New Drug Doubly Effective Against Heart Attacks

A new drug, t-PA, stops heart attacks in progress nearly twice as effectively as the drug currently available, according to the results of a multicenter, 316-patient study reported in the April 4 issue of The New England Journal of Medicine.

Tissue plasminogen activator, t-PA, stops heart attacks by dissolving blood clots lodged in a coronary artery. Such clots cause 80 percent of heart attacks. Rapid dissolution of the clot spares the heart from damage and thus significantly improves the patient's chance for recovery.

In the just-completed clinical trials, done at Washington University and 12 other clinical centers nationwide under the direction of the National Heart, Lung and Blood Institute, 143 patients received intravenous t-PA while 147 received intravenous streptokinase. Streptokinase is currently the drug-of-choice for dissolving clots during a heart attack.

"t-PA was more effective by a substantial margin," says Burton E. Sobel, M.D., chief of cardiology at Barnes Hospital and Washington University. "Within 90 minutes of administration, the clot was dissolved in 2/3 of the patients who received t-PA and only 1/3 of the patients who received streptokinase."

"The advantages of t-PA are so substantial that it quite likely will replace the agents we have used in the past," adds Phillip Ludbrook, M.D., a cardiologist who has served as Washington University's principal investigator in the study. Chief among these advantages is t-PA's specificity. Streptokinase's lack of specificity puts patients at substantial risk of systemic bleeding. In addition, streptokinase is a bacteria-derived substance that can cause an allergic response in some patients and make it difficult to determine a proper dose.

Although t-PA has proved to be an effective and safe clot dissolver, "it is not a panacea," Sobel warns. "The coronary arteries where these clots occur are abnormal to start with. The clots generally form where the vessel is narrowed due to plaque build-ups. We're still going to have to deal with the long-term widening or repair of these arteries." Coronary artery bypass surgery and balloon angioplasty are among the techniques currently used to correct coronary artery stenosis.

This clinical study constitutes Phase I of the Thrombolysis in Myocardial Infarction (TIMI) trials sponsored by the National Heart, Lung and Blood Institute. According to the journal article, the advisory committee directing the study decided to end Phase I a month ahead of schedule because the significant contrasts between t-PA and streptokinase became apparent.

Cardiac catheterization was performed on t-PA and streptokinase recipients during a recent clinical trial in which t-PA was shown to be the superior thrombolytic agent. Phillip Ludbrook, left, principal investigator of the trial at Washington University, here awaits final preparation of a patient for catheterization.
Genetic Disease: Sniffing Out Clues

Gene therapy will eventually become a reality, but it won't be the first line of treatment for genetic diseases that respond to dietary manipulation. Uncovering these conditions requires a trained nose and a dose of "old-fashioned" medicine.

Ins and Outs of Cell Traffic

The movement of cell traffic looks chaotic but in fact is carefully orchestrated. Molecules that act like barges ferry substances into, and around, cells and deliver their cargo when they encounter a change in charge in the cell's soupy interior.

Resculpting the Head

Disease or trauma to the head often produces cosmetic or functional defects. But because of innovations in surgical restoration, deformity no longer goes hand in hand with tissue loss.

Student Stage: Match Day

An annual rite of passage brings few breaks with tradition in 1985.

Personal Outlook: Dan McKeel

The declining rate of autopsies should be reversed in order to preserve excellence in medical education.
GENETIC DISEASE

sniffing out clues

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ometime this year, federal health agencies are expected to approve the first authorized attempts to treat cases of rare, devastating genetic disease through the use of gene therapy. When it comes, this approval spells hope for persons with certain unusual, catastrophic illnesses — hope that a feat of genetic engineering can straighten out their jumbled genes.

But the fanfare heralding this revolutionary treatment obscures gene therapy's limited importance. Fewer than 500 new cases of the five genetic diseases under federal scrutiny are diagnosed each year — a mere thread in the sizable fabric of genetic disease. Nearly 10 years ago, it was estimated that 12 million Americans had a genetic disorder, and that life-years lost to such diseases are almost seven times those lost to heart disease. An estimated 30 percent of pediatric hospital admissions are for genetic disorders.

Thus, feats of gene therapy may eventually bring hope to hundreds suffering from extremely rare diseases. But tens of thousands others suffer from diseases like cystic fibrosis or muscular dystrophy. Although traditional medical treatment can help alleviate the symptoms of these diseases, a cure from gene therapy is still the stuff of science fiction. A few metabolic disorders like the genetic disease phenylketonuria (PKU) are treatable, but there is no cure. The plain truth is, except for diseases like PKU — for which all newborns are screened, and which can be effectively treated by dietary manipulation — genetic diseases often remain undiagnosed, or are misdiagnosed.

"Children with genetic disease often present with symptoms like unexplained vomiting," says Richard E. Hillman, M.D. "In many cases, they are mistakenly diagnosed with pyloric stenosis. Then, they undergo surgery for this condition, surgery which may be unnecessary — and potentially dangerous."

Hillman, director of medical genetics at Washington University Medical Center, is often called in on these puzzling cases. He points out that besides problems with eating, children with genetic diseases — especially a defect in metabolic processes — often have a peculiar odor stemming from an accumulation of certain metabolic products.

In some cases, Hillman's primary tipoff is the first symptom that captures attention — the patient's odor. To be sure of his initial hunch, though, he always runs appropriate clinical tests.

"Many genetic diseases have been named for their odors," discloses Hillman. "Osthaus disease, for example. An osthaus is a place where malt is cured before beer is made, and patients with this disease have an odor distinctly like malt. There's also maple syrup urine disease, in which an accumulation of certain acids causes the patient's urine to have a caramel-like smell. Another very rare condition — a defect in fat metabolism — is sometimes called 'sweaty feet disease.'" he continues. "It causes affected infants to smell like a locker room."

Cystic fibrosis, a genetic disease that occurs in about 26 out of 100,000 white infants born in the U.S., causes the infants' stools to be fatty and foul-smelling. A fruity aroma on the breath is characteristic of persons with untreated diabetes, which has a strong pattern of inheritance between generations.

"There are many inherited diseases in which a distinct odor is part of the clinical picture," says Hillman. "The physician does need a trained nose — that's a big factor."

Megan suffered from delayed development and had an unusual odor. These symptoms motivated her mother to seek their cause, a quest that eventually brought her to the Clinical Research Unit at Children's Hospital.
Sniffing out genetic disease requires noting a combination of symptoms. Often the most obvious are neurological signs, like irritability and failure to develop motor skills at a typical age — parents seek medical attention because their baby fails to roll over or sit up or stand. In addition, these children will have a problem with eating: either they eat very little, or they vomit. But tragically, parents whose children have these symptoms may be rebuffed when they seek medical attention. Case in point: Megan, age two-and-a-half.

Megan's parents first sought help for their irritable baby when she was nine months old. Megan had always eaten poorly, and she still didn't stand alone. A series of specialists consulted by this midwestern couple either ignored the parents' pleas or were hostile: "One doctor told me that I was just overly conscientious," remembers Megan's mother. But when she pointed out the odor in her daughter's clothes, doctors agreed it wasn't normal; they suspected, they said, maple syrup urine disease.

Megan was flown to Colorado for a series of developmental tests which confirmed the abnormal development reported by her parents. "They told us that Megan was about a year behind in skill development," says her mother. "But they still didn't know what was causing the peculiar odor." Finally, last summer, Megan was referred to Hillman. By practicing what he refers to as "old fashioned medicine," Hillman was able to diagnose Megan's rare disorder. It wasn't maple syrup urine disease, but instead was an inability to perform a key "last step" in one of the pathways of fat metabolism.
The diagnosis was all the more remarkable considering that Megan may be the only living child with this particular defect.

There are only 75 Clinical Research Centers in the U.S. — places where metabolic defects like Megan's can be diagnosed. These centers, funded by competitive federal grants, are each "hospitals-within-a-hospital." They consist of a core laboratory, a metabolic kitchen, treatment rooms, nurses station, and outpatient section. The laboratory and kitchen provide the controlled environment necessary to study complex metabolic and nutrition-related disease processes, in a multidisciplinary setting. Washington University Medical Center has "one of the oldest, largest, and most productive Clinical Research Centers in the U.S.,” according to Philip E. Cryer, M.D., the center's director. Established in 1960, the center has both adult and pediatric units in which a wide spectrum of abnormal conditions is studied and treated: epidermolysis bullosa, a rare childhood disease in which the skin blisters and fingers fuse; growth hormone deficiency in children; immunodeficiencies, such as the "bubble boy" disease; bone diseases; neuromuscular conditions like muscular dystrophy and multiple sclerosis; and a host of other disorders, including one of the most comprehensive diabetes research and treatment programs in the country.

Megan was hospitalized in the Clinical Research Unit at the medical center's Children's Hospital, and Hillman began his methodical search for the cause of Megan's problems. Besides Megan's odor, the other distinctive clue was her diet: "Megan's dietary history was confusing because whenever you eat protein, you also eat fat," says Hillman. "Megan had limited her protein intake dramatically, but this apparent aversion to protein was really nature's way of limiting her fat intake. We loaded her with milk to fill her up with protein, thinking we'd find a defect in amino acid metabolism. Instead, the concentration of fatty acids in her blood and urine went up."

Hillman analyzed the compounds in Megan's blood and urine, and discovered a high concentration of butyric acid. This buttery-smelling substance accumulates because of a genetic defect in Megan's fat-processing enzymes. Hillman sent a sample of Megan's tissue to William Rhead, at the University of Iowa, to test for the fat-digesting enzymes that he suspected of being missing or low. While awaiting results from Rhead, Hillman put Megan on a special diet, low in fat and high in sugars. He also added supplements of glycine, an inexpensive amino acid which helps clear fatty acids from blood serum. Since Megan fortunately has a relatively mild form of the disease, Hillman suspects that she will do well on the diet. But as to how reversible her symptoms are, Hillman is unsure.

"Since there are so few children with this particular defect," says Hillman, "we have to work by analogy with other diseases. We don't know exactly how toxic butyric acid is to the brain. All we know is that currently, Megan is about a year behind where she should be. But once her diet is adjusted, she might catch up. Other children with similar diseases have shown striking improvement once their diet is corrected."

On a recent followup visit to the medical center, Megan seemed as happy and healthy as any other toddler, and her mother confirmed that the dark-haired, long-lashed little girl had improved substantially since beginning her low-fat, high-carbohydrate diet. "She's much less irritable now," said her mother. "She doesn't cry when strangers approach. And the odor has disappeared."

Besides careful examination of the patient and attention to any odors they carry, Hillman stresses the importance of taking a good dietary history. "It's old-fashioned medicine, really," he says. "And believing mothers — that's probably the key to the whole story."
Cell TRAFFIC: INS & OUTS

BY KAREN FREEMAN

Molecules — big and small — rush in and out of cells at a dizzying pace. And within each cell, vital components are constantly shuttled between compartments. The frantic pace would stump a traffic controller, but mechanisms within each cell impose order and structure upon the apparent pandemonium. Two research groups at the School of Medicine are deciphering these traffic patterns and pinpointing the junctions where the cell posts its “traffic cops.”

One way cells sample their environment and take in the molecules they need is by coating their surface — the plasma membrane — with receptors, the cell’s “barges.” Receptors ferry metabolically important molecules — the ligands — into cells, shuttling them between cell compartments. But once the loaded barge reaches its destination, its cargo must be delivered and the barge must return for another load. Researchers at work in the laboratories of Philip D. Stahl, Ph.D., and Jacques U. Baenziger, M.D./Ph.D., are trying to understand the cell’s system of routing barge movement and directing cargo delivery.

Once this is understood, there may be widespread application: “Although the receptors are highly specific, many appear to utilize the same general mechanism for entry into the cell,” Baenziger points out. The receptors studied by Baenziger’s and Stahl’s groups transport glycoproteins — proteins with groups of sugars attached. For two of these glycoprotein ligands, sugar components appear to be the shipping labels assuring that the cargo reaches its proper destination.

The cell has to solve the problem of how to transport ligand-cargo through hostile environments. Ligands are at home in the cell’s liquid interior, but they cannot freely move into a cell or between cell compartments. That’s where the receptor comes in. The receptor is at home in both environments; part of it prefers to be submerged in the membrane, while the other parts can drift into the aqueous milieu on either side of the membrane, looking for ligands. Loading the ligand...

Gold particles stipple the edge of a cell organelle (center). These particles trace the pathway followed by molecules transported inside the cell. Using John Heuser’s quick-freeze technique, Clifford Harding employed two sizes of gold particles to differentiate phases of transport. Here, a vesicle called a CURL can be seen curling off the lower right side of the organelle. (Micrograph courtesy of Philip Stahl)
piggyback, the receptor gives its ligand a ride into the cell.

**FROM HERE TO THERE**

Research in Stahl's lab has traced the path of two receptors that bind glycoproteins. Clifford Harding, M.D./Ph.D. (a former MSTP student) and Marilyn Levy, A.B., have been working on one of these — the transferrin receptor. This receptor lets a glycoprotein called transferrin into the cell to deposit its cargo of iron.

Unlike the role of many receptors, the function of the transferrin receptor is clear: it carries iron into the cell. Receptors such as the one for transferrin are in constant motion, with only a small percentage exposed on the cell surface at any one time. Like barges moving from the cell surface to the cell's interior, they recycle back to the surface once they deliver a load of freight. (But not all receptors recycle; some make one-way trips.) To get a clear idea of what happens to a receptor when it ferries its ligand inside the cell, Harding and Levy bring cell traffic to an immediate halt by quick-freezing the tissue.

Tom Wileman, Ph.D., a postdoctoral fellow, is studying the mannose receptor. But the mannose receptor's role is less clear than transferrin's. Since it's found on macrophages — cells that migrate into inflamed areas — it may play an important role in inflammation. And the mannose receptor may also be important for picking up pathogens and transporting them to lysosomes — the cell's "garbage disposals" — to be destroyed. "We have a receptor here that can be regulated by a number of things, and that might be important for host defense," muses Stahl.

A ligand's journey starts at the cell surface and proceeds through the murky interior of the cell. Receptors begin the journey on the plasma membrane, and the initial steps in the ligand's ride have been documented in a number of systems. The ligand binds to its receptor, the membrane forms a pit by invaginating, and the receptor-ligand complex moves into the cell in a vesicle formed from the pit.

First identified in 1964, these vesicles...
are coated with clathrin molecules (see diagram). Greatly enlarged, clathrin molecules appear as a honeycomb-like basket supporting these vesicles and pits. Under lower magnification, this clathrin coating looks like dark fuzz surrounding the vesicles.

The formation of coated vesicles explains how many receptor-ligand complexes gain entry to the cell. But after the vesicles lose their clathrin coat, how does the cell steer the naked vesicle (which contains the receptor-ligand complex) to its proper destination?

**ACIDITY AFFECTS ROUTING**

The mannose and transferrin receptors follow different routes, Stahl has found, because they respond differently to acidity. Under neutral conditions found at the cell surface, the mannose receptor securely binds its ligand; under acidic conditions, the receptor frees its freight.

By contrast, transferrin (with iron in tow) stays tightly bound to its receptor over conditions ranging from acidity to neutrality. (Transferrin without iron binds well to its receptor only under acidic conditions.)

Stahl proposes the following itinerary for cell traffic: The mannose receptor binds its ligand under neutral conditions, then ferries it into an acidic compartment within the cell. The ligand is dumped, and the receptor recycles to the cell surface. This receptor recycling can be very fast. In macrophages, each mannose receptor can be reutilized about every 12 minutes.

Stahl's route for transferrin is somewhat different: Transferrin binds its receptor at the cell surface, under neutral conditions, then travels with the receptor to an acidic compartment. The iron dissociates from the transferrin in the acidic environment, but the iron-free transferrin remains bound to its receptor and gets a ride back to the cell surface. Once there, it is freed into the extracellular space, where it can bind iron again and repeat its journey.

These models both assume that the cell has acidic compartments that are not lysosomes, because a side trip into a lysosome by a receptor would degrade it. Stahl has used electron microscopy to find such compartments, whimsically called a CURL — Compartment of Uncoupling of Receptor and Ligand.

CURLs, unlike other cell organelles, carry no easily identifiable markers. So how can they be studied? Harding uses a double-labeling technique and prepares the tissue for electron microscopy with a quick-freeze method developed by John Heuser, professor of cell biology and physiology. Cells are dosed with ligands that are labelled with small gold particles. These ligands help identify electron micrographs. These membrane fragments presumably carry the mannose receptor, or iron-free transferrin and its receptor, back to the plasma membrane.

Stahl's laboratory can partially purify CURLs to study their properties. And he wants to know more about the mannose receptor and how it's regulated. "We've isolated the mannose receptor and some day we hope to clone the gene," he says.
Stahl, after 14 years at Washington University, has a new job and a new department — or, rather, an old department under a new name. He's the new chairman of the Department of Cell Biology and Physiology, formerly the Department of Physiology and Biophysics, and was recently named Edward Mallinckrodt Professor.

Baenziger has also been at Washington University for a considerable time. He received the M.D./ Ph.D. degrees here in 1975 and is now professor of pathology. Most recently, he received the Warner-Lambert/Parke-Davis Award from the American Association of Pathologists in recognition of his work on the interaction of carbohydrate molecules and ligands at the cell surface.

Baenziger is mapping the route for another glycoprotein receptor, one that will bind sugar chains that end with galactose. He is interested in glycoproteins' carbohydrate components and their ability to act as shipping labels for protein transport, "even though they're just a few percent of the molecular weight of the glycoprotein," he says.

The physiological role of the galactose receptor has yet to be worked out. Although it appears to pick up a type of antibody and transport it into the cell, Baenziger will need more convincing before he'll be ready to call the antibody the natural target of the galactose receptor. The physiological role of the galactose receptor is still mysterious, but much is known about the physical properties of the receptor in liver cells.

Baenziger is using a novel method to study the recycling of the receptor, a technique he stumbled upon while studying something else. Unlike Stahl's traffic-freezing method, Baenziger alters the ions bathing the cells, halting traffic by causing the cargo, but not the cargo-bearing proteins, to stall; the ligand accumulates inside the cells, and the journey is halted in midstream. Baenziger found that ligands pile up in uncoated vesicles that are not lysosomes, vesicles analogous to the CURLs analyzed in Stahl's lab.

This discovery armed Baenziger with a new tool for purifying the vesicles. (The vesicles are hard to purify because their density is similar to that of other cell components, and standard separation methods sort them according to differences in density.) He is trying to link ligands for the galactose receptor to dextran beads that are bonded to iron. This magnetic cargo accumulates in vesicles and will enable him to separate these cell compartments. By passing the cell contents through a column in a strong magnetic field, Baenziger can remove the iron-loaded vesicles for further study. Eventually, he may be able to map out the route that receptors follow in their journey from the plasma membrane to their intracellular destination and back again. He knows, though, that receptor recycling is a reality: "Otherwise, the cell couldn't make receptors fast enough to keep up with the traffic," Baenziger says.

So far, Baenziger has found evidence that the vesicles he studies are of two types. He is scanning the membranes of the vesicles, looking for proteins that may differ from those found on the plasma membrane, but he has yet to find unique components. "The differences may be quantitative instead of qualitative," Baenziger says. "The membranes may have the same complement of proteins, but they may be present in different amounts."

**TREASURE MAPS**

Trying to decipher the coding involved in handling traffic in the cell is an attempt to understand one of the cell's most fundamental processes. Will such work lead...
to cures for disease? Probably — a long way down the road. Receptor systems are medically important because pathogens can use them to get into cells. Defective receptors play a role in many common diseases, such as some forms of diabetes. But does faulty receptor recycling cause disease? The answer to that must await more basic research into normal receptor processes. Discovery of defective receptor recycling in an animal would be significant, because understanding the glitches in a system often leads to an understanding of how to correct disease processes.

Eventually, research could allow the dissection and reconstitution of such receptor systems, so scientists could learn how to manipulate them. What keeps receptors and their ligands going in the right direction? Do differences in the environments encountered by receptors and ligands keep traffic moving in the right direction? Or does the cell exert control by putting the right things in the right place at the right time? When the controls over this most basic mechanism of cell physiology are understood, the bounty will undoubtedly spill over into many fields of biology and medicine.

Karen Freeman is a St. Louis freelance writer.
In a high-tech era, surgery without computers and other electronic wizardry may seem almost an anachronism. Even today, more than electronic gadgets and technical skills are required — ingenuity and creativity are among the surgeon's less tangible tools.

Such traits have helped surgeons in the Department of Otolaryngology at the School of Medicine produce innovations in microvascular reconstructive surgery of the head and neck, fashioning new body parts out of tissue taken from elsewhere in the patient's body. They continue the tradition begun by the late Joseph Ogura, former head of otolaryngology, who pioneered the use of more conservative surgical procedures to treat laryngeal cancer.

Richard Hayden, M.D., assistant professor of otolaryngology, points out that this emphasis on reconstruction is a radical departure from traditional care of patients with head or neck cancer: “Earlier in this century, the emphasis was on removal of the tumor, without much attention paid to restoration. In the last two decades, this has changed. Now, the emphasis is on less radical removal of tissue for cure, a movement pioneered by people like Ogura.

“The other major thrust has been in reconstructive surgery,” continues Hayden, on staff at Barnes Hospital. “But microvascular surgery of the head and neck has had some peaks and valleys. The enthusiasm generated in the early ’70s waned, partly because of the limited number of free flaps available, and partly because of the time-consuming nature of microvascular surgery and the expertise needed by the surgical team. The new enthusiasm for microvascular surgery was probably generated by the development of more versatile free flaps. These flaps carry larger vessels that make the transfer easier to perform and increase the success rate.”

A recent landmark in reconstructive surgery occurred when Hayden and John M. Fredrickson, M.D., fashioned functional tongues for three patients whose cancerous tongues had to be removed. Although other surgeons have reconstructed this organ by a variety of methods, none used Fredrickson and Hayden's technique: an implant of skin-covered muscle, with microsurgical attachment of nerve and blood vessels in the implanted tissue. Sufficient nerve growth occurs in the new tongue.
to restore function, so that activities like swallowing — and speaking — are now possible.

Bobby R. Alford, M.D., head of otolaryngology at Baylor College of Medicine in Houston, points out the importance of the W.U. team’s success in fashioning a functional tongue for amputees: “For the first time in medical history, these patients have the opportunity for a useful life. They can swallow and speak — do all the things we take for granted.”

They also connected the tongue stump nerve to the nerve in the implant. One year after her surgery, Mrs. Foster is back at work, speaking intelligibly and swallowing well.

In performing such procedures, ingenuity comes into play when the donor site for the transplanted tissue is chosen. In the case of the artificial tongue, the donor muscle section has been a long-time ‘workhorse’ of reconstructive surgeons. Good results come from selecting and preparing new donor tissues which can be microsurgically reconnected in such a way as to stimulate nerve regrowth and subsequent muscle function.

Mrs. Pearline Foster was the first patient for whom Fredrickson and Hayden fashioned a new tongue, using a piece of large muscle (the latissimus dorsi) taken from where it crosses the side of the chest. One group of head and neck surgeons, headed by Gershon J. Spector, M.D., professor of otolaryngology, removed the cancerous tongue. Hayden and Fredrickson’s team removed and prepared the donor tissue, trimming and tailoring the muscle and overlying skin to fashion the new tongue. Then, under the operating microscope, they laboriously joined blood vessels in the implant to suitable matching vessels in the tongue stump.

Mrs. Pearline Foster (left), pictured here with her supervisor at Bellefontaine Habilitation Center, is back at work after recovering from surgery. Mrs. Foster was the first patient for whom a new, functional tongue was created by surgeons from the Department of Otolaryngology.

In performing such procedures, ingenuity comes into play when the donor site for the transplanted tissue is chosen. In the case of the artificial tongue, the donor muscle section has been a long-time ‘workhorse’ of reconstructive surgeons. Good results come from selecting and preparing new donor tissues which can be microsurgically reconnected in such a way as to stimulate nerve regrowth and subsequent muscle function.

Microsurgery is being used in neurosurgery, obstetrics and gynecology, orthopedics, and plastic and general surgery. Hayden sees the technique applied to various aspects of head and neck reconstructive surgery, not just the tongue. Facial reanimation, for those whose faces have been paralyzed by facial nerve paralysis or affected by cancer surgery, is one example of another application of this technique. Using an inner thigh muscle — the gracilis — as donor tissue, or other muscles from the chest, surgeons can restore movement to a frozen face. “This is a burgeoning field and in time, we’ll know the best donor sites,” Hayden speculates.

In addition, microsurgery can be used to reconstruct the cervical esophagus when a patient loses this structure to cancer, which happens when the larynx and pharynx are removed. “Using microvascular techniques, we have used skin flaps from the thigh, or loops of jejunum, to produce good conduits from mouth to esophagus,” says Hayden.

The technique has been invaluable in reconstructing the jaw after its loss in an accident or after cancer surgery. And it’s in developing this technique that creativity comes into play.

In the past, most facial bone reconstruction has been done using rib, a technique developed by Fredrickson in 1973. (This was the first demonstration that free bone could be revascularized to repair bone defects.) But a rib is too small and weak to really be an ideal substitute for the sturdy jawbone. Patients with the so-called Andy Gump deformity, named for the chinless cartoon character, needed something better.

Fredrickson’s team was able to extend and improve a technique developed by Australian physician Ian G. Taylor to utilize another source of bone — the crest of the pelvic girdle. By meticulous anatomical studies, Fredrickson was able to elucidate the complete arterial and venous blood supply of this region to calculate the maximum area of the bone that could be harvested and survive when it was transplanted. This bone has proven to be a far more effective mandibular substitute than rib. So far, the technique has been used to reconstruct the jaw in seven patients, most of whom had jaw defects resulting from cancer surgery.

One of the principal advantages of the larger-sized ribbone graft is that unlike transplanted rib, it has the strength to accept the titanium metal pegs which support dentures.

“If you work as a team,” explains Fredrickson, “you can do some very good things for patients with complex needs. That’s the beauty of an institution like this...
Richard Hayden (left) instructs Cecil Yeung, fellow in otolaryngology, in microsurgical technique. Washington University Medical Center is one of few academic health centers where this technique is taught to head and neck surgeons.

require this skill. But completely trained head and neck reconstructive surgeons of the future will be required to be skilled in microsurgery. Otherwise, they will not be able to provide the ultimate in care to patients who require these treatments.

"The great advantage of this technique compared to conventional reconstructive techniques like flaps or grafts is that survival of the transplanted tissue is greatly enhanced," says J. Gail Neely, M.D., head of otorhinolaryngology at the University of Oklahoma. "Also, smaller pieces of tissue are required. Flaps are the great workhorses of our field, but they require an implant six to 10 times the size of the defect and must be in an area close enough to be swung around and reach the defect."

Neely, a consultant to the journal Microsurgery, says that a principal disadvantage of microsurgery — the time required to complete meticulous procedures — will lessen as additional surgical tools are developed: "The laser, properly focused, can weld together tiny blood vessels in a fraction of the time required for sutures. Eventually, microsurgery will probably evolve to the point where someday we can do surgery on individual cells."

That day is far in the future, as is the time when advances in immunology solve the problem of tissue rejection, the surgeon's nemesis. "If someone can solve the problem of tissue rejection, they will surely win the Nobel Prize," comments Fredrickson. "And when it is accomplished, that will bring about a renaissance in reconstructive surgery. Then, one could take human tissue at the time of death and replace loss of like tissue for a patient in need. For example, if a surgeon could use another human tongue to replace a tongue, the advantages would be tremendous. Patients would be much better off than what we can do now, even with the strides in microsurgery that have been made. That's going to be a terrific advance when it happens."

(Ed. note: some of the results of the bone graft and reconstructive tongue surgery are published in ACTA OTOLARYNGOLOGICA, Volume 99, 1985.)
STUDENT STAGE

Match Day 1985

This year, as in the past, the idea of Match marked Match Day — the event at which fourth-year students find out where they'll begin their residencies. Tradition persisted in the pattern of choices. Medicine topped the list, with nearly half the 130 students opting for internal medicine.

Fifteen students chose pediatrics, and 12 decided on surgery. Transitional residencies (formerly called flexible residencies) attracted 12 students. Seven picked radiology. Pathology was chosen by six students, five picked psychiatry, and four chose family practice. Obstetrics/gynecology attracted four, and two chose anesthesiology. Otolaryngology, orthopedics and urology each attracted one.

This year, many more students than usual will be staying in the Midwest, although fewer will remain in St. Louis than in years past. Washington University Medical Center hospitals attracted 34 students. One-third of the students will remain in Missouri and nearly half will be staying in the Midwest.

"Married graduates are more likely to stay in this area, for two reasons," says John Herweg, M.D., associate dean. "Their spouses are usually working and don't want to leave their jobs. And they know that they can get a better value for their housing dollar here than on either coast."

In 1985, only 11 graduates of the School of Medicine will be moving to California; in 1980, nearly twice that number headed west. A similar decline in numbers held for points south: Houston beckoned only two students this year, compared with 11 in 1980. But the Big Apple is a powerful attraction, possibly because so many fourth-year students are from New York. Twelve will be heading for that city in July.

The geographical pattern to this year's matching was one of few unusual features characterizing the class of 1985. Their choice of specialty conformed to traditional patterns established and molded over the years. And this is a big surprise because many had predicted that the exponential rise in indebtedness of medical students would influence their choice of specialties.

Contrary to prediction, higher-paying specialties like surgery have not lured graduating students in great numbers, at least not immediately upon graduation from medical school. This is the conclusion reached from an analysis of trends in specialty choices over the past 20 years at Washington University School of Medicine.

The percentage of fourth-year students entering surgery has held steady between 10 to 15 percent, with a slight decline evident. But some students who enter medicine now, says Herweg, may not stay there: "Many will take one year of medicine, then go into some other specialty."

Not as many students — usually between five to 10 percent — choose family practice, but the number has held steady over the past decade despite predictions to the contrary. Part of the reason for this, says Elmer Brown, M.D., associate dean for postgraduate medical education, is that "no one here acts as an advocate for family practice. And that needs to happen before any specialty becomes a popular choice."

The most precipitous decline has been in the number of students choosing transitional residencies: From a peak of 33 percent of the class of 1967 choosing rotating internships, fewer than 10 percent of any class within the last decade has opted for a transitional residency. Brown speculates that this is due to a transitional residency's image now as something "for students who can't make up their minds. And the decline in transitional residencies," he continues, "probably reflects the elimination of high-quality rotating internships beginning in 1975."

Surprisingly, this drop in transitional residencies has not been mirrored by a rise in any specialty choice. The number of students choosing medicine has hovered around 40 percent, with a slight increase in numbers evident...
over the past two decades. Thus, predictions that high-paying specialties would be chosen over the less lucrative have not held true, at least at Washington University. “Our patterns pretty well conform to what is seen nationwide,” says Brown. “For example, few of our students go into psychiatry, but then, that's the national pattern.”

However, speculation that student indebtedness would continue to rise has proven true, to the chagrin of many. According to John Walters, assistant dean, 33 fourth-year students are more than $30,000 in debt, and one owes more than $50,000. But whether these students finally end up in lucrative specialties as a result of their indebtedness is anyone's guess. “This is potentially masked by the numbers of students entering preliminary medicine or transitional residencies,” says Brown. “Some who choose medicine internships may eventually end up in a field like ophthalmology, which surveys show to be near the top in income potential.”

“I see the beginning of a trend this year in the large numbers of third-year students expressing interest in ophthalmology or radiology,” discloses Herweg. “But in the future, these may not remain such high-income specialties because of the growing numbers of salaried physicians working for corporations. So even if a student enters a high-paying specialty now, the growth of corporate medicine may mean that in the future, those specialties may not guarantee a high income.”

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<td>West Suburban Hospital  Susan Locke, Family Practice  Larry Schertz, Transitional</td>
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Dave Milstone (foreground) looks for his match.
Marisa Klein and Darren Gitelman are husband-wife fourth-year students who want their matches to match.
As this issue went to press, we were notified of the death of Elisabeth Demonchaux. We extend our sympathy to her family and friends.
The autopsy — a traditional mainstay of medical education — is being eroded by several forces. Some say it is in danger of becoming extinct.

The autopsy rate has fallen substantially in the past 20 years at Washington University Medical Center. In 1966-67, autopsies were performed in 68 percent of deaths; in 1984, postmortem exams were conducted in only 33 percent. Our statistics reflect the national trend. But the wisdom of avoiding autopsies was challenged dramatically by recent studies.

In one of these, Zarling et al (JAMA 250: 1171-81, 1983) documented that at the Baptist and University of Tennessee hospitals in Memphis, only 53 percent of autopsy-proven myocardial infarction had been correctly diagnosed. And another hallmark autopsy survey from the Harvard hospitals showed similar results. This study highlighted common medical entities most usually overlooked or misdiagnosed — pulmonary emboli, certain cancers, fatal septicemias, and myocardial infarction (Goldman et al, NEJM, 308: 1000-5, 1983). Evidence indicated that despite the advent of computed tomography (CT or CAT scans), clinical diagnoses and autopsy results showed a steady rate of discrepancy — about 22 percent — during three decades (‘60s, ‘70s, and ‘80s). Goldman’s team concluded that patient survival may have been adversely affected in about half those cases.

Thus, roughly 10 percent of these discrepancies could reflect an inherent error rate of clinical diagnoses that could not be lowered by any means. Or, as I believe, the discrepancy rate would be even greater if more autopsies were performed. An ongoing, real increase in the accuracy of many aspects of medical diagnosis may have kept the discrepancy rate artificially low. Data supporting these conclusions have emerged from an ongoing study at 32 medical centers, sponsored by the College of American Pathologists.

These figures defy the emerging mythology that the advent of powerful diagnostic laboratory technology has perfected clinical diagnosis. The existing error rate should not be accepted as immutable and therefore unworthy of serious concern, but instead should be vigorously assailed. Zero discrepancy should be the target, yet it is difficult to convince pathologists and clinicians of this. The death of a patient — and attendant autopsy — represents a certain degree of failure and an admission of our limited, albeit very powerful, diagnostic and therapeutic capacities.

Currently, when autopsies are performed, the results usually consist of 10 to 15 hematoxylin- and eosin-stained histologic slides, a few photographs, and a report. Thus, not only are too few autopsies performed, but the information gleaned from postmortem exams is woefully lacking in substance.

We pathologists must acknowledge our role as both the cause of, and the solution to, the problem of declining postmortem exams. However, we can help medicine’s phoenix re-emerge from its ashes with resurrected youthful vigor, having been consumed by its own hand as was the ancient bird of Egypt.

First, we must recognize the value of autopsies in refining and perfecting clinical diagnosis. We can reinforce the autopsy’s importance in our communications with clinical colleagues by acting as trusted and expert consultants with valued insights into the anatomic expressions and basic mechanisms of disease.

The revolution in digital electronics allows us to use computer technology to instantly transmit autopsy images — with voice and digital data — anywhere in the world. Routine procedures for procuring data should include electron microscopy; immunology and biochemistry ought to be within the scope of our inquiries. The addition of these untapped resources would supply information that could improve teaching conferences, and the improved communication derived from use of electronics would enhance diagnostic accuracy and patient care.

Obviously, my suggestions would significantly escalate autopsy costs, which are already substantial: At Washington University Medical Center, the overall cost per case is nearly $2000. Currently, families are not assessed for an autopsy, and the economic burden falls directly on us. Thus, we must aggressively seek creative means for funding state-of-the-art autopsies. Since postmortem examinations directly verify accuracy of clinical diagnoses — thus providing an objective means of monitoring quality and controlling costs of medical care — they provide a potential for establishing a salutary cost-benefit ratio. Accordingly, third-party payers should be recruited to share in these costs.

The rightfully honored status of the autopsy in first-rate medical education and patient care deserves to be reinstated. The challenge? How best to promote communication between colleagues, disseminate autopsy information, and obtain critically needed funding to advance the diagnostic armamentarium of the modern autopsy pathologist. When this occurs, then medicine’s dodo will indeed have been transformed into a phoenix.

Daniel W. McKeel, M.D.
Associate professor of pathology

This is the opinion of the author, not necessarily shared by Washington University, Washington University School of Medicine, Washington University Medical Center, or the policy of any of these entities. Outlook welcomes replies to this editorial and invites contributions from its readers on other subjects.
Radiologist Receives Award

Michel M. Ter-Pogossian, Ph.D., director of the Division of Radiation Sciences at Mallinckrodt Institute of Radiology and professor of radiation sciences in radiology and biophysics in physiology, has received the distinguished Hermann L. Blumgart Pioneer Lecture Award.

This award was created by the New England Chapter of the Society of Nuclear Medicine in honor of the late Dr. Blumgart, widely known as the "father of clinical nuclear medicine." Since 1978, it has been presented annually to outstanding innovators in the field of medical instrumentation.

A physicist and nuclear scientist, Ter-Pogossian is recognized for his key role in the introduction and use of radioisotopes for biomedical research and also in the development of PET (positron emission tomography) scanners, which plot the path of these radioactive substances in living tissue. His contributions have enabled the study of biochemical processes occurring in the body, including the metabolism, circulation and permeability of the brain.

In 1951, Ter-Pogossian was a partner in the construction of one of the first scanning devices capable of detecting concentrations of radioactive material in living matter. Since then, his research has progressively advanced the practice of nuclear medicine. He was one of the first to use radioisotopes to detect brain tumors, and was the first in the world to report the biomedical application of the sodium iodide detector for the diagnosis of these tumors. An early promoter of stationary imaging devices, Ter-Pogossian was pivotal in the development of gamma devices.

As a result of successful preliminary studies conducted by Ter-Pogossian using radioactive oxygen, W.U. Medical Center was the first medical facility in the United States to install a biomedical cyclotron. The cyclotron produces the short-lived radioisotopes which identify, or label, molecules in the body for observation. In 1978, W.U. became the first medical center to utilize two biomedical cyclotrons.

Ter-Pogossian received his doctorate in physics from W.U. A member of the staff at Mallinckrodt Institute since 1950, he has published nearly 200 papers and over 50 book chapters regarding his work. In 1976, Ter-Pogossian was honored with the Paul C. Aebersold Award, the highest recognition for science bestowed by the Society of Nuclear Medicine.

Probsteins Create Oncology Lectureship

Mr. and Mrs. Norman K. Probstein have honored two physicians by creating an oncology lectureship at the School of Medicine.

The Probstein Oncology Lectureship was established in appreciation of professional services provided by William Fair, M.D., former head of the urology division of the Department of Surgery, and Carlos Perez, M.D., professor of radiology and head of radiation oncology at the medical center's Mallinckrodt Institute of Radiology.

"We are truly honored that Mr. and Mrs. Probstein have chosen to praise the work of Drs. Fair and Perez by establishing this lectureship," said William H. Danforth, M.D., chancellor of Washington University. "By sharing valuable medical information, programs like this one help physicians and other health care professionals, and are of immeasurable benefit to patients and their families."

Fair is now a physician at Memorial Sloan-Kettering Hospital in New York City. Perez is on staff at Barnes, Children's and Jewish hospitals.

In creating the lectureship, the Probsteins also expressed appreciation to the staff of Barnes Hospital and of Washington University Medical Center.

The annual lectures,
to begin this summer, will disseminate state-of-the-art information on concepts in cancer prevention, diagnosis and treatment, with an emphasis on genitourinary diseases. Outstanding investigators will be selected as speakers for the lectures, which will be offered to members of the medical community of St. Louis and the bi-state area. The lecture series is organized by Perez.

Klahr to Head Nephrology Society

Saulo Klahr, M.D., director of the renal division at the School of Medicine, has been named president-elect of the American Society of Nephrology.

Klahr is professor of medicine at Washington University and a physician at Barnes and Jewish hospitals.

He will serve as president of the American Society of Nephrology in 1986. The 4,000-member organization was formed in 1967 for physicians and basic scientists who conduct kidney-related research.

Klahr's research expertise includes urinary tract obstruction, renal metabolism and physiology, chronic renal disease, and parathyroid hormone metabolism.

He joined the faculty at Washington University in 1963 as an instructor in medicine and became professor of medicine and director of the renal division in 1972.

Klahr received the doctor of medicine degree in 1959 from the Universidad National de Colombia School of Medicine in Bogota, Colombia. He interned at Hospital San Juan de Bogota, Colombia, and served a residency in medicine with University Hospital of the Universidad del Valle School of Medicine in Cali, Colombia.

He holds appointments with several government agencies and voluntary organizations, among them the American Heart Association and the National Kidney Foundation. He has served on a number of committees for the National Institutes of Health, and currently chairs a planning committee for a clinical study on how diet modifies the course of progressive renal disease.

He is a fellow of the American College of Physicians, a member of many other professional societies, and on the editorial boards of numerous journals, including Kidney International, Renal Physiology, American Journal of Nephrology, Clinical Update in Nephrology and Clinical Journal of Hypertension. He also has edited six textbooks on general nephrology, one of which has been translated into Russian. Klahr serves frequently as a visiting professor and lecturer for universities and organizations throughout the country.

Volunteers Needed for Alzheimer's Disease Study

Elderly volunteers suffering from memory loss are needed for research that may help scientists learn more about normal aging as well as the effects of Alzheimer's disease on the brain.

The on-going study is being conducted by the Memory and Aging Project at the School of Medicine. Researchers have been investigating Alzheimer's disease, milder forms of memory impairment, and healthy aging. The study is directed by Leonard Berg, M.D., professor of clinical neurology at the School of Medicine and staff physician at Barnes, Children's and Jewish hospitals.

According to Berg, five to 10 percent of the U.S. population is affected by Alzheimer's disease, the most common cause of severe intellectual impairment and institutionalization among the elderly.

Currently, the Memory and Aging Project is recruiting volunteers aged 65-84 who have intellectual impairment but are in good general health. Studies include a clinical examination by a physician specializing in dementia, psychometric tests of memory and other thinking functions, brain wave tests and a special CT scan of the head. Also, researchers will assess participants' abilities in daily living activities, as well as stress levels of family members.

Some participants will be selected for positron emission tomography (PET) scanning of the brain. All of the studies will be done at no charge.

Elderly volunteers, their relatives or physicians may call the Memory and Aging Project office (telephone 314-362-2683) for more information.

Sobel to Hold New Professorship

Philanthropist Tobias Lewin has established an endowed professorship to further heart research at Washington University School of Medicine. The first Lewin professor will be internationally renowned cardiologist Burton E. Sobel, M.D.

Creation of the Tobias and Hortense Lewin Distinguished Professorship in Cardiovascular Disease was announced March 19 during a dinner at the St. Louis Club. In the last decade Lewin and his late wife, Hortense Cohen Lewin, have provided major funding to nurture the arts.
and humanities in the St. Louis area. The Lewins are both alumni of Washington University. This is their first endowment in the field of medicine.

The Lewin professorship at the School of Medicine was made as a part of the Alliance for Washington University, a $300 million fund-raising campaign.

In announcing the gift, Washington University Chancellor William H. Danforth, M.D., remarked, "Through the years, Toby Lewin and the late Hortense Lewin have become recognized in St. Louis as benefactors of the arts. Because of their generosity, Washington University has been able to offer programs that enrich the lives of its students and the public. It is quite fitting that the Lewins now lend their support to the medical arts, helping ensure progress in research on cardiovascular disease."

Burton Sobel, professor of medicine and director of the cardiovascular division at the School of Medicine, is well known for his research on thrombolytic therapy, a new treatment that could save thousands of lives each year. In 1984, he published results of a pilot study using an experimental chemical called t-PA, tissue plasminogen activator. (See inside-front cover.) Subsequently, comparable results were obtained in additional studies of more than 200 patients in collaborative trials involving 15 medical centers.

At the medical school, Sobel is director of a Specialized Center of Research (SCOR) that is investigating the heart's response to ischemic injury and trying to identify new therapeutic approaches for heart disease. The research involves 40 scientists from 12 departments, and has received $9.2 million in renewed funding for the next five years from the National Heart, Lung and Blood Institute.

A faculty member at Washington University since 1973, Sobel is chief of cardiology at Barnes Hospital. He received the doctor of medicine degree *cum laude* from Harvard Medical School, held an internship and residencies in medicine at Peter Bent Brigham Hospital, and trained as an assistant in medicine at Harvard Medical School.

Sobel is a member of many professional societies, research advisory committees and editorial boards. Currently editor of the journal *Circulation*, he has lectured nationally and internationally, and has written more than 300 articles on his research.

He is recipient of the 1971 National Heart and Lung Institute's Career Development Award, the 1981 Heart Research Foundation's International Award, and the 1984 American Heart Association's Distinguished Achievement Award.

**Stahl Heads Cell Biology and Physiology Department**

Philip D. Stahl, Ph.D., has been named Edward Mallinckrodt Jr. Professor and Head of the Department of Cell Biology and Physiology at the School of Medicine. His appointment was announced by William H. Danforth, M.D., chancellor of Washington University. Stahl has been on the faculty of the School of Medicine for almost 15 years, most recently as professor of physiology and biophysics.

Stahl's research has centered on the mechanisms of protein transport and degradation in macrophages, cells which help eliminate worn-out components in the body, repair injured tissue and aid in defense against infectious agents. Protein digestion in cells involves digestive bodies called lysosomes. In 1978, Stahl and his colleagues discovered a new receptor on macrophages which binds sugar-coated proteins (glycoproteins) as well as certain microorganisms and transfers them into the cells to lysosomes where they are digested. These studies have been influential in our understanding of the mechanism by which cells recognize and transport proteins.

Stahl received his doctorate in pharmacology from West Virginia University in 1967. He has been on the faculty of Washington University since 1971, when he was hired as an assistant professor, and has been professor of physiology and biophysics since 1982.

In 1980, Stahl was a Senior International Fogarty Fellow of the Sir William Dunn School of Pathology at Oxford University. During this period he and his colleagues at Oxford developed the first macrophage hybridoma, which allowed for the production of these cells and their products in large quantity. His training also includes postdoctoral fellowships with the Arthritis Foundation in the molecular biology department at Vanderbilt University, and with the Space Sciences Research Center and pharmacology department at the
University of Missouri.

His research on the macrophage hybridoma is supported by the Monsanto Corporation. He also holds grants from the Muscular Dystrophy Association of America, Inc., the National Institute of Allergy and Infectious Disease, and the National Cancer Institute. He is a member of the Pathobiology Study Section of the National Institutes of Health, and co-chairman of the Gordon Conference on Glycoproteins.

Stahl is author of more than 60 journal articles and over 30 abstracts describing his research.

Audiologists Monitor Effect of Drugs on Patients' Hearing

The Department of Otolaryngology is beginning a program to monitor patients who are taking medications that may damage their hearing. The division of audiology is sponsoring the program to prevent or reduce drug-induced hearing loss, and in cases of irreversible hearing loss, to provide immediate therapy and counseling. The program is approved by the school's Medical Advisory and Pharmacy and Therapeutic Drug Committees.

"Patients who are at highest risk of drug-induced hearing loss are those taking certain antibiotics or one of the anticancer drugs," said Margo Skinner, Ph.D., assistant professor of otolaryngology and director of audiological services at the School of Medicine.

For example, she said, the antibiotics gentamycin and tobramycin — used for a broad range of bacterial infections, and critical for treating some life-threatening infections — are ototoxic, meaning they can cause severe and sometimes irreversible hearing damage. Another ototoxic medication is cis-platinum, which in the last five years has been increasingly prescribed for chemotherapy patients, she noted.

According to Skinner, patients who use these drugs are particularly at risk when they have decreased renal function, and when they take them in increased daily doses or for more than 14 days. They also are at risk when their blood tests show high peak and trough levels of the drugs, and when they combine or take the drugs consecutively with other ototoxic drugs, such as loop diuretics and medications toxic to the kidney. Other patients at special risk include those who already have hearing loss, severe visual impairment, advanced age or diabetes, as well as those who report tinnitus, hearing loss or dizziness.

Skinner recommended that physicians schedule hearing evaluations for patients whose conditions place them at greater risk of drug-induced hearing loss. Ideally, she said, patients should be evaluated before the start of treatment, or within 72 hours after medication begins, and then at regular intervals.

Hearing evaluations will be given in the audiology clinic, located at 805 McMillan Hospital at Washington University Medical Center, or at the patient's bedside if necessary. To schedule evaluations, physicians may call 314-362-7489.

Sloan and Klingenstein Fellowships

Two young neuroscientists at W.U. School of Medicine have received prestigious foundation fellowships to support their research.

Paul Taghert, Ph.D., assistant professor of anatomy and neurobiology, has been named a Sloan Research Fellow by the Alfred P. Sloan Foundation; and Lawrence Salkoff, Ph.D., assistant professor of neurobiology, has been named a Klingenstein Fellow in the Neurosciences by the Esther A. and Joseph Klingenstein Fund, Inc.

Since 1955, the Sloan Foundation has awarded over $42 million to more than 2,000 young researchers of extraordinary promise. The fellowships were established as a means of encouraging
basic research by young scholars at a time in their careers when their creative powers are often most acute and when other support is difficult to obtain.

This year, 90 winners were selected from among 400 nominations by a committee of recognized scientists and economists including Gerald D. Fischbach, M.D., Edison Professor of Neurobiology and head of the Department of Anatomy and Neurobiology at W.U. Each fellow will receive $25,000.

Taghert, using the simple nervous system of insects, is trying to isolate genes of neuropeptides, substances made by nerve cells. He is studying how the nervous system makes neuropeptides and how they act on other cells, as well as the regulation over expression of these substances.

Taghert received his bachelor's degree from Reed College in 1975, and a doctorate in zoology from the University of Washington-Seattle in 1981.

Salkoff, one of six junior investigators to be named a 1985 Klingenstein Fellow, will receive $100,000 to pursue his research.

Klingenstein awards are given to encourage both clinical and basic science investigators to engage in research that may lead to a better understanding of the cause, treatment and prevention of epilepsy.

Salkoff's research involves the use of fruit flies with genetic mutations affecting the nervous system to investigate the molecular properties of membrane ion channels. Ion channels, the "transistors of the brain," are responsible for the electric excitability in the nervous system.

Salkoff received his bachelor's degree from the University of California-Los Angeles in 1967, and his doctorate in genetics from the University of California-Berkeley in 1979. He completed postdoctoral training in biology at Yale University.

The Lipid Research Center Laboratory has been awarded a two-year accreditation by the College of American Pathologists (CAP).

CAP is a national medical specialty society of physicians certified by the American Board of Pathology. The Washington University laboratory, previously accredited by the Centers for Disease Control and the World Health Organization, is now recognized by all three accreditation groups.

The accreditation, based on results of an on-site inspection by the CAP Commission on Laboratory Accreditation,
oratory safety and laboratory therapies evaluate workers to determine their physical abilities, then retrain them with the physical skills necessary to perform their jobs. After the half-day evaluation, workers attend training sessions for an average of one month, or until work-related goals are met.

“Many of the workers we evaluate are appealing social security benefits,” explained Cole. “The IWJ program works closely with lawyers handling these cases. We strive to provide an objective evaluation in order to report the worker’s maximum capabilities.”

Cole foresees an increased role for the work assessment program in such cases, as well as in worker’s compensation and insurance cases.

The program receives referrals from neurologists, internists, orthopedists, worker’s compensation and insurance carriers, and rehabilitation councils. Workers suffer from stroke, hand and nerve injuries, burns, fractures or back injuries.

Further information on the Work Performance Assessment and Training Program is available by sending a self-addressed, stamped envelope to Doug Cole, IWJ Rehabilitation Institute, 509 S. Euclid Ave., St. Louis, MO 63108.

Julio V. Santiago, M.D., professor of pediatrics and codirector of the division of endocrinology and metabolism, and a member of the National Diabetes Advisory Council, has been elected to the Board of Directors of the Diabetes Treatment Centers of America Foundation.

The nonprofit foundation will provide grants for research on the treatment of diabetes and for the career development of health-care professionals. Composed of leading specialists in research and treatment of diabetes and its complications in the United States, the Board of Directors will establish criteria for the grants and oversee the appropriateness of research and career development programs.

The foundation was established by Diabetes Treatment Centers of America, headquartered in Nashville, which operates hospital-based centers nationwide that provide treatment, education, diet and family counseling, and instruction in self-care for persons with acute diabetes mellitus and its complications.

James Grier Miller, M.D., Ph.D., delivered the fifth Estelle Brodman Lecture. The Brodman Lecture is sponsored each year by the medical school library in honor of Estelle Brodman, director of the medical school library and professor emeritus of medical history at Washington University from 1961-81. The lectureship was established in 1981 to recognize her achievements at Washington University and her contributions to biomedical communications and medical history.

Miller is professor of psychiatry and behavioral sciences, psychology, and computer sciences at the University of California, Los Angeles. Best known for his book, Living Systems, Miller was co-founder and later executive director of EDUCOM, the Inter-university Communications Council for academic information management. He has made substantial contributions in the behavioral sciences, especially in psychopharmacology, human information processing and general systems theory. He has also been involved in international science policy as an advisor to the United Nations and to foreign governments.

Miller received his medicine and psychology degrees from Harvard University. He has held professorships at the University of Chicago, where he was chairman of the psychology department; the University of Michigan, where he was director of the Mental Health Research Institute; and the University of Louisville, where he was president of the university.

He is author or co-author of 161 scientific papers and seven books.

The Visiting Nurse Association of Greater St. Louis has honored several faculty members for contributions and service on VNA's Medical Advisory Committee.

Those receiving special recognition were James R. Want, M.D., Lawrence Kahn, M.D., Stephen A. Kamnetzky, M.D., Robert E. Shank, M.D., and Franz U. Steinberg, M.D.

The Medical Advisory Committee consists of 16 physicians representing different specialty areas and hospital appointments. The committee actively provides in-service education for home care nurses and expands its medical expertise and guidance in all VNA medical policies and procedures.
Charlie Ruggieri isn't sure where or when he was born — he knows it was somewhere in Italy, and he thinks it was in 1899. But Charlie is certain of two things — the affection and the loyalty of "his boys." And that goes both ways.

Ruggieri, a widower with no children of his own, considers as family the generations of medical students who lived and ate at the Phi Beta Pi fraternity house at 4933 Forest Park Blvd. For 38 years, beginning in 1931, he was cook, assistant house manager, and often, father confessor.

The house no longer exists, and Charlie no longer has foster sons to watch over. But his memories of those years stay green. So do those of the scores of young men whom he served, many of them now grown grayer and more distinguished, with busy medical practices, homes and families of their own.

The fraternity's property was sold to Washington University many years ago, and the funds (carefully husbanded by Richard Bradley, M.D. '52) accrued to a sizable figure. Now, the Phi Beta Pi alumni — 400 strong — want to express their gratitude to Ruggieri in a tangible way. A revocable trust of $65,000 has been established that provides a modest stipend to Charlie each month as long as he lives. Also, the principal can be used to meet any special needs, such as unusual health care costs. (Other Phi Beta Pi monies will be used to establish a student loan fund and to endow an Evarts Graham lectureship.)

Since the death of his wife Hilda, in 1980, Ruggieri has lived alone at the Hawthorne Apartments, only a few blocks from the big old house where he spent the happiest years of his life, often working from before dawn to after dark.

That life, especially in his early years, wasn't easy. His first memories are of an orphan's home in Memphis, Tenn., yet he knows he was brought to the states from his native Italy. He never knew his mother. And because his father didn't learn English and Charlie never learned Italian, their communication was sparse. His formal education ended in fourth grade.

"When I was 14, I left home and got a job as a special delivery carrier at the post office, telling them I was 16."

He had his first cooking lessons as a griddle boy at Childs Restaurant, flipping pancakes in the front window. Then, although he wasn't an American citizen and couldn't prove he was old enough to fight, he went off to war.

"I was standing in line and the other fellows were asked their birthdates, so I just pulled one out of the air — May 22," he said.

"I was naturalized when I was in the army."

He was in the ambulance corps in Belgium, serving near the front. "The people I served with were from the University of Pennsylvania," he said with a grin. "I was the only blockhead."

After his return to the United States, he learned that his brother had moved to St. Louis. So Charlie followed him here and got a job which, ultimately, would lead him to Phi Beta Pi and 4933 Forest Park Blvd.

"I worked as a waiter at a restaurant at 313 Locust St. I didn't make much money but I got room and board. Then I looked for a better job and went to work as a counterman for a man named Bloomer, who had a restaurant at Eighth and Locust."

When Bloomer moved to High Point, Ruggieri was placed in charge of the delicatessen, and later managed Bloomer's new place on Natural Bridge.

"But he went bankrupt, and I was out of a job. That was when a man who sold meat called me and said a fraternity out on Forest Park was looking for a cook and would I be interested? I went out there and I was hooked."

As with his other jobs, the work wasn't easy. With 28 students living in the house, and 36 who had their meals there, he had little free time. Although he didn't live at the house, he would arrive early enough to serve breakfast from 7 to 9 a.m., then begin to prepare lunch — from 11:30 to 1:30 — and when that was cleared away, start on dinner. But he remembers no drudgery.

"I became the house manager, and I would help the president and the treasurer. I made a tremendous number of friends, and several have told me, 'Charlie, if it hadn't been for you, I wouldn't have gotten through medical school.' "

"Charlie was a wonderful, personable and cooperative character," remembers Eugene Bricker, M.D. '34, clinical professor emeritus of surgery. Bricker's memories of Charlie date back to his student days as a resident of Phi Beta Pi: "Charlie was totally absorbed in his job. One of the great things was that he knew how to deal with suppliers. This certainly helped, especially in the middle of the Depression, when we were in a real financial bind. He got us through that crisis."

As an "elder statesman" of Phi Beta Pi, and with all those years of experience at a fraternity house, what does Charlie think about young people of today?

"I'm not pessimistic about them," he said. "They'll be all right."

What else could a foster father say about "his boys?"

Mary Kimbrough is a St. Louis-based freelance writer.
Last August, Robert M. Filler, M.D., led a 43-member surgical team in a breathtaking operation which captured world attention. At Toronto’s Hospital for Sick Children, where Filler is surgeon-in-chief, the team separated two-and-a-half year old Lin and Win Htut, conjoined twins whose bodies were fused in a Y-shape at the abdomen and pelvis. It took 17½ hours to complete the intricate separation, as complex as any ever attempted.

Without the surgery, Filler says, the children might have survived for years, but what quality of life would they have had? “If one sat up, the other had to lie down. They couldn’t crawl or walk or do anything,” he says. “They were like a human seesaw: One went up and the other was down; up, down; up, down…”

Many of Filler’s patients live seesaw existences, teetering between whole and partial lives or between life and death. His pioneering surgical techniques and broad research interests, which have brought international acclaim to this 1956 School of Medicine graduate, have also given these children health. The Htut twins, for instance, who have spent their lives in hospital rooms, are beginning to walk and will soon be ready to live in their parents’ home for the first time.

“My children have the freedom to do anything they want that I never thought I would have,” Filler says with satisfaction.

Unlike his patients, Filler has no doubts about the stability in his own life. Since childhood, medicine has fascinated and absorbed him. It’s an “all-consuming” commitment which exacts 12-hour days, steals evenings and weekends, and leaves little time for hobbies. Yet he hasn’t regretted it. “It was absolutely the right thing to do,” he says.

Filler, 53, was born in Brooklyn during the Depression, a good experience since it taught him to “hustle a little.” His grandmother, so the story goes, made an early prediction about his career. “When I was two years old, she saw me walking along and said, ‘There goes my little doctor.' I don’t know whether that was imprinted on my brain, but that’s the only thing I really wanted to do.”

For college, he chose Cornell University — a beautiful place but a disappointment to him, since the pre-med courses were still far from real medicine. When it came time to select a medical school, a fraternity brother first suggested Washington University School of Medicine. After he’d been accepted, he says, he discovered what a fine reputation the school had.

“It was fantastic,” he recalls. “From the very instant I put my foot in the door, I was in love with what I was doing. Do I remember my first dissection — I do. Do I remember the first time I looked at a patient? I do. The whole thing — every day — was more excitement as far as I was concerned.”

He remembers with pleasure courses.
in anatomy from Mildred Trotter, pharmacology from Oliver Lowry, medicine from Carl Moore. But he has most vivid memories of a fellow student, two years his senior, who also lived in the medical students' dormitory on Forest Park Boulevard. His name was Daniel Nathans "and he was really a genius. He knew more about my courses than I did after studying all night long. He knew more than the professors." Filler was not surprised when Nathans, who went on to Johns Hopkins in microbiology, was awarded the Nobel Prize for Medicine in 1978.

Filler himself graduated first in the class. Although he'd always wanted to be a surgeon, he had found internal medicine most exciting in medical school. Hedging, he applied for internships in both fields. Sol Sherry, formerly director of the division of medical services at Jewish Hospital (and now dean at Temple University School of Medicine), offered an intriguing option which nearly kept him in St. Louis: a specially created internship, half in medicine and half in surgery. In the end, surgery won when Filler captured one of six spots at Harvard University School of Medicine's teaching hospital, Peter Bent Brigham.

He discovered pediatric surgery during a second-year rotation to Children's Hospital Medical Center in Boston; his future was sealed two years later by a phone call from Robert Gross, M.D., then surgeon-in-chief at Children's and, Filler says, "probably the most famous pediatric surgeon who ever lived." The offer was hard to refuse: "I see you're about to finish at Brigham. How about coming back here for a few more years?"

For 21 years, with one break, Filler stayed at Children's, Harvard and affiliated hospitals. The exception was a drastic one. Deferred from military service during his residency, he planned to do his two-year stint at Walter Reed Army Institute of Research in Washington, D.C. After one year, though, the war in Vietnam broke out. With two weeks' notice, he was whisked out of the lab and overseas.

He found M*A*S*H-type conditions in the Army Evacuation Hospital: primitive tents or quonset huts, five operating tables to a room, persistent electrical failures, and steamy days when they operated shirtless. The intense and varied experience was "fantastic," he admits, though difficult personally since his wife and three sons (ages 6, 4, and 1) were back home. He spent spare hours visiting leper colonies and establishing a cleft lip/palate program which repaired abnormalities in some 100 Vietnamese children. He was awarded a Bronze Star for his work.

Back at Harvard, now the youngest person in his department, he began a rapid climb through a series of academic and clinical positions. He branched out in new directions as consultant in surgery at the Sidney Farber Cancer Center in Boston. At 45, he was already associate professor of surgery and chief of clinical surgery at Children's. But the head of pediatric surgery was also a young man — and Filler wanted a chance to run his own department.

"When they first asked me about Toronto, I wasn't even quite sure where it was. But I knew the hospital because it's the largest children's hospital in North America, double the size of the next largest. It has a very excellent reputation and there was a lot of work to be done," he says.

Upon his arrival in 1977, he quickly enhanced its reputation for excellence. In 1979, for example, he operated on Herbie Quinones, a Brooklyn infant born with an esophageal defect that had nearly choked him to death some 30 times during his first seven months of life. After surgery which involved, in part, pulling his heart forward and stitching it to his breastbone, Herbie today is "terrific," Filler says.

The Hutt twins posed another challenge. Joining from the diaphragm down, they shared a pelvis, parts of small and large intestines, urinary tract, and (in addition to one good leg each) a vestigial third leg. Their livers were fused, though each half had its own gall bladder and bile duct. Still more complicated, the twins — both genetically male — each had his own testes but shared a penis.

The surgery, Filler's third on conjoined twins, went "absolutely perfectly," he says. Relays of doctors spent 12 hours severing and reshaping shared internal organs and constructing a vagina for the twin who will be raised as a female. They used the remaining five and a half hours to close up yawning incisions with tissue and muscle taken from the useless leg.

Filler was on hand throughout, watching and working, though "I was so pumped up about this whole thing, to make sure everything went right, that it certainly didn't seem like 17 hours," he says.

Along with his wide-ranging clinical skills, he has more than 160 publications on "almost every pediatric surgical subject you can think of." He has done pioneering work in total parenteral nutrition, working out a system to feed infants special formulas intravenously. He has also taught a variety of courses, most recently as professor of surgery at the University of Toronto, using his own "modified Socratic method." "I prefer an interaction with the students," he says, "so it's always a lot of questions and 'What do you think of this?' or 'What would you do and why?'"

Now, every day is different. "Some mornings I might say, 'Wow, this looks like a great day; there's hardly anything scheduled,' and by 8:30 a.m. I'm up to my ears in emergency surgeries or administrative problems." He keeps fit through tennis and exercise to make this workload possible. The morning after he finished the exhausting surgery on the twins, he jogged five miles, then came back to repair a bleeding blood vessel in one of the children.

His wife, June, is coordinator of fund-raising for the Toronto hospital. None of his three sons (now 25, 23, and 20) will be a doctor — and that doesn't trouble him a bit. "If you don't really love it, you can't do it," he says.

For himself, "my goal is to carry on with exactly what I'm doing," says Filler, who sees fetal surgery and organ replacement surgery as new frontiers in his field. "I just want to remain a pediatric surgeon."

Candace O'Connor is a St. Louis-area freelance writer.
Paul C. Sheldon, M.D. '35, writes to say that he's proud to have been a Century Club member for many years. He sends a "God bless you all" to his former classmates.

Richard A. Sutter, M.D. '35, chair of his fiftieth class reunion, points out that the Sutter Clinic has joined Barnes Hospital, "thereby upgrading Barnes Hospital's reputation in the fields of occupational medicine and worker's compensation practice." Sutter, board-certified in occupational medicine, says that he is the only staff physician at Barnes so credentialed.

Lawrence Breslow, M.D., '36, writes that he is looking forward to his fiftieth class reunion next spring. After finishing a residency at the U. of Illinois, he served in the U.S. Army (1942-6), European theatre, achieving the rank of major. He is a member of the part-time faculty at IU and maintains a practice in Northbrook, IL.

V. Terrell Davis, M.D. '36, continues to teach and practice psychiatry part time. He writes that he plans to attend the fiftieth reunion of the class of 1935, with whom he studied for two and a half years, and the half-century reunion of the class of 1936, with whom he graduated.

J. Robert Mangum, M.D. '38, has been busy selecting and supporting medical teams sent to Ethiopia in 1984-5 under the aegis of World Vision.


Edgar H. Keys, M.D. '39, retired from the practice of ob/gyn, is now medical director of the Hospice of Adams Co. Project, Blessing Hospital, in Illinois.

Benjamin S. Greenwood, M.D. '43, retired since 1981, is an industrial medicine consultant.

Martin P. Meisenheimer, M.D. '43, has recently retired from family practice, and writes that he's "gone fishin'." Meisenheimer lives in Cherokee Village, AR.

Bernard S. Lipman, M.D. '44, writes that the seventh edition of his book Clinical Electrocardiography; Year Book Medical Publishers (Chicago), is included in the recommended tomes for "Library for Internists V."

Gladden V. Elliott, M.D. '46, is president-elect of the California Medical Association, a 33,000-member organization. In private practice in San Diego, Elliott is clinical professor of radiology at UCSD.

Alan R. Laurain, M.D. '49, has retired from practice. He lives in Johnson City, TN.

Charles M. Lederer, M.D. '50, retired recently after 34 years of practice in Warrensburg, MO. The Daily Star-Journal, in a front-page story and accompanying editorial, cited Lederer's lifetime of practicing general medicine in the community. At a retirement party in his honor, Lederer was presented with many mementos, including a letter and pair of cuff links from President Ronald Reagan.

Dorothy D. Reister, M.D. '50, writes that she is the first woman to be named president-elect of the Jackson County (MO) Medical Society. She also represents her district at the Missouri State Medical Association.

William R. Cheek, M.D. '51, is president of the pediatric section of the American Association of Neurological Surgery. He also serves as secretary of the American Society for Pediatric Neurosurgery and is a member of the editorial board of Child's Nervous System, the journal of the International Society of Pediatric Neurosurgery.

James H. Dunley, M.D. '51, has been appointed clinical assistant professor of family practice at the U. of Iowa School of Medicine. He is also in full-time private practice at the Fairfield Clinic, Iowa.

Edgar Draper, M.D. '53, is president of the Mississippi Psychiatric Association. He resides in Jackson, MS.

Seina L. Kaplan, M.D. '55, is president of the Pediatric Endocrine Society. Kaplan, a resident of San Francisco, has also been appointed to the advisory council of the National Institute of Child Health and Development.

Melvin C. Dace, M.D. '62, is chief of staff at North Florida Regional Hospital (Gainesville). Dace is an internist specializing in cardiology.

David Danoff, M.D. '62, is chief of staff at North Memorial Medical Center in Minneapolis. A neurosurgeon, he lives in Golden Valley, MN.

Brian H. Gross, M.D. '65, waxes enthusiastic about a recent trip to Australia and New Zealand. An anesthesiologist, Gross lives in Winchester, MA.

Lawrence M. Kotner, M.D. '68, has co-chaired the monthly cancer conference at Jewish Hospital for the past three years. He invites the medical center staff to attend.

Bruce D. Fisher, M.D. '70, has been appointed chief of medical education at Muhlenberg Hospital, Plainfield, N.J. A specialist in infectious diseases, Fisher has been promoted to clinical associate professor of medicine at the University of Medicine and Dentistry of New Jersey (Rutgers Medical School).

Robert G. Harmon, M.D. '70, has recently been re-elected president of the National Association of County Health Officials and holds the same office in the Arizona County Health Officials Association. A resident of Scottsdale, Harmon specializes in public health.

William V. Roberts, Jr., M.D. '72, is a neuropsychia-
trist in private practice with Albert A. Lorenz at Eau Claire Clinic (WI).

Roslyn Kaplan Yontovian, M.D. '74, is president of the Minnesota Association of Blood Banks. Her article, "Establishing a successful autologous blood transfusion program in a community hospital," was published in the January 1985 issue of Medical Laboratory Observer.

James M. Barton, M.D. '75, has completed residencies in medicine at UCSF and anesthesiology at Massachusetts General Hospital. He also wrote "Anesthesia and Renal Disease," a chapter in an anesthesiology manual for Mass General. Currently, Barton is in private practice in Highland Park, IL.

Linda A. Hershey, M.D. '75, has recently been elected a member of the Central Society for Neurological Research. CSNR is a select group of medical neurol'ogists.

Edward H. Kovnar, M.D. '77, has recently joined the staff at St. Jude Children's Research Hospital in Memphis, where he is section head of neurology and a member of the hospital's new program to treat brain tumors. Formerly, Kovnar was assistant professor of neurology at the Medical College of Wisconsin and director of EEG at Milwaukee Children's Hospital.

Carol Grammer Stull, M.D. '78, is an ob/gyn at the naval hospital in Bremerton, WA.

Gaylord T. Walker, M.D. '78, is serving a two-year fellowship in surgical oncology at Memorial Hospital in New York.

1980s

Myron Tanenbaum, M.D. '81, will soon finish an ophthalmology residency at the Bascom Palmer Eye Institute and begin a fellowship in oculoplastic and reconstructive surgery at Emory University.

Linda M. Olson, M.D. '82, will soon complete a residency in family practice and has accepted a fellowship in adolescent medicine.

Stuart Sherman, M.D. '82, has completed a residency in internal medicine at the University of Pittsburgh and will begin a fellowship in gastroenterology at UCLA after finishing the Physician Investigator Training Program at U. Pitt.

FORMER HOUSE STAFF NOTES

Leopold Hofstatter, FHS, presented a paper on neuro-endocrinological rhythms of the menstrual cycle and an exhibit on the psychoneuro-endocrinology of pregnancy last fall at a professional meeting in New Orleans.

Charles A. Johnson, FHS, was recently re-elected chairman of the Sarasota (FL) County Public Hospital Board. Johnson specializes in thoracic and cardiovascular surgery.

William R. Platt, FHS, is now semi-retired from the practice of clinical pathology (hematology). A resident of Baltimore, Platt recently was educational leader for medical seminars for primary care physicians held in Portugal. A guest lecturer for the Medical Student Aid Society-Florida, he was also visiting scholar in pathology at the Chinese University of Hong Kong Medical School. Platt is also editor-in-chief of the journal, Pathology Update, published in Princeton, NJ.

Alumni Win Pfizer Award

Two graduates of the Medical Scientist Training Program (MSTP) at Washington University School of Medicine have been named Pfizer Scholars under a new program sponsored by the company to support young faculty members. Donald A. Kennerly and Ira A. Tabas are the MSTP graduates who were selected from 134 applicants for the award. Kennerly and Tabas, who selected the University of Miami School of Medicine, will each be supported by a $50,000 annual grant covering two years of research.

The Pfizer Scholars Program for New Faculty, first announced in early 1984, encourages physicians to pursue research careers in academic medicine during the early part of their professional lives. The awards are open only to physicians with faculty appointments below the rank of associate professor.

The 1985 Pfizer Scholars were chosen by an advisory board chaired by Robert I. Levy, M.D., (FHS), Columbia University. Burton E. Sobel, M.D., professor of medicine and director of the cardiovascular division at the School of Medicine, was a member of the advisory board.

Donald Kennerly is assistant professor of internal medicine at the University of Texas Health Science Center at Dallas. He received the A.B. degree from Harvard in 1974 and the M.D./Ph.D. in 1980 from Washington U. Named to Alpha Omega
Kennerly's research interests concern the mechanisms of allergy and inflammation. As an M.S.T.P. student, he worked under the direction of Charles W. Parker, M.D. '53, professor of medicine and microbiology/immunology. In his research with Parker, he investigated intracellular metabolic changes that occur when mast cells release inflammatory substances such as histamine that provoke inflammation and are important to the development of allergic responses. Besides their involvement in inflammation, mast cells also serve as a model of secretory cells. Kennerly found that in mast cells, secretion of histamine parallels incorporation of radioactive phosphate into several specific classes of phospholipid. In collaboration with Philip W. Majorus, M.D. '61, professor of medicine and biological chemistry, he discovered a novel pathway for the release of arachidonic acid—a substrate for prostaglandin formation—thus explaining how cells may regulate synthesis of inflammatory substances.

Together with Aubrey R. Morrison, associate professor of medicine and pharmacology, Kennerly investigated the effect of renal ischemia in rabbits. Specifically, he examined injured kidney cortex and looked for changes in the phospholipid and fatty acid compositions of cell fractions.

Recently, Kennerly developed techniques to permit examination of cell fragments—cytoplasts—containing only plasma membrane and cytoplasm. Characterizing cytoplasts will enable him to construct a model to explain how mast cells can be triggered to release their inflammatory substances. This knowledge will also illuminate the way that other secretory cells function.

Ira Tabas is assistant professor of medicine at the College of Physicians and Surgeons at Columbia University. He received the B.S. degree from Tufts University in 1975, and earned the M.D./Ph.D. in 1981 from Washington University. Elected to Alpha Omega Alpha, he served his residency at Columbia Presbyterian Medical Center and was a research fellow in Columbia University's Specialized Center of Research.

Tabas' thesis research centered on the processing of complex sugars during cell manufacture of glycoproteins (protein/sugar molecules), and resulted in two fundamental findings. Collaborating with thesis advisor Stuart A. Kornfeld, M.D. '62, professor of biological chemistry and medicine, Tabas discovered the pathway by which certain complex sugars in glycoproteins are manufactured in cells. Two of these sugar chains, although dissimilar in chemical structure, are not manufactured by different pathways, as had previously been thought. Instead, they are both derived from a common precursor. This ancestral molecule is transferred from a lipid carrier to the newly manufactured protein, is extensively processed in situ, and eventually forms the final product. Tabas isolated and characterized two of the enzymes involved in this processing.

In addition, he discovered the mechanism by which phosphate units are added to carbohydrate components of certain enzymes (acid hydrolases). Previously, it was known that certain phosphorylated sugar residues on acid hydrolases serve as important recognition signals, allowing these enzymes to be sent from their site of synthesis in the cell to their eventual destination: lysosomes, cells' "garbage disposals." But the way in which the sugar residues were phosphorylated was unknown. In elucidating it, Tabas opened the way for Kornfeld and others to uncover the enzymatic defect responsible for important genetic diseases known as lysosomal storage diseases.

Now, Tabas' research interest is atherosclerosis. He investigates the low-density lipoprotein (LDL)/macrophage interaction involved in atheroma foam cell formation, a prominent feature of atherosclerotic lesions on blood vessel walls. The cholesteryl ester-loaded foam cell is believed to be derived from macrophages. However, no one had developed a model system consisting of macrophages that accumulate cholesteryl esters after induction by LDL. Tabas found a macrophage cell line which accumulates large amounts of cholesteryl ester when human LDL is added to the cell culture.
The courtyard near the old Maternity Hospital teems with life, especially on a sunny spring afternoon around lunchtime. Then, it becomes a favorite place to eat, meet friends for a chat, or just relax and listen to the splash of falling water.
This polyhedron, a complex of five- and six-sided figures, was designed by Leonardo da Vinci around 1501. Remarkably, it is an exact replica of the shape assumed by a protein called clathrin. Clathrin supports cell compartments—pits and vesicles—that contain substances which the cell absorbs and sends to specific destinations. (See micrograph, page 10.)