Downstate EXAMINER

September 1980 STATE UNIVERSITY OF NEW YORK

Downstate Doctors Work to Discover What Drugs Really Do to Us

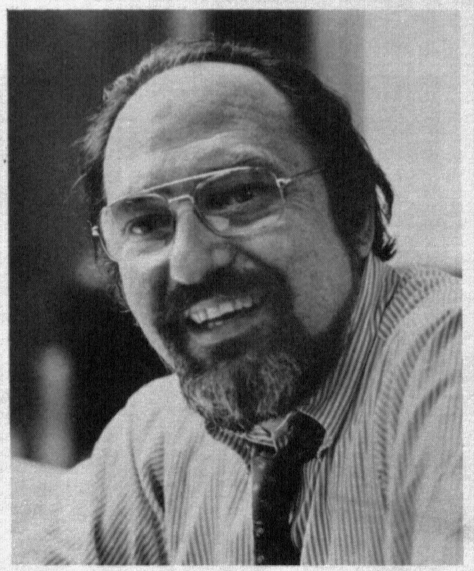
For years and years now, we have all been haunted by the spectre of drug addiction. Every area of life has been affected by the problems that go hand-in-hand with substance abuse—from fear of crime in the streets to the fate of the unborn fetus. Substance abuse—its origins, its practices, and perhaps its cures—is a high-priority area for research and study.

The scientists who work with the New York State Division of Substance Abuse Services (DSAS) Testing and Research Laboratory in Brooklyn often lead the way in this priority area. Asked what the lab is involved in, its director, Dr. Salvatore J. Mulé, professor of psychiatry, has a quick response: "We are always involved in some phase of the drug-dependence problems seen out there in the streets." In other words, even though they are doing basic research, these scientists are working with the stark, ugly realities of the drug scene—which, by the way, includes alcohol.

Dr. Gerald Deneau with "self-administering" monkey.

New affiliation for psychiatry

The DSAS Laboratory is the newest adjunct of the Department of Psychiatry. Why psychiatry? Because, says Dr. Mulé, "the typical drug addict has needs beyond the physiological one for a fix. They have psychological and socio-economic problems, too." Dr. Eugene B. Feigelson, professor and chairman of the Department of Psychiatry, is delighted to welcome the laboratory and the six new faculty members associated with it. Says Dr. Feigelson, "It enormously strengthens our expertise and capability in biological issues related to psychiatry, drug abuse, and alcoholism and creates new opportunties for research collaboration and education."



Dr. Salvatore J. Mulé

Cocaine can kill

Those who believe that cocaine is a benign, "safe" drug might think again if they could see what happens when rhesus monkeys (primates biologically very similar to humans) are allowed to dose themselves with as much coke as they want.

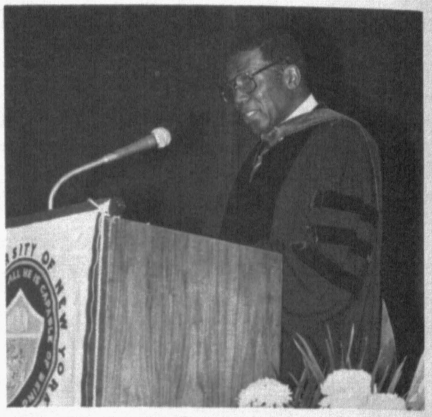
This is precisely what has happened in the lab run by Dr. Gerald Deneau, associate professor of psychiatry. Each animal was connected to a system where, by

(continued on page 4)

Commencement 1980

Commencement exercises for the Colleges of Nursing and Health Related Professions were held on Monday, May 19, at 7 P.M. in Walt Whitman Auditorium of Brooklyn College. One hundred twenty-eight graduating nurses and sixty-four health professionals from the various CHRP programs received their hard-earned degrees. Dr. Alden N. Haffner, SUNY associate chancellor for the health sciences, delivered the commencement address. Lawrence Joseph Bock, Class of '80 of the College of Health Related Professions, and Patricia Jane Peacock, Class of '80 of the College of Nursing, addressed their respective classes. One of the highlights of this program was the presentation of the Chancellor's Award for Excellence in Teaching. Dr. Stanley L. Lee, acting president, gave the certificate and the check to Dr. Jacqueline S. Jakway, assistant professor of anatomy and cell biology.

Commencement exercises for the College of Medicine and the School of Graduate Studies were held on Monday, June 2, at 7 P.M. in Avery Fisher Hall at Lincoln Center in Manhattan. Two hundred twenty-two new doctors entered into the practice of medicine and nine students from the graduate school received D.M.Sc., Ph.D., or combined M.D.-Ph.D. degrees. Dr. Louis C. Lasagna, professor of medicine and professor and chairman of the Department of Pharmacology at the University of Rochester, delivered the commencement address. Hunter Scott Tashman, Class of '80 of the College of Medicine, gave the greetings from the graduates. AJA □

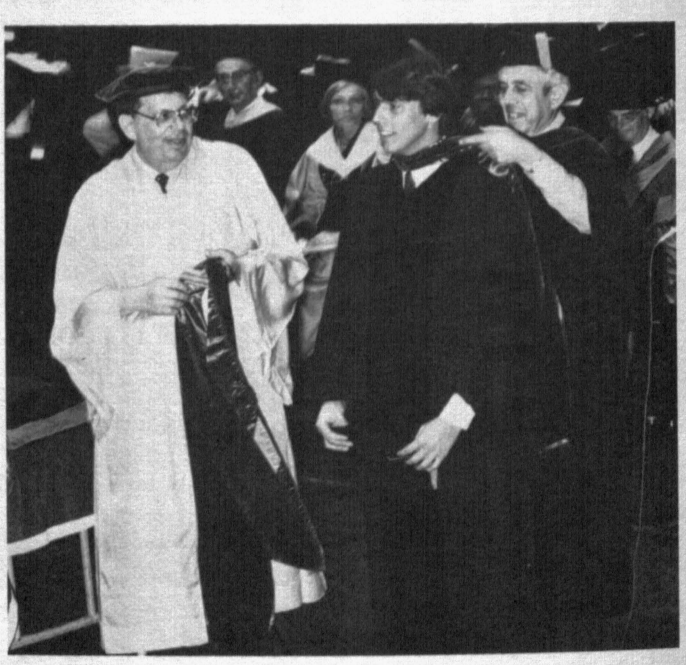


Dr. Charles R. Greene, dean of students, applauded both the students and their families at the College of Medicine/ School of Graduate Studies Commencement.

Right, CHRP students await the awarding of their degrees.

Below, Dr. Stanley L. Lee, acting president, presented diplomas at both Commencements.

Below right, Dr. Eli A. Friedman (left), professor of medicine, looks on as Dr. Seymour S. Cutler, clinical professor of medicine, hoods a candidate.



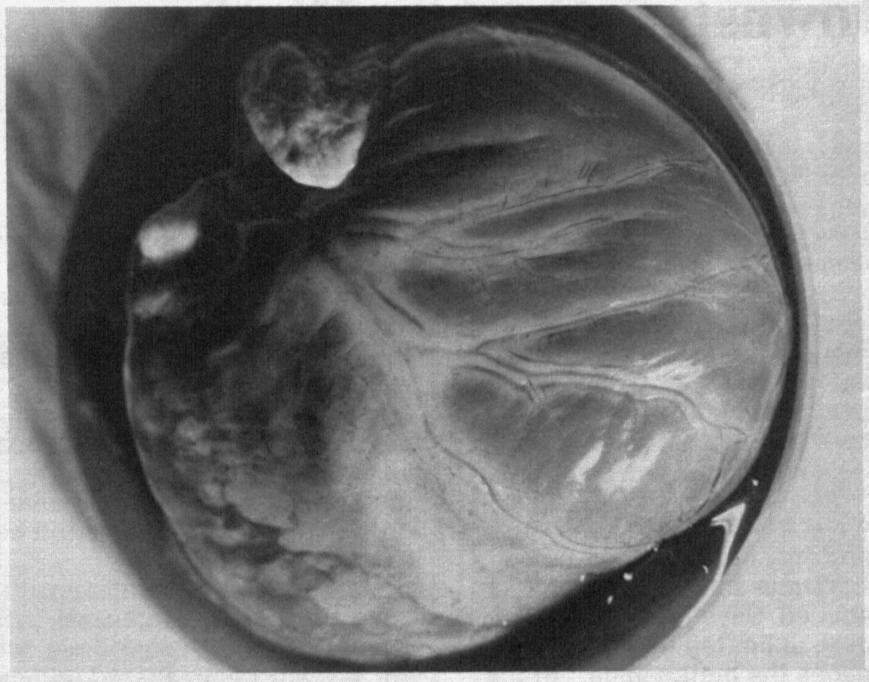
New Clue to "Sudden Death" Heart Attack Discovered at Downstate

One of the great mysteries of medical science is "sudden death ischemic heart disease (SDIHD)," which kills about 600,000 Americans (mostly young men between 20 to 50 years of age) every year. Most people, doctors included, have assumed that these people died of a heart attack so severe that there was no time to get to the safety of a hospital or doctor's office. But the baffling fact is that at least 10 to 25 percent of the victims turn out to have had perfectly normal coronary arteries—no plaque, no clot, no sign that they have experienced a heart attack, or a stroke, or any other trauma, for that matter.

Obviously, there are many unanswered questions when it comes to ischemic heart disease. ("Ischemic" simply means that the heart muscle isn't getting enough blood and oxygen, for whatever reason.) Now, a real clue has been provided by Drs. Prasad D.M.V. Turlapaty and Burton M. Altura. They have evidence that at least some of these sudden deaths may be caused by a magnesium deficiency.

The two physiologists had noted numerous studies showing that the heart muscle and coronary arteries from patients who died suddenly of ischemic heart disease had lower than normal magnesium levels. Then there were numerous epidemiological studies that pinpointed the highest incidence of sudden death to those areas with soft water (low magnesium) and soil with little magnesium content.

The two Downstate researchers then began to review the latest theories on spasm. As a cause of heart attacks, spasm—a kind of cramp that constricts the artery wall and prevents enough blood from getting through to the heart muscle—was not a particularly new idea; a number of theories tried to explain the cause: too much cholesterol, too much smoking, too much emotional stress, too much physical exertion. Says Dr. Altura: "We began to suspect that one of the causes of spasm might be too *little* of a crucial trace mineral—magnesium.



Dog heart showing coronary artery.

Dr. Burton M. Altura

In the laboratory

As reported in the April 11, 1980 issue of *Science*, the Brooklyn investigators isolated four different coronary vessels, both large and small in size, from each of several dogs, to test the idea that a magnesium deficiency can produce blood vessel constriction. These vessels were exposed to normal and high concentrations of magnesium as well as to a sudden withdrawal of all magnesium from the fluid medium surrounding them. The vessels were also exposed to several neuro-humoral substances, including norepinephrine, acetylcholine, serotonin, angiotensin, and potassium, all known to cause coronary vessel spasm.

Dr. Turlapaty, an assistant professor of physiology, and Dr. Altura, a professor of physiology, found that a sudden removal of magnesium caused all of the coronary vessels to constrict. The removal also enhanced the response of these vessels to the known vasoconstrictors.

But just how does magnesium deficiency lead to coronary artery spasm at the cellular level? Drs. Turlapaty and Altura aren't sure, but their research suggests that extracellular calcium ions move across the arterial muscle cell membranes to promote spasm.

(continued on page 7)

Downstate Doctors Work to Discover What Drugs Really Do to Us (continued from page 1)

pushing a button, the drug was injected directly into the bloodstream.

"They didn't like hallucinogens (LSD, etc.) at all," reports Dr. Deneau. "And they quickly settled down to a steady level of opiates such as heroin. But with cocaine—they went wild!"

The test monkeys pushed the button over and over, even after convulsions. They went without sleep. They ate five to six times their normal amount, yet became emaciated. Says the doctor, "Obviously, unlimited use of cocaine damages the metabolism." In the end, they began to mutilate themselves and, eventually, died of cocaine abuse. "Of course," cautions Dr. Deneau, "few people could afford the massive doses of cocaine these monkeys were able to obtain." But we know little, as yet, of the cumulative effects of cocaine usage. In any case, every indication is that cocaine is *not* harmless.

Dr. Masaji Matsuzaki

Changes in brain waves

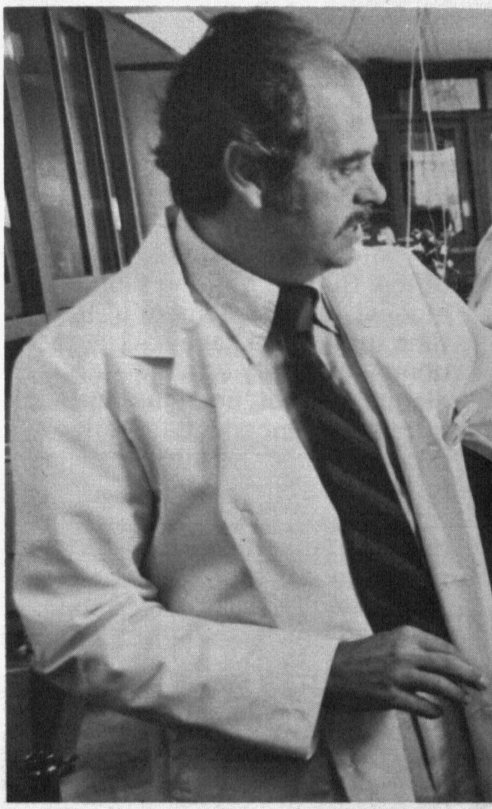
While Dr. Deneau looks at drug-related behavior, Dr. Masaji Matsuzaki, assistant professor of psychiatry, looks into the electrical activity of the brain itself—in an effort to find out *why* addiction changes peoples' behavior. Dr. Matsuzaki is an expert in neuropharmacology and he, too, works with rhesus monkeys which have had electrodes permanently implanted in various parts of the brain. This way, measurements can be made of the long-term effects of a particular drug on the primate brain and behavior patterns.

Many studies were made with cocaine. Says Dr. Matsuzaki, "We are not certain whether brain cells are actually being altered or destroyed by cocaine. But we do see that long-term use results in an alteration of the EEG (a measurement of electrical activity in the brain)." The animals in the study became extremely placid or profoundly depressed. Dr. Matsuzaki feels that these changes may be related to a drug-induced malfunction in the limbic system. (The limbic system, sometimes called "the visceral brain," is composed of various pathways and glands inside the brain near the brain stem. It seems to be associated with those responses essential to self-preservation, such as mating, eating, and the care of offspring.)

Most recently, Dr. Matsuzaki has been concerned with PCP, better known as Angel Dust. This substance, too, had deleterious effects . . . among them, "within five to ten minutes after injection, major components of visual, auditory, and somatosensory evoked potentials . . . were depressed significantly."

How long in the brain?

How quickly is Angel Dust (or any other drug of abuse) absorbed into various tissues in the body? And then, once there, how long before it is excreted? How much goes into the brain and how long does it stay there?

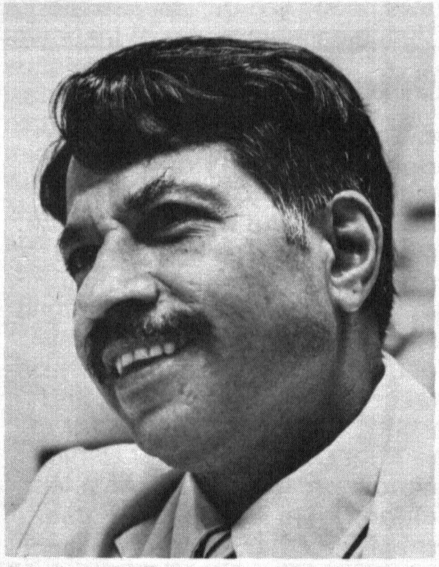


Dr. Karl Verebey monitors a HPL (High Pressu

These questions are being asked and answered by Dr. Anand Misra, associate professor of psychiatry and head of drug disposition and metabolism at the DSAS. Right now, his lab is working on PCP, which is "labeled" with a tritium radioisotope, injected, and then studied in the tissues. Says Dr. Misra, "We have seen Angel Dust and its metabolites remaining in the brain for two weeks. And we see that large amounts of it go into the body's fatty tissue, from where it is released very, very slowly." This slow release may be the cause of sudden and delayed reactions to the drug, weeks after it is taken.

According to Dr. Misra, drug interactions (i.e., the taking of more than one drug at a time) pose a potentially dangerous situation, because one drug can change the metabolism of the other and so can enhance or neutralize the action of the other drug. In particular, combinations of alcohol with

d Chromatograph).



Dr. Anand Misra

sleeping drugs or tranquilizers or anti-depressants can be very hazardous. An Angel Dust-marijuana combination is also dangerous—and this is the way Angel Dust is usually taken. "As we collect more and more information about how the body handles a particular drug or combination," says Dr. Misra, "we can try to figure out the proper treatment."

Opiates as treatment in mental illness?

In the clinical pharmacology lab run by Dr. Karl Verebey, associate professor of psychiatry, opiates and their antagonists are getting a great deal of attention. One of their major interests is Naltrexone, the narcotic antagonist that blocks the "high" opiate addicts live for. With the widespread use of Naltrexone, we could probably eradicate the use of opiates totally and forever. But there's a problem and it's a big one: addicts won't stay on Naltrexone. They *want* that "high!" In spite of that, though, two studies using actual addicts continue and a long-term antagonist, which would be implanted under the skin and last for five or six months, is being looked into.

Should the day ever arrive when we no longer have any opiate addicts, Dr. Verebey sees a different use for that class of drugs: as therapy for certain kinds of psychoses. This is, needless to say, highly controversial. Rare is the committee who would willingly allow schizophrenics to be "shot up." "Yet, we all produce opiates in our own brains," says Dr. Verebey. "That's how sane human beings are able to cope with stress and pressure." It is his belief that probably some of us simply don't produce or can't release these natural opiates, called endorphins.

Dr. Doris Clouet, assistant director of the DSAS Lab and professor of psychiatry, examines the basic neurochemical mechanisms underlying the addictive processes. She has one ongoing study in which blood levels of endorphins are measured in human patients. By combining animal and human experimentation, she

Dr. Doris Clouet

says, the researchers at the lab hope to define the neurochemical states that lead to the abuse of drugs, and suggest ways in which brain neurobiological deficiencies can be normalized without resorting to addicting and harmful drugs.

What's next on the drug scene?

Further tests are planned with Angel Dust, as more and more American youths (most of them male) are rendered psychotic by its use. In fact, opiates will be tried as treatment in those cases. And further physiological work on PCP will continue, using evoked response testing. Pregnant rats will (one hopes) show how various substances affect the unborn baby through its mother. Since science recently rediscovered Fetal Alcohol Syndrome, we now know this to be of prime importance.

In fact, if you want to know which are the most abused substances at any given time, you need only look at the DSAS Lab agenda. Whatever the worst current problem, that's what they'll be working on. MKH/SB □

Martin Newborn Appointed Director of Computing Center

Martin Newborn speaks three foreign languages: Assembler, COBOL, and RPG. This may not get him through many foreign countries in the world, but they are certainly crucial to his new position as director of the Computing Center.

With an appointment that became effective on June 5, Mr. Newborn takes charge of a staff of some 40 people and an IBM 370 computer with some 100 terminals throughout the State University Hospital—all of whom (and which) operate in perfect synchronization to keep the medical center functioning without a hitch. "The challenge," he believes, "is to meet the current and future demands of the medical center in the most efficient way possible. That means predicting future needs and trying to update our present system to make it even more reliable and accesible."

Commenting on this appointment, Howard Dorfman, vice president for administration, said: "Martin Newborn assumes the position of director, having already demonstrated his ability through a series of accomplishments during his tours of duty first as assistant director and subsequently as acting director.

"I am confident that as director he will contribute significantly to the advancement of computerized informational systems and that all will find him a willing collaborator in searching for a method to achieve a speedier, more precise 'way', fully utilizing the resources of the Downstate Computing Center."

Before coming to Downstate in 1967, Mr. Newborn was employed at the International Paper Company and the Mutual Life Insurance Company of New York. He holds a Bachelor of Arts degree from Brooklyn College.

The revolution in home computers has not bitten Martin Newborn who prefers to spend his leisure time with his wife Angela and his 12-year-old daughter Joanne. His favorite pastimes are photography, gem cutting, and travel. SB □

Fifth Annual Tyler Lecture to Be Delivered on October 6

Dr. William N. Spellacy, professor and chairman of the Department of Obstetrics and Gynecology at the Abraham Lincoln School of Medicine, University of Illinois Medical Center, will deliver the Fifth Annual Tyler Memorial Lecture and serve as visiting professor in the Department of Obstetrics and Gynecology.

Dr. Spellacy will give this year's Tyler Lecture, entitled "Diabetes and Pregnancy—1980," on Monday, October 6, at 4 P.M. in the First Floor Lecture Hall. He will also participate in a staff conference, discussing "Intrauterine Growth Retardation."

A nationally prominent physician specializing in both gynecologic endocrinology and perinatology, Dr. Spellacy is a member of numerous professional societies, including the American Federation for Clinical Research, the American College of Obstetricians and Gynecologists, the American Fertility Society, the Society for the Study of Reproduction, and the American Association of Planned Parenthood Physicians. He also serves on the American Board of Obstetricians and Gynecologists Division of Maternal and Fetal Medicine; the Biomedical Advisory Committee of the Population Resource Center, New York; and the Test Committee of the National Board of Medical Examiners. Dr. Spellacy is the author/coauthor of over 300 published articles in medical and scientific journals.

The Tyler Lectureship

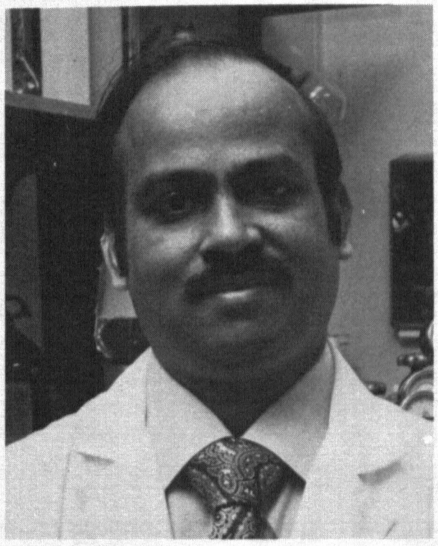
The Tyler Memorial Lectureship is endowed by a gift from Lillian Tyler in memory of her husband Dr. Edward Tyler, who died in August 1975. Dr. Tyler was an alumnus of the Class of 1938 at The Long Island College of Medicine (LICM), which became the nucleus of Downstate Medical Center in 1950, when LICM merged with the State University of New York. He was a noted authority on oral contraception, sterility, and fertility, and had been director of the Tyler Clinic and Tyler Clinic Foundation, Inc., of Los Angeles, California. He was the first president of the Association of Planned Parenthood Physicians and a member of the Royal Academy of Medicine, the British Fertility Society, the International Fertility Association, and the International Planned Parenthood Federation.

A reception will follow the lecture. AJA □

New Clues to SDIHD...

(continued from page 3)

Prior to this time, Dr. Altura, Dr. Bella T. Altura, an assistant professor of physiology, and Dr. Turlapaty had shown that when the magnesium content in the arterial smooth muscle cell membranes is lowered, calcium flows into the cells in abundance and causes arterial muscle spasm.



Dr. Prasad D.M.V. Turlapaty

Diet and SDIHD

Can diet cause or prevent sudden death ischemic heart disease? Possibly so. Dr. Burton Altura believes: "It may become important to provide magnesium supplements to people who, for various reasons, may not be receiving enough of this important mineral in their diets." In the August 1979 issue of *Medical Hypotheses*, he noted that fats and refined sugars, which are readily consumed as a source of caloric energy by people in the Western world, are virtually devoid of magnesium. Other foods that are low in magnesium are fruits, legumes, dairy products, meats, and "junk foods," all of which are commonly ingested in large amounts, particularly in the Western world. Foods high in magnesium, on the other hand, are nuts, unprocessed cereals, and bony fish. "The high intake by the Japanese and Bantu natives in South Africa of foods which are high in magnesium may serve to explain why these populations have the lowest incidence of sudden death ischemic heart disease in the world," says Dr. Altura. SB □

Downstate Views

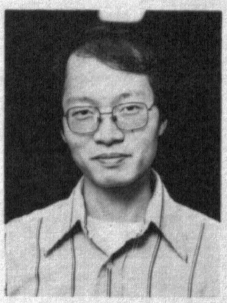
by Martha J. Thomas

In the past decade, the U.S. has taken in a large number of immigrants from Southeast Asia and Latin America... How do you feel about this?

Marguerite A. Kelly, Assistant to the Dean, College of Nursing

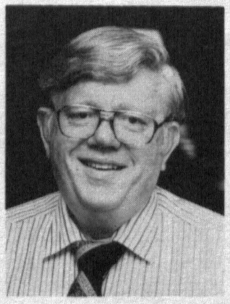
We should take more. We've intervened in those countries and disturbed their natural order, so we have a moral responsibility to undo some of the harm we've caused.

Christopher Chan, Instructor, Department of Anatomy and Cell Biology

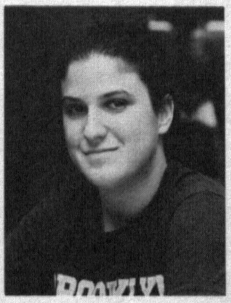


It's the culmination of many events... war, intervention, etc. And I would be disappointed if the United States did not pick up the refugees. I'm not saying this with any bitterness or approval, but the influx is all just part of the history.

Steward Crawford, Assistant Manager, Computing Center



Since it's the tradition of this country... I'm in favor of it. We should take anyone who wants to come here, that's what's made our country so great—and we have the room.



Karen Alpert, College of Health Related Professions, Class of 1982

I think it is the right thing to do. They're in a time of need and should be helped. We can never let what happened in Europe during Hitler's reign happen again.

Dianne Gleitman, College of Health Related Professions, Class of 1982

Immigrants can contribute a lot to this country... in fact my parents are immigrants from Europe. If there had been a lot more "boat people" during World War II maybe more lives would have been saved... including my grandparents'.

Dr. Courtney Fisher, Assistant Instructor, Department of Urology

It depends on what is being offered to these individuals. If this country's idealistic policy was really one of equal opportunity... then fine. But realistically it is not. So, before the U.S. takes in others, it should first be able to take care of its own. This does not mean, however, it shouldn't lend or extend help to the outside.

"Downstate Views" is a random sampling of the Downstate community and the opinions expressed are those of the individual—not those of the editors or of the institution.

POTPOURRI

New Appointments in Public Affairs

Dr. Stanley L. Lee, acting president of Downstate, has announced the following appointments in the Office of Public Affairs:

Renee Meltzer, director of the Grants Advisement Office and assistant director of public affairs, has been named acting director of public affairs and acting director of medical illustration and photography.

Martha J. Thomas, assistant for media relations and community relations, has been named acting assistant director of public affairs.

Barrie Jacobs Kelly, the former director of public affairs and assistant to the president, has left Downstate to become executive director of public affairs for The College Board.

Werthamer Fellowship Awarded

Dr. Mark J. Lema, a Ph.D who is now a third-year medical student, has been awarded a stipend of $1,000 to study tumor cell sharing of nonhistocompatible surface antigens. He will be working in the laboratory of Dr. Michael Howe, associate professsor of microbiology and immunology. The information gained from these studies will aid in the elucidation of how viruses induce cancer and the possible relationship between autoimmunity and leukemia.

The funds for this award were set aside by the friends of Dr. Seymour Werthamer, a clinical professor of pathology who died on July 3, 1976. The fund monies, which are deposited in the Beneficial Fund, are to be used to encourage research in tumor immunology.

Downstater Named "Family Doctor of the Year"

Dr. Eugene Fanta, clinical associate professor emeritus of family practice, was recently honored by President Jimmy Carter as the 1980 "Family Doctor of the Year." Dr. Fanta is the fourth physician to be so honored and the first from a major metropolitan area. The annual award is co-sponsored by the American Academy of Family Physicians (AAFP) and *Good Housekeeping* magazine. Dr. Fanta was chosen by the editors of *Good Housekeeping* from numerous nominees from AAFP chapters across the country.

The director of the Department of Family Practice at Lutheran Medical Center, Dr. Fanta has specialized in family practice for forty years in the Sunset Park and Bay Ridge neighborhoods.

Brooks Award Presented

Owen Glenn Peller, Class of 1982 of the College of Medicine, received the seventh Chandler McCuskey Brooks Award at a brief ceremony on June 6. He was presented with a check, a certificate citing his "outstanding attainment in physiology," and a copy of *Research in Physiology: A Liber Memorialis in Honor of Professor Chandler McCuskey Brooks,* edited by Professors Frederick F. Kao, Kiyomi Koisumi, and Mario Vassalle of the Department of Physiology.

The Chandler McCuskey Brooks Award, which is presented annually, was established in 1973 with the proceeds from the distribution of the above book. Dr. Brooks, who was chairman of the Department of Physiology for 25 years, is now a distinguished professor of physiology.

Have Fogarty, Will Travel

Dr. James P. Quigley, associate professor of microbiology and immunology, has been awarded a Fogarty Senior International Fellowship to continue his tumor cell research. Dr. Quigley, who was chosen from a large number of applicants, will work at the Sir William Dunn School of Pathology at the Medical School of the University of Oxford, England. While at Oxford (for the next academic year—September through June), Dr. Quigley, who studied the biochemistry of malignant cells in culture while at Downstate, will turn his attention to the genetics and biochemistry of tumor cell invasions and metastasis. He will be working with Professor Henry Harris, a pioneer in the field of malignant cell genetics. AJA □

The Downstate Examiner is published monthly during the academic year by the Office of Public Affairs for the Downstate community—faculty, professional staff, support staff, and students—and its friends.

Editor: Barrie Jacobs Kelly, Director
Editorial Advisor: Renee Meltzer, Assistant Director
Editorial Associate and Designer: Antoinette J. Alesi
Feature Writers: Susanne Berkman and Marcia Kamien Hechtman
Photography: Bob West and DMC Medical Illustration and Photography
Masthead Design: Tony Villapaz, Medical Illustrator

Office of Public Affairs
Downstate Medical Center
State University of New York
450 Clarkson Avenue
Brooklyn, N.Y. 11203
(212) 270-1176

Non-Profit Org.
U.S. Postage
Paid
Brooklyn, N.Y.
Permit No. 10045