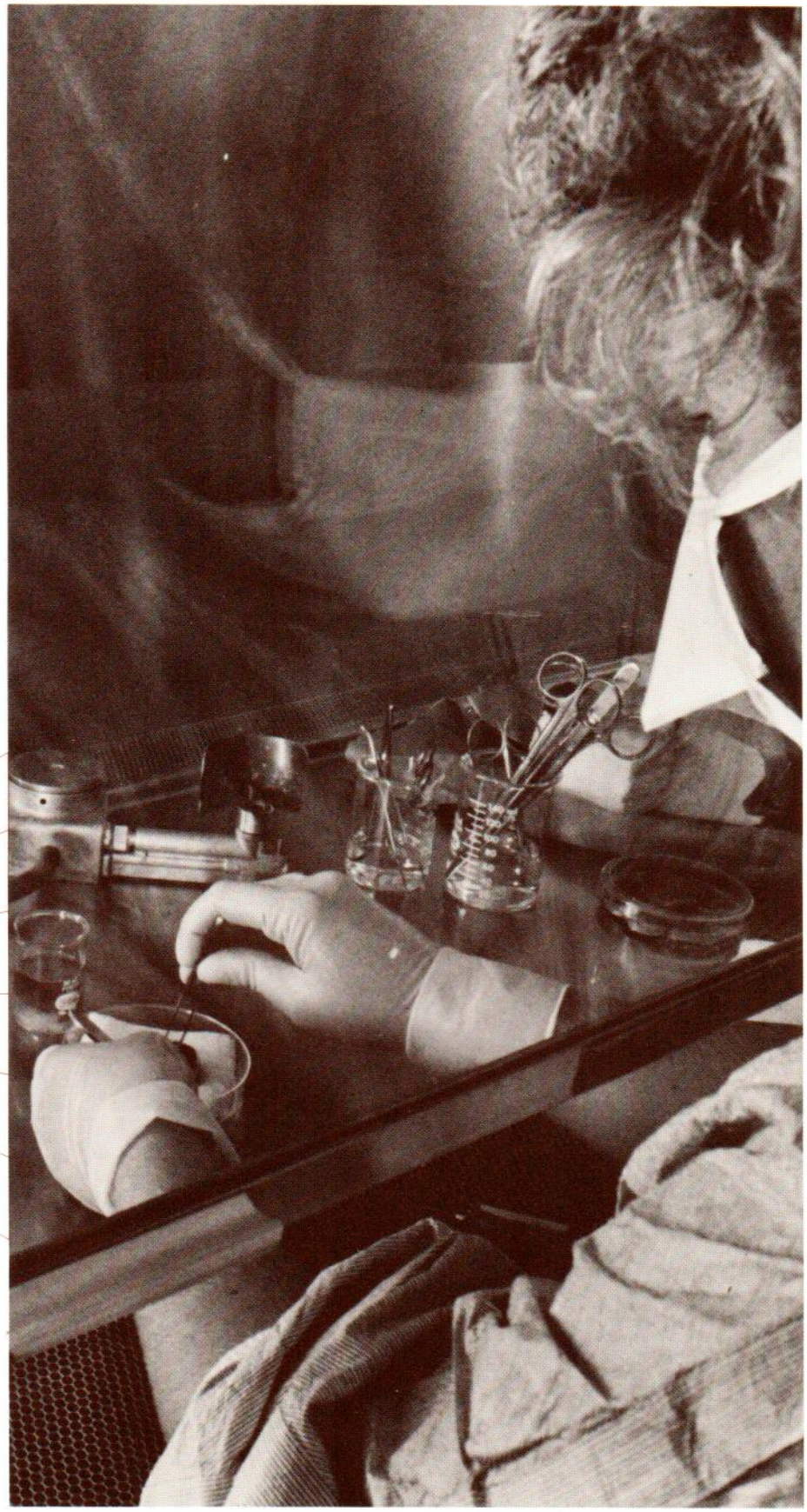
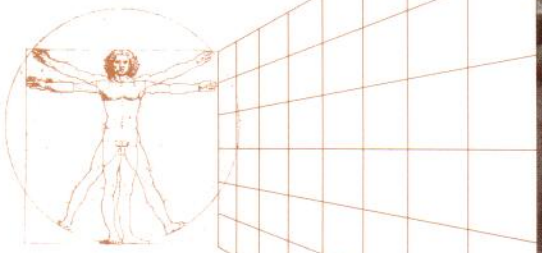
BOSTON BIOMEDICAL RESEARCH INSTITUTE

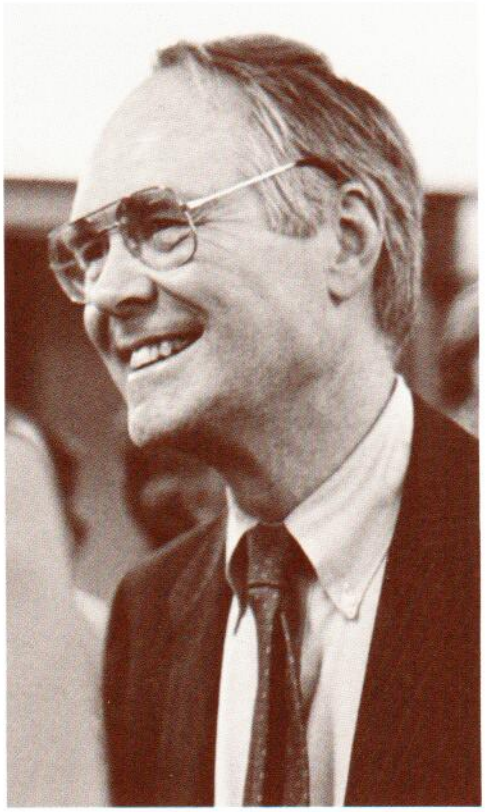




1985 ANNUAL REPORT

CONTENTS

Boston Biomedical Research Institute is an independent, non-profit organization with a staff of M.D. and Ph.D. investigators who carry out a broad program of basic and applied research in biology and medicine, and provide highly specialized training for future physicians and scientists. For over a decade the Institute has maintained its position among the leaders in the world-wide effort to prevent and cure disease. Areas currently under investigation range from the study of birth defects to the biology of aging. The findings of Institute scientists are used by others in clinical projects including those aimed at helping people suffering from cancer and diseases of the heart, muscles, liver, and eye. The Institute's research programs will ultimately bring lasting benefits to the future well-being of mankind.



Report of the President

John French, President

While this past year at BBRI has seemed relatively calm and "routine," it is instructive to remind ourselves what occurs at the Institute in the regular course of events. The results of grant applications by the staff as outlined in John Gergely's letter, while in keeping with the Institute's past record, are, on any absolute scale, an impressive achievement. This is particularly so in light of the increasing competition for government funds. These grants are decided upon, not by administrative funding committees, but by ad hoc scientific review boards consisting of academic peers of the applicants – a further testimonial to the scientific work being undertaken at the Institute. The number and range of scientific papers and publications presented at meetings and in scholarly journals, also mentioned by John Gergely, reinforce the conclusion as to the calibre of the work at BBRI. Clearly, a "normal" year does not mean one without significant activity and scientific achievement!

This year has also seen a potential new source for funding which may be even more important in future years. The NIH has a Small Business Innovation Research Program, funded at 1% of its basic research program. This program is particularly significant for the Institute because it may be utilized by our heretofore inactive commercial subsidiary – Boston Biotechnology Corporation – as the "small business" which applies for the grants. Three applications for grants under this program have been made. While no final decisions have been reached on these applications, the reports to date are encouraging. If funding does, in fact, materialize, we will have the start of active operations for that venture, as BBC will then explore whether projects initially developed by BBRI staff members can be profitable.

Our Development Committee has had another successful year. After raising a record $150,000 last year, they immediately raised their sights to $175,000 for this year, presumably applying the adage of Browning that "a man's reach should exceed his grasp." This turned out to be the case, but the final report does show we exceeded slightly last year's amount, establishing a new high for annual giving. Our grateful best wishes to all our donors who participated in achieving these solid results. The Institute's financial picture remains sound, with our investments and our fund balances (the equivalent of net worth for a business corporation) standing at all-time high levels. This record is due both to the able management of our investments by Treasurer Ernest Henderson, and also to prudent management of the Institute's operations by the staff. As a result, we are making some progress toward our long-term goal of having unrestricted funds on hand in an amount equal to one year's operating budget.

This goal was a challenge left for us by David Crockett, former Chairman of the Trustees of the Institute who retired as a Trustee at this year's Annual Meeting. His long and distinguished career with BBRI was detailed at the Annual Meeting, and it won't be repeated here. However, no report on the year's operations would be complete without acknowledging, with overwhelming gratitude, David's service to BBRI. We are all in his debt for his contributions and his example to the rest of us.

Report of the Executive Director

John Gergely, M.D., Ph.D., Executive Director

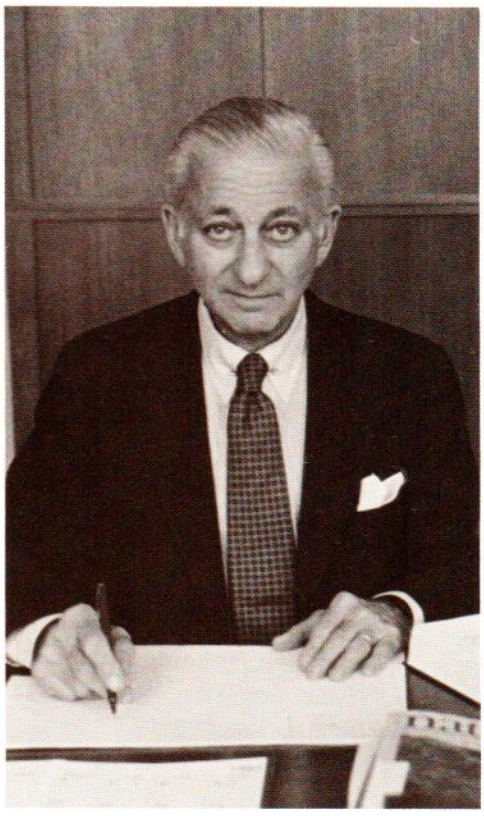
In keeping with the practice of the past few years, this Annual Report focuses on a selected facet of BBRI's activities. While the main mission of BBRI is the advancement of knowledge in the basic biomedical field, not infrequently, and sometimes quite unexpectedly, the research of BBRI scientists contributes to the solution of an immediate medical or environmental problem. A few examples of projects with relatively direct practical benefits are presented on the following pages.

Because the importance of the advancement of basic knowledge is not fully appreciated by the general public, BBRI depends on a small group of far-sighted supporters, not only in terms of direct financial assistance but also by influencing public policy, which often is preoccupied with short-range goals. The impact of this kind of influence was well illustrated in the past year, when public pressure – including letters written by members of BBRI's Board of Trustees and Corporation – led to Congressional action which was finally approved by the President just before the end of the fiscal year and which annulled an attempt by the Office of Management and the Budget to reduce the number of research grants to be funded in 1985 by more than 20%. This episode exemplifies the vulnerability of the scientific enterprise and highlights the need for additional non-government support. However, one hopes that the public's response to this threat to basic research may have helped to educate our lawmakers to the importance of long-term stability of the funding for basic research.

The quality of the work of BBRI's staff can be gauged by a variety of objective standards. In the past year, 38 publications by BBRI scientists appeared in top-ranking scientific journals that typically reject about 50% of the submitted manuscripts. Many members of the staff were invited to present their research at national and international meetings, in countries ranging from Hungary to Japan. The number of successful grant applications has been well above the national average so that our research budget has topped for the first time the $5-million mark. Furthermore, several younger members of our staff who previously were recipients of 3-year grants have been awarded support for 5 years – a clear sign of confidence in their productivity.

The growing contacts between the United States and China have left their mark on BBRI too. A number of Chinese scientists have joined us for varying periods of time partly to receive post-graduate training, partly, in the case of more senior individuals, to lend their expertise in collaborative research efforts.

Again on behalf of the staff I should like to express our appreciation for the support – intellectual and material – received from Trustees and Corporation Members, Foundations, and other friends, more formally acknowledged elsewhere in this Annual Report.



"He who falls in love with practice without science is like a sailor who gets on a ship without a helm or a compass and never can be certain whither he is going."

Leonardo da Vinci

Fighting Tumor Growth through Clear Vision

Bernard Jacobson, Ph.D.

One of the fascinations of basic research is that, although one begins with a clear idea of the path to be taken, the final destination is often a surprise. Dr. Laurie Raymond and I set out to answer the question: why does the vitreous body of the eye remain a clear gel? We would indeed have been greatly surprised had we known that we would end up trying to answer the question: how might one possibly slow the growth of solid tumors? In retrospect, the two questions are actually closely related.

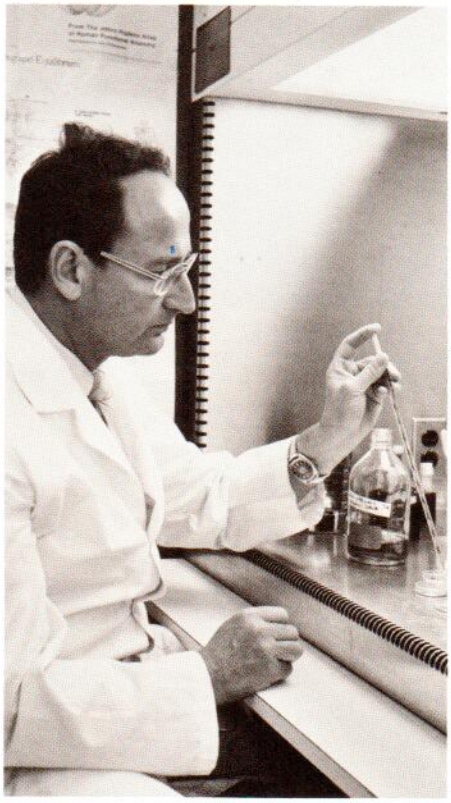
What, then, is the connection between clarity of the vitreous on the one hand and growth of solid tumors on the other? In one word, angiogenesis – the formation (genesis) of blood vessels. The vitreous body, a clear gel occupying most of the volume of the eye and lying between the lens and the retina, contains a system of small blood vessels during embryonic development. These blood vessels disappear after birth, and the vitreous – under normal conditions – becomes a clear tissue.

Dr. Raymond and I decided to investigate whether the vitreous contained an agent that could prevent the growth of blood vessels, and, if so, whether this agent might be responsible for maintaining the clarity characteristic of healthy vitreous and so essential for clear vision. From vitreous of bovine eyes – readily available from the slaughterhouse – we were able to identify a substance that stops the growth of endothelial cells. These are one of the two types of cells that build the walls of large blood vessels and smaller blood capillaries. If the growth of this type of cell could be stopped, then the growth of blood vessels should, in turn, be inhibited. We were soon able to determine that the inhibitory material was produced by the cells called hyalocytes located within the vitreous. This aspect of the research was greatly aided by my long-time collaboration with Dr. Endre Balazs, former Director of BBRI's Connective Tissue Research Department, in growing hyalocytes in the test tube.

It appears to be impossible for solid tumors to grow large unless they manage to acquire a supply of blood through new vessels that the tumor itself must induce to grow. These new blood vessels bring nutrients needed by the tumor. If the development of new blood vessels is blocked, growth is prevented and tumors remain small. Our current research is designed to determine whether the vitreous material that inhibits endothelial cell growth may be able to counteract the blood vessel-stimulatory activity of tumors. If this proves to be the case, we would then begin studies on how best to deliver the purified vitreous inhibitor to a site in tumor-containing animals where its anti-angiogenesis effect might be exerted.

We recently found that the material that stops the growth of endothelial cells exists as a family of substances containing molecules that differ in their size. We are currently engaged in determining whether molecules of one particular size may have a greater inhibitory activity than others.

Finally, in a fruitful collaboration with Dr. Prasanta Basu and his associates at the University of Toronto Department of Ophthalmology and cooperating Toronto ophthalmologists, we have been able to identify endothelial cell growth inhibitory material in normal and pathological human vitreous. This suggests that our results obtained with bovine vitreous represent the situation in our own species as well.



Bernard Jacobson culturing endothelial cells from a calf aorta.

Jane Fogg isolating the vitreous gel from cattle eyes.

Frank Sreter homogenizing a sample from a muscle biopsy.

Katsuhide Mabuchi removing a frozen muscle biopsy sample from liquid nitrogen.

Reducing the Hazards of Anaesthesia

Frank A. Sreter, M.D., D.V.M., Ph.D.

Malignant hyperthermia is a little-known hereditary disease. Nevertheless, there are many families with sad memories of loved ones who suddenly died on the operating table or shortly after surgery. At first the cause was not known, but surgeons and anaesthesiologists soon found out that certain specific anaesthetics must be responsible for the symptoms. More than a decade ago, we initiated research to find out what goes wrong in this disease and how to determine whether a person is susceptible to it. Since the disease is hereditary and some members of susceptible families usually inherit the disease, it seemed important to be able to screen the susceptibility of all members of families known to be at risk.

Through years of research we learned that the disease is due to a biochemical defect in the function of the skeletal muscle, and that this abnormality involves the system responsible for calcium metabolism in muscle cells, the sarcoplasmic reticulum.

It is interesting that some pig strains exhibit the same type of susceptibility and thus serve as excellent "guinea pigs" for our research. During the past year, with the help of Dr. Lopez and his colleagues from Venezuela, who were visiting scientists at BBRI, we demonstrated that the calcium level in susceptible pigs was approximately 3 to 5 times higher than in control pigs. When we triggered a "malignant hyperthermia episode" by administering halothane, an anaesthetic agent widely used during surgery, the usual symptoms – high fever and muscle rigidity – were accompanied by an almost 100-fold increase in the calcium level inside the muscle cells of the susceptible pigs as compared to the calcium level in the control pigs.

In the past, the mortality from this disease was exceedingly high – more than 50% – and the outlook even now is not very bright. Occasionally we read in the newspaper that a young person has suddenly died of high fever during, or immediately after, surgery. It seemed to us that the best way to prevent such accidents would be to develop a diagnostic test that could be made on a biopsy sample taken prior to the proposed surgery.

Our first step in developing a test was to study calcium uptake by fragmented sarcoplasmic reticulum prepared from muscle biopsies. Years of study showed that calcium uptake by the sarcoplasmic reticulum is indeed significantly different in susceptible patients and in normal individuals, thus providing us with the basis for a test that can in fact be used for diagnostic purposes. The test we developed initially required a relatively large muscle sample. Dr. Mabuchi and I have now developed a technique to measure calcium uptake from a much smaller sample by using sectioning of frozen tissue, a method widely used in histology. The advantage of this method is that small muscle biopsies can be taken in any medical laboratory, frozen, and shipped in dry ice to our laboratory for examination. Each year we carry out several hundred such diagnostic tests for anesthesiologists across the country and protect many patients from being subjected to a potentially fatal procedure.

Can We Disarm Asbestos?

Philip Graceffa, Ph.D.

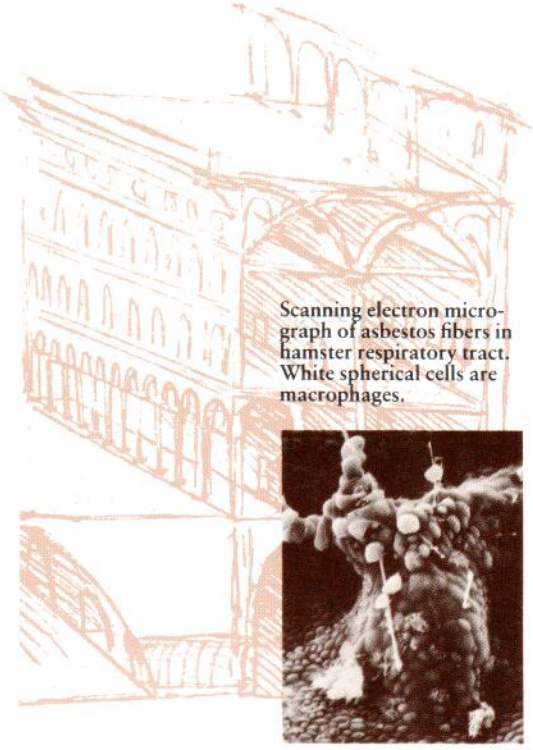
Asbestos is a useful but toxic mineral. It is excellent for use in insulation and fireproofing, and it imparts high tensile strength and durability to many products. However, inhalation of microscopic asbestos fibers can lead to asbestosis, lung cancer, and mesothelioma. Asbestosis involves scarring of the lungs that makes breathing difficult and can lead to heart failure by affecting the pulmonary circulation. Both asbestosis and asbestos-caused lung cancer result from prolonged and intense exposure to asbestos and thus develop mostly in asbestos workers. Mesothelioma, a rare cancer of the linings of the lungs that is always fatal, can be caused by much more casual exposure. Thus there has been increasing concern that members of the general public are also at risk of developing mesothelioma since low levels of asbestos are released from materials used in the construction of schools, homes, and other buildings.

My research has long been concerned with the properties and measurements of free radicals. Free radicals differ from ordinary chemical compounds in that they have an incomplete complement of electrons, causing them to be magnetic and highly reactive. Unexpectedly, my interest in free radicals brought me to the study of asbestos toxicity.

A discussion with Sigmund Weitzman, M.D., an oncologist at Massachusetts General Hospital with an interest in the human organism's reaction to invasion by foreign bodies, led us to suspect that a highly toxic free radical might be produced as a result of the body's reaction to asbestos. Our reasoning went as follows. Inhaled asbestos fibers are engulfed by macrophages, cells in the respiratory tract that are stimulated to destroy and remove foreign bodies. It is known that stimulated macrophages produce hydrogen peroxide, which can react with iron to form a highly toxic substance, the hydroxyl radical. Hydroxyl radicals can react with, and thereby change, almost any tissue component. In particular, they can chemically change the genetic material, DNA, initiating events that may lead to cancer. Since asbestos contains iron, we decided to test whether asbestos mixed with hydrogen peroxide in a test tube generates hydroxyl radicals. We monitored for the presence of hydroxyl radicals with electron spin resonance spectroscopy, a technique that takes advantage of the magnetic properties of radicals. Hydroxyl radicals were indeed produced.

We then treated asbestos with desferrioxamine, a compound that can bind to iron and render it chemically inactive. Treated asbestos no longer produced hydroxyl radicals when mixed with hydrogen peroxide. After we published these findings, we and others demonstrated that, in the test tube, asbestos can chemically alter both the DNA of cells and the membranes surrounding cells and can even cause cell death, and that these effects are reduced when the asbestos is first treated with iron-binding compounds. These findings suggest that the iron in asbestos contributes to its toxic properties and that this toxicity may be reduced by treating the asbestos with iron-binding compounds – either during processing or else after it is in place in buildings. We are now planning experiments to determine whether the treatment of asbestos with desferrioxamine reduces its ability to produce cancerous tumors in mice.

Since asbestos toxicity is the result of an interaction of a chemical with a living organism, the collaboration between a medical biologist, Sigmund Weitzman, and a physical chemist, myself, has been complementary and helpful in investigating this important environmental health problem.



Scanning electron micrograph of asbestos fibers in hamster respiratory tract. White spherical cells are macrophages.

(Photo: Brooke T. Mossman, Univ. of Vt.)

Sigmund Weitzman (left) and Philip Graceffa (right) examining the electron spin resonance spectrum of hydroxyl radicals generated in the gap of the large magnet in the background.

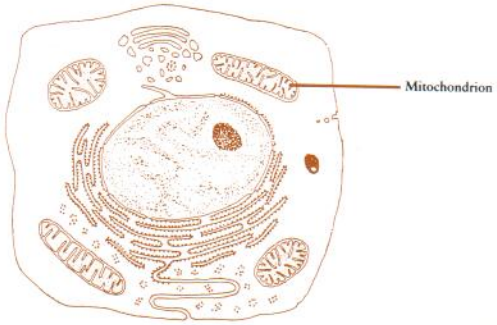


Diagram of the anatomy of a liver cell.

From Mitochondria to Liver Disease

D. Rao Sanadi, Ph.D.

Basic investigations of mitochondria led us to develop a means for diagnosing a chronic liver disease that primarily strikes women over thirty and at present inevitably leads to death. This is another example of basic research leading to discoveries that can have immediate application to the diagnosis and treatment of certain diseases.

Mitochondria occur within most of our cells and are compact structures comprising highly organized collections of enzymes. The function of mitochondria is to convert food energy to other forms of energy that sustain life by maintaining body temperature, fueling contraction of muscles, promoting cell division, and even enabling brain activity. For many years, our laboratory has studied the molecular mechanism of the energy conversion that occurs in mitochondria. During this study we have examined several of the proteins that help to bring about the energy conversion.

In 1979, we were contacted by Dr. Harold Baum, Professor of Biochemistry at the University of London, who was studying certain diseases in which patients develop immune responses to components of their own tissues (autoimmunity). One of these diseases is known as primary biliary cirrhosis. The blood of over 90% of the patients suffering from this condition contains antibodies against mitochondria. It seemed that the detection of such antibodies might be a useful way of diagnosing this disease. Unfortunately, antimitochondrial antibodies are also seen in some other chronic liver disease conditions, seriously limiting the value of such a diagnostic procedure. However, if the antimitochondrial antibodies produced in primary biliary cirrhosis could be defined more precisely so as to distinguish them from antibodies produced in other chronic liver diseases, a reliable diagnostic tool for primary biliary cirrhosis might result.

Dr. Baum proposed a collaborative project to determine whether these antibodies react specifically with any of the mitochondrial proteins that we had characterized. In a screening program, Drs. James Hughes and Saroj Joshi of our laboratory and Jules Dienstag, M.D., of the Massachusetts General Hospital tested antibodies from patients with primary biliary cirrhosis for reaction with the approximately 100 proteins that make up mitochondria. No reaction was observed with any of the few proteins we had previously studied extensively. But in the course of the screening experiments, we identified one protein amongst the 100 which was uniquely reactive with antibodies from patients suffering from primary biliary cirrhosis. We have been able to purify this protein to some extent for use in a diagnostic test which will differentiate primary biliary cirrhosis from other chronic liver diseases. This test is expected to be simple and suitable for automation. It is our hope that it will permit routine screening of all patients with chronic liver disease to enable early detection of primary biliary cirrhosis.

Rao Sanadi, Saroj Joshi, and James Hughes analyzing reaction of patient's blood against mitochondrial proteins.

Antibodies with a Split Personality

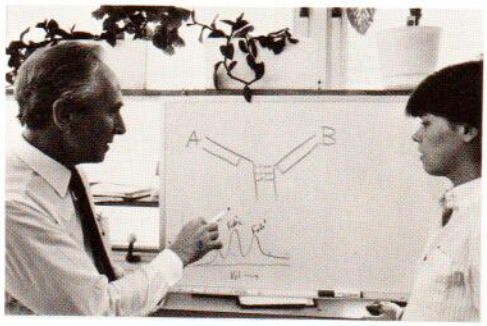
Henry Paulus, Ph.D.

In recent years, monoclonal antibodies have become an important research tool by virtue of the very high specificity with which they can bind to enzymes and other protein molecules, and in addition they are beginning to find many practical applications in medicine and biotechnology. While thinking about potential uses of monoclonal antibodies, it occurred to me that their utility and range of applications would be considerably enhanced if one could construct hybrid antibody molecules that contained portions of two different antibodies.

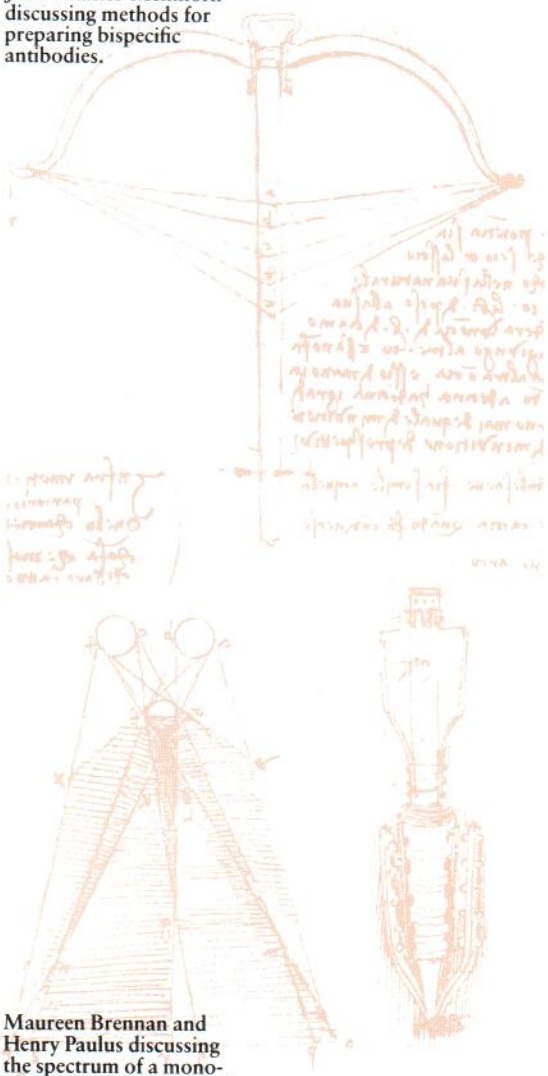
Antibodies are proteins produced by certain cells in the blood and some tissues as a defense against foreign substances – the so-called antigens, which may be proteins, viruses, or cells. The antibodies have two special regions on their surfaces, each of which strongly binds to the antigens and so initiates removal of the foreign matter from the bloodstream. The two binding regions on each antibody molecule are identical, and an antibody can therefore bind to only one kind of substance. Nevertheless, I wondered whether it would be possible in the test tube to cleave an antibody molecule in half and link it to half of another kind of antibody to create a hybrid molecule with two different binding regions.

In searching for ways to achieve this objective, I collaborated with Maureen Brennan and Peter Davison of BBRI's Fine Structure Department. In the context of our other research programs aimed at understanding the basic properties of normal cells and their constituents, we had achieved considerable expertise in protein chemistry and immunology. This helped us develop methods for carrying out what was essentially transplant surgery on an antibody molecule, namely to remove one of the antigen binding regions from an antibody and replace it with the antigen binding region from a different molecule. The technical problems we had to face were difficult ones, because multiple chemical bonds had to be cleaved and then restored exactly to their original condition without damage to any other part of the molecule. We were therefore pleased when we finally succeeded in constructing a hybrid (or bispecific) antibody which had the desired property of being able to link together two different proteins or enzymes as a stable complex. This linkage can be very strong and exceedingly specific. As a result, an appropriate mixture of different bispecific antibodies and proteins will assemble spontaneously into a unique three-dimensional complex, like a jigsaw puzzle assembling itself as if by magic.

We have now accomplished the synthesis of many different bispecific antibodies and studied their properties, and it is clear that we have developed a class of reagents that may have numerous applications in medicine and biotechnology. For example, it should be possible to construct a bispecific antibody that could attach a toxic molecule to a specific protein on the surface of a malignant cell and thus act as a highly selective agent for cancer chemotherapy. Another application would be in diagnostic procedures in which bispecific antibodies would link an enzyme or a fluorescent protein as an indicator to a substance to be analyzed, thus facilitating the measurement. Many other potential uses of bispecific antibodies have suggested themselves, leaving little question that these reagents, developed through methods that we had learned in the course of answering basic biological questions, will also be of great practical utility.



Peter Davison and Jean Thaxter-Mehlhorn discussing methods for preparing bispecific antibodies.



Maureen Brennan and Henry Paulus discussing the spectrum of a monoclonal antibody recorded with a spectrophotometer.

THANK YOU!

The generosity of far-sighted foundations, individuals, and businesses this year provided over $150,000 for basic medical research at BBRI. Each gift contributes to the excellence which is the hallmark of BBRI's research. Each donor is a valued partner in BBRI's work.

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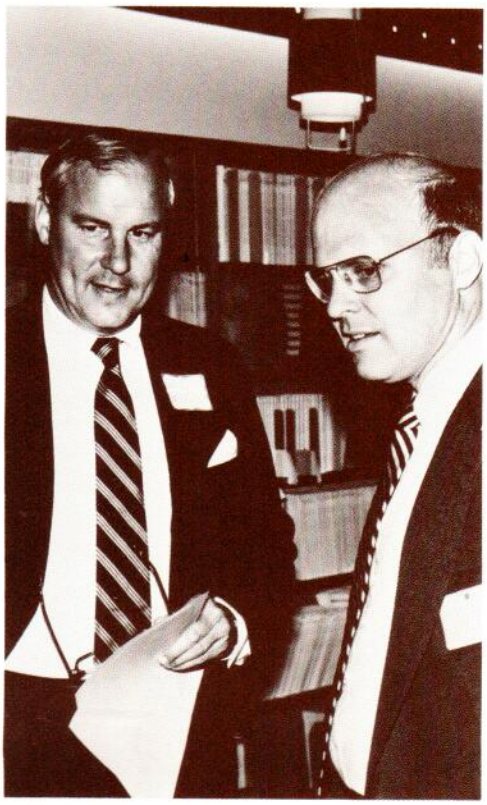
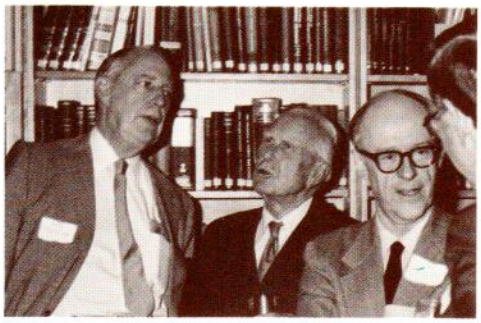
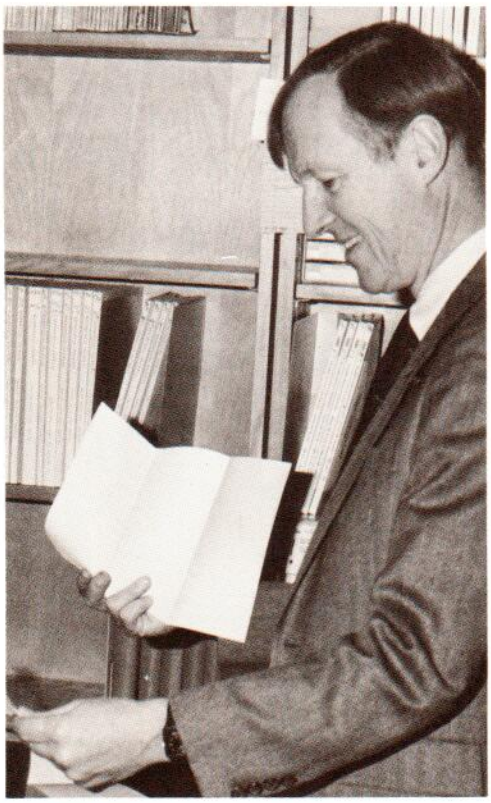


Eustis Walcott, Vice President, and Samuel Talbot.

John Taplin and Sidney Felton, members of the Corporation. At right, William Jencks, member of the Visiting Committee.





Vice President
Chilton Cabot.

Anne Smith, Corporation member, with John Gergely, Executive Director, and William Jencks, member of the Visiting Committee.

Service For The Public Good

The distinguished professional, academic, and community leaders who serve the Institute as Trustees and Corporation members share generously their expertise, wisdom, and resources with BBRI. Through their work with BBRI, they are contributing to a healthier future for everyone.

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BBRI's dedicated staff contribute in many different ways to the advancement of biomedical knowledge.

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Metabolic Regulation

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Cell Physiology

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Maria Bozzella
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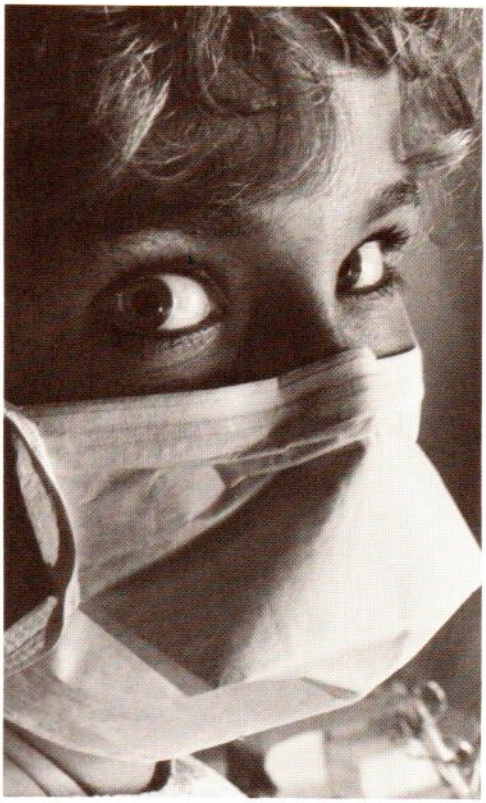
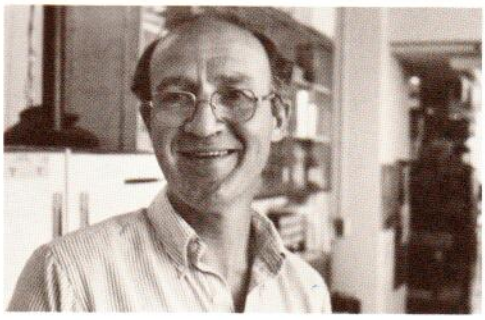


Jane Fogg

Hartmut Wohlrab



Boston Biomedical Research Institute
Balance Sheets
August 31, 1985 and 1984

	1985	1984
Assets		
CURRENT ASSETS		
Cash	$ 506,680	$ 566,939
Grants receivable	4,605,476	4,054,098
Pledges receivable	32,352	26,000
Prepayments, deposits and other receivables (note 6)	141,269	130,298
Investments, at market value (cost 1985 – $2,121,810 1984 – $1,344,663) (note 5)	2,295,756	1,433,116
Total current assets	7,581,533	6,210,451
FIXED ASSETS (notes 1 and 2)		
Leasehold improvements	1,935,632	1,935,632
Research equipment	3,329,969	3,103,710
Furniture and fixtures	47,129	47,129
Total	5,312,730	5,086,471
Less accumulated depreciation and amortization	3,410,411	3,030,130
	1,902,319	2,056,341
	$9,483,852	$8,266,792
Liabilities and Fund Balances		
CURRENT LIABILITIES		
Accounts payable and accrued expenses	$ 40,000	$ 40,703
Overhead and fringe benefit adjustment payable	417,988	287,002
Deferred grant income (note 4)	4,650,251	3,908,190
Deferred fund (building) (note 4)	115,702	115,702
Total current liabilities	5,223,941	4,351,597
FUND BALANCES (note 1)		
Operating	495,306	315,555
Plant and equipment	1,501,682	1,224,969
Permanent research	360,604	318,330
Fixed assets (notes 1 and 2)	1,902,319	2,056,341
Total fund balances	4,259,911	3,915,195
	$9,483,852	$8,266,792

See accompanying notes to financial statements.

Boston Biomedical Research Institute
Statements of Revenues, Expenses and Changes in Fund Balances
for the Years Ended August 31, 1985 and 1984

	1985	1984
REVENUES		
Grants	$4,777,605	$4,371,936
Equipment replacement	98,850	108,127
Contributions and pledges	153,129	150,292
Property and equipment purchased (notes 1 and 2)	226,259	77,877
Investment income	279,007	139,904
Total	5,534,850	4,848,136
EXPENSES (by department)		
Muscle Research	2,240,021	2,110,150
Cell Physiology	1,161,248	1,127,505
Fine Structure	458,045	427,003
Metabolic Regulation	777,387	581,048
General Research	118,915	47,207
Fund Raising	40,149	31,975
Purchase of fixed assets (note 1)	14,088	10,431
Depreciation and amortization (note 2)	380,281	381,855
Total	5,190,134	4,717,174
NET ADDITION TO FUNDS	344,716	130,962
FUND BALANCES, BEGINNING OF YEAR (note 1)	3,915,195	3,784,233
FUND BALANCES, END OF YEAR (note 1)	$4,259,911	$3,915,195

See accompanying notes to financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
NOTES TO FINANCIAL STATEMENTS
AUGUST 31, 1985 AND 1984

(1) – Significant Accounting Policies:

Fund Accounting:

The accounts are maintained on the accrual basis and in accordance with the principles of fund accounting. Funds that have similar characteristics have been combined into the following fund groups:

*Unrestricted funds include two groups representing the portion of expendable funds available for support of operations: a) The operating fund includes unrestricted contributions and investment income less the cost of grants not reimbursed in full by granting agencies, and further reduced by transfers to other funds; b) Other unrestricted funds represent reserves transferred from the operating fund, and a building program fund derived from unrestricted contributions.

*Restricted funds represent resources restricted for research grants or building additions. These funds are deemed to be earned and reported as revenues when the Institute has incurred expenditures in compliance with the specific restrictions. Amounts received but not yet earned are reported as restricted deferred amounts (See note 4).

*Fixed assets fund represents the undepreciated cost of leasehold improvements, equipment and furniture and fixtures.

Other Matters:

All income, gains, and losses arising from the sale, collection, or valuation at market of investments are allocated to the fund owning the assets.

A portion of the overhead chargeable to research grants is deemed to be reimbursement for equipment and is shown as an addition to the Equipment Replacement Fund. This amounted to $98,850 in 1985 and $108,127 in 1984. In addition, $14,088 of equipment was charged to the operating fund in the year ended August 31, 1985, $10,431 in 1984 and added to the plant fund.

(2) – Plant Assets and Depreciation:

The Institute, under an agreement dated June 16, 1970, shares with Retina Foundation the use of research facilities for fifty years at 20 Staniford Street, Boston, and of a research farm in Townsend, Massachusetts.

The leasehold improvement asset category represents the cost of the Institute's long-term leasehold in the building and improvements, and is being amortized over the 50 year lease term. The furniture and equipment categories represent, at cost, acquisitions from operating funds and restricted research grant awards. Depreciation is primarily on the straight-line basis over the estimated ten year useful life of the assets. All depreciation and amortization is charged to the plant fund.

(3) – Government Grants:

All grant costs to the U.S. government and most private grants are subject to audit by the granting agency.

(4) – Changes in Deferred Restricted Amounts:

	1985			1984
	Building Fund	Grants & Contracts	Total	Total
Balance, beginning of year	$115,702	$3,908,190	$4,023,892	$3,150,291
Additions:				
New grants awarded		5,442,509	5,442,509	5,142,152
Contributions and pledges		1,000	1,000	1,000
Investment income	15,344	34,132	49,476	33,022
	131,046	9,385,831	9,516,877	8,326,465
Deductions:				
Funds expended for designated purposes		4,735,580	4,735,580	4,292,913
Transfer of investment income from Building Fund	15,344		15,344	9,660
Balance, end of year	$115,702	$4,650,251	$4,765,953	$4,023,892

(5) – Investments:

Investments consist of corporate and government bonds and listed stocks. Also included is an $800 investment made in 1982 in Boston Biotechnology Corporation. This company was formed to utilize and commercialize certain technical processes originated at Boston Biomedical Research Institute and elsewhere.

The investment holding represents the entire outstanding stock of Boston Biotechnology Corporation and is shown at cost since Boston Biotechnology was inactive through the Institute's year end.

(6) – Advances to Subsidiary:

The Institute has advanced $81,903 to Boston Biotechnology Corporation. This amount is included in the category Prepayments, deposits and other receivables.

Board of Trustees
Boston Biomedical Research Institute
Boston, Massachusetts

I have examined the balance sheets of Boston Biomedical Research Institute as of August 31, 1985 and 1984, and the related statements of revenues, expenses and changes in fund balances for the years then ended. My examinations were made in accordance with generally accepted auditing standards and accordingly included such tests of the accounting records and such other auditing procedures as I considered necessary in the circumstances.

In my opinion, the aforementioned financial statements present fairly the financial position of Boston Biomedical Research Institute as of August 31, 1985 and 1984, and the results of its operations and changes in fund balances for the years then ended, in conformity with generally accepted accounting principles applied on a consistent basis.

John Vecchi/Certified Public Accountant
400 Hillside Avenue, Needham, Massachusetts 02194
(617) 449-5545

October 2, 1985

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