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## INTRODUCTION



**Transforming the vision** of a model urban health center of the twenty-first century into reality has required restructuring the curriculum, streamlining the clinical service, and focusing the research enterprise. This Dean's Report examines the School's research initiatives. Now, more than ever before, basic medical research at the School of Medicine targets the molecular and cellular aspects of urban diseases while clinical care links innovations in the laboratory to clinicians practicing in a network of neighborhood health centers and community hospitals.

The clinical research programs in amyloidosis and sickle cell disease described in this issue exemplify a continuum of bench-to-bedside research in which a dynamic and productive interchange between basic scientists and clinical investigators trims the time from concept to capsule. The breast cancer research program now under way illustrates how, with motivation and leadership, the faculty can mobilize to address important research problems. Only a few years after start-up, the initiative in women's health has recruited more than two dozen investigators in a bold, broad, and comprehensive investigation of the causes and treatment of breast cancer. On an even larger scale, several initiatives in health services research permit population-scale studies to examine issues of access, quality of care, outcomes, and costs of care. In these endeavors, we continue to enjoy strong academic and research links with the Veterans Administration medical centers.

Increasingly, the School's research enterprise attracts students, and we find that about 20 percent of our students choose to participate in basic science or clinical investigation during their academic careers. Some take electives, while others structure their education to include earning a PhD in a basic or clinical science. I am pleased to introduce you to some outstanding young scientists and leaders from the student body.

Also in this issue you will find a description of the School's Master Plan illustrating how BioSquare and Boston Medical Center fit into the design of our modern urban medical campus.

*Aram V. Chobanian*

Aram V. Chobanian

**BOSTON**  
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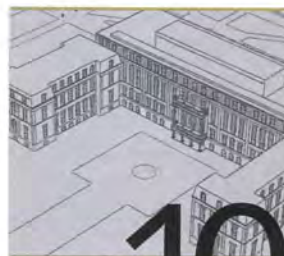
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# CLINICAL RESEARCH

Bridging the gap between research and patient care

Determining how a commonly prescribed drug therapy will affect a patient's health in years to come and whether a drug therapy can activate long-dormant genes are but a few of the questions regularly answered by clinician-scientists at Boston University School of Medicine (BUSM). Bridging the gap between basic researchers working behind laboratory doors and physicians practicing on the front lines of disease management, BUSM's impressive cadre of clinical researchers has made remarkable strides in creating effective therapies for disease and in buttressing the epidemiological evidence for those therapies.

Clinical research is often referred to as "bench-to-bedside" practice. It combines the meticulous and rigorous principles necessary in basic research with the hands-on empathy of practicing clinicians. At BUSM, these seemingly disparate, yet ultimately complementary, approaches among its various clinical research teams—three of which are profiled here—are cultivated every day.

## THE CLINICAL RESEARCH MISSION

Clinical research is an integral part of BUSM's mission. As understanding of basic cell functions grows and new therapies become reality, it becomes essential to translate these advances into patient care. However, bridging the gap between laboratory work and effective therapy can only be accomplished via safe, careful clinical trials and rigorous epidemiological analyses.

To support this mission and continue its widely established reputation as a center of interdisciplinary cooperation, BUSM, together with Boston Medical Center (BMC), formally established the Office of Clinical Research (OCR), under the direction of Deborah J. Cotton, MD, MPH, in July 1998. Cotton, a 1976 BUSM graduate who was recruited from the Massachusetts General Hospital, is a world-renowned researcher in the area of the clinical epidemiology of AIDS and HIV/AIDS in women. Cotton, professor of medicine, epidemiology and biostatistics, and assistant provost of the medical campus, is the former chair of the Antiviral Advisory Committee of the Food and

Drug Administration, which reviews drug licenses for AIDS treatments in the United States, and is a long-standing member of the Board of Health Services Policy at the Institute of Medicine.

Cotton sees the OCR mission as threefold. "First, we need to enhance the infrastructure of the medical campus to promote the most efficient conduct of clinical research. We need to re-engineer everything from grant administration to research planning to patient recruitment," says Cotton. "We must aggressively seek new clinical research opportunities, including incubating new ideas with the help of the Community Technology Fund—Boston University's in-house venture capital group—to assist clinical investigators in developing novel therapies, tests, and medical devices."

Finally, Cotton wants the OCR to respond to a national shortage of physician-researchers. "Studies have now conclusively documented this critical shortage," says Cotton, "and we're committed to developing new programs to integrate training in clinical investigation into all stages of

*Deborah Cotton, MD, MPH*



medical education—from undergraduate through residency and specialty fellowships.”

Cotton emphasizes that the OCR is situated in a superb research environment. “BUMC ranks twentieth in the nation in receipt of federal funding,” she says. “In the 1998 fiscal year, we received more than \$100 million in research funding from federal and other sources.” BUMC has hosted an NIH-funded general Clinical Research Center for thirty years, and Boston University is known for a large number of

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*“We must aggressively seek new clinical research opportunities, including incubating new ideas with the help of the Community Technology Fund...to assist clinical investigators in developing novel therapies, tests, and medical devices.”*

Deborah Cotton, MD, MPH

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National Centers of Excellence. It is within this long-standing framework of excellence that the accomplishments of many unique research teams have grown and developed.

Although the three teams profiled here are treating very different disease conditions—amyloidosis, sickle cell disease, and breast cancer—they have much in common: a multidisciplinary approach, the highest standards of professional support within the team and among the disciplines, and, above all else, supreme dedication to patient care.

## UNCOMMON DISEASE, COMMON COMMITMENT

On the third floor of the Preston Building, the warmth and quiet found in the hallways of the Center for Cancer Care and Blood Disorders belie the aggressive treatment many of its patients undergo—particularly those patients being treated for amyloidosis. This group of diseases, in which one or more of the body’s organ systems accumulate abnormal protein deposits, is so rare that most patients diagnosed with it have little or no information about its pathology or treatment. It can also be a baffling diagnosis for physicians to make, because the various forms of the disease affect a variety of the body’s systems.

Martha Skinner, MD, professor of medicine and staff member in the Department of Rheumatology at BUMC, is the director of the Amyloid Treatment and Research Program, one of the largest and most successful amyloid treatment centers in the world, and has been with the program since its earliest days. Skinner, a rheumatologist by training, first became involved with the program when she worked under the direction of Alan S. Cohen, MD, ’52.

Cohen, the program’s founder, first director, and former head of the Rheumatology Department, was interested in determining what proteins were responsible for amyloidosis. Skinner began work on developing a method for isolating the proteins from tissue, and subsequently performed the initial biochemistry. As Skinner points out, “I wasn’t trained as a biochemist, but was very lucky to have tremendous support from the Biochemistry Department to teach me the techniques necessary to accomplish this work.”

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*“We’ve been able to create a treatment program because of this careful coordination of research and treatment—and through the assiduous follow-up and study of the approaches we’ve developed.”*

Martha Skinner, MD

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### Treatment and research

Because the program combines the best of basic research with ongoing treatment, Skinner and her colleagues have seen tremendous growth in both the treatment potential for patients and the Amyloid Program itself, which cared for more than 300 patients in 1998.

“We’ve been at the forefront of amyloid research and treatment for more than twenty-five years,” Skinner adds. “What makes this department so successful is the teamwork: teamwork among our researchers, teamwork in caring for our patients. We’ve been able to create a treatment program because of this careful coordination of research and treatment—and through the assiduous follow-up and study of the approaches we’ve developed.”

The clinical research component of the Amyloid Treatment and Research Program is essential. “Frequently, by the time our patients get to us, they are very, very ill,” admits Skinner. “We can’t afford not to consider the immediate benefits of our basic research.”

### Combining skills

The interdisciplinary approach of the amyloid team's clinician-researchers has led to significant advances in the use of chemotherapy (to destroy plasma cells producing amyloid proteins), and the relatively novel program of stem cell rescue for treatment of primary amyloidosis—the most common form of the disease. “The stem cell rescue program is the front-runner for patients who are well enough to undergo the procedure,” says Skinner. “We were looking at a group of patients who were getting better with oral chemotherapy, but many of them were so sick that they literally did not have time for the oral therapy to disrupt the formation of the abnormal plasma protein. We changed our approach to deliver the drug intravenously to obtain a more expedient and readily available effect.”

Concurrently, stem cell rescue was being used for treatment of a variety of other blood disorders. “Our hematologists proposed that stem cell rescue would be appropriate for those patients who could tol-

*“We’ve made incredible strides, and it is because we have the unique qualities found in a clinical research center.”*

Martha Skinner, MD

erate it,” she says. As a result, a new, highly effective treatment has become available for many primary amyloid patients.

### Expanding the scope of treatment

The treatments developed by the Amyloid Program are not limited to primary amyloidosis. Research on secondary and hereditary amyloidosis is also being conducted at the center.

Secondary amyloidosis results from a chronic infection or inflammatory condition, such as rheumatoid arthritis, osteomyelitis, or familial Mediterranean fever. Treatment and research for secondary amyloidosis concentrate on managing the underlying cause of the

condition. As the infectious and inflammatory diseases responsible for causing secondary amyloidosis are eliminated, the disease has become increasingly uncommon in the Western Hemisphere.

Understanding how the protein is produced has resulted in successful treatment of hereditary amyloidosis. “In this type of condition, we have established that the abnormal protein production takes place in the liver,” says Skinner, “so we were able to pioneer liver transplants in hereditary amyloidosis patients—the only currently available treatment.”

The commitment to team effort shows in the progress the Amyloid Treatment and Research Program has made in a relatively short period of time. “I started this work before it was known that primary amyloid originates in the bone marrow,” says Skinner. “We’ve made incredible strides, and it is because we have the unique qualities found in a clinical research center.”

*(Left to right)  
Vaishali Sanborawala,  
MD, Martha Skinner, MD,  
and Rodney Falk, MD*

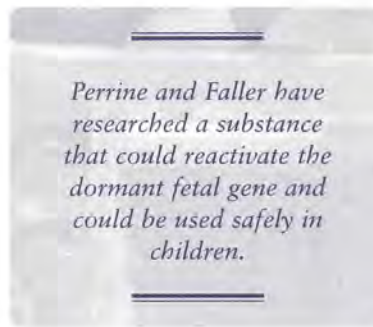


Focusing on another group of blood disorders is clinician-researcher Susan P. Perrine, MD, who has devoted a significant portion of her career to developing safe, long-term, and effective treatments for sickle cell disease and thalassemia. Perrine is the director of BUMC's Hemoglobinopathy Thalassemia Research Unit, and associate professor of medicine, pediatrics, and pharmacology. She is also an associate professor of experimental therapeutics.

Afflicting millions worldwide, this group of blood disorders is among the most common of the genetic diseases. Also referred to as beta-hemoglobinopathies or the beta-thalassemias, the conditions result from mutations in the adult beta-globin gene, or a region controlling the expression of that gene.

Though both diseases are genetically linked, they differ in their presentation. Normally, oxygen-carrying red blood cells are doughnut-shaped and flexible. The flexibility allows them to pass through arterioles and capillaries. However, in sickle cell disease, a genetic mutation causes red blood cells to become stiff and curved—like a sickle—after delivering oxygen to the peripheral tissues. Unlike their healthy counterparts, these cells cannot easily pass through arterioles and capillaries, and may obstruct them.

While sickle cell disease is the result of a genetic mutation that affects the shape of red blood cells, thalassemia is related to the rapid death of these cells. The bone marrow produces massive quantities of red blood cells that die relatively quickly, leaving the patient extremely anemic and usually dependent upon blood transfusions to live.



#### Turning on dormant genes

Perrine, along with Douglas Faller, MD, PhD, director of BUMC's Cancer Center, professor of medicine, biochemistry and pediatrics, and research professor of pathology and laboratory medicine, has been working on ways to reactivate a fetal hemoglobin gene as a long-term treatment for sickle cell and thalassemia. According to Perrine, it was well known that infants born with both diseases did not show any signs or symptoms of disease until after they were about four to six months old. No signs of disease or illness existed *in utero*. "It is also well known that fetal hemoglobin is switched off at this time. In rare cases, when fetal hemoglobin continues to be expressed (approximately 20 percent of cases), the disease does not cause problems," says Perrine. Extensive work in the laboratory and in rare cases has subsequently shown that fetal hemoglobin prevents red blood cells from sickling.

Perrine and Faller have researched a substance that could reactivate the dormant fetal gene and could be used safely in children. Perrine's work led to the discovery that when a metabolite (similar to the natural fatty acid butyrate) is present in high levels in developing infants, it prevents fetal hemoglobin from "switching off." This in turn led to the development

of new drugs and new clinical trials to carefully evaluate their effects. As a result, Perrine and Faller are currently working on several multicenter, international Phase II clinical trials that involve regulating genes with drugs to potentially benefit sickle cell disease and beta-thalassemia, as well as a specific type of lymphoma. The goals of these current trials are to determine if specific therapies can heal refractory leg ulcers in



*Susan Perrine, MD*

patients with sickle cell disease, increase red blood cell counts and eliminate blood transfusions in beta-thalassemia, and cure patients of usually fatal Epstein-Barr virus-associated malignancies.

A recently concluded trial examined the effect of pulsed butyrate therapy in sickle cell patients. According to Perrine, "In nine out of eleven adult patients with severe sickle cell, a regimen of pulsed butyrate reactivated the fetal hemoglobin gene to the necessary level of 20 percent or more. In treated subjects, the number of days of hospitalization for pain crises associated with sickle cell disease decreased by 75 percent—from eighty days per year to nineteen days per year."

**B**reast cancer may be a disease with which clinicians and the lay public have more familiarity than they do with the beta-hemoglobinopathies or amyloidosis; however, it is no less challenging for those attempting to find preventive and curative therapies. Maureen T. Kavanah, MD, associate professor of surgery, and Marianne Prout, MD, associate professor of public health and medicine, and assistant professor of surgery, have seen their work benefit from the integrated, multidisciplinary approach central to BUSM's mission.

That mission was particularly evident to Kavanah, who completed the two-year surgical oncology fellowship at BUSM in 1981—one of the original surgical oncology training programs in the United States—under the direction of Peter J. Mozden, MD, professor emeritus of surgery. As one of the first women trained in surgical oncology, Kavanah emphasizes, “The members of the Section of Surgical Oncology were highly skilled surgeons and oncologists who also had the warmth and compassion necessary to help patients and their families deal with the complexities of cancer diagnosis, treatment, and follow-up care.” During the program, Kavanah also received training in multidisciplinary approaches to care, including medical oncology and radiation oncology. At the basis of each treatment plan was a thorough analysis of the underlying pathology and radiologic studies.

*The extensive clinical research conducted by Kavanah, Prout, and their colleagues has shed the first light on a new era in breast cancer chemoprevention.*

#### **A new era of preventive oncology**

The comprehensive approach to treatment clearly evident in Kavanah's fellowship training has contributed to the clinical research she and Prout conduct. “We work closely with our colleagues in an integrated, multidisciplinary method,” says Kavanah. “We have also had a long experience participating in National Cooperative Clinical Trials, founded by the National Cancer Institute.”

The extensive clinical research conducted by Kavanah, Prout, and their colleagues has shed the first light on a new era in breast cancer chemoprevention. As chemoprevention has been successful in other areas of medicine, so now it is occurring within oncology. Kavanah is hopeful about the future of this preventive approach. “We know that a lot of research effort and attention will continue in this direction as we concomitantly move toward treating patients with diagnosed malignancy,” she says.

Toward that end, Kavanah's and Prout's association with the National Surgical Adjuvant Breast and Bowel Program (NSABP) center at BUSM has been crucial. The NSABP, a cooperative group formed in 1971 to conduct clinical trials in breast and colorectal cancer research, is funded primarily by the National Cancer Institute (NCI). BUSM was first designated a NSABP site in 1971. Kavanah was the protocol chairman of the NSABP's Breast Cancer Prevention Trial (BCPT). “The NCI recently termed this the ‘hallmark study of the century’ as far as breast cancer prevention is concerned,” says Kavanah. In addition, Kavanah was made national chairman of the BCPT in 1994; later that year, Prout took over the role of principal investigator. Owing to the scrupulously careful manner in which that trial was conducted, BUSM's NSABP center has been selected to participate in the upcoming Study of Tamoxifen and Raloxifene (STAR) trial. This twelve-year, multicenter clinical trial will study the effects of tamoxifen and raloxifene on postmenopausal women considered at risk for breast cancer.

*Below left: (left to right) Deborah A. McDonald, certified clinical research associate, Maureen Kavanah, MD, and Elizabeth Pottier, certified clinical research associate*

*Below right: (left to right) Marianne Prout, MD, and Christine Hamori, MD*



# HEALTH SERVICES RESEARCH

Supporting changes in practice and policy

**H**health services. To some, the term might sound more like a university clinic than a university department. However, this relatively new area of study has occupied the time and attention of many researchers at Boston University School of Medicine (BUSM) and the Boston University School of Public Health (SPH).

Health services is a growing field aimed at using both traditional, basic methodologies and nontraditional methods to answer a broad range of questions about the practice, policy, financing, and delivery of medicine. Investigators studying the field look at a complex web of issues ranging from macroeconomic concerns about how governments approach health care financing to front-line clinical problems, including ever-shrinking patient appointment lengths and concerns about the safety of certain drugs.

BUSM, in conjunction with the SPH, has been at the forefront of this unique and far-reaching field since the early 1970s. Faculty and clinicians involved with this research include practicing primary care physicians, Veterans Administration (VA) research staff, policy and legal analysts, epidemiologists, and biostatisticians.

**Leading the way in health services**  
Mark Prashker, MD, MPH, is associate professor of medicine and public health at BUSM, and chair of the SPH Health Services Department. In addition to overseeing the department and its staff of thirty-six full- and part-time faculty, Prashker also

*"We want to be certain that the tools we provide are based on sound, logical, and methodically appropriate reasoning based in valid data."*

Mark Prashker, MD, MPH

heads the Center for Health Quality Outcomes Economic Research, a VA Field Service Program.

The Health Services Department's course of study offers students opportunities for field practice experience, as well as directed research projects in long-term care, administration, public-private sector agencies, and maternal and child health. Training students for this incredibly diverse field is more important now than ever before.

According to Prashker, "This is really the golden age of health services research, ironically due in part to the failed Clinton health care reform proposal." Although the attempt to reform health care delivery, policy, and practice on a national level did not succeed, Prashker does see the attempt as spurring both the funding and interest in this area of study. "Consider that although we did not have a drastic overhaul of the health care system, the public and

private sectors have moved forward on a number of the issues surrounding the ideas proposed in the Clinton reform package. One great example is the VA—they've consolidated from 128 hospitals into 22 integrated delivery systems," says Prashker.

In addition, recent trends toward the consolidation of the private health care industry will also result in significant changes in both the way patients access care and the manner in which that care is provided. "With the mega-mergers occurring in health care insurance, people are actually facing what they claimed would be the downfall of health care reform: reduced choices," comments Prashker. It is precisely those kinds of consolidations—and the resulting effects on patient and provider—that health services researchers study. However, they examine these macro-trends (and other microscale effects) in hopes of gleaning valuable clues about how similar decisions might affect structure, patient care, clinical responses, treatment decisions, and standards of care in other health care organizations.

Health services investigators, though, are concerned with more than simply understanding cause and effect—they seek to provide clinicians, policy-makers, and health care administrators with tangible tools to support appropriate and beneficial changes. "We want to be certain that the tools we provide are based on sound, logical, and methodically appropriate reasoning based in valid data," says Prashker. The programs at BUSM and SPH rank among the best in the United States in terms of assessing health care quality, policy,



Mark Prashker, MD, MPH

economics, management, and issues associated with access to care. "We're conducting very cutting-edge work in terms of developing the methodological framework for addressing health services questions," Prashker adds.

Prashker also emphasizes that the work is not limited to analysis of existing data. "We also do a great deal of primary data collection in large cohorts of patients." The VA is one large patient cohort that provides a substantial population that Prashker's colleagues can use to collect such invaluable primary data. "The relationship between SPH, BUSM, and the VA network is symbiotic," Prashker emphasizes, "and we're very aware of our good fortune in having that kind of relationship."

#### Impact of health services

Addressing the direct impact of health services research on his clinical practice is Mark Moskowitz, MD, professor of medicine and public health at BUSM, and chief of the Section of General Internal Medicine at BUMC.

Like Prashker, Moskowitz has conducted primary data collection, but concentrates more frequently on the use of large administrative databases. His belief is that health services applications should be used to support changes implemented in various aspects of medical care. "We need a logical, methodical approach to the changes we decide to make. We should not simply base change on one physician's notion that something is a good idea. Health services data allow us to use a very scientific methodology to support change," says Moskowitz.

Moskowitz and his colleagues have made liberal use of a unique outgrowth of health care informatics in the United States: the accumulation of, and access to, large administrative databases. Within that framework, they have focused on three very specific issues: access to care, quality of care, and outcomes of treatment. The idea that nonbasic, nonclinical

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*"We should not simply base change on one physician's notion that something is a good idea. Health services data allow us to use a very scientific methodology to support change."*

Mark Moskowitz, MD

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research will effect change in that triumvirate may appear unusual to a "traditional" basic researcher; however, Moskowitz points to several large databases as key to understanding the enormous value inherent in this kind of approach.

"In 1997, there were 39 million people enrolled in Medicare, 37 million in Medicaid," says Moskowitz, "and of those patients, we have access to data for about 700,000 cases of congestive heart failure, 450,000 cases of pneumonia, and 370,000 cases of chronic obstructive pulmonary disease."

Moskowitz and his colleagues also identified the VA database and other Health Care Finance Administration databases as equally rich veins of material to be mined for health services analyses.



Mark Moskowitz, MD

#### Tangible impact on practice

There is a growing body of clear evidence that these very large data collections will continue to result in studies that will have a tangible impact on clinical practice. The VA population was recently the subject of a study Moskowitz conducted in cooperation with Daniel Berlowitz, MD, MPH, associate director of the VA Center for Health Quality, Outcomes and Economic Research at the Bedford VA Medical Center, and an associate professor of medicine at BUSM.

The study, published in the December 31, 1998, issue of *The New England Journal of Medicine*, provided some interesting findings about the management of hypertension. It determined that physicians failed to adequately control hypertension in many patients even though excellent medications are available to achieve such control. Access to care and cost of care were both ruled out as impediments to treatment. Because so many clinical trials have proven the efficacy of treating hypertension to prevent cardiovascular disease and stroke, the study findings are significant in their call to physicians to reassess their treatment for, and management of, hypertensive patients.

It is precisely this practical application, derived from health services research, that Moskowitz and Prashker believe must become a vital part of medicine — particularly when there is sound evidence that prevention can dramatically alter disease pathology and outcomes. In turn, costs for tertiary care can be dramatically reduced when prevention is so clearly proven to be effective. "We can all agree that hypertension is a condition that needs to be treated, and that the failure to do so results in serious consequences," says Moskowitz. "Yet our study clearly demonstrates that physicians are not aggressively treating hypertension or taking the simple, necessary steps to reduce high blood pressure."

### Arthritis research

The accuracy of the recently completed Framingham Heart Study (FHS) has been so well established that it continues to be used extensively by BUSM researchers to provide very reliable conclusions about a number of health concerns. David Felson, MD, MPH, professor of medicine, epidemiology and biostatistics, would not necessarily refer to the work he conducts as "health services"; however, his is the kind of close, careful analysis of existing data that is the essence of appropriately applied health services work. As director of the NIH-funded Multipurpose Arthritis Center, Felson has had the opportunity to work with Framingham data with the goal of developing preventive measures for this debilitating condition.

His recent study, conducted in collaboration with BU researcher Christine Chaisson, MPH, examined the correlation between grip strength in the proximal hand joints (metacarpophalangeal joints and thumb base) and the development of osteoarthritis. According to Chaisson, this is the first study to examine the relationship of osteoarthritis and grip strength in different types of hand joints. "The forces at the joint and the frequency those forces are applied is new territory in arthritis research," notes Chaisson. "We've had some studies about hand biomechanics that show force along the joints, but no one has evaluated this particular association before."

The fact that Felson and his colleagues can conduct research programs that look at such previously unexamined connections is intimately tied to one of the primary goals of health services research: effecting change in outcomes based on solid evidence that practical preventive measures do exist and should be implemented, and that via that implementation, tertiary care costs would be greatly reduced.

### Drug epidemiology

While access to large administrative data sources provides health services researchers with an existing pool of information for analysis, other contributions to health services data are being made at the Slone Epidemiology Unit (SEU). Founded in 1975 at BUSM, SEU is a multidisciplinary, internationally recognized research group with specialists in epidemiology, adult and pediatric medicine, nursing, pharmacy, biostatistics, and computer science.

Currently under the direction of Allen Mitchell, MD, professor of pediatrics, epidemiology and biostatistics, the SEU has been involved with a number of groundbreaking studies. "The work here is a complementary approach to the work being conducted by health services researchers at BUSM," says Mitchell.

The mission of the SEU is to identify and quantify the occurrence of diseases caused by medications and lifestyles and to provide estimates of the risks and safety of drugs in relation to specific diseases. According to Samuel Shapiro, MBCh, director emeritus of the SEU, and professor of epidemiology and biostatistics, "We test hypotheses and try to discover previously unsuspected associations involving drugs." Proving out those hypotheses requires careful and assiduous epidemiological work. "We must be constantly vigilant against error, and against the temptation to make inferences where none exist," he adds.

### Programs at SEU

The many programs currently underway at the SEU have the potential to provide health service investigators and front-line clinicians with information that can be used to identify interventions, both on a policy level and in daily clinical practice, that can reduce the burden of disease caused by medications and lifestyles. The tangential relationships with which health services researchers are con-

cerned are inherent in some of the large case-control and cohort studies SEU is overseeing.

One such program is the birth defects case-control study. This ongoing study has accumulated information on more than 18,000 infants born with birth defects in more than eighty institutions in Boston, Philadelphia, and Toronto. The program is designed to provide a national data source for both the identification of previously unsuspected associations and the testing of hypotheses relating environmental agents—particularly medications—to birth defects. This research has supported the now-accepted observation that folic acid intake in pregnant women can decrease the likelihood of an infant developing spina bifida by 30 to 40 percent.

Another current study, which will eventually provide investigators with an invaluable collection of data, is the Black Women's Health Study. This study is following more than 65,000 African-American women to assess risk factors for heart disease, cancers, and other major illnesses. It will also provide information on demographic factors, reproductive and contraceptive histories, cigarette and alcohol use, physical activity, height, weight, and use of certain medications.

Other research programs at SEU have investigated the effects of cigarette smoking, alcohol, and oral contraceptives on cardiac health and certain cancers in women; rare but serious adverse effects of ibuprofen in children; and the effectiveness of health promotion campaigns designed to modify parents' behaviors to reduce the risk of sudden infant death syndrome. Health services investigators may be able to pose difficult questions based on the data gathered by SEU, and if previous efforts shown by SPH and BUSM researchers are any indication of success, they will come up with some valuable, practical, and applicable answers.

# BOSTON MEDICAL CENTER PLANS FOR THE FUTURE

*New outpatient facility and quadrangle to connect campuses*

**B**oston Medical Center (BMC) is moving forward with plans to construct a new ambulatory care facility to help maintain and improve the quality of care provided to patients for many years to come.

The new facility is the current focus of a BMC master plan project, which will create new space for the hospital, modernize existing facilities, and remove some of the unusable vacant buildings that currently form a physical barrier in the middle of the BMC campus. Construction of the new ambulatory care facility is slated to begin in July 1999, with a projected completion date of March 2001.

The master plan is progressive in its vision to unify the medical campus by creating a central campus quadrangle and integrating existing facilities with a new ambulatory care facility. The plan is respectful of the neighborhood's past in re-establishing an important urban design relationship with the adjoining South End Landmark District. "Boston's South End has a rich and vibrant architectural history," says Elaine Ullian, BMC president and CEO, and associate professor of public health.

"We are working very closely with the local historical associations and preservation experts to retain the grandeur and architectural integrity of our neighborhood."

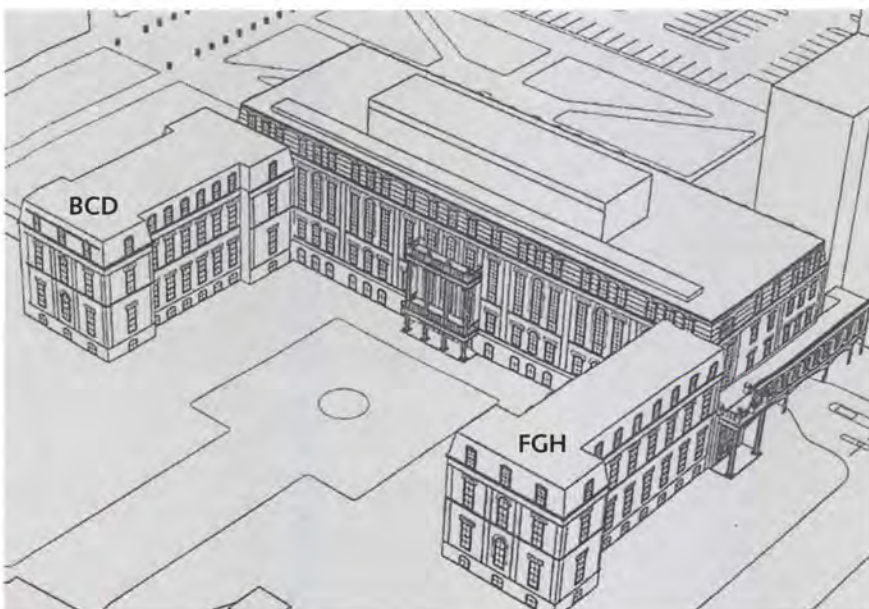
The Administration Building, located between the BCD and FGH buildings on Harrison Avenue, will be demolished to make way for the state-of-the-art ambulatory care facility. The new construction will provide much-needed additional space for ambulatory and critical care, the areas of largest growth at BMC.

Renovations to the BCD and FGH buildings also play important roles in the new plan. BCD has been vacant for twenty years and exterior stabilization and facade restoration, along with various interior repairs, are needed. It is envisioned that the space will be used for clinics and doctors' offices.

The proposal also calls for the demolition of the Thorndike, MRI, and Sears buildings lining East Concord Street. With the removal of these buildings, the various existing small open spaces on each of the separate campuses will be combined to form a central quadrangle.

"Unlike many urban medical centers, which have little real estate space for new projects and campus development, Boston University Medical Campus (BUMC) has sixteen acres of available land on the BioSquare site and a number of existing campus buildings, all of which provide us with a wide array of options for development and renovation," says Richard Towle, vice president, Administrative Services, Boston University. "As a result, BUMC is well positioned to meet its space needs through the next decade."

*Architect's rendering  
of the new ambulatory  
care facility.*



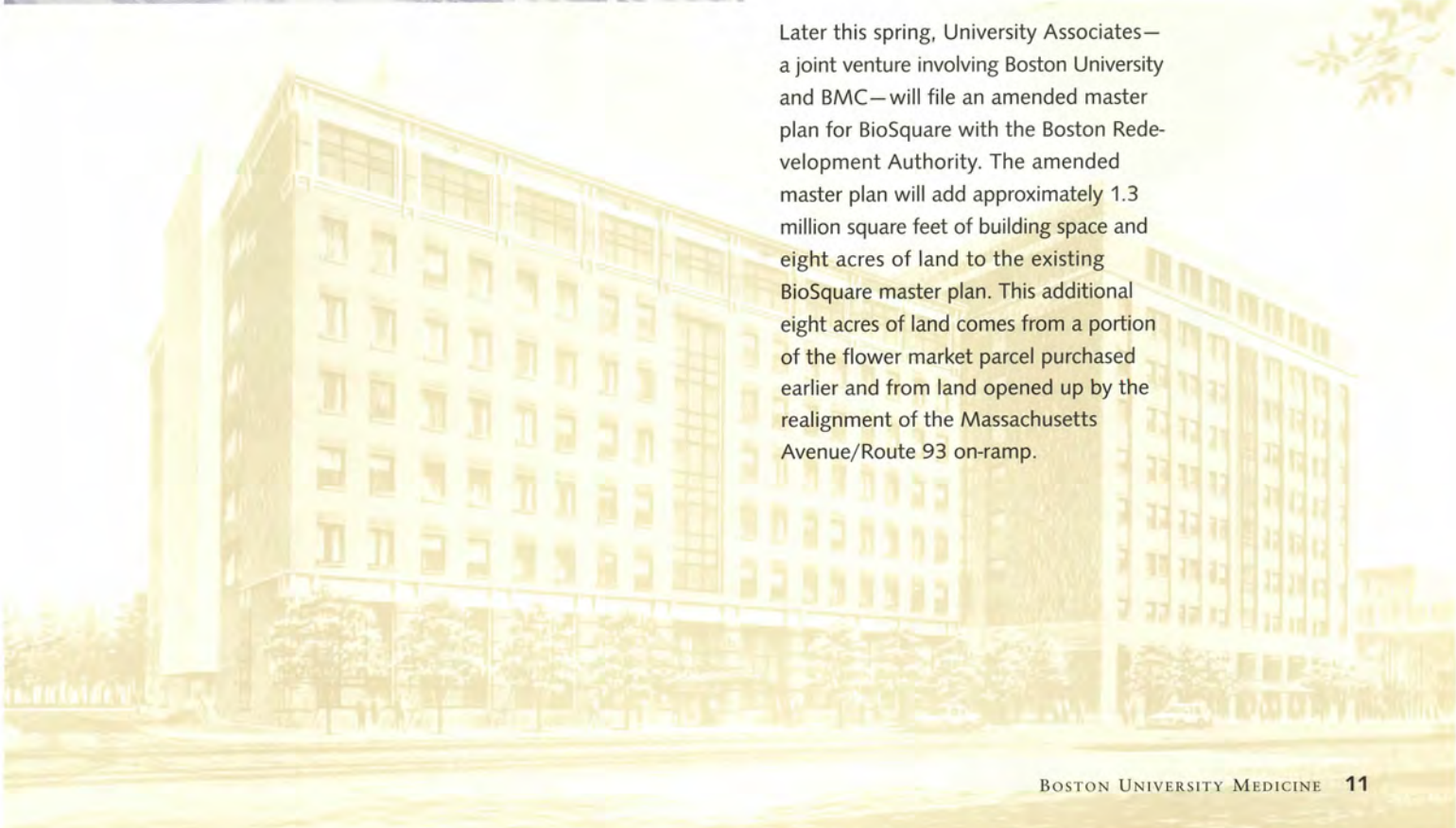


## BIO SQUARE PROGRESS REPORT

BioSquare's current master plan provides for the development of 1.2 million square feet of building space on eight acres of land along Albany Street. The plan includes four research/office buildings, a 1,000-space parking garage, 5,600 square feet of retail space, and a 230-room hotel.

The second BioSquare building, to be known as Evans Biomedical Research Center, is currently under construction and scheduled to be completed in January 2000. In addition to housing the Evans Medical Foundation at Boston Medical Center (BMC), the Evans Biomedical Research Center will be the new home of Oncogene, Inc., a life-sciences company based in San Diego.

Later this spring, University Associates—a joint venture involving Boston University and BMC—will file an amended master plan for BioSquare with the Boston Redevelopment Authority. The amended master plan will add approximately 1.3 million square feet of building space and eight acres of land to the existing BioSquare master plan. This additional eight acres of land comes from a portion of the flower market parcel purchased earlier and from land opened up by the realignment of the Massachusetts Avenue/Route 93 on-ramp.



# BUSM AFFILIATES OFFER STUDENTS GREATER OPPORTUNITIES FOR LEARNING

Medical education shifts from inpatient to outpatient settings

It used to be that medical school students primarily trained by seeing patients and following attending physicians in large teaching hospitals. These days medical students are seeing patients in a variety of settings—community hospitals, doctors' offices, neighborhood health centers, and even patients' homes—as well as in the traditional, tertiary care hospital. Much of the reason for this change is the recent shift in patient care delivery from inpatient to more outpatient treatment, which has had a direct effect on the education of medical students.

At Boston University School of Medicine (BUSM), that shift is the force behind the School's decision to form affiliations with several area community hospitals and neighborhood health centers, which offer medical students the opportunity to see patients in outpatient settings. BUSM has as its principal hospital affiliates the Boston Medical Center and the Boston Veterans Administration Medical Center. In addition, BUSM now has affiliations with more than twenty hospitals throughout New England and twelve neighborhood health centers through the Boston HealthNet. Some of the larger affiliated institutions include Roger

*“Developing relationships with other hospitals ensures that BUSM students are exposed to a greater selection of patients, especially in the primary care field.”*

John McCahan, MD

Williams Medical Center in Rhode Island; Bedford Veterans Administration Hospital; Beverly Hospital; and Brockton Hospital. In addition to regional hospital affiliations, BUSM also has limited affiliations with several international medical schools and hospitals in Israel, Italy, Hong Kong, Armenia, and the Camerouns.

## Adapting to changes in delivery

The enormous economic pressure that health care institutions have faced since the 1980s has profoundly changed the health care delivery system, resulting in an ongoing trend to have fewer patients admitted to hospitals for shorter lengths of stay. This, in turn, translates into an inpa-

tient population with greater severity of illness, which is more skewed and less representative of the general population. A larger percentage of patients who are admitted to the hospital come in for specific procedures that are relatively technical or for treatment of end-stage disease.

Another important health care trend in recent years is the emergence of family medicine and primary care as key specialty areas. BUSM's growing affiliates network allows students to see family medicine and primary care patients in smaller community hospitals, as well as in neighborhood health centers and doctors' offices.

“Due to shifts in health care trends, BUSM has adapted its medical curriculum to meet the needs of tomorrow's physicians, with a change from students following doctors around the large teaching hospital to that of students being trained in settings that offer primary care,” says John McCahan, MD, associate dean for Academic Affairs and professor of family medicine. “Developing relationships with other hospitals ensures that BUSM students are exposed to a greater selection of patients, especially in the primary care field.”





John McCahan, MD

In response to the growing importance of family medicine, BUSM was the first medical school in Boston to develop a full-fledged Department of Family Medicine. Formed in 1997, the department was established as a specialty for training future physicians to care for patients across the board, with an emphasis on outpatient care.

BUSM's Department of Family Medicine works closely with the Boston HealthNet, a partnership between BUSM, Boston Medical Center, and twelve community health centers, which provides a broad spectrum of primary health care services in neighborhood settings. The HealthNet health centers are the primary teaching sites for most community-based learning for first- to fourth-year BUSM students in pediatrics, internal medicine, and family medicine. Through grants from the Robert Wood Johnson Foundation and the Kellogg Foundation, these centers have become a national model for the development of academic community health centers.

"Boston HealthNet health centers provide students with an opportunity to learn about the communities they are serving, to understand the connection between environment and health, and to understand multicul-

turalism and its connection to health and health belief," comments Lisa Levine, MPH, associate director, Generalist Physician Initiative of the Center for Primary Care. "This experience allows students to really be part of a community service organization, and to follow through with continuity of care, since students who start in a health center in the first year of medical school usually stay for the duration of their four years."

#### **Clerkships provide opportunities**

Another vehicle for medical students' hands-on experience, third-year BUSM clerkships have evolved in recent years to give students more training at newly affiliated institutions. For example, third-year students currently serve in clerkships at Roger Williams Medical Center through the departments of Medicine and Surgery.

A vital part of the Rhode Island community for more than one hundred years, Roger Williams is recognized throughout the nation for innovative programs in cancer research and treatment, health care, education, and medical research. It has been a fully operational major clinical affiliate of BUSM since July 1997. The 220-bed acute care hospital includes a 14-bed intensive care unit and the only bone marrow transplant unit in Rhode Island. Since the affiliation, more than forty

Roger Williams physicians have been appointed to faculty positions at BUSM. Under the partnership, BUSM students rotate through clinical clerkships at Roger Williams, receiving instruction from the hospital faculty.

This year, Roger Williams was named as one of the one hundred best hospitals in the United States in an annual study conducted by HCIA, Inc., and William M. Mercer, Inc., to establish industry benchmarks and identify those institutions that have demonstrated superior performance.

"Roger Williams is not a typical community hospital because it has a long academic tradition and a strong teaching faculty," says Michael Macko, MD, site director for Medical Clerkship and director of Continuing Medical Education at Roger Williams, and associate clinical professor of medicine at BUSM. "We get feedback from BUSM students that they are very satisfied with their clerkships at Roger Williams because of the teaching level and the high ratio of direct mentoring of students by faculty."

The expanding relationships with BUSM affiliates also support the School's philosophical intent to get students immediately involved with practicing physicians from the first day of medical school. The School is more able to accommodate those students who want exposure to different types of patients in a variety



Roger Williams Medical Center

of settings, as well as other students who wish to have continuity with particular patients and facilities over prolonged periods.

For Betsy Ciarimboli, a fourth-year student anticipating a career in psychiatry, rotations in community hospitals such as the MetroWest Medical Center, the Bedford VA, Brockton Hospital, and Roger Williams Medical Center have broadened her exposure to patients in smaller facilities. It is a more personal approach. Students are not assigned to one doctor, but rather follow different attending physicians, each treating his or her own patients. "During my clerkship at Roger Williams, I got to see patients alone in their rooms, to talk to them one-on-one about what was happening to them each day during their hospital stay, and really develop a relationship with them," says Ciarimboli. "We saw general medicine patients, ranging from pneumonia to end-stage cancer, what I think of as 'bread and butter' medicine."

Another important affiliate agreement is with the Family Practice Residency Program at Beverly Hospital, which went into effect in July 1998. As an academic partner in family medicine, BUSM supports the Family Practice Residency Program's faculty teaching and affords faculty and residents more extensive research and clinical opportunities than in the past. As part of the partnership,



*Betsy Ciarimboli*

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*"During my clerkship at Roger Williams, I got to see patients alone in their rooms, to talk to them one-on-one about what was happening to them each day during their hospital stay, and really develop a relationship with them."*

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Betsy Ciarimboli

BUSM students serve clerkships in family medicine at the hospital and its residency practice. Likewise, family medicine physicians have received faculty appointments at BUSM.

"Because we are a community-based residency program, student interest in the Family Practice Center is notably high," says Mark Mengel, MD, MPH, program director of the Beverly Hospital Family Practice Residency Program. "Through the unique academic, clinical, and research programs at Boston University School of Medicine, we look forward to training a new generation of family physicians who will provide high-quality family practice services to the residents of Beverly and surrounding communities."

#### **A unique partner in the VA**

One of the established affiliate relationships is the School's association with the Boston Veterans Administration (VA) Medical Center, a 250-bed facility established in 1950. The partnership has served both institutions well. BUSM's affiliation with the VA provides a faculty with advanced knowledge and expertise to participate in the care of veteran patients. Most of the veteran patients who receive medical care at the VA are elderly, and by and large suffering from advanced stages of disease. The students, residents, and physicians who work at the VA are often challenged by the complexity of these cases, and learn a great deal about

pathophysiology and management. The patients' ages and social situations are also important factors.

"Caring for these patients, especially on the Surgical Service, requires a great deal of consideration of the risks versus the benefits of intervention," explains Nancy L. Cantelmo, MD, associate professor of surgery and director of Surgical Clerkships at BUSM, and associate chief of Surgery at the Boston VA Medical Center. "As a result, trainees participate in the care of patients with complex medical and social problems. Sharing faculty in patient care, lectures, and conferences has benefitted both institutions."

Research is another area of shared benefit for the VA and BUSM. VA grants for both clinical and basic science provide residents and students with research opportunities. Annually, the VA receives approximately \$10 million in VA research funds, and Boston VA principal investigators receive another \$4 million in funds from the NIH.

"The VA has a distinctive patient population," says Robert Arbeit, MD, associate chief of staff for research at the Boston VA Medical Center, and professor of medicine at BUSM. "Research conducted by VA principal investigators is targeted to problems and issues that are relevant to this special patient



# BOSTON MEDICA

population, and the result is that it's focused on cutting-edge research in basic and clinical science and health services that relate to the specific problems that are a challenge to the VA."

## Trend toward outpatient care

The trend toward more outpatient care is also evident at BUSM's principal affiliate, Boston Medical Center (BMC), which itself is a vital resource for learning opportunities for BUSM students. As the anchor patient-care institution on BUSM's campus, BMC is devoted to training future generations of health care professionals. BMC operates thirty-eight residency training programs with more than 450 resident positions. The central role that BMC plays administratively and clinically is illustrated in the fact that all clinical chiefs of service at BUSM are also clinical chiefs of service at BMC.

BMC has responded to the same forces in health care that other institutions have by increasing its outpatient service for patients in all specialties (see story on page 12). "BUSM students are afforded an opportunity to experience a variety of health care settings in placements throughout the network of affiliates, including BMC," says McCahan. "This experience establishes some sense that what they are learning is universal and is applicable in different settings. It's a much more enriching learning experience."

BMC and BUSM have developed a long-standing relationship in the area of geriatrics, both in patient care and medical training. BUSM is one of only a handful of medical schools that require a fourth-year rotation in geriatrics with the unique feature of taking outpatient medicine, including medical students, to

patients in their homes, as well as to those in Boston-area nursing homes. The home-care program was established in 1875 and is the oldest continuously operating home medical service in the United States.

Geriatric home and nursing home patients have a wide range of chronic medical problems, such as diabetes, congestive heart failure, dementia, urinary incontinence, and immobility. Students are exposed to a collaborative practice model that includes physicians, nurse case managers, nurse practitioners, and social workers with advanced training in geriatrics.

Home visits give the geriatric team an opportunity to evaluate aspects of the patient's care, both medical and nonmedical, that may not be apparent during a traditional office visit. Medical students are exposed to nonmedical issues that include transportation problems,

insurance issues, and community resources. Many of the students are able to spend an observational day in the field with nurses from the Visiting Nurse Association of Boston, and most spend time at an adult day health program.

Nursing home care gives the medical students an opportunity to care for the institutionalized frail elderly who need ongoing primary care, with additional exposure to Alzheimer's disease and other dementias, which are growing at an exponential rate.

Through the experience gained during clerkships at affiliated institutions, medical students gain access to more diverse patients. Another added benefit is that students gain exposure to a larger group of faculty so that the student-to-faculty ratio is very low. Students often have an opportunity to work one-on-one with an experienced physician. "The undiagnosed, undifferentiated patient is the best teacher for students," explains McCahan. "These types of patients are most often seen in outpatient settings. We need to be able to have our students work with patients before they require the highly specialized care usually given in a hospital."

*The central role that BMC plays administratively and clinically is illustrated in the fact that all clinical chiefs of service at BUSM are also clinical chiefs of service at BMC.*

# BUSM HONORS SENATOR KENNEDY

Concluding a year-long celebration of BUSM's 150th anniversary, the school honored Massachusetts Senator Edward Kennedy last November for his longtime commitment to biomedical research and medical education, as well as his overall support of Boston University School of Medicine.

At a ceremony held in the Hiebert Lounge, Kennedy was presented with a special Sesquicentennial Gold Medallion from Dean Aram Chobanian and Boston University President Jon Westling. "This is the most fitting way I could imagine to close our year-long sesquicentennial celebration—by awarding this medal to Massachusetts' senior senator, with whom this campus has had such a long-standing, close relationship," Chobanian said. Kennedy also received praise from Boston University Chancellor John Silber, BMC President and CEO Elaine Ullian, Boston Mayor Thomas Menino, and Westling.

Lauding the School's commitment to public health, community-based medicine, and advancing medical research, Kennedy said he will continue to support BUSM to the best of his abilities. "One in \$10 from the National Institutes of Health comes to Massachusetts—and much of this funding supports research at Boston University," he said. "Our goal over the coming years in Congress is to double the budget of the NIH. The potential benefits are vast, and I am optimistic that we will succeed. At Boston University, that support is an especially wise investment in the future—for patients, for doctors, dentists, nurses, and other providers, for researchers, and for taxpayers—and I intend to do all I can to see that it is strengthened."

During the presentation, Chobanian highlighted some of Kennedy's legislative accomplishments, which have been of great importance to biomedical research and medical education. His achievements include being the original sponsor of the Comprehensive Health Manpower Act of 1971, which assisted medical schools in designing new programs responding to the demands of the changing health care environment; being the original author of the National Health Service Corps, through which financially disadvantaged students attend medical school in exchange for providing care for the underserved in rural and urban areas after they have completed their training; and supporting health care and educational programs for minorities and women.



*Senator Edward Kennedy*

Silber praised Kennedy's record in Congress, saying, "Senator Kennedy has been, for more than thirty years, in a position to influence the passage of health care legislation for all. Additionally, he has been effective in preventing the passage of legislation that would have been harmful to medical students, public health, and medical research."

The ceremony marked the end of a year of events celebrating the sesquicentennial milestone, including the first Alumni Career Day, the Women in Medicine Awards ceremony, the Rebecca Lee 5K Road Race, the Convocation, the gala, a piano recital, a Cardiovascular Symposium in honor of the twenty-fifth anniversary of the Whitaker Cardiovascular Institute at BUSM, an international symposium on the brain, and numerous other scientific conferences.



*From left: Boston University President Jon Westling, Senator Kennedy, and Dean Aram Chobanian*

The student body at BUSM comprises a number of outstanding individuals. Featured here are some of the talented students and their varied interests in science and medicine.

### Nicholas Husni, '99

Nicholas Husni, who will graduate this month with a combined MD-PhD degree, was invited to speak at the thirty-fourth Annual Meeting of the European Association for the Study of Diabetes, in Barcelona, Spain, last fall. He presented a portion of his PhD thesis work on tumor necrosis factor alpha and its effects on skin fibroblasts from patients with diabetes.

"My fascination with the carefully orchestrated cascade of cellular and biochemical events that culminate in the



wound-healing process began on my second day of pathology class," recalls Husni. "Not being satisfied with simply memorizing the

various stages, cytokines, and cells involved in healing by primary and secondary intention, I decided to transfer into the MD-PhD curriculum so that I might design a course of study that would satisfy my curiosity. I was able to find an ideal mentor in Barbara Corkey, PhD, director of Metabolic and Obesity Research, and professor of medicine and biochemistry at BUSM, who helped me to shape my clinically based questions into hypotheses that could be investigated by basic biochemical methods.

"Skin fibroblasts were obtained from diabetic patients, and their response to stimulation with inflammatory cytokines intimately involved in the wound-healing process was compared with cells taken from non-diabetics. Interestingly, the cells from the two donor groups varied markedly in response to stimulation with these cytokines, which caused significant differences in agonist-

mediated calcium responses and in basic calcium homeostasis itself. A tissue culture medium designed to mimic the metabolic environment encountered in diabetic patients further augmented the differences in cytokine response between control subjects and diabetics. These findings have implications for the vast array of diabetic pathologies found throughout the natural history of the disease, ranging from the inflammatory reaction that destroys the pancreatic islets in type 1 diabetes, to the recalcitrant wound healing observed in older patients."

Husni graduated from Boston College magna cum laude in 1990, and entered the combined degree program in fall 1991. During his years here, he has served as a cellist in the BUSM string ensemble and won the Karin Grunebaum Research Foundation Fellowship in 1996. He plans a career as an academic surgeon.

### James S. Chen, '02

James Chen's work as an MD-PhD candidate in the Department of Microbiology and in the Biomolecular Pharmacology Training Programs helped him earn two awards from the Pharmaceutical Research and Manufacturers Foundation. He is both an advanced predoctoral fellow and a medical student research fellow. He carried out his research in the laboratory of Douglas Faller, PhD, MD, director of the BUSM Cancer Research Center.

"I am studying a protein dubbed RING3, short for Really Interesting New Gene 3," Chen reports. "As a kinase, RING3 phosphorylates other molecules in the cell, thereby regulating their activity. Since it resides in the nucleus, RING3 probably can act on a class of cellular proteins called

transcription factors, molecules that are important in determining what types of new proteins are made in the cell. Indeed, forcing cells to produce large amounts of RING3 actually causes those cells to transform, or become neoplastic, suggesting that RING3 has an impact on proteins that are important in directing cell growth. In addition, RING3 is activated by extracellular signals, including interleukin-1 (IL-1), an inflammatory cytokine. These observations together suggest a potential role for RING3 in the development of hyperproliferative inflammatory disorders such as atherosclerosis.

"My focus is on what controls RING3's activity. By studying its regulation, I will be examining RING3's part in inflammatory signaling and will be investigating whether defects in these signals can lead to the dys-



regulated proliferation seen in atherosclerotic plaques. My preliminary results indicate that a new class of drugs, the CSAIDs (cytokine sup-

pressive anti-inflammatory drugs), can down-regulate the RING3 signaling axis by inhibiting various MAP kinase pathways, thus highlighting potential targets for intervention in RING3-mediated maladies. Intensive investigation of these pathways for IL-1 signaling will provide us with some new insight into inflammation and atherosclerosis, with the potential for developing a whole new class of therapeutics."

Chen graduated from Stanford University with a BS in 1992 and an MS in 1993 (both in biological sciences), then entered the combined degree program. His research

has won other awards, including the American Heart Association Research Fellowship, 1997; American Society of Hematology Research Fellowship, 1997; Karin Grunebaum Foundation Research Fellowship, 1996; and American Cancer Society Foundation Summer Research Fellowship, 1994.

#### Margaret S. Lee, '99

This academic year Margaret Lee, '99, who represented the student body in a performance at the Sesquicentennial Gala Ball, has made significant moves toward building her dreams of integrating cultures, sciences, and arts in medicine.

Lee was the 1999 winner of the Leah J. Dickstein Award from the Association of Women Psychiatrists, recognizing creativity, energy, and leadership.

As a first-year medical student, she cofounded the Creative Arts Society (CAS) to advance recognition of the healing potential of art and creativity. Two very successful products of CAS are the publication *Whorl* and the popular Kick Back Kafé coffeehouse event. A new project, the Arts-Healthcare Alliance brings Boston Medical Center faculty and staff and Boston artists together for performances at the hospital. "Music and poetry have been central to my personal development and well-being," says Lee, "so it is natural for me to want to share and encourage the healing power of art as a medical student and doctor."

When Lee graduated from MIT in 1992, she had already gained substantial experience in laser treatment of tatoos at the MGH Wellman

Laboratories of Photomedicine. She has continued to develop her interest in photomedicine and is currently working at the Department of Dermatology lab, studying the protective effects of thymine dimer treatment in cell cultures from exogenous oxidative damage, such as hydrogen peroxide solutions. She has already begun work for a PhD in the Department of Pathology and Laboratory Medicine.

Lee extended her fourth year of medical school to study traditional Chinese medicine in South Korea, where she was born. Although she grew up in the United States, her Korean heritage has been an important part of her identity and extends to her professional goals. She plans to combine her studies in allopathic medicine with traditional Chinese medicine and conduct research on alternative and integrative therapeutics.

In her remarks at the Gala Ball on October 10, Lee expressed her confidence in the future: "From the first class of twelve, 150 years ago, we have now grown to more than 600, coming from many backgrounds and from all across this great nation. We are informed, we are prepared, and we are ambitious. The courage and vision of these past 150 years are ours today as we carry the tradition of leadership and excellence into the next 150 years."

#### Eric R. First, '00

Botulinum toxin was once known only as a potent poison, but now it is bringing relief to thousands of patients with a variety of neuromuscular disorders as a result of some vigorous research by Eric First, '00.

First entered BUSM in fall 1994, having graduated magna cum laude from Boston University's MMEDIC program. While an undergraduate, he began a productive collaboration with L. Bruce Pearce, PhD, now an

adjunct professor of pharmacology, characterizing clinical preparations of *Clostridium botulinum* toxin, and developing an assay to assess potency. The team is also developing new and unique formulations of botulinum toxin. "Billionths of a gram of toxin are injected into a muscle or muscles affected by spasm, contraction, or intractable pain," explains First. "This causes a localized, reversible paralysis through the inhibition of acetylcholine release, which restores the muscle back to a near-normal state. Since this is a localized injection, there are virtually no side effects. The long duration of action (months versus hours of standard drugs) makes this a truly unique treatment. Botulinum toxin was approved in 1989 for the treatment of strabismus (cross-eyes). It is now used in more than 125 different indications, ranging from various dystonias, excessive sweating, and gastrointestinal sphincter disorders to cosmetic wrinkle reduction and, most recently, migraines.

"My research has focused on developing new formulations of toxin to increase the duration of action and potency, and therefore decrease the

frequency of injections.

Current clinical research focuses on botulinum toxin and pain—how the toxin decreases pain signals.

"After my first year of medical school, I took two years off to continue my research, publishing more than a dozen papers in journals such as *The Lancet*. In addition, I founded Theratox Corporation, a company specializing in botulinum toxin. Now in my third year, I continue extensive clinical research and publishing, manage an Internet site dedicated



exclusively to botulinum toxin ([www.botulinum-toxin.net](http://www.botulinum-toxin.net)), and continue to pursue the business aspects of my company.”

#### Michelle S. Hirsch, PhD, '99

During her undergraduate experience at the University of California, Davis, Michelle Hirsch became a teaching assistant in anatomy. There she met Hugh Patterson, MD, a 1977 graduate of BUSM's Division of Graduate Medical Sciences, who encouraged her to seek a doctorate in anatomy here. She entered BUSM in fall



1991. After earning her doctorate in anatomy and neurobiology in 1996, she entered the medical curriculum and will graduate in May 1999.

Hirsch's research focuses on fetal skeletal development. "The fetal skeleton is a cartilaginous tissue," she explains, "composed of chondrocytes surrounded by an extracellular matrix. I was able to create a unique organ culture model that allowed investigation of terminal chondrocyte differentiation without disrupting the cells from their natural environment. I determined that communication with the extracellular matrix, specifically through integrin receptor signaling, was important for this step in development by allowing subsequent changes in the synthesis of many proteins, including collagen molecules, metalloproteinases, and the tissue of metalloproteinase inhibitors. Changes in these proteins have been shown to be necessary, before replacement of cartilage by bone, in the developing fetal skeleton."

Hirsch plans a career as an anatomic pathologist in either surgical or forensic pathology.

#### Pedram Salimpour, '00

Pedram Salimpour is the only medical student ever to have twice received the American College of Physicians' Medical Student Research Award. Over the course of the past four years, Salimpour's research in sexual dysfunction has resulted in numerous scientific publications and several fellowships, including an Alpha Omega Alpha Medical Honor Society Fellowship and several educational



awards from pharmaceutical industry leaders. Additionally, he has been interviewed a number of times in the popular press about his research projects. This exposure has provided the opportunity for him to present papers throughout the United States and in Europe.

In the Department of Urology, Salimpour led several projects, including a study of the association between lumbosacral disc disease and impotence; the effects of compressive forces on perineal contents; erectile and urinary problems in bicyclists; the correlation of body mass index and erectile dysfunction; and a study of novel 3-D imaging systems for use in laparoscopic surgery. He has presented the findings of these studies at local, national, and international scientific meetings and has succeeded in conveying a clear message to an interested public: "For years people thought that sexual dysfunction was psychological. Working with Dr. Irwin Goldstein, professor of urology, BUSM, we've shown that it is the result of physiological components: bicycling, cholesterol, drug interactions, and high body mass index. These findings have had a remarkable social impact."

As an undergraduate at the University of California, Riverside,

Salimpour served as chairman of student government and upon graduation was inducted as a member of the Chancellor's Honor Society. Later, he earned a master's degree in pharmaceutical economics at UCLA. Before medical school, Salimpour worked as a lobbyist in Washington, DC, as well as in advertising in Los Angeles. He continues his interest today as a medical consultant to BBDO Advertising, among whose accounts is that of the British Health Service.

#### Janetta Cureton, '00

Janetta Cureton will enter the third year clinical clerkships in a few weeks with a year's experience as a Congressional Fellow in the US House of Representatives.

Last spring she won a fellowship through the Congressional Black Caucus Foundation. Later in the summer, she began her fellowship in the office of Congressman Edolphus Towns (D-NY)—the ranking minority member of the Human Resources Subcommittee of the Government Reform and Oversight Committee. As a Congressional Fellow, Cureton



used her strong science background to conduct research and shape public policy on the safety of the US blood supply and the shortage of immunoglobulins currently available. "It gives you a different perspective on the issues," says Cureton. "I understand the process now, and see that a proposal might sound really good, but when you apply it, it may not work."

During the recess and into the new year, she spent time at the National Cancer Institute in the Office of Special Populations Research. "I've been doing some

data analysis on the importance of the underserved in clinical trials and becoming familiar with the grants process. You could call it a lesson in the politics of cancer.”

Cureton graduated from Clark Atlanta University in 1996 with a BA in biology and entered BUSM through the Early Medical School Selection Program.

### Selene Parekh, '99

Selene Parekh will graduate this spring as one of a new breed of alumni: MDs with MBAs. For Parekh, the MBA program was a nice complement to the MD education—teaching different teamwork skills, and problem-based case evaluations



to reinforce creativity and “thinking outside the box,” a skill useful in both medicine and business. “I plan to continue my involvement with outcomes-

type research as a resident,” says Parekh. “As an attending physician, I hope to add value to the hospital and department I work with, using business skills to acquire funding for research from the private sector and developing algorithms of care for more efficient management.”

Parekh entered the Combined BA-MD Program in 1991, and during his undergraduate education worked as a research assistant at Massachusetts General Hospital's Department of Orthopedic Surgery. He took time off between his second and third years to work as a research fellow in the MGH Wellman Laser Center of Photomedicine.

### C. Charles Wen, '00

C. Charles Wen, who will graduate from BUSM next spring, earned his BS from Boston University, magna cum laude, in 1995. He then took time off after completing the preclinical years at BUSM to obtain an MBA from the Boston University School of Management.

“During my MBA study, I learned how medicine worked from the business side, how medical organizations are currently structured,



and how the medical system has evolved into what it is today. I also learned management techniques that are widely applicable to efficiency, opera-

tions, quality management, and information technology,” he says. “As I was completing my MBA, I accepted an internship at Boston Scientific Corporation to apply what I've learned from business school in a practical setting. At Boston Scientific, I worked in the urology division evaluating future markets, analyzing competitor positions, and implementing new programs to improve data gathering.”

### Rishi P. Singh, '01

Rishi Singh won first prize in the basic science section of the NIH-AAMC 1998 Research Poster Session program held during the AMSA Conference in Washington, DC.

The poster presented was titled “What Role Do Ras and Rho Proteins Play in Corneal Wound Healing?” and was based on research conducted over the previous summer in the laboratory of Vickery Trinkaus-Randall, MD, an associate professor of ophthalmology.

The award recognizes work accomplished by Singh funded by the

Fight for Sight Research Fellowship to examine corneal wound healing at a molecular level. He has continued his research efforts this year as a recipient of the 1998–1999 Research to Prevent Blindness Fellowship.

“Using confocal laser scanning microscopy, protein separation and purification, and antisense technology, my research elucidated the chain of events that occurs after an ocular injury,” reports Singh. “Since the cornea is a highly innervated structure, this process is usually accompanied with a great deal of pain and discomfort. I have concluded from my research that Ha-Ras proteins play a major role in cellular migration after an ocular injury. This knowledge can be used to enhance the injury response by reducing the pain and the complicating infections that normally follow an ocular injury, while also reducing the healing time necessary for these wounds.

“The method I've used for transfecting cells is a novel drug delivery system, and thus could be used to deliver more of this helpful protein to an injured eye. Moreover, this protein may play a major role in other



fields, such as in the healing of skin after burns or cuts. Through my examination of the biochemical and cellular events following wounding, I hope to promote

repair in corneal disease and corneal wounds. This year has given me the opportunity to attend various research seminars and conferences so that I may share the results of my work with others and learn about other research being conducted in ophthalmology.”

Singh entered Boston University's Combined BA-MD Program in 1993.

## 1999 DISTINGUISHED ALUMNUS AWARDS

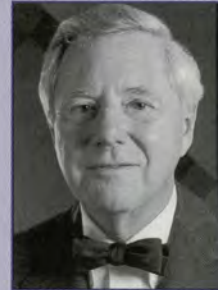
Every year, the Alumni Association and BUSM recognize the outstanding accomplishments of three graduates. The honorees, through their determination and insight, have made important contributions to medicine.



**Joseph L. Jorizzo '75** is professor and chairman of the Department of Dermatology at the Bowman Gray School of Medicine of Wake Forest University in Winston-Salem, North Carolina. An internationally recognized expert on dermatologic disease, he has focused his research on such areas as immunodermatology, neutrophils and immune complex reactions in the skin, vasculitis, Behcet's disease, dermatomyositis, and lupus erythematosus. The author of more than 150 articles and abstracts, he is a diplomate of the American Board of Dermatology, a member of the Medical Advisory Board of the American Behcet's Disease Association, a member of the Scientific Advisory Board of the Congress of International Society of Cosmetic Dermatology, and a member of the Board of Trustees of the American Academy of Dermatology. He served as president of the southern section of the Society of Investigative Dermatology and was chosen one of The Best Doctors in America for dermatology. He is on the editorial boards of numerous professional journals, including *Archives of Dermatology*, *Clinical and Experimental Dermatology*, *Journal of the European Academy of Dermatology and Venereology*, and *Skin Research and Technology*.



**Burton I. Korelitz '51** is professor of medicine at New York University Medical Center and chief of Gastroenterology at Lenox Hill Hospital in New York City. A recognized leader in gastroenterology, he is an internationally renowned expert in the study and treatment of inflammatory bowel disease (IBD). He has written three textbooks on the topic and has developed new and innovative therapeutic approaches to the treatment of IBD. He is also the author of more than 150 published articles and sixty book chapters. A former president of the American College of Gastroenterology, he also served as chairman of the National Scientific Advisory Committee of the Crohn's and Colitis Foundation. He is on the editorial board of *Current Concepts in Gastroenterology* and the *Journal of Clinical Gastroenterology*. He also serves as associate editor for *Inflammatory Bowel Diseases*. In 1996 he received the Clinical Achievement Award from the American College of Gastroenterology, and in 1998 he received the Distinguished Clinician Award from the American Gastroenterological Association.



**Luigi Mastroianni Jr. '50** is the William Goodell Professor of Obstetrics and Gynecology at the University of Pennsylvania School of Medicine and was chairman of the Department of Obstetrics and Gynecology there for twenty-two years. A highly renowned fertility specialist, he has a considerable body of research, including more than 140 published articles and chapters, and has earned international recognition. He has served as president of the International Academy of Human Reproduction, president of the IXth World Congress of Fertility and Sterility, and president of the IXth World Congress on Human Reproduction. He has also served as president of the American Fertility Society, vice president of the American Gynecological and Obstetrical Society, and president of the American Gynecological Club. He is a fellow of the World Academy of Art and Science and a senior member of the Institute of Medicine, and was chairman of the National Academy of Science and Institute of Medicine Committee on Contraceptive Development. He is on the editorial board of numerous journals and served as editor-in-chief of *Fertility and Sterility*.

**K**enneth M. Grundfast, MD, a nationally known pediatric otolaryngologist, who has most recently focused his interest on ear and hearing disorders in children and adults, will assume leadership of the Department of Otolaryngology on July 1.

He brings an expertise in evaluating patients with hereditary hearing impairment, as well as his surgical skills for treating cholesteatoma and chronic ear conditions. His vision for the department includes enhanced teaching, research, and clinical service.



“Otolaryngology now incorporates many new technologies such as use of lasers for surgery on vocal cords, a technique first developed at BUSM,” notes Grundfast.

“Otolaryngology is a vibrant specialty with an ever-expanding array of innovative methods for diagnosis and treatment. In fact, use of the laser to operate on the larynx was pioneered at the BUSM by Dr. M. Stuart Strong, who had been chairman of the Department of Otolaryngology from 1956 to 1985. Today, otolaryngologists use microscopes and telescopes to operate in the ear, the larynx, and the sinuses. Computer-guided systems are used for precise localizing of instruments during surgery in the paranasal sinuses. New technology enables otolaryngologists to alleviate snoring and sleep apnea using a device in the office that reduces the size of soft palate muscles. Also, new devices are being used to perfuse medications directly to the inner ear in order to alleviate symptoms of vertigo in some patients.

“I want to develop a department that is always moving forward and is continually responsive to the needs of physicians and patients at the School of Medicine and Boston Medical Center,” says Grundfast. “The department will have a personality: it will be friendly, caring, responsive, have high energy, and be open to new ideas. While continuing to pursue my own area of interest in hearing impairment, I plan to expand basic research programs investigating the etiology of head and neck cancer and seek to identify the molecular mechanisms involved in hereditary deafness. I hope to work with collaborators at BMC in developing outcomes research projects to monitor and continually improve the efficacy of alternative methods of managing patients with otolaryngic disorders.”

Grundfast received his AB degree from Johns Hopkins University and MD degree from the State University of New York at Syracuse. After internship and residency training in general surgery at the New England Medical Center in Boston and the Sibley Memorial Hospital in Washington, DC, he trained as a resident in otolaryngology at BUSM with M. Stuart Strong, MD, and Charles Vaughn, MD. He then completed a fellowship in pediatric otolaryngology at the Children’s Hospital of Pittsburgh before joining the faculty at the George Washington University School of Medicine and accepting an appointment as chairman of the Department of Otolaryngology at the Children’s National Medical Center. After attaining the rank of professor with tenure at the George Washington University School of Medicine, Grundfast moved to Georgetown University Medical Center, where he currently serves as professor and interim chairman of the

Department of Otolaryngology. In 1998, Grundfast received the award for excellence in education at Georgetown University Medical Center.

He spent a sabbatical year in 1989 working at the National Institute on Deafness and Other Communication Disorders at the NIH, and he has published more than one hundred articles on topics ranging from the molecular genetics of hearing disorders to the management of common ear problems in children. Grundfast’s many honors and awards include the presidential citation and the distinguished service award of the American Academy of Otolaryngology–Head and Neck Surgery. He has been president of the Society for Ear, Nose, and Throat Advancements in Children; the American Society of Pediatric Otolaryngology; and the International Society for the History of Otolaryngology. In 1995 he was elected vice president of the American Academy of Otolaryngology–Head and Neck Surgery. Grundfast has served as a member of several national advisory panels, including the Alexander Graham Bell Association for the Deaf, and he was a member of the panel convened by the Agency for Health Care Policy and Research (AHCPR) to develop practice guidelines for management of otitis media in children. In addition, he has been appointed an associate examiner for the American Board of Otolaryngology, and he serves on the editorial boards of numerous journals including the *Journal of Otology*, the *Archives of Otolaryngology–Head and Neck Surgery*, and the *International Journal of Pediatric Otolaryngology*.

## NEW SURGEONS JOIN BOSTON UNIVERSITY MEDICAL CAMPUS

Building upon an already prestigious surgical staff, the Boston University Medical Center (BUMC) has added to its roster four surgeons, formerly of Beth Israel Deaconess Medical Center and Harvard Medical School. R. Armour Forse, MD, PhD; Timothy Babineau, MD; Stephen Sentovich, MD; and Peter Burke, MD, joined BUMC as of March 1, 1999.

Along with their medical center positions, all four surgeons will hold academic titles at Boston University School of Medicine. Their reputations as outstanding physicians, surgeons, and academicians are well known throughout the medical community and will advance the academic mission of the school.

Forse received both his MD and PhD from McGill University in Montreal, and completed his internship and residency at Royal Victoria Hospital in Montreal—serving as chief resident in surgery. He was a research fellow and PhD candidate in experimental surgery at McGill and a research fellow in surgical metabolism at Columbia University College of Physicians and Surgeons in New York. Most recently, Forse was an associate professor of surgery at Harvard Medical School. He specializes in the surgical treatment of morbid obesity and gastrointestinal disorders and has an active basic research program in metabolism.

Babineau, who specializes in digestive disorders and minimally invasive surgery, received his MD from the University of Massachusetts.

He completed his internship and residency in general surgery at the New England Deaconess Hospital, where he also served as a fellow in surgical nutrition and metabolism. Babineau became an assistant professor of surgery at Harvard Medical School in 1995 and served on the active staff of New England Baptist Hospital. He also served as chief of surgery at Vencor Hospital in Brighton.

Sentovich received his MD from the University of California, Los Angeles School of Medicine. He completed his internship and residency at the University of California Irvine Program in General Surgery, where he served as chief resident in surgery. Following a fellowship in the fields of colon and rectal surgery, Sentovich joined the faculty in surgery at Harvard Medical School in 1994. He specializes in colon and rectal surgery, and his major research interests include anorectal physiology, pelvic floor disorders, and outcome/quality-of-life issues.

Burke received his MD from Tufts University School of Medicine and completed his internship and residency at the New England Deaconess Hospital, serving as chief resident in surgery. He became an assistant professor of surgery at Harvard Medical School in 1995 and specializes in trauma surgery and critical care. Burke's research interests include gene regulation in injury and molecular, metabolic, and immunological responses to sepsis and injury.



*R. Armour Forse, MD*



*Timothy Babineau, MD*



*Stephen Sentovich, MD*



*Peter Burke, MD*

## IN BRIEF

**Joel Alpert, MD**, professor of pediatrics and public health, was elected president of the American Academy of Pediatrics.

**Robert Beazley, MD**, professor of surgery and section chief of the Department of Surgical Oncology and Endocrinology, received the 1998 Stanley L. Robbins Award for Excellence in Teaching. This award is given annually to an outstanding educator at BUSM for his or her excellence in teaching and devotion to the students.

**Dick A. J. Brown, MD**, director of medical student education in the Department of Obstetrics and Gynecology, and associate clinical professor of OB/GYN, received the 1998 Frederick Jackson Faculty Award for excellence in teaching the clinical sciences.

**Paul O'Bryan, PhD**, associate professor of physiology, received the 1998 Thomas Robitscher Faculty Award for his excellence in teaching the preclinical sciences.

**Larry Culpepper, MD, MPH**, professor and chairman of the Department of Family Medicine, was elected to the Institute of Medicine.

**Thomas Einhorn, MD**, professor and chairman of the Department of Orthopedic Surgery, received the Elizabeth Winston Lanier Award for developing new strategies to treat broken bones that have not healed properly and for documenting the complex physiological process involved in the normal healing of fractures.

**Barbara Ann Gilchrest, MD**, professor and chairwoman of the Department of Dermatology, has been appointed president of the Society for Investigative Dermatology (SID). The SID has more than 2,500 members and is the major resource organization for dermatology and skin biology. Additionally, Gilchrest was elected to the Institute of Medicine.

**Lillian Caldeira McMahon, MD**, associate clinical professor in the departments of Medicine and Pediatrics, and program director of the Boston Comprehensive Sickle Cell Center at BMC, received the Distinguished Community Award for Outstanding and Dedicated Service to Sickle Cell Patients and the Community from the Community Sickle Cell Support and Awareness Center of Boston.

**Robert Meenan, MD, MPH**, and dean of SPH, was appointed secretary of the Arthritis Foundation. In this role, Meenan will lead more than 600,000 volunteers and staff nationwide in the foundation's mission to support research to find the cure for and to prevent arthritis and to improve the quality of life for those affected by disease.

**John Noble, MD**, director of the Primary Care Center and professor of medicine, received the 1999 Robert J. Glaser Award for his exceptional contributions to research and education in the field of generalism in medicine. This is the highest award given by the Society of General Internal Medicine.

**Domenic Scrceni, EdD**, director of the Educational Media Center, accepted the International Teleconferencing Association's Excellence Award for the novel use of teleconferencing in the audiovisual/multimedia category. The award recognized BUSM's project titled "International Medical Education and Harmonization Program for Nuclear Accident Preparedness." The project helped train medical professionals from fifteen countries to handle aspects of a radiation accident.



# Match Day '99



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