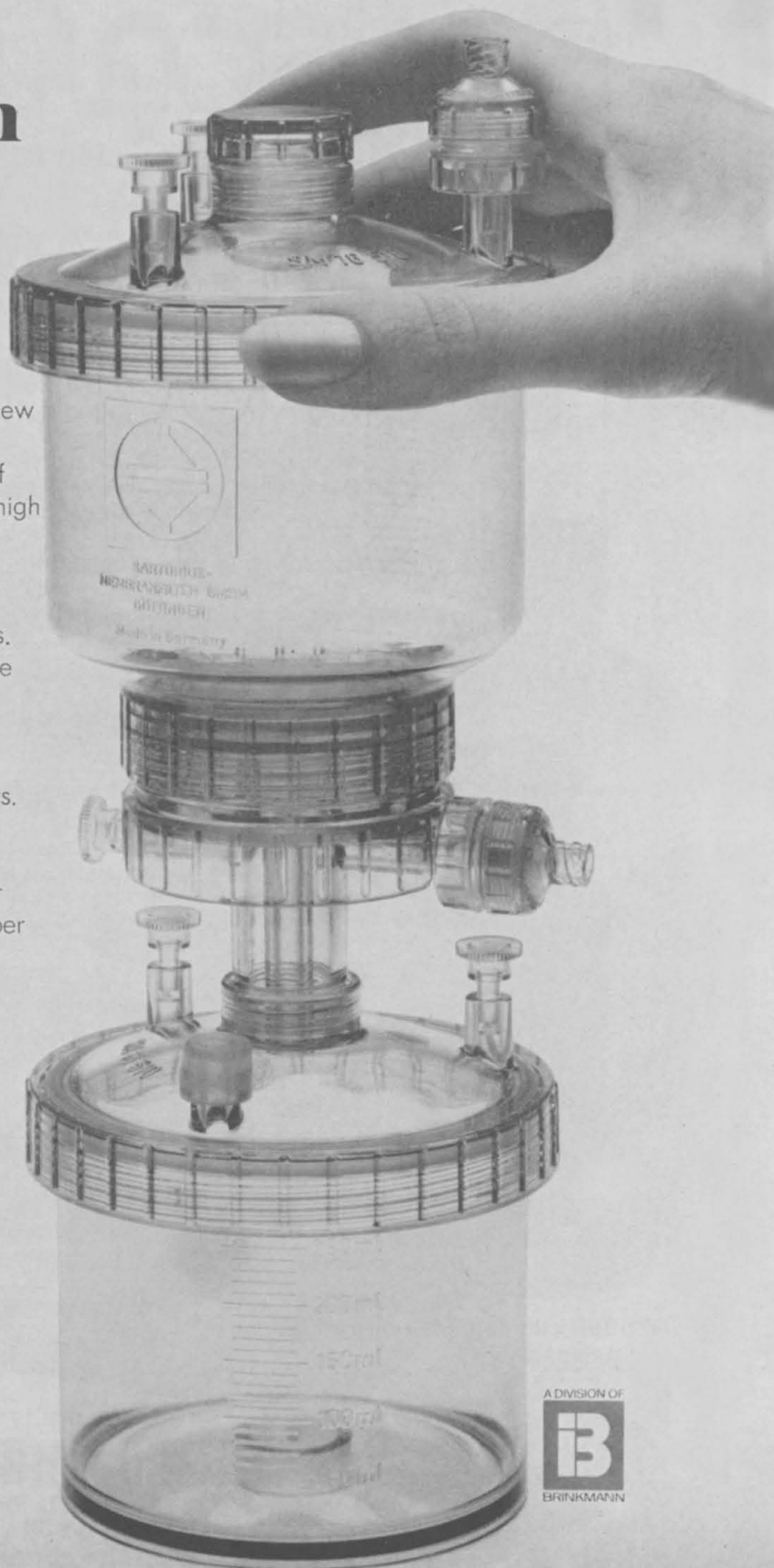
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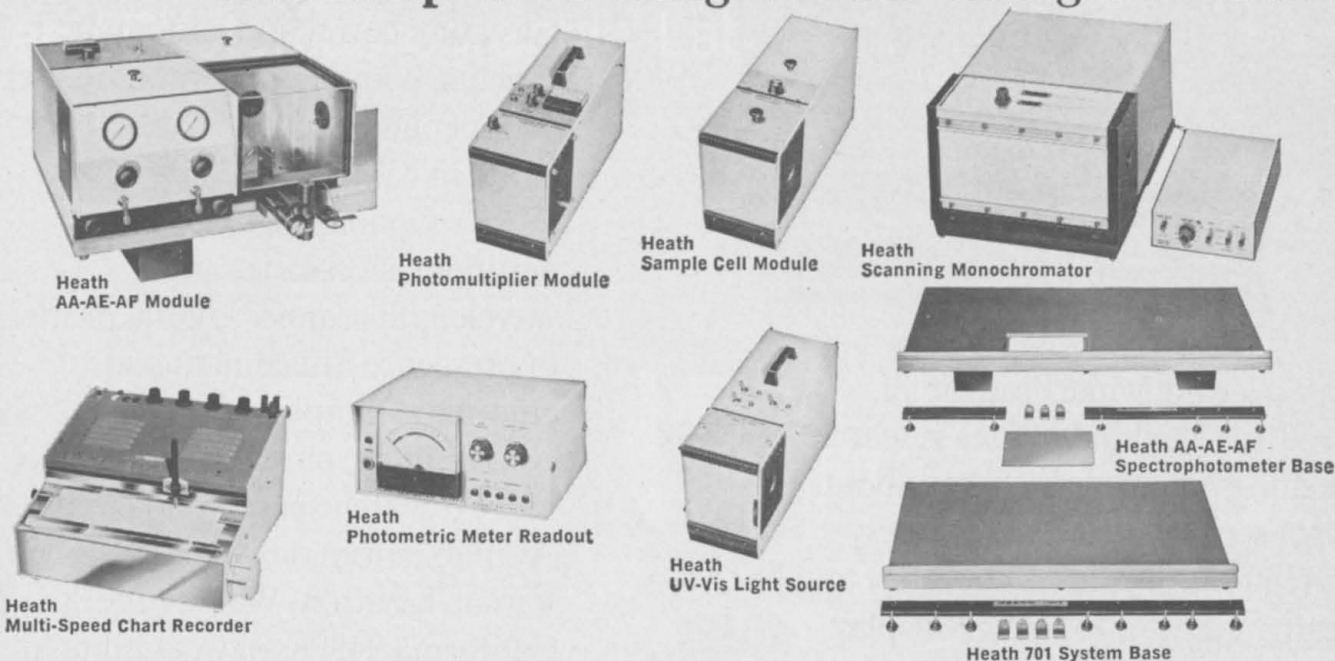
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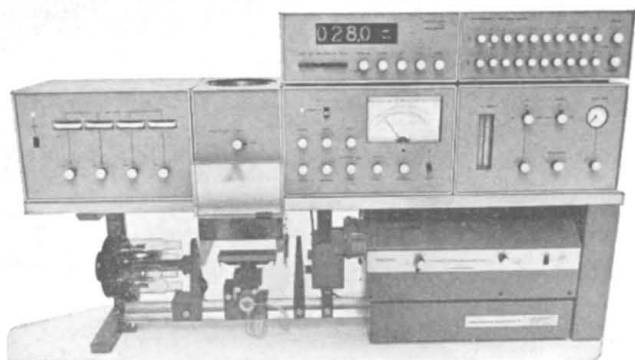
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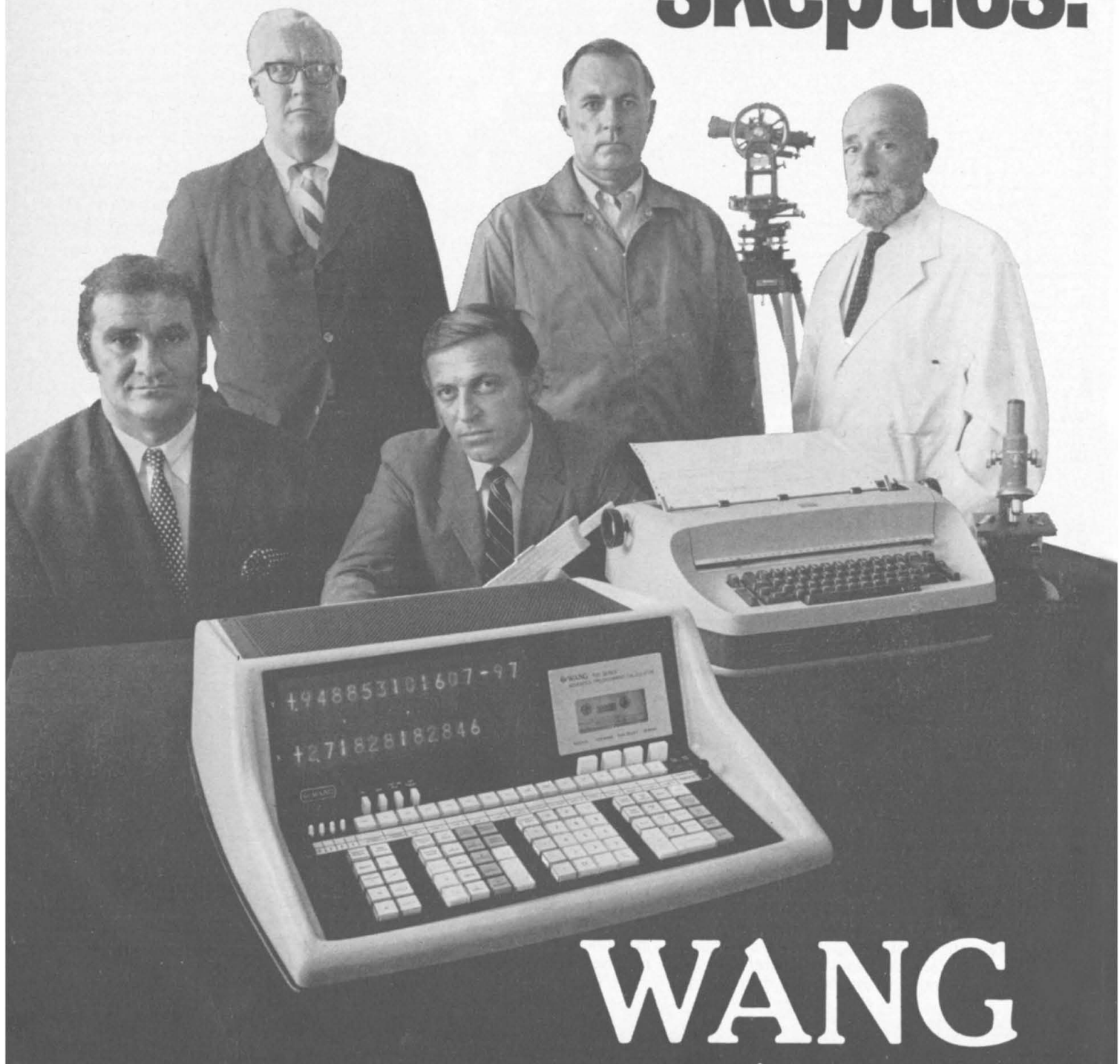
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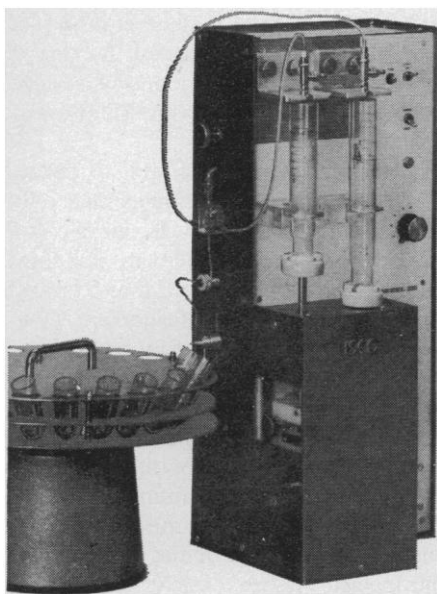
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bilities to their minimum"), it is highly rational to turn to an oracle to terminate the decision process ("after that, do as you please" to "bring the decision to uniqueness"). In fact, failure to appeal to chance when the possibilities of analysis have been exhausted is clearly irrational, since continued circular thinking about unsolvable problems only leads to dithering and frustration.

First, the effectiveness of transcendental meditation is demonstrated (27 Mar., p. 1751). Now, the use of the I Ching seems to be rational. Is science slowly finding its way back to the wisdom of the ancients?

WILLIAM OPHULS
*Department of Political Science,
Yale University,
New Haven, Connecticut 06520*

Hooke's Premises

The issue of political stands by scientific societies is naturally important, but I believe Robert Hooke's letter to *Science* (17 July) decrying any political action ought to have been rejected on grounds of prior publication, for, in a document regarding the founding of the Royal Society, he states its ends (1):

To improve the knowledge of natural things, and all useful Arts, Manufactures, Mechanick practices, Engynnes, and Inventions by Experiments (not meddling with Divinity, Metaphysics, Moralls, Politics, Grammar, Rhetorick or Logic).

Anyone dead 267 years is probably out of touch with the present situation anyway.

E. J. DEVINNEY, JR.
*Department of Astronomy,
University of South Florida,
Tampa 33620*

Reference

1. A. Pannekoek, *A History of Astronomy* (Interscience, New York, 1961), p. 250.

Vietnam: Judged by Reason

Carroll E. Izard in his editorial "The Cambodian crisis: Reason and emotion" (5 June, p. 1157) is pretty shaky in his reasoning. I object to the implication that one must abandon reason to oppose the Asian war. Nixon's Cambodian decision may indeed have been in accordance with reason, but it was based on shaky assumptions. Aristotle said 2200 years ago: "The chain of reason must begin somewhere, other-

wise it would be endless. We begin with assumptions that are agreed on, but not proven. These are called axioms, or first principles." Thus, if it can be proven, it is not a first principle. Principles cannot be derived logically, but they can be examined in the light of their logical consequences, and thus reason can assist emotion in arriving at them.

A simple assumption would permit us to withdraw from the Asian war and stay out of others like it, while still adhering to reason. This would be the recognition that a corrupt and self-serving military dictatorship such as that in South Vietnam is not preferable, either to its own people or to ourselves, to its Communist alternative. There are capitalist democracies worth defending, besides our own, in which the creation of wealth is the ruling economic motivation, such as those of Western Europe and Japan. Other so-called capitalist regimes still play the old zero-sum game of exploitation of the poor, and they do not deserve our support. Fortunately, those worth defending are strong enough not to need much bolstering by us of their regimes.

We might well consider the assumption that we could do ourselves the most good by helping those regimes which are helping their own people, without regard for whether or not they are Communist.

FREDERICK J. HOOVEN
*Thayer School of Engineering,
Dartmouth College,
Hanover, New Hampshire 03755*

Hoooven has presented some cogent arguments for ending the Indochina war, but he has misunderstood a central point in my editorial. He missed the distinction between rejecting reason for emotion and allowing the emotions to play their proper role in human affairs. Hoooven's rationale for ending the war is indeed admirable. I am concerned with a more general point—the need to be careful not to dehumanize our logic and reason or to deceive ourselves into thinking that being completely rational and nonemotional will end war and other human problems. Our modern age of rationalism and science has been as war-torn and bloody as the Dark Ages. Our age has produced a superabundance of rational-logical information including the "technologic" for a superkill, an Armageddon. It has failed to produce the means to predict and prevent wars. Paradoxically, it is illogical and irrational to

attribute the failure to lack of logic and reason.

The psychobiological unity of human personality makes it very improbable that there is such a thing as reason totally uninfluenced by emotion. When the rationalistic view of man leads to undue suppression of the emotions or inadequate utilization of their inherently adaptive functions, they tend to become mysterious and adventitious forces that misguide our thoughts and overdetermine our actions.

CARROLL E. IZARD

Department of Psychology, Vanderbilt University, Nashville, Tennessee 37203

Crude Altimeter

While flying at altitude in an unpressurized airplane a few years ago, I was surprised to discover that by using my mouth I could improvise a crude altimeter. Because I have yet to run across anyone who has noticed this, it is perhaps worth describing.

I first became aware of this phenomenon while flying at 7.5 km waiting to make measurements above a growing cumulus cloud. As we flew back and forth, for something to do I idly produced a suction in my mouth by retracting my tongue with my lips closed. At lower altitudes, it is impossible to pull the tongue back very far because of the strong force exerted by the atmosphere. At altitude, to my surprise, I found that I could pull it back rather easily, thus creating a cavity filled with airless vacuum, or, more accurately, with water vapor, which at body temperature has a partial pressure of 47 torr. On subsequent flights I could begin to observe this effect at altitudes of 6 km or even a little lower.

In laboratory experiments it is possible to reduce pressure in one's mouth by about 400 torr. This indicates that at altitudes above 5.4 km, where the total pressure is this value or less, it is possible to overcome the force of the atmosphere and produce a vacuum, thus forming a rudimentary aneroid barometer. It would be interesting to know if some organisms, for example, leeches, may be capable of producing similar vacuums against even higher pressures, perhaps utilizing this phenomenon to some advantage.

BERNARD VONNEGUT

Department of Atmospheric Science, State University of New York at Albany, Albany 12203



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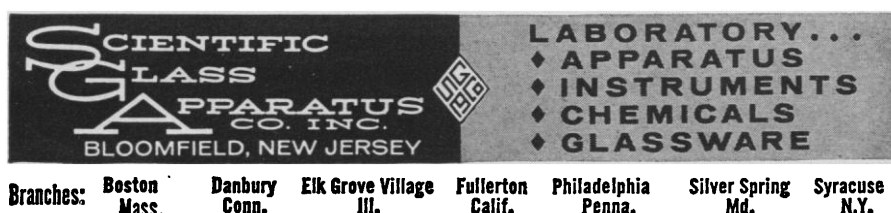
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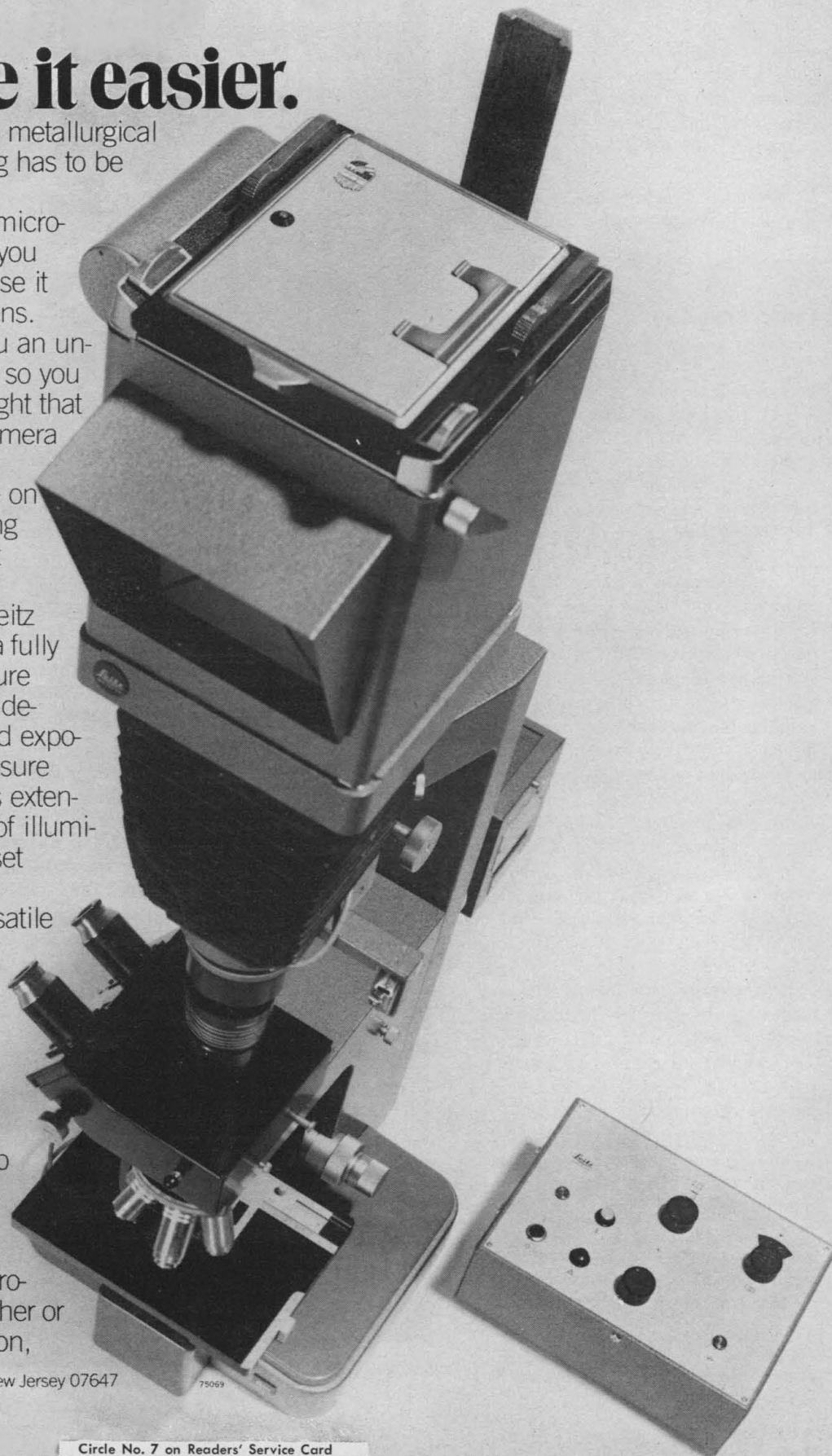
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National Family-Planning Programs: Where We Stand

Most qualified observers believe that the rate of population growth in the developing countries is too rapid and that something must be done. The something has usually taken the form of national family-planning programs, which now exist in about 25 countries, from India and Pakistan to Tunisia and Mauritius. Where does this effort now stand?

The present state of national family-planning programs is *impressive*, in that a great deal of development has occurred in a very few years; *frustrating*, in that many things that need to be done and are in principle do-able are simply not being done because of weak will or bureaucratic limitations or personality conflicts or inadequate funding or some other unworthy reason; *uneven*, in that a few countries have been able to achieve important targets, whereas others have been unable to do so or have not really tried; *inadequate*, in that "the population problem" has not been "solved" by such programs in most of the countries at issue, and the efforts in several key countries are not adequate to the essential requirements of the task; and, finally, *doubtful or unknown*, in that we simply do not know how well or badly things are going in several places for lack of a proper system of evaluation.

As for the prospects, they are simultaneously *promising*, in that the momentum of effort is still running, though not so strongly as in the mid and late 1960's; and *dubious*, in that the problem itself is terribly resistant, the positive results tend to be concentrated in the more favorably situated countries, the field may be hitting a plateau of effort and results, and the measures beyond family planning—like education or tax incentives or shifts in the status of women—are unlikely to be helpful in the short run.

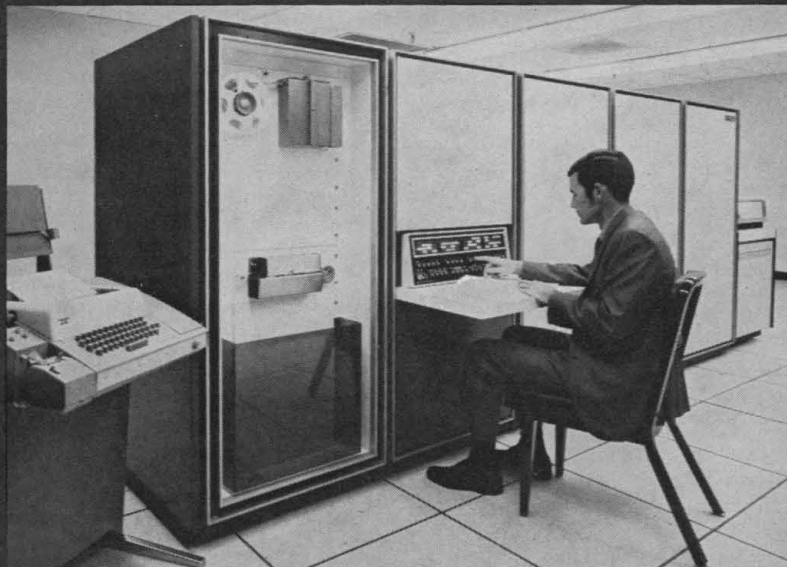
With so much having gone on in so many places in so few years, workers in this field are now trying to digest the experience to date, to assimilate it, to balance the achievements and the shortfalls, to appraise alternatives even as they seek to advance beyond what is now being done. Nor do they lack for critics on all sides—politicians who suspect the enterprise of impure motives, international civil servants who think the "population problem" has been oversold, financial supporters who want more results, program administrators who want more freedom, demographers who feel the effort has become captured by the medical men, medical men who feel the effort has been captured by the demographers, social scientists who say that family planning will never work in the absence of deep structural changes, doctors who say it will never work in the absence of a complete medical infrastructure.

Where does that leave us? It leaves us, as usual on complex social problems of great magnitude, in a mixed position. Science, both social and biological, has made and will make notable contributions but probably cannot "solve" the problem by itself. Beyond knowledge, the world needs at least the will and the time. At present, the will seems to be greater where it is less needed, namely, among those in the developed world seeking to help. Similarly, the time frame allowed to do the job is perceived as much shorter among those not directly involved. Thus the mixed picture: much done, much more remaining. The honeymoon is over, and the partners in the developing and the developed countries need to settle down to the hard and long task of attacking a consequential problem with no easy solutions.—BERNARD BERELSON, *Population Council*, 245 Park Avenue, New York 10017

This editorial is adapted from a paper presented at a Conference on Technological Change and Population Growth held at the California Institute of Technology.

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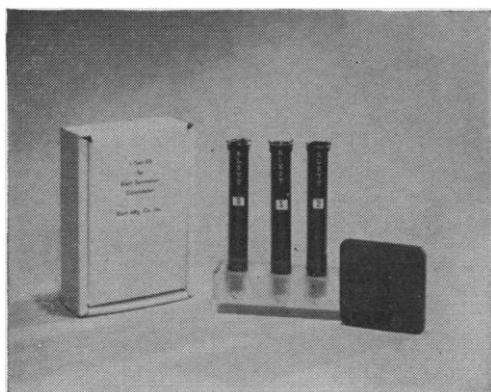
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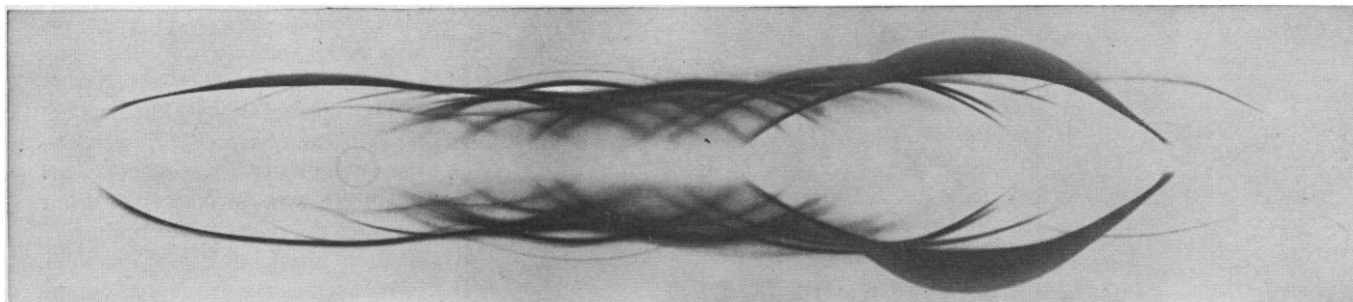
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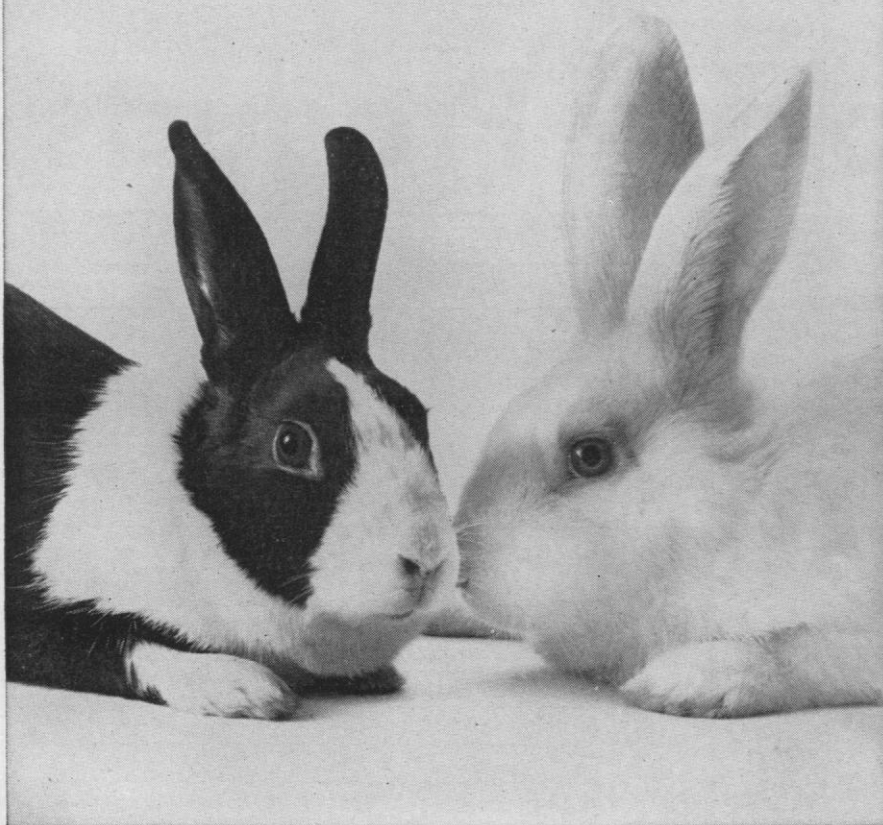
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play. According to this ingenious scheme, specific antigens of a tumor cell, for example the T1 antigen, can be regarded either (i) as a genotypic error, whereby a deviant product is inserted into a grid representing a repeating feature of cell surface topography or (ii) as a phenotypic defect due to the erroneous assembly of normal gene products resulting in aberrant juxtaposition of units comprising the normal grid pattern of the somatic cell's surface. Such structural anomalies were postulated to account for defective recognition in various developmental steps in ontogeny as well as in a surveillance mechanism of a nonimmunologic character.

Triggering events which might lead to the operation of an immunologically mediated surveillance mechanism were identified by Möller, and the various means by which the triggering threshold might be lowered so as to increase the efficiency of the response were considered. Evidence was presented that both "thymus-derived" (T) and "bone-marrow-derived" (B) lymphocytes, which participate in a cooperative immune response, have specific receptors for antigenic determinants. The T lymphocyte function, including memory, could be inhibited by treatment with antiserum directed against theta (θ), for example, a surface determinant specific for T lymphocytes. The interaction of T and B lymphocytes was considered a helper mechanism rather than a mandatory one which makes for increased efficiency of immune reactions by lowering the triggering threshold through multivalent binding. In these cell-cell interactions, the T cell might be replaced by another B cell, a macrophage, or an immunoglobulin-antigen complex, particularly if the antibody were the pentameric, decavalent immunoglobulin M (IgM).


The current status of specificity as opposed to nonspecificity of action of the cytoactive effector agents of cellular immunity was considered by Bloom in terms of the relevance of these agents to effector mechanisms of surveillance. Lymphocytes from immune donors cultured in the presence of specific antigens elaborate factors such as migration inhibitory factor (MIF), lymphotoxin, (LT), and skin reactive factor, as well as others that are mitogenic or that inhibit DNA synthesis or cloning of cultured fibroblasts; these factors have a variety of effects on different cells. The destruction of innocent-bystander fibroblasts exposed to lymphoid cells from tuberculin-immunized isologous donors that

are triggered by purified protein derivative (PPD) was cited as an example of the nonspecific action of cytoactive substances. What is not clear, however, is how a cellular immunity mediated by nonspecific substances could evoke destructive effects that are seemingly highly specific for "target" neoplastic or normal tissue cells both in vitro and in vivo—for example, the survival of a small minority of histocompatible tumor cells in the midst of a much larger number of histoincompatible tumor cells undergoing violent rejection.

Various options that might be involved in mechanisms of surveillance were discussed by Mitchison, including (i) killing by a nonspecific mediator released by a specific reaction between immune lymphocyte and haptenic determinant; (ii) killing by a specific mechanism at the target cell surface permitting entry of nonspecific mediators; (iii) killing due to direct entry of specific mediators; (iv) adding on to a tumor target cell a "prosthetic" grouping to which an immunity already exists and thereby assisting in the induction of immunity to a specific tumor antigen by an adjuvant effect or some other mechanism that promotes antigen handling.

Examples of situations where tumors apparently escape the consequences of a surveillance mechanism, despite an immune response directed against them, were considered by Hellström. Human tumor cells grown in culture can be destroyed by lymphocytes obtained from the tumor host but not in the presence of the patients' own serum, an indication that cell-mediated immunity had been elicited against the tumor but is inoperative because of serum factors. In addition to cell-mediated immunity, tumors can also elicit the production of antibodies that block the destructive effects of activated lymphocytes. Other situations where tumor cells seem to escape the destructive activities of killer lymphocytes include (i) too few tumor cells to evoke immunity, (ii) masking of tumor cells by mucopeptide surface components making them inaccessible to immune recognition or attack, (iii) various serum factors which cause a depression of cell mediated immunity, and (iv) a state of tolerance to tumor-specific antigens.

A unifying hypothesis accounting for the generation of immunologic diversity, nonreactivity to self antigens, and the functional importance of histocompatibility antigens was developed for the first time by Jerne. It relies on the premise that the germ line contains struc-



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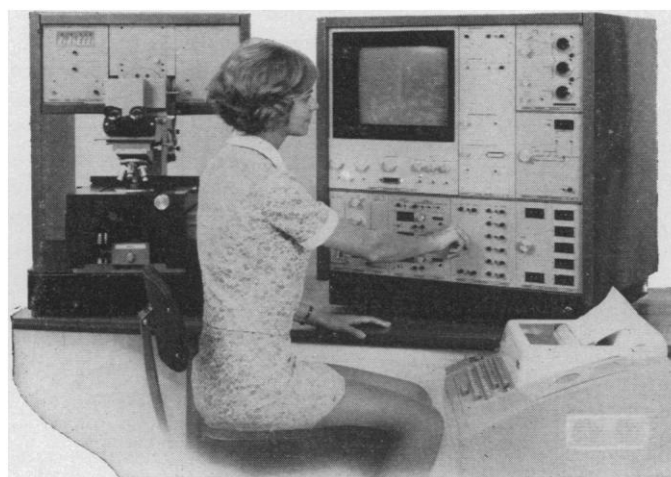
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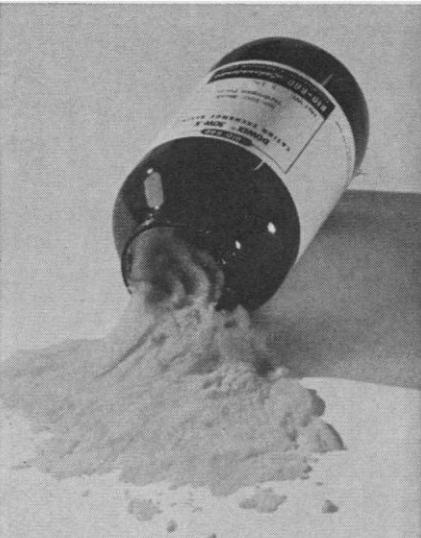
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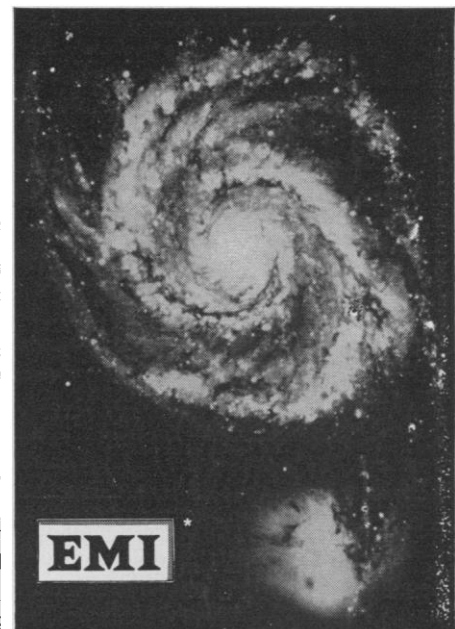
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tural genes which code for antibody molecules specifically directed against the histocompatibility (H) antigens of the species; that mutations occur involving the variable portion cistrons (v), resulting in antibody molecules which code for specificities other than toward H antigens; and that the selective survival of mutant cells is favored by the suppression of non-mutant self-recognizing clones. Jerne postulated that suppression of stem line lymphocytes containing nonmutant gene products takes the form of tolerance to self antigens induced in ontogeny. Since no one individual possesses all the H antigens of his species, the v genes of his germ line must code for antibodies to all of the host's species antigens to insure reactivity against those he does possess. Jerne's model therefore proposes that the portion of germ line cells with v genes determining antibodies against self H antigens are suppressed, and thereby favoring the survival of mutants of this germ line. On the other hand, cells expressing the other set of v genes, coding for H antigens of the species that the individual lacks, are not suppressed and are therefore available in large numbers for reactivity against H antigens of other members of the species. These could be considered as the cellular basis of a surveillance mechanism against neoplasia.

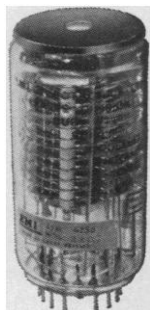
This theory was considered by most of the conferees to be a quantal leap forward in current immunological concepts and to provide a novel and particularly acceptable explanation for two basic immunologic phenomena heretofore inexplicable, namely, the large number of lymphocytes reactive to H antigens in graft-versus-host reactions in vivo and in mixed lymphocyte interactions in vitro, and the special relationship between H antigens and the responder-nonresponder status of animals immunized with antigens having a restricted degree of heterogeneity. In Jerne's model, individuals have different ranges of antibody patterns because they possess different H antigens and because diversity evolves from mutation. Accordingly, each individual (or inbred strain) expresses only a fraction of the antibody diversity range available to the entire species; this could account for the genetic nonresponsiveness of certain inbred strains to certain antigens and for responsiveness, under autosomal dominant genetic control, to others.

A number of basic predictions emerged in the lively discussion of



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Jerne's hypothesis. For example, antibody to H antigen should be monoclonal; the frequency of plasmacytomas producing myeloma proteins with specificity directed against H antigens should be high; and progeny of matings between parental responders and non-responders of different allotype, or allophenic mice derived from these parental strain animals, should be responders and make specific antibody of the nonresponder allotype. Information presented at the conference supports the first two of these predictions. Ramseier and Lindenmann's experiments demonstrated that serum obtained from A/B F₁ animals that had been inoculated with immunologically competent parental strain A lymphocytes contains factors which specifically block stimulation of A strain lymphocytes by B strain antigens. The explanation offered for this intriguing finding was that A/B animals were making antibody against receptors on A strain lymphocytes specific for B strain H antigens; this implies that receptor sites on A lymphocytes for B strain antigens are relatively homogeneous. Walford presented data indicating that of ten human myelomas thus far examined, three were directed against HLA antigens, and two of these three were directed against HLA-5.

The large number of host lymphocytes reactive to H antigens of other members of the same species was discussed extensively. Essentially four different points of view emerged as possible explanations: the Jerne model; the Möller-Mitchison view that the high density of H antigen determinants on lymphocyte membranes activates cells with low affinity binding sites and causes them to undergo blastogenic transformation and to produce mediators of cellular immunity; the Cohn-Good-Lawrence hypothesis that the large number of reactive cells represents prior antigenic experience of the animal with cross-reacting environmental antigens or with tumor specific antigens on neoplasms suppressed successfully; and finally the "antyclonalist" concept of Simonsen that these cells are basically multipotential.

The edited proceedings of this conference will be published by Academic Press as the third volume of the series "Perspectives in Immunology."

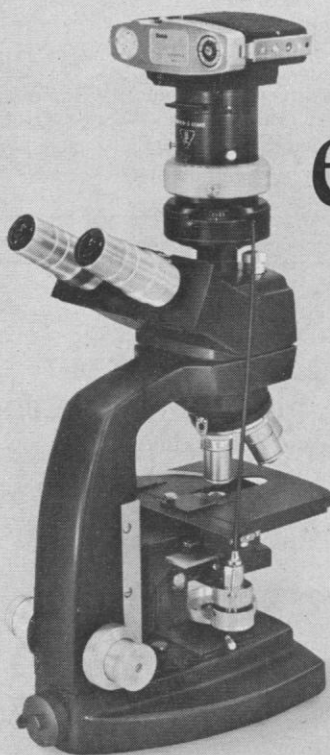
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Electronic Flash, Strobe. Harold E. Edgerton. McGraw-Hill, New York, 1970. xvi + 368 pp., illus. \$22.50.

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¹ Benesch, R. and Benesch, R. E., Nature, 618, 221 (1969).
² Krinsky, I., In H. U. Bergmeyer, Methods of Enzymatic Analysis, p. 238, Academic Press, N.Y. (1965).

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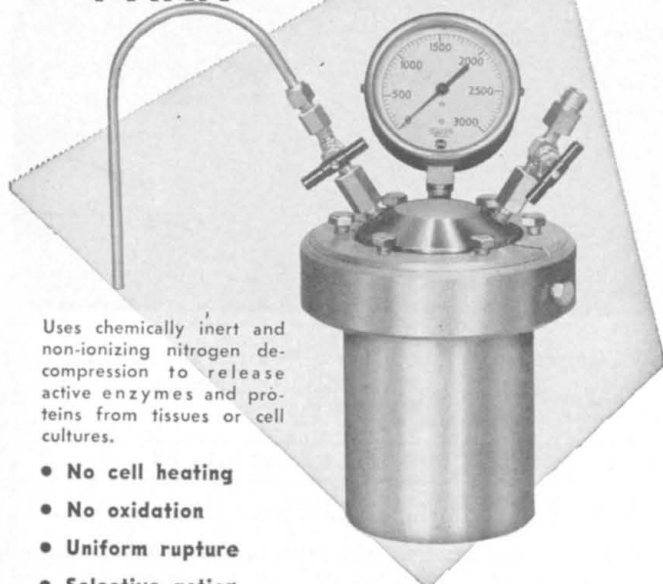
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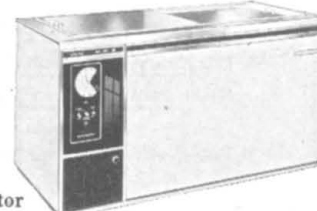
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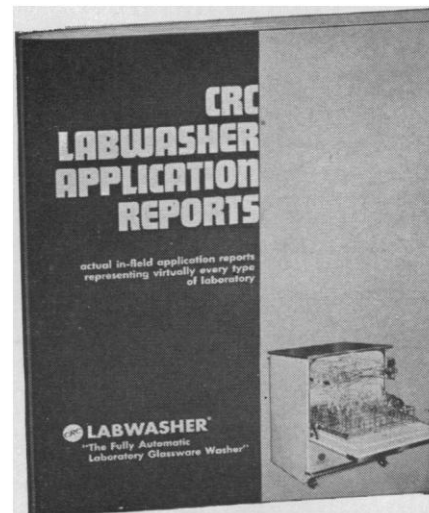
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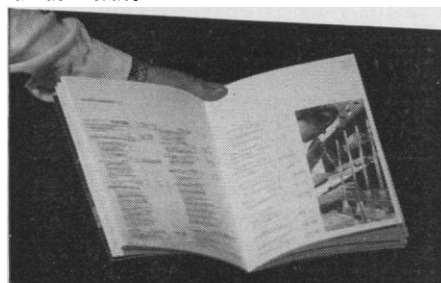
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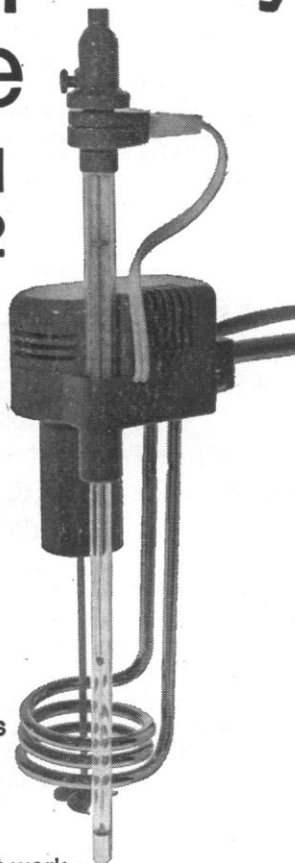
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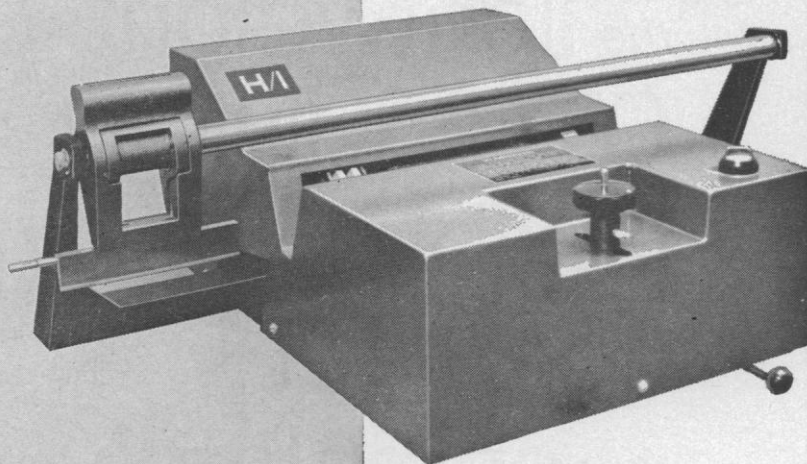
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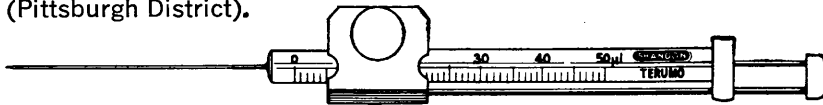
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