

# Beckman L8 Ultracentrifuges-High Performance in the 80's

From every aspect of performance, the L8 ultracentrifuges are unsurpassed. Whether you choose the 80,000rpm Model L8-80, or the 70,000 or 55,000-rpm models, you get the most advanced drive system, programming capability, over 40 rotors to choose from, and a host of built-in features which assure you top performance in the years ahead.

The Ultra-Smooth<sup>™</sup> drive system is the most successful ever designed — a frequency-controlled induction motor that drives the rotor directly from *inside* the vacuum system. Its smoothness is unsurpassed, and we warrant the *complete* drive for 16 billion revolutions.

Programmability comes from microprocessor control using the Memory-Pac<sup>™</sup> module. You insert a Memory-Pac

in the L8 control panel, and seconds later it is programmed with whatever rotor speed, temperature, etc., you wish. You're assured of error-free duplicate runs with no time spent in set-ups.

L8 features include a Dry Cycle to remove



moisture from the chamber, an  $\omega^2 t$  Integrator for accurately reproducing runs in sucrose gradients, and internal diagnostic systems for simple servicing.

For high performance rotors, no one comes close to Beckman. There are two 80,000-rpm rotors: the 80Ti fixed angle which generates 602,000 g at 80,000-rpm — highest force of any rotor — and the VTi-80 for rapid density gradient runs with such materials as steroid receptors. For the Model L8-70 ultracentrifuge, the 70,000-rpm Type 70.1 Ti rotor has an outstanding combination of volume (163 mL) and force (450,000 g) for such separations as plasmid DNA.

Add a superb line of tubes and adapters, topped by the unique Quick-Seal<sup>™</sup> tubes for sure sealing with-

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### COVER

Tassel-eared squirrel (Sciurus aberti) in ponderosa pine tree. Ponderosa pine twigs are used as a food source by these squirrels, but only Ponderosa pines containing smaller amounts of monoterpenes qualify as food source trees. See page 1273. [R. C. Faren-tinos, National Oceanic and Atmo-spheric Administration, Boulder, Colo-rado 80303]

# Baked Apple.

Last Thanksgiving, a designer from Lynn/Ohio Corporation took one of the company's Apple Personal Computers home for the holidays.

While he was out eating turkey, it got baked.

His cat, perhaps miffed at being left alone, knocked over a lamp which started



a fire which, among other unpleasantries, melted his TV set all over his computer. He thought his goose was cooked.



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11 SEPTEMBER 1981

# Where biological problems find answers,



Two new instruments from Varian: the VISTA Chromatography Series with the 401 Data System and the DMS 90 UV-Vis Spectrophotometer

Life scientists have trusted Varian instruments for decades – and for good reasons.

First, Varian offers the widest range of research and analytical instrumentation available today; so you can select state-of-theart performance to suit the needs of your laboratory. Second, Varian puts the operator first by making ease and speed of operation a design commitment; you benefit from the increased productivity. Most important of all, you can rely on the accuracy of your results; they carry the authority of long-standing leadership in scientific instrumentation. In other words, we've earned the trust. And intend to keep

earning it.

The results you see here are examples of answers found to problems in the biosciences – from instruments designed to make them all seem routine.

### **ULC:** Analyze nucleic acid constituents

The separation of nucleotides, nucleosides, and bases shown was achieved in a single run in less than 90 minutes. The threesolvent capability of the *Model 5000 Liquid Chromatograph* was used to sequentially program two gradients. Flow programming was used to separate bases and nucleosides at a reduced flow during initial solvent gradient.

The Model 5000 is fully compatible with the new VISTA 401 Chromatography Data System

### Circle No. 63.

### **2** LC: Identify and purify peptides

With the *Model 5000*, peptide species differing in only a single amino acid are sharply separated by reverse-phase chromatography. Circle No. 64.

#### **OLC:** Separate proteins by molecular size

The new Varian *HPLC System* for protein and peptide chromatography gives you complete molecular-size exclusion, anion exchange, and reverse-phase capabilities. For example, you can separate proteins with a wide MW-range in minutes, with excellent recovery of protein mass and enzyme activity. Circle No. **65**.

### **UV-Vis:** Measure enzyme activity at 0.0005 A/min

The new easy-to-operate *Cary 219/210-PLUS Spectrophotometer/Computer System* offers fully computerized spectrophotometry. All experimental data are accurately collected, processed, and reduced to give you final results automatically. The superior optical performance that's part of the Cary tradition accommodates low enzyme activities just as easily as highly turbid samples. Circle No. **66**.

### **O UV-Vis:** Do derivative spectrophotometry at the touch of a button

A derivative spectrum enhances spectral detail like the shoulders on this BSA spectrum, and they are easy to do with the low-cost *DMS 90 UV-Vis Spectrophotometer!* Just touch a button, and the microcomputer calculates true wavelength derivative data – both first and second derivative. Circle No. 67.

### **O** AA: Measure electrolytes in tissue, cells, and fluids

With the new Varian AA-875 Atomic Absorption Spectrophotometer, you can study toxicity, nutrient and metabolic activities, and the therapeutic effects of some 67 elements. This AA spectrum shows a typical determination of chromium in urine, using the Carbon Rod Atomizer accessory. Sample volume is 20  $\mu$ l. Sensitivity: 6 pg Cr in the urine matrix; precision: 10–20% RSD at 1  $\mu$ g/24 hr sample level. Circle No. 68.

# you'll find Varian instruments



### DEPR: Study RBC internal viscosity

In spin label studies of slow molecular motion, like investigations of red-blood-cell internal viscosity and the effects of chemotherapy on membrane fluidity, the saturation-transfer EPR (ST-EPR) experiment has been proven extremely useful.

The Varian *E-150 Induction EPR Accessory* now brings high sensitivity to dispersion ST-EPR, which makes it possible to use  $90^{\circ}$ -out-of-phase first-harmonic ( $\mu'$ ) detection. This technique offers easier interpretation and simulation and makes spectrometer adjustment less critical.

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optimize spectral sensitivity to slow molecular motions ( $10^{-3} \sec T_c > 10^{-6} \sec$ ). Circle No. 69.

### **3** GC: Identify bacteria by methylated fatty acids

Superb resolution achieved with the fused-silica capillary column on the *Model 3700 Capillary Gas Chromatograph* and the data presentation capabilities of the *VISTA 401 Chromatography Data System* make bacteria fingerprinting a routine procedure.

The easy-to-read printout includes peak names, run conditions, and quantitative chromatographic data. All can be stored on a floppy disk for instant retrieval and precise reproduction of the analysis. Circle No. 70.

### **ONMR:** Elucidate peptide structure

The exceptionally sophisticated software of the XL-200 Superconducting NMR Spectrometer gives the researcher a high dynamic range and unsurpassed data processing capabilities.

The XL-200 proton spectrum shows 6 x  $10^{-3}$ M arginine vasotocin in 90% H<sub>2</sub>O/10% D<sub>2</sub>O, using 32-bit double-precision acquisition and floating-point Fourier transform. Direct time averaging allows automated variable-temperature experiments to be performed without resorting to organic solvents or presaturation of H<sub>2</sub>O. You can observe temperature dependence of NH proton shifts and determine vicinal NH-CH spin couplings—information which can help you determine peptide structure in aqueous solution. Circle No. 71.

To have a representative contact you about *any* Varian instrument, Circle No. 312.



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For literature, write: Eppendorf Division, Brinkmann Instruments, Inc., Subsidiary of Sybron Corporation, Cantiague Road, Westbury, NY 11590; or call 516/334-7500. In Canada: Brinkmann Instruments (Canada), Ltd.

# To spin for minutes, set the timer,

# To spin for seconds, touch the butt

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Published in Cooperation with the International Plant Growth Substances Association Editor-in-Chief: Thomas C. Moore, Oregon State University

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### Plant Cell Reports

Managing Editors: Klaus Hahlbrock, Freiburg i. Br., FRG; Oluf L. Gamborg, San Carlos, CA, USA

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**Advanced Applications** 

20.00004

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SCIENCE, VOL. 213

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SCIENCE, VOL. 213



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### **Field Centers**

### Western Circuit

- OGC—Oregon Graduate Center for Study and Research, Nicholas J. Eror, Department of Materials Science, 19600 N.W. Walker Road, Beaverton, Oregon 97006. Tel: (503) 645-1121.
- ANA—Santa Ana College, David Dobos, Division of Social Science, 17th at Bristol, Santa Ana, California 92706. Tel: (714) 667-3279.
- UUT—University of Utah, E. Allan Davis, Department of Mathematics, Salt Lake City, Utah 84112, Tel: (801) 581-5809.
- TXA—University of Texas at Austin, James P. Barufaldi, Science Education Center, EDB 340, Austin, Texas 78712. Tel: (512) 471-7354.

### **Central Circuit**

- UIA—University of Iowa, Robert E. Yager, Science Education Center, 450 Physics Building, Iowa City, Iowa 52240. Tel: (319) 353-4921.
- PAR—Parkland College, Delores C. Schoen, Life Science Division, 2400 W. Bradley Avenue, Champaign, Illinois 61820. Tel: (217) 351-2465.

- **DAY—University of Dayton**, George K. Miner, Chautauqua Field Center, Department of Physics, Dayton, Ohio 45469. Tel: (513) 229-2327.
- **CBC—Christian Brothers College**, John Edward Doody, Division of Science and Mathematics, 650 East Parkway South, Memphis, Tennessee 38104. Tel: (901) 278-0100, ext. 290.

### **Eastern Circuit**

- UGA—University of Georgia, W. R. Zeitler, Department of Science Education, Athens, Georgia 30602. Tel: (404) 542-1763.
- **TUCC—Temple University,** Leonard Muldawer, Chautauqua Short Course Program, Barton Hall BA-407, Philadelphia, Pennsylvania 19122. Tel: (215) 787-7668. *Courses will be conducted at Temple University Center City (TUCC).*
- **POL—Polytechnic Institute of New York,** Bernard J. Bulkin, Polytechnic/Westchester, 456 North Street, White Plains, New York 10605, Tel: (914) 949-1775.
- HAM—Hampshire College, Arthur H. Westing/Jim Matlack, Chautauqua Program/CA, Amherst, Massachusetts 01002. Tel: (413) 549-4600, ext. 562.

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### Schedule of Classes

- 1. Astronomy Bizarre R. EDWARD NATHER, University of Texas at Austin 12-14 Nov./TXA
- 2. Advances in Coherent Optical Science and Engineering BRIAN THOMPSON. University of Rochester 16-17 Nov. & 11-12 Mar./TUCC
- 3. Qualitative Physics VICTOR F. WEISSKOPF. MIT 24-26 Mar./HAM
- 4. The Personalities of 20th Century Physics: Their Interactions and Struggles MAX DRESDEN, SUNY, Stony Brook 12-14 Nov./PAR; 25-27 Mar./CBC
- 5. Historical Foundations of Modern Science DUANE H. D. ROLLER. University of Oklahoma 18-20 Mar.1/UIA
- 6. Industrial Organic and Pharmaceutical Chemistry in College Chemistry Teaching HAROLD WITTCOFF. Koor Chemicals. Israel. and University of Minnesota 4-6 Nov./DAY; 11-13 Nov./POL
- 7. Chemical Phenomena: Presentations and Explanations BASSAM Z. SHAKHASHIRI. University of Wisconsin 25-27 Feb./TXA; 12-14 Apr./UIA
- 8. Thermodynamics, Art, Poetry, and the Environment HENRY BENT. North Carolina State University 8-10 Mar./PAR; 11-13 Mar./POL
- 9. Plate Tectonics: History of, Evidence for, and Function as Rock-Generating Machine PETER J. WYLLIE. University of Chicago 19-21 Nov./UUT; 4-6 Mar./PAR
- 10. The Evolution of Life on Dynamic Earth JAMES VALENTINE, University of California, Santa Barbara 8-10 Mar./OGC; 15-17 Mar./ANA
- 11. Cosmology:>Protobiology:>Biology SIDNEY FOX, University of Miami 16-17 Nov. & 15-16 Feb./PAR; 19-20 Nov. & 18-19 Feb./DAY
- 12. Life in the Oceans EUGENIE CLARK, University of Maryland 3-5 Mar./UGA
- 13. Ecology and Evolution in the Tropics JOHN KRICHER. Wheaton College 29-31 Mar.<sup>2</sup>/TXA; 29-31 Mar.<sup>2</sup>/UGA
- 14. Ecology of Terrestrial Microcommunities DANIEL DINDAL. SUNY College of Environmental Science and Forestry 22-24 Nov./ANA; 17-19 Nov./TXA; 5-7 Apr.3/UGA; 8-10 Nov./TUCC
- 15. Immunobiology: Evolutionary, Developmental and Molecular Perspectives RICHARD GOLDSBY, University of Maryland 16-18 Nov/OGC; 12-14 Nov/ANA; 4-6 Nov/CBC; 8-10 Nov/TUCC

- 16. Genetics and Society: A Dynamic Interaction ROBERT F. MURRAY, JR., Howard University 15-17 Mar./PAR; 24-26 Mar./UGA
- 17. Ethical Issues in Death and Dying THOMAS L. BEAUCHAMP, Kennedy Institute, Georgetown University 22-24 Nov./TXA; 10-12 Mar./TUCC
- 18. Arms Uncontrolled: Causes and Remedies of the Arms Race EVERETT MENDELSOHN, Harvard University 18-20 Mar/UIA; 19-21 Nov/PAR
- 19. Soft Energy Paths: How to Enjoy the Inevitable AMORY LOVINS and L. HUNTER LOVINS. Friends of the Earth 4-6 Mar./UUT
- 20. Energy and Society GEORGE TSONGAS, Portland State University 9-10 Nov. & 8-9 Mar./DAY; 12-13 Nov. & 11-12 Mar./HAM
- 21. Science, the Media, and the Public SHARON DUNWOODY. University of Wisconsin. and CAROL ROGERS. Office of Communications. AAAS 28-30 Mar./UIA; 15-17 Nov./TUCC
- 22. Cognition and Teaching RUTH DAY, Duke University 4-6 Mar./UUT; 28-30 Oct./CBC
- 23. Patterns of Problem Solving MOSHE RUBINSTEIN, UCLA 7-9 Dec./ANA; 11-13 Mar./UUT
- 24. Combinatorial Problem-Solving in the Mathematical Sciences ALAN TUCKER, SUNY, Stony Brook 5-7 Apr.<sup>3</sup>/UGA; 19-21 Nov./TUCC
- 25. Calculus for Non-Majors in the Physical Sciences ROBERT ROSENBAUM. Wesleyan University 19-20 Nov. & 18-19 Mar./HAM
- 26. Computers as an Aid in Learning Science ALFRED M. BORK, University of California. Irvine 22-24 Mar./OGC; 16-17 Nov. & 25-26 Mar./ANA
- 27. Microcomputer Interfacing in the Undergraduate Laboratory ALBERT S. WOODHULL, Hampshire College 29-30 Oct. & 25-26 Feb./HAM
- 28. Microcomputers in the Laboratory **ROBERT TINKER**, Technical Education Research Centers 9-10 Nov. & 25-26 Feb./PAR; 12-13 Nov. & 1-2 Mar./DAY
- 29. A Laboratory Lecture Approach to Microcomputer Education DAVID G. LARSEN and PAUL E. FIELD, Virginia Polytechnic Institute 25-27 Mar./UUT; 12-14 Nov./CBC
- 30a. Introduction to Microcomputers and Microprocessors ROGER CAMP. Iowa State University 10-12 Mar./UIA
- 30b. Introduction to Microcomputers and Microprocessors ROGER CAMP. Iowa State University 15-17 Mar./UIA

<sup>1</sup>Course will be conducted at the University of Oklahoma. <sup>2</sup>Course will be conducted at Ossabaw Island. Georgia. Applications should be sent to the University of Georgia OR the University of Texas, but not to both. <sup>3</sup>Course will be conducted at the University of Puerto Rico. Rio Piedras. Applications from Puerto Rico and the Virgin Islands should be sent to Dr. Manuel Gomez, Director. Resource Center for Science and Engineering in Puerto Rico, University of Puerto Rico, Rio Piedras, Puerto Rico 00931.





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\*Many of these systems are already installed in major research institutions... and conversion to these ventilated animal racks is accelerating.

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the capital costs of construction). Even the City of Cambridge subsidizes federal research programs, since Harvard's laboratories are exempt from real estate taxes.

I have always been puzzled about the manner in which universities are reimbursed for the costs of research. The federal government sponsors research at a variety of institutions. At least for private industry and the federal laboratories essentially all the costs are reimbursed, and in private industry, at least, the level of indirect support is substantially greater than it is at typical universities. Much of this research is of a kind that is not appropriate to universities, but there are at least a few areas (for example, plasma physics) where university, federal, and industrial researchers compete for the same funds. Why then, in some cases, are all costs reimbursed in a rather straightforward manner, but in the case of universities it is only with the greatest difficulty (at least that is the impression one gets) that less than the entire amount can be recovered?

In my opinion, universities are underfunded in both direct and indirect categories by some factor. This issue will be particularly vexing in the coming years, when university finances will be in bad shape generally. Yet we as a society face critical technical issues and research problems of a kind traditionally addressed in the university environment. Weakening the universities in any way cannot help.

HERBERT GURSKY

Harvard/Smithsonian Center for Astrophysics, 60 Garden Street, Cambridge, Massachusetts 02138

... Brown's analysis rests on the use of a percentage of either the direct research support as a total of federal research support or of the indirect costs as a total of federal research support. The former appears to be declining, the latter rising, thereby proving the hypothesis. What Brown does not point out is that the universities are trying to maintain a high level of research at a time when outside funding is not keeping up with general growth in university costs. At Washington University, a recent analysis showed that the indirect cost of federally sponsored research taken as a percentage of the total university budget has remained constant over a 10-year period. . . .

Brown states that universities have no incentive to minimize indirect costs. Indirect costs in universities are allocated across three pools: organized research; instruction and departmental research; and other institutional activities. Very few costs are allocated only to the research pool. Therefore universities do indeed have a significant incentive to minimize overhead since, depending upon their research activities, they are responsible for paying a significant portion of it.

Brown raises a number of important issues, some of which we can all agree on: that the current environment is fraught with excessive regulation; that there is a tendency for accounting principles to be applied without an understanding of the research process; and that the requirement for 100 percent effort reporting is without merit. However, in an effort to solve these problems, it is essential that we recognize the complexity and individuality of our universities. The currently recognized accounting principles have evolved in part because of a recognition that these essential differences in our universities make a unique contribution to our society. Attempts to oversimplify the determination of indirect costs could lead to pressures on universities to fit all university work and faculty responsibilities into a standard mold. This could result in a uniformity that most faculty members would resist just as strenuously as they now do the effort reporting requirements.

SAMUEL B. GUZE

Department of Psychiatry, School of Medicine, Washington University, St. Louis, Missouri 63110

Brown performs a valuable service by exposing the increasing proportion of the federal research budget that has been consumed by indirect costs over these past few years. If these trends continue, a linear least-squares projection-which. by the way, accounts for 97 percent of the variance---indicates that we shall attain Nirvana on 17 November 2048. On that landmark date, only 67 years hence, the entire research budget will be allocated to indirect costs, and none will remain for the conduct of research! I recommend that, after that date, indirect costs be justified as necessary to support the preparation of new proposals for research that might have been carried out if any funds had remained for actual research.

JOHN W. DONAHOE Department of Psychology, University of Massachusetts,

Amherst 01003

The letters of Guze and Gursky raise several points that require further discussion.

Guze overstates, then challenges, my



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article's point that "... there is inadequate incentive for universities to be cost-efficient with respect to indirect costs of grant-supported research," especially by comparison with direct costs. In my view this is a clear and fundamental flaw in the federal indirect cost policy. Direct costs of National Institutes of Health (NIH) grants undergo a prospective three-step review by study sections, institute councils, and NIH intramural personnel, and specific items are cut that are inadequately justified as necessary to the proposed research. Indirect cost rates are approved in the renegotiation process, where the review is largely retrospective, and there would naturally be great reluctance in disallowing, for example, indirect cost funds for salaried persons already hired. More important, I am informed by federal personnel who conduct these negotiations that it is not feasible to determine whether any given item of indirect costs is justified as part of an efficient operation, or even whether it is needed at all. They can only determine whether an item falls within accepted definitions of indirect costs. If a similar approval system were applied to research equipment, for example, an investigator could purchase any equipment desired, providing only that he could demonstrate at a later date that it fell within the definition of research equipment. It would not be necessary to show that it improved the efficiency of his research or even that it was needed in any way for his research. Clearly this would be an unsound policy that would lead to obvious abuses. Yet that type of policy is currently applied to indirect costs, where the consequences are less obvious. Under these conditions it is hardly surprising that many university administrators are reluctant to accept a change of policy. There is no adequate information on the percentage of indirect costs of federally supported research that is actually covered by universities. It undoubtedly varies greatly but is probably small in most cases. Even if a university paid as much as 25 percent of its total indirect costs, it could not realistically be expected to be as careful and efficient about costs of 25 cents on the dollar as about costs it must pay in full. This inevitably seems an important factor behind the steady upward spiral of indirect costs.

Under regional uniform indirect cost rates, as proposed in my article, universities would have strong incentives to place as many costs as possible in the "direct" category. Rather than a "serious defect" of the proposal, as stated by Gursky, this is an advantage because the direct costs are much more stringently controlled. Administrative excesses in shifting costs could be prevented rather simply by defining costs that cannot be put into the "direct" category. Some definitions of direct and indirect costs are necessary under any policy and are currently provided by Circular A-21 of the Office of Management and Budget (OMB).

Guze expresses the belief that diversity among universities requires diversity of negotiated indirect cost rates. This view seems more emotional than logical, since significant diversities rest primarily upon faculty and upon university policies. This view also ignores history, unless Guze considers that the desired diversity among universities has existed only since 1966, when the current indirect cost policy became effective. Guze goe on to predict that faculty members will esist my proposal as strongly as they now resist effort reporting. In fact, the response of nonadministrative faculty has been strongly supportive, the letters of Jaffe and Donahoe being typical of many I have received. Opposition to date has been almost exclusively from among those like Guze and Gursky, who have long held administrative posts.

Instead of diversity among universities, the more basic issue is, What policy would treat all universities the most fairly in reimbursing their indirect costs? Defenders of the current policy often assume that it does this very well, but I doubt it. Based upon differing goals and educational policies, universities will inevitably hold differing views concerning the desirability of seeking maximum indirect cost rates. Also, among the universities that do seek maximum rates. there will inevitably be differences in diligence and abilities that are applied in the negotiations. All these factors will result in inequitable indirect cost rates. So it is not at all clear that regional uniform rates would be any less equitable than the current policy. Certain inequities would probably occur in both cases, with the nature of the inequities probably differing somewhat under the two policies. In short, it appears that equity considerations cannot be decisive in rationally comparing these two policies. On the other hand, my proposal would remove or alleviate most of the serious problems that have developed under the current policy, as described in my article. These perceived advantages of the proposal seem to require particularly close attention, since they offer a much more decisive basis for evaluating the proposal in relation to current policy.

In Gursky's letter many statements

need correction or comment. He says I would "... allow a single, indirect rate for all universities . . . ." Instead, my proposal is for uniform rates within each geographical region that has reasonably uniform fuel costs. He also says that my proposal would ". . . eliminate accountability to the government." On the contrary, it would eliminate only the need for specific cumbersome mechanisms that the universities must now use under OMB Circular A-21 in demonstrating accountability for indirect costs. The basic accountability to all major groups affected by indirect costs would, of course, remain. And accountability to the federal government would continue to be assured by the information required from universities in establishing regional indirect cost rates. Since Gursky seems impressed that his university pays for some faculty salaries, it should also be noted that federal grant policy reimburses faculty salaries for the portion of time spent on grant-supported research. That policy pertains even for tenured faculty, whose salaries might be regarded as the exclusive responsibility of the university. This important and complex salary issue was not discussed in my article because grant-supported faculty salaries are normally charged to direct costs.

Gursky says he has always been puzzled by the different indirect cost policies applied to federal research at universities and in private industry. But why? As mentioned in my article, universities have always accepted faculty-initiated research as a primary responsibility and in former times paid both the direct and indirect costs of much of that research. Also, universities are nonprofit institutions. Unless Gursky's institution has given up its avowed dedication to faculty-initiated research, and its nonprofit status as well, it hardly seems eligible for the same indirect cost rates as private industry.

Finally, Gursky implies that my proposal would weaken the universities. Instead, this proposal would stimulate a healthy competition between universities in the efficiency of using their indirect cost funds. Through this, and a variety of other factors that were described, indirect costs would be reduced. More federal research funds would thus become available to support the direct costs of research. These changes, augmented by others that were cited, should considerably strengthen, not weaken, the universities.

KENNETH T. BROWN Department of Physiology, University of California, San Francisco 94143

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### **Genetic Effects of Atomic Bombs**

The evaluation of the genetic implications for humans of increasing exposures to ionizing radiation and complex chemicals presents one of the most difficult epidemiologic issues ever faced by biomedical science. In an article in this issue we report the results of a 34-year follow-up study of children born to the survivors of the atomic bombings of Hiroshima and Nagasaki. We found no clearly statistically significant effects of parental exposures on the offspring characteristics which we studied, but the various indicators of possible genetic damage all are in the direction expected if an effect was indeed produced. On the basis of the enormous body of data concerning the genetic effects of radiation on experimental organisms, we feel there can be no doubt that some genetic damage was sustained by the survivors of the bombings; hence we have taken the findings in their children as the basis for an effort to estimate the genetic doubling dose of acute radiation for humans. This involves assumptions concerning the contribution, in each generation, of spontaneous mutation to the indicators in question. Although we feel that we have been suitably conservative in this regard, these assumptions may have to be altered as understanding of human genetics improves. Despite the duration of the study and the expense and labor involved, we can only regard the present estimate as preliminary.

The estimate of the genetic doubling dose for humans is 156 rems. This is approximately four times higher than the estimate in current usage based largely on experiments with selected strains of mice. Accordingly, the estimate has the kinds of implications for regulations regarding permissible exposures, and for legal actions brought on the suspicion of genetic damage from inadvertent exposures, that are certain to elicit discussion.

Where do we go from here? Certainly, all possible efforts must be made to improve the data base on which the estimate rests. These include not only continuing studies along the lines described in the accompanying article, but the application of a number of new techniques for screening for protein variants. Time, however, is running out. The cooperation of the citizens of Hiroshima and Nagasaki has been magnificent, but because both parents must be available for study in case of a suspected mutational event, the sample size is shrinking year by year.

Should similar studies be undertaken on other populations of children at suspected genetic risk from parental exposures? It must at this point be clear to any responsible government official that the issues are highly complex; there are no easy answers to the question of induced, transmitted genetic damage. In particular, the relevance of positive findings in the body cells (say, lymphocytes) of exposed persons to the prediction of transmitted genetic damage in their offspring is highly ambiguous. Chromosomal damage has been obvious in the lymphocytes of survivors of the atomic bombings, but the demonstration of corresponding genetic damage has been difficult.

On the basis of present knowledge, it seems unlikely that any other study can be more revealing than that in progress in Japan. On the other hand, so widespread and pervasive are public concerns, and so great their impact on government actions and regulations, that a case can be made for additional studies of carefully selected groups. The issues are now as much social and political as scientific. There is, in this context, no such thing as a "negative" study; every epidemiologically sound study helps put the problem in perspective. The issue of credibility is major; in some quarters any government-financed, government-directed study will be suspect. We recommend that a blue-ribbon committee, of wide representation, be appointed by either the executive or the legislative branch to consider the entire issue of additional studies. In these deliberations, the opportunities for international collaborative efforts should not be overlooked. The human and financial costs, reckoned in various ways, of not conducting additional studies may far outweigh those of continuing to try to extrapolate from present knowledge.—JAMES V. NEEL, Department of Human Genetics, University of Michigan Medical School Ann@Arbor 48100

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