Offering Hope To The Homeless
Perhaps the single biggest sign of the School of Medicine's impend­
ing centennial celebration hangs in the new Medical Library and 
Biomedical Communications Center, scheduled to be dedicated on 
Saturday, October 12.
In Defense Of Self
The story of two proteins in the immune system’s complement component and their far-reaching implications for medicine.

Long Way Home
How can homeless families be helped most efficiently? A new study takes the most practical route to finding out.

Men Of Science
Recalling what was written about three of the medical school’s most prominent researchers almost 50 years ago.

Newsbriefs
2
Personal Outlook
24
Silhouette
27
Alumni Report
28
Parents still using polystyrene-filled cushions, banned last year by the Consumer Products Safety Commission, are endangering their babies’ lives, warn the authors of a recent report in the New England Journal of Medicine.

The cushions may cause accidental death by limiting infants’ ability to move their heads, thus preventing them from obtaining fresh air, say the researchers.

James S. Kemp, M.D., and Bradley T. Thach, M.D., studied the deaths of 25 infants, most of whom had died face down on polystyrene bead-filled cushions. Autopsies had been conducted on 23 infants; in 19, the death was attributed to Sudden Infant Death Syndrome (SIDS). However, Kemp and Thach’s study concluded that the majority of the deaths were due instead to rebreathing, a form of accidental suffocation.

“These deaths from rebreathing appear to have occurred in a manner not previously reported in infants,” they write. “Our findings challenge the basic assumptions used to distinguish SIDS from accidental suffocation and emphasize the need for new safety regulations for infant bedding.”

That the deaths had been diagnosed as SIDS on post-mortem examination is not surprising, Kemp and Thach say. Standard thinking is that on typical bedding, normal two to three-month-old babies are easily able to turn their heads when they need fresh air. Suffocation is not generally considered unless the baby’s head has been entrapped or its nose and mouth are covered by impermeable material, such as plastic. Very often there are no marks, making it impossible to distinguish between SIDS and suffocation.

This study provides new information that Kemp and Thach hope will help in making that distinction.

“Medical examiners can now consider whether the baby’s access to fresh air might have been limited in more subtle ways than having something impermeable over its face or having its head entrapped,” Kemp explains. “They can begin to think in new ways about possible deaths due to low oxygen. That could benefit SIDS research by allowing us to focus on children whose deaths are for more obscure reasons.”

Kemp and Thach’s study was based on information about the 25 deaths made available by the U.S. Consumer Products Safety Commission, as well as their own laboratory studies. Using mechanical and animal models, they simulated infant breathing on two polystyrene-filled cushions. Their tests enabled them to measure the effects of softness, malleability, airflow resis-
tance and rebreathing of oxygen-poor air.

Their findings indicate that if an infant is lying face down with the nose and mouth resting on the cushion, the material can mold about the infant's head so closely that head movement is hindered. That forces the baby to rebreathe expired air, which contains low levels of oxygen. The amount of rebreathing they estimated to have occurred in the infants was lethal in an animal model.

"The Consumer Products Safety Commission had a very strong hunch that these cushions were a threat to babies and were in fact fatal to them," comments Kemp, an instructor in pediatric pulmonary medicine. "We've shown the mechanism by which these cushions can be fatal, namely rebreathing."

Polystyrene-filled cushions were marketed as a gentle restraint to keep babies from rolling, Kemp says. He adds that though no longer manufactured, the cushions are reportedly still available secondhand.

Kemp and Thach, a professor of newborn medicine, are calling for new safety standards for infant bedding. "These polystyrene-filled cushions have been banned, but we need to make an effort to learn whatever lessons we can from these tragedies," says Kemp.

"Until new safety standards have been developed, the lessons haven't been fully put into practice."

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Lacy Elected To Academy

Paul E. Lacy, M.D., Ph.D., Robert L. Kroc Professor of Pathology, has been elected a fellow of the American Academy of Arts and Sciences. The academy is one of the nation's oldest societies of leaders in science, scholarship, the arts and public affairs.

"This is a richly deserved honor for Paul Lacy, one of Washington University's true investigative pioneers and a most distinguished department head," says William A. Peck, M.D., vice chancellor for medical affairs and dean of the School of Medicine. "His research offers great promise for the successful treatment of diabetes mellitus, a major public health problem."

Lacy, one of 195 new fellows elected to the 211-year-old academy, is recognized worldwide as a leader in the study of insulin-dependent diabetes mellitus. One of his most significant contributions has been the transplantation of islets — cells in the pancreas that produce insulin — for the treatment of diabetes. Lacy devised many of the techniques used to isolate and purify human islets. Islet transplantation has temporarily eradicated the need for insulin injections in several patients with juvenile-onset diabetes. His current studies also are focused on developing novel approaches to forestall the rejection of transplanted islets and the isolation of animal islet cells as a source of tissue for human transplantation.

The American Academy of Arts and Sciences conducts studies that reflect members' interests and respond to societal needs. There are currently 20 faculty members at Washington University who are academic fellows.

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Jay S. Pepose, M.D., Ph.D.

Pepose Receives Cogan Award

Jay S. Pepose, M.D., Ph.D., associate professor of ophthalmology and visual science, recently received the Cogan Award for his outstanding contributions to ophthalmic research.

Pepose is the fourth scientist to receive the award, which is presented annually by the Association for Research in Vision and Ophthalmology (ARVO), an international society of vision scientists. Researchers are nominated by their colleagues.

Pepose, who is also assistant professor of pathology, studies infectious and inflammatory diseases of the eye. His pioneering studies of the ophthalmic manifestation of AIDS demonstrated that the cotton-wool spots that affect the vision of many AIDS patients are caused by microvascular lesions, not cytomegalovirus (CMV) infection of the retina.
Six years ago, Don Cohn exchanged his researcher's lab coat and test tubes for a high school classroom and textbook because he wanted to experience a broader scope of science and be in touch with people.

This summer Cohn, a biology teacher at Kirkwood High School, is out of the classroom and back in a lab at Washington University School of Medicine, where he is refreshing his relationship with research so he can become a better teacher.

A former bioenergetics researcher and now a Kirkwood High School biology teacher, Don Cohn was back in a lab at the medical school this summer brushing up on his science so he can become a better teacher.

Researchers Clone Gene That Controls Cell Signaling

Researchers here are the first to clone a member of a family of human genes that may restrain runaway cell growth.

The scientists have cloned an enzyme that removes phosphate groups from several messenger molecules inside cells. Scientists have known for two decades that the addition of phosphate groups to specific molecules, a process called phosphorylation, is a critical event in the propagation of signals inside cells. In response to the extracellular demands of hormones, phosphorylation is orchestrated inside cells, activating some molecules and immobilizing others and ultimately leading to cell growth or cell movement.

The work done at Washington University in the laboratory of Philip W. Majerus, M.D., professor of biochemistry and molecular biophysics and head of the division of hematology/oncology, may give scientists an edge in understanding the intricate cellular communication processes that regulate cell growth.

A goal of the research is to understand the function of all the inositol phosphates, a family of at least 21 molecules, says Theodora S. Ross, an M.D., Ph.D. student in...
Majerus' laboratory who performed the experiments. Inositol phosphates are released inside cells in response to signals received from outside the cell.

Although many inositol phosphates have been identified, scientists are still uncertain about their function. But they believe quite a few are crucial to the physiology of the cell.

The Majerus group has already expressed the 5-phosphatase in cells, with the hope of understanding whether it controls the levels of its target, or substrate, and the subsequent products.

"Now that we can express this protein in cells and manipulate the levels of its products we have a new way of approaching the problem," Ross says.

It's still not known what regulates the expression of the 5-phosphatase, Ross says, but having the clone will allow her to examine the problem.

"The future is in overexpressing, or knocking out, this enzyme in cells and looking at the cells to see what the true functions of the substrates for this enzyme are," she says. "The 5-phosphatase may decrease the level of the signal molecules, but of course we don't know that yet."

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**ACTU Facility Open At Regional**

The AIDS Clinical Trials Unit (ACTU) at Washington University School of Medicine has opened a satellite facility at St. Louis Regional Medical Center. The facility, located in Regional Medical Center's Infectious Disease Clinic at 5535 Delmar, is open from 8 a.m. to 12:30 p.m. Mondays and Thursdays, with plans to expand hours to 8 a.m. to 4 p.m. Mondays, Wednesdays and Thursdays.

The satellite facility is open to anyone who qualifies for care at Regional Medical Center. The purpose of the facility is to make it easier for underrepresented populations, in particular the medically indigent, blacks and IV drug users, to participate in AIDS-related drug studies while receiving primary care for HIV infection at the regional clinic.

Currently, 12 percent of Washington University's ACTU patients are black. However, in 1989, 35 percent of all Missourians who tested positive for HIV, the virus that causes AIDS, were black, and researchers say there is a need to increase access to drug studies.

Patients now being seen at the regional clinic are about evenly split between black and white.

All research costs, including experimental drugs and related tests, are provided free of charge. Routine care provided by the Infectious Disease Clinic is billed as normal. In addition to primary care and clinical trials, the AIDS satellite facility provides individual case management coordinated by a social worker.

The satellite facility was made possible by a $244,400 grant jointly funded by the National Institute of Allergy and Infectious Diseases and the National Institute of Drug Abuse. It is a supplement to the existing AIDS Clinical Trials grant with Gerald Medoff, M.D., and Lee Ratner, M.D., Ph.D., as co-principal investigators.

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**Csernansky Receives Research Award**

John G. Csernansky, M.D.

Csernansky is studying alternative drugs for schizophrenic patients who do not respond to neuroleptics. Neuroleptics, antipsychotic medications discovered in the 1950s, are widely used to treat delusions and hallucinations that are common with schizophrenia. He is also studying disease-related biochemical markers present in patients with severe schizophrenia and developing animal models that will enable direct measurement of specific elements of brain circuitry thought to be involved in schizophrenia.

In addition, Csernansky is involved in developing a clinical research ward at St. Louis' Malcolm Bliss Hospital to provide care for the severely mentally ill. The 25-bed ward will provide training for residents and fellows in the Department of Psychiatry at the School of Medicine.
Blood Test May Diagnose Neuropathy

Scientists have identified a blood test that will help in diagnosing and perhaps in treating some forms of peripheral neuropathy. According to a report published in Neurology, results of a 180-month multicenter study indicate that the blood test — which can reveal high levels of antibodies that may attack the nervous system — provides a new means of diagnosing peripheral neuropathy, says principal investigator Alan Pestronk, M.D., professor of neurology.

Peripheral neuropathy, a term for a variety of ailments that damage nerves and impair muscle movement and sensation, causes widespread numbness, tingling and pain, particularly in the hands and feet. Often the cause is unknown, but peripheral neuropathy can be hereditary or brought on as a manifestation of diseases such as diabetes and Guillain Barre. A few peripheral neuropathies are treatable, but for the majority there is no treatment.

The research, funded by the National Institutes of Health, was conducted at Washington University's Department of Neurology, the University of Michigan Medical Center and the Johns Hopkins School of Medicine.

Alan Pestronk, M.D.

The researchers examined a group of patients with sensory abnormalities — damage predominantly to their sensory nerves — and discovered that approximately 30 percent of them had antibodies that may cause damage by binding to human nerve tissue.

"Antibodies normally protect you from foreign invaders," Pestronk explains, "but sometimes antibodies are directed instead at your own tissue. We've identified peripheral neuropathy syndromes in which people have antibodies against a specific component of nervous tissue. Identifying those antibodies in the blood associated with neuropathy has helped us make a diagnosis of what the neuropathy was caused by and also has provided the suggestion that some of these disorders are treatable.

"In the past, there have been few diagnostic tests for these patients that provided positive results, but this is a test and a set of results which indicate that peripheral neuropathy may be caused by an immune-mediated disorder." Pestronk says. "It allows researchers to take a step forward in diagnosing these patients. In the past we had no idea what was causing their problem."

It may be three to five years before researchers can determine whether effective treatment is possible, Pestronk notes. "This test is a big first in that it will allow us to do treatment trials in the next several years and select a specific group of patients with neuropathies that might be likely to respond."

As the studies continue, he hopes to learn more about what causes the neuropathies and to identify similar antibodies in patients with other types of neuropathy.

Prostate Cancer Runs In Families

Men who have relatives with prostate cancer are at an increased risk of developing the disease and should consider screening early in life in order to treat it at its earliest stages, report researchers.

In a study that further establishes the role of genetics as a predisposing factor for prostate cancer, urologic surgeons William J. Catalona, M.D., and David W. Keetch, M.D., found that family history may increase an individual's risk of prostate cancer as much as eightfold. The
findings were presented at the annual meeting of the American Urological Association in Toronto.

"There appears to be a definite familial tendency among certain cases of prostate cancer, and men who have relatives with known prostate cancer should undergo early and regular screening," Keetch says.

Three hundred fifty-five prostate cancer patients and 339 controls were interviewed for the study. Among the prostate patients, 76 had one or more affected family members and 24 had two or more affected family members. The incidences were significantly smaller among controls: 31 and 7, respectively.

According to the study, the overall risk of developing prostate cancer for men with one affected first degree relative (brother or father) is 2.8 times that of the general population. The risk if a first and a second degree relative (uncle or grandfather) are affected increases to 6.1 times. One affected second degree relative only slightly increases the chance of developing prostate cancer.

This study follows others at the Johns Hopkins University and the University of Utah which also showed a genetic component to prostate cancer. The disease is the second most common malignancy among men in the United States and results in 30,000 deaths each year.

Eduardo Slatopolsky, M.D., has been named the Joseph Friedman Professor of Renal Diseases in Medicine.

Slatopolsky is professor of medicine and director of the Chromalloy American Kidney Center at Washington University. In his appointment as Friedman Professor, he succeeds Saulo Klahr, M.D., now chairman of the Department of Medicine at Jewish Hospital, a sponsoring institution of the Washington University Medical Center. The Friedman professorship was established in 1986.

A native of Argentina, Slatopolsky has been affiliated with Washington University since 1963. He has been director of the Chromalloy American Kidney Center since 1967, co-director of the renal division since 1972 and professor of medicine since 1975. His contributions to the fields of parathyroid hormone metabolism as well as bone and mineral metabolism have brought him national and international recognition.

Test Shows Metabolism Of "Bad" Cholesterol

A powerful method for determining how humans, metabolize dietary fats is being pioneered by investigators here.

Scientists with the university's Lipid Research Center have succeeded in measuring the rate of production of apolipoprotein B (apoB) using amino acids labeled with stable isotopes. ApoB is an important component of LDL, the "bad" cholesterol in blood. Information on apoB amounts gives scientists a better idea of how much LDL cholesterol enters and leaves a person's blood in a given time period.

They have found that stable isotope labeled amino acid testing used in conjunction with a complex mathematical model is the best way to measure apoB turnover. Because the studies are non-radioactive, scientists can study apoB metabolism in children and in women of child-bearing age. Also, repeat studies can be done providing scientists with valuable information about the effects of drugs or changes in diet on LDL levels.

"These studies are very important because there's the potential to get information on people who have never been studied before," says Gustav Schonfeld, M.D., Kountz Professor of Medicine and director of the Atherosclerosis and Lipid Research Center. "These kinds of studies were not possible several years ago. Our testing then was limited because it involved radioactivity."

Doctors using this technique are not restricted to studying lipoprotein metabolism. They also can study the effects of genetic disorders, drug treatment, exercise or dietary interventions on the metabolism of any type of protein.

Schonfeld's group plans to use the tests to study people with very low cholesterol levels in hopes of learning why they are different. "We know there are certain genetic defects that cause low cholesterol levels, and we know at the DNA level what the defect is, but we don't know why that particular defect produces low cholesterol in people's bodies," he says. "We have to do these kinds of studies to get that answer."

These stable isotope labeled amino acid studies can help because they give reliable information about why people have the cholesterol levels they do.
Researchers Harness The Body’s Guardians

By Steve Kohler

Twenty-five years ago, the movie “Fantastic Voyage” put forth its outlandish premise — Raquel Welch and her submarine crew, shrunk to fit inside human blood vessels for a rescue mission, come under attack by their host’s defenses. Campy as the film’s concept and execution were, its allegory was accurate. The human immune system really is a corps of automatically deployed defenders protecting the body from invaders. Powerless against the immune system’s sophisticated cascade of weapons, Raquel and her crew would have been cleared from a real body in short order — and not in a teardrop.
Small protrusions, called villi, attach placental tissue to the womb. Here, via its fluorescence, an antibody to the protein MCP shows how densely coated placental tissue is with that protective protein.

What they lacked was stealth technology — a means by which to convince the host immune system that their submarine was really "self" to be protected, not "non-self" to be destroyed. Again, such a concept has actual roots in elegant but complex reality. Research by John P. Atkinson, M.D., and his colleagues has revealed that two proteins displayed on the membranes of self cells protect them from an otherwise immediate attack by the immune system.

The two proteins — called MCP for membrane cofactor protein and DAF for decay accelerating factor — are proving to be of broad importance in areas of medicine ranging from organ transplant rejection and tumor immunology to infertility and the protection of damaged tissue from further assault. The implications of the work surprise even Atkinson, who says, "We were just purifying proteins from blood cells and certainly didn't expect all of these other potential applications."

Immune System Distinctions

Atkinson, a professor of medicine and chief of rheumatology, describes the immune system as comprising two halves. One, cellular in nature, includes the famous helper T-cells and killer T-cells that attack certain types of invaders. The other is the humoral component that functions in extracellular fluids, such as blood plasma.

For many modern investigators, the stunningly efficient cells of the immune system are the stars. The humoral element's circulating proteins were well studied during the first half of this century and today are sometimes regarded as having the equivalent of walk-on parts. But the ingenuity MCP and DAF — the surprisingly important new players —
I, exploring the many advantages that will come from harnessing two regulators of the immune system’s complement component.

John P. Atkinson, M.D., explores the many advantages that will come from harnessing two regulators of the immune system’s complement component.

John P. Atkinson, M.D., explores the many advantages that will come from harnessing two regulators of the immune system’s complement component.

An ancient protection device that can function independently, the complement system is one of the body’s first lines of defense against infection. Its proteins function by signaling for help from other parts of the immune system and by attaching themselves to threatening foreigners, coating them and preparing them for elimination. As if on sentry duty, complement proteins circulate constantly in the body’s fluids. Able to amplify themselves rapidly whenever they find an invader, they also can damage foreign cells directly.

MCP and DAF belong to that subgroup that regulates the system. Control of the ever-present complement system is so important that nearly half of its total number of proteins is devoted to down-regulation. Atkinson explains: “You only want the complement system to work on an infecting organism. It must respond to invaders, but it can’t attack your own blood cells or tissue.” Toward that end, MCP and DAF are expressed on the surface of the body’s cells. In fact, Atkinson says, one or both almost always are present on the membranes of any cell that directly contacts the environment. Stationed there, they guard against action by the attack proteins of the system.

MCP’s specific mechanism is to aid in degrading an essential element in the complement system’s cascade into two ineffective pieces; DAF works by preventing critical components from getting together. Atkinson says. The two regulator proteins, along with others of their ilk, allow the complement system to tick over watchfully but keep it from blossoming into a full immune-system response unless a foreign invader is present.

According to Douglas M. Lublin, M.D., Ph.D., assistant professor of pathology and internal medicine and another complement-system investigator, complement proteins inevitably do alight on self cells. In fact, research has shown that a red blood cell, in its average lifespan of 120 days, takes from 200 to 400 hits from complement. That many, it can withstand. Because of the regulators on a cell’s surface, those complement strikes remain mostly innocuous and don’t amplify, Lublin says. In his words, the regulator proteins allow the complement system to remain at “idle,” always ready to kick in when confronted with an invader. Another of the body’s defenses — antibodies — lack the ability to “idle” and may take weeks to come to strength.

Atkinson’s lab identified MCP in 1985. Since then, researchers in his lab have cloned the genes for both proteins and have shown that the genes reside near one another on human chromosome one. They also have sequenced the amino acids of the proteins and developed ways
to make enough of the substances for additional study.

**Medical Implications**

What good is knowing all of this? The implications are particularly far-reaching and fall into four groups.

First, Atkinson says, “The complement system sees damaged tissue the same way it sees foreign tissue. It will try to eliminate damaged tissue just as it tries to eliminate a foreign organism so healing can be completed.” However, given time and protection from an immune system trying to finish it off, damaged tissue sometimes can recover.

The possibility exists to down-regulate the complement system by injecting MCP, DAF, related proteins or a combination of the molecules into the blood as medicine. Injected with regulator proteins, a patient suffering from a stroke, acute respiratory distress syndrome or even an ischemic heart event might gain a temporary reprieve from his own immune system. Thereby, damage to the brain or heart could be limited. In one study of a related molecule administered to dogs, heart damage was reduced by 25 to 50 percent, Atkinson reports. To illustrate why such control is necessary, Atkinson says, “The complement system is ancient; heart attacks are a product of the American diets of the past 80 years. To the complement system, a heart attack looks like a bad cut.”

Research into the potential for using MCP and DAF as therapeutic medicines is just beginning. Unfortunately, when MCP is made soluble to be injected as medicine, it no longer is capable of binding to cells as it does naturally. Lublin explores the prospects for getting soluble MCP to bind to cell membranes. Work on soluble DAF has shown that its efficacy is reduced to one-twentieth or less of the same regulator expressed on cell membranes.

A second promise for the two newly respectable proteins concerns their applications in tumor immunology. Tumor cells often turn out to be heavily coated with MCP and DAF, sometimes in concentrations 10 to 100 times those found on mature blood cells. “That may be one reason why it’s so hard to kill your own tumor cells,” Atkinson says. “After all, if I put a rabbit tumor cell into your system, it would be cleared by the immune system immediately.”

Already available are antibodies that block the action of MCP and DAF. If such antibodies could be delivered to the MCP and DAF molecules only on the membranes of tumor cells, those cells would then be seen as foreign. An excited complement system would in turn alert the rest of the immune system, with the result that tumors might be controlled internally.

“It works great in a test tube,” Atkinson says of this approach. But the trick remains making the antibodies tumor-cell specific in the body. MCP and DAF are so widespread and so important that any overall assault on them would have disastrous consequences; tumors must be the only targets. Still, Atkinson points out, tumor cells are considerably different from healthy cells, so he hopes that an answer to the specificity question will be forthcoming.

Reproductive immunology is the third area in which the two regulators are having a major impact. A fetus is a heterograft — made of tissues that are half foreign to the mother — and immunologists have wondered how the mother’s system is able to support the fetus without activating an immune response, Atkinson says.

At least part of the answer lies in the discovery that MCP and DAF coat the critical cells of the placenta — those that

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Douglas M. Lublin, M.D., Ph.D.
Stolen Secrets

Scientists are not alone in having figured out how MCP and DAF work to protect cells from attack by the immune system. Two clever viruses — the herpes simplex virus that causes herpes and the vaccinia virus that causes measles — both display proteins on their membranes that closely mimic human MCP and DAF.

John P. Atkinson, M.D., theorizes that the viruses somehow captured the primate genes bearing the instructions for making the two proteins and put them to their own uses. “There is no other purpose for that gene than to shut off the human complement system,” he says. “It’s been shown that without the gene, the two viral agents are not nearly so infectious as they are with it.”

Both viruses display analogs to human MCP and DAF but also are capable of coating cells they invade with the proteins. In that way, they evade detection and gain time to replicate inside cells that would otherwise be destroyed. When an infected cell finally lyses, a huge number of copies of the virus is released.

Once control of the complement system has been gained, other species may be called upon to provide organs for transplantation into humans. The hearts and lungs of pigs in particular are similar to human organs.

interface with the mother. The issue of protecting the fetus is so crucial to the species that the two proteins are just one of the many schemes evolution is likely to have devised for the task, Atkinson believes. But, he adds, they provide a window on the question and point to other possible mechanisms. It is also possible, though unproven, that a deficiency of MCP, DAF or both might be a factor in early miscarriages, Atkinson says.

The two proteins are important not only to baby and mother. They also can be found in abundance on the head of sperm, a location that Atkinson says was a “complete surprise,” but one that makes sense in retrospect.

When sperm are injected during intercourse, they require approximately 24 hours to reach the egg while undergoing the acrosome reaction, a dissolution of the outer membrane that enables them to fertilize an egg. During that time, they are exposed to the complement system of the female and perhaps subsequently to antibodies. Atkinson explains that complement proteins are common in the female genital fluid, almost certainly there to “fight the load of bacteria that comes along with intercourse.”

But when the outer membrane dissolves, a coating of MCP and DAF is revealed, protecting the sperm and preserving them for their task of fertilization. In collaboration with Atkinson and his colleagues, groups of investigators in France, England and Australia are exploring the relationship between these protective proteins and male infertility.

Perhaps the most striking potential for MCP and DAF, however, rests in the fourth arena: their applicability to organ transplantation and the creation of transgenic animals as a source for donor organs. A lack of organs for transplantation currently limits the good that medicine can do. And an otherwise promising source — organs from other species — is unavailable due to the hyperacute rejection that the complement system initiates when it encounters foreign tissue. MCP and DAF may resolve the dilemma.

Research into the possibilities of creating transgenic animals, especially pigs, is promising. Simply put, the process goes like this: Scientists inject human genes for the two protective proteins into pig embryos. In some cases, the human genes are taken up by a pig embryo and assumed as its own. When both male and female pigs that have adopted the human genes become available, the two are bred to produce a strain with cells that express human MCP and DAF. In other ways, the pigs are like all pigs, and they suffer no ill effects from making the two human proteins. The hope is that with the human
proteins expressed on the pig heart or kidney, the organ will not be rejected by a human complement system.

Research in several labs recently has shown that cells from other species expressing human MCP and DAF are, in fact, protected from assault by the human complement system. The most difficult step — getting the human gene to be accepted into the pig embryo — has been accomplished in collaboration with researchers in Great Britain and Australia. Atkinson says. And medical science already has good success controlling longer-term rejection mechanisms with immunosuppressants.

Luckily, both the hearts and lungs of pigs are similar to those of humans. Says Atkinson, “Clearly, using transgenic animals as organ donors is the way to go. We will never solve the transplant problem as we approach it now.” Imagining the future only five years away, he adds, “There are even miniature strains of pigs that could save the lives of children and infants who must have replacement organs to survive.” And he predicts that the advanced techniques of animal husbandry could be brought to bear humanely on the problem.

Work today centers on producing transgenic animals and on discerning the significance of the four minor variations of the proteins present in each of our systems. It is “not coincidence,” Atkinson says, that the MCP and DAF on sperm have a slightly different molecular weight from that found elsewhere.

He also wants to know where the active sites in the proteins are and why they have two different “tails” — sections that protrude through the membranes of cells while most of the protein remains outside the cell wall. One form of MCP’s tail is 16 amino acids long; the other is 23.

In Lublin’s lab, work centers on getting animal cells to express human regulators and on exploring the possibility of making MCP that binds to cell membranes. V. Michael Holers, M.D., assistant professor of medicine, analyzes animal models of human autoimmune diseases mediated by the complement system, explores the mouse homologues of the two proteins and creates mice that lack the equivalents of MCP and DAF in order to investigate the consequences of deficiency.

What might have been science fiction 25 years ago is science fact today. Organs donated across species, tumor-specific medicines and treatments for infertility — all are concepts that might sound no more believable than miniaturized submarines navigating in veins. But they are based in science and rooted in the mechanics of the complex and efficient system that protects the only organism capable of both pure fancy and real solutions.

Electron scanning microscopy of the bacteria E. coli reveals (A) intact bacteria; (B and C) the bacteria killed by purified complement proteins; and (D) E. coli exploded by the combined effects of the immune system. Illustration courtesy of the Journal of Experimental Medicine, vol. 149, p. 878, Robt. D. Schreiber, et. al.
An hour past noon on a hot and steamy Wednesday, the hunger of the people at Grace Hill center is apparent in the boisterousness of children and the grumblings of adults. More than the usual 35 women and children have shown up for lunch today, and Ann is manning the kitchen as best she can. The midday meal, she has learned, is much like the monthly assistance check she receives to support her family of three: It lasts longer when it’s divided into small portions.
Whether Ann is in the kitchen divvying up salmon croquettes and salad or at the bank withdrawing cash from her new savings account, she is practicing her basic life skills. There’s a lesson in every task at Grace Hill center. That’s the theory behind this novel therapeutic community for homeless, substance-abusing women and their children, part of a study being conducted through Washington University School of Medicine. The project’s purpose is threefold: To assist women in leading clean, sober, drug-free lives; to help them find employment and become self-sufficient, and to locate stable housing for them.

An unemployed special education teacher, Ann had just been released from a 30-day treatment program for drug and alcohol abuse when she learned of the program. She was one of an initial 34 eligible to participate in the study run cooperatively with St. Louis University Medical Center, Grace Hill Neighborhood Services and the Salvation Army.

Some 240 St. Louis-area women with 600 children eventually will be served by the project that began in April. The study here is one of 14 nationwide receiving funding from the National Institute on Alcohol Abuse and Alcolobism (NIAAA) and the National Institute on Drug Abuse (NIDA) as pilot projects on substance-abusing homeless people. This is the only site focusing on women and children.

“At Grace Hill, the focus is on providing a therapeutic community where the women get in touch with feelings and motivations that led them to abuse substances,” says Washington University’s Elizabeth M. Smith, Ph.D., the study’s principal investigator. “Issues like self-esteem are terribly important, as well as parenting, poverty and lack of education. We’re trying to develop a sense of community among this small group where the women and children live together and develop some spirit of cooperation.”

Ann and her children are among five families residing at Grace Hill. Physically and verbally abused by her husband, she left her marriage and a secure teaching position 2½ years ago, and hasn’t been inside a classroom since. For half of her 36 years, Ann has used marijuana and been addicted to cocaine and alcohol. She has remained drug-free only during her pregnancies with her son, 12, and her daughter, eight. Recently, Ann learned she is pregnant again. The baby is due in January.

Like Ann, Ronda had just completed treatment for substance abuse when she was accepted into the program. A 31-year-old mother of four, Ronda is separated from her husband and has worn out her welcome living with relatives following her treatment. Although she was working as a waitress and a chauffeur before going into treatment, she postponed getting back into the workforce in order to put some structure back into her life.

“When I was using (cocaine) I didn’t care; I didn’t want to care; I didn’t have any emotions,” Ronda explains. “Nothing anybody said would bother me, because I just didn’t have a heart. I tried to take care of the kids, but with their father leaving everything... I wanted attention, and I guess I couldn’t get the attention I wanted. I just couldn’t handle it anymore and the addiction got worse.”

According to Smith, women like Ann and Ronda are becoming all too familiar in cities and towns across the country. She says women and children are among the fastest growing segment of the homeless population today. Nationally, about one-third of the homeless are families headed by women. Locally, about half of the estimated 10,000 homeless are families.

In her study, Smith hopes to examine the effectiveness of four programs — including two at Grace Hill — that offer different combinations of services to homeless women and their children. At Grace Hill, there also is a group of outpatients who live at other centers but receive Grace Hill’s support services. Through the Salvation Army, outpatient programs involve extended case management, family therapy and family and child development.

Initially, 19 women were accepted into the programs at Grace Hill — seven residential and 12 outpatient. Eight have dropped out for a variety of reasons but will be followed by the researchers at six-month intervals. All of the women will be followed for one year after they leave the center.

Smith says substance abusing, homeless women are challenging to work with because they don’t like structure and some are not ready for a program that doesn’t allow them to use substances.
“At Grace Hill, we’re offering an incentive to come into the program. Women are allowed to remain with their children,” she says. “Children are an important motivator for women. Often, it’s the fear of losing their children that prevents them from seeking treatment.”

Ronda, who gave birth to her fourth child in late July, says being at Grace Hill has helped her re-establish her relationship with her daughter and two sons. “We’ve been missing each other for so long,” she says. “There are four beds in our room but we all huddle into one at night so we can read or toss a ball around just to let out frustration and keep the family going.”

Because Grace Hill does not offer detoxification, only women who are already recovering are accepted into the program. Random drug screenings make sure women do not resume their habits while at the center.

In the residential program, women adhere to a daily schedule that begins before 7 a.m. and ends at 10 p.m. Meal preparation, grocery shopping, budgeting and money management, maintaining a household and learning how to be good mothers are just some of the subjects taught. Each family has its own room and is responsible for its upkeep, which is also a necessary part of the program. As many as seven families at a time live at the center.

“Initially, they don’t want to do anything for themselves, but we make them work in the center — plan meals, cook, do laundry and maintain their living quarters,” says Carolyn Franklin, coordinator for homeless services at Grace Hill and the primary case manager. “Some of the things you and I would do without even thinking are foreign concepts to these women. They’ve never been taught to make a bed, balance a checkbook or hang up clothes.”

Though it’s apparent the women love their children, Franklin says they often are irresponsible and harsh when caring for them. She tells of the time when one of the mothers went to cash her welfare check. Without notice, the woman left on a Thursday and didn’t come back until the following Monday. When she finally did return to the center and learned that her children had been placed with Protective Services, she was livid.

Ann and Ronda have never abandoned their children, but they admit to neglecting them while they were abusing substances. Ronda used to leave her 11-year-old daughter in charge of the house for hours at a time. The girl prepared meals, changed her brothers’ diapers and cleaned house regularly during her mother’s absences. “She never really had a childhood,” Ronda laments. “I put a lot of responsibility on her, and it’s hard for her to let go of that mother role and be a little girl again.”

Ann also feels guilty, but her philosophy is, ‘don’t look back.’ “I feel bad and I’m mad at myself because I broke a lot of promises to my kids,” she says. “There were times they needed clothes for school or something for a field trip, and I’d tell them there was no money when I had spent it on drugs. But I can’t dwell on that. I have to forget the past and make what restitution I can and go on.”

Smith says children are one of her greatest concerns because of their emotional vulnerability that could lead to eventual substance abuse. Group discussions that give children an opportunity to talk about their feelings and the effects of drugs and alcohol are held daily, sometimes twice a day. Day care and a day care specialist who conducts play activities are also available at the center.

Franklin says the most rewarding aspect of her work is the blossoming she has witnessed among the children. Hugging and other displays of affection are a common sight in the center’s corridors. “We do a lot of touching and nurturing of the children and it’s beautiful to watch them grow,” Franklin says. “Very seldom can you walk down the hall out here without receiving a hug or being asked for a hug.”

Another area Franklin has emphasized is helping the women to develop a workable system of values. “We want them to begin planning their lives,” she says. “It may not always go as planned, but they should plan anyway.”

Ann is doing just that. Recently, she was hired to teach special education at a school outside the city, and she is looking forward to getting an apartment. With the support she’s received from the program and the Alcoholics Anonymous and Narcotics Anonymous meetings she regularly
attends, she says she's ready to go.

"It's been good for the time that I've been here, but I'm tired of this place and want to be situated," she says. "I want this start real bad. I came here for a certain reason and my mind was set for the duration of the program, but now that's been accomplished."

The obstacle stall ing Ann's release is housing. Because most of the debts incurred during her marriage are in her name, she is considered a credit risk. In the months she has been at Grace Hill, Ann, like all of the women, has been required to save at least 35 percent of the money she receives from welfare. Still, it will be difficult, if not impossible, to come up with enough money for a deposit on an apartment and first month's rent in short order.

Valorie Robinson, a peer counselor who assists with locating housing, pores over the classified section of the newspaper every day looking for safe, affordable apartments and homes — rare commodities in St. Louis, she says. Women at the center receive from $236 to $688 a month in welfare, Robinson says, but with an average of five mouths to feed, little is left for rent and other essentials.

Theresa Heaton, project director, says the women sometimes hold unrealistic expectations about what type of housing they should have. When the women talk about the apartment they want, they often describe a place that costs $750 a month. Recently, Robinson found an affordable apartment for a woman who declined it because she would have had to pay utilities, something she had never done before.

"All of the women come with great hopes that they are going to get the chance to start over," says Heaton, "but they may have unrealistic expectations. They think because they've gotten into a shelter we're going to be able to perform magic and get them their dream house with the white picket fence. That just doesn't happen."

Ronda says she never thought she'd be addicted to drugs or without a home. Now she has vowed not to take her home and her children for granted, and she wants people to know that addiction and homelessness can happen to anyone. But, "you can recover and survive," she says. "I feel I've gotten a second chance to live, so I'm going to take that opportunity. It's almost like being a disciple. Now I want to go back and let people know what happened, how it happened and let them know that they can make it too."

Ronda's new awareness represents a success for the fledgling program. Says Smith: "We hope the project will show us how to lead women with problems back into productive, substance-free lives. We know we have a long way to go; however, I think we've made a good start."
In 1948, as the golden era of medical science was beginning, the St. Louis Post-Dispatch published a series of articles profiling the city's eminent researchers. Many of the subjects were members of the Washington University School of Medicine faculty, and the articles reveal much about the school and the state of medical research of the day, as well as that time's writing style.

With the exception of the article that concerned his father, the stories were all written by Evarts A. Graham, Jr. The younger Graham was then a reporter; 20 years later he went on to become the paper's managing editor. Outlook thanks Graham and the St. Louis Post-Dispatch for permission to reprint here abbreviations of three of the articles.
Dr. Leo Loeb

"It is impossible," said the late Dr. Walter B. Cannon, great Harvard physiologist, "to view cancer research from any angle whatsoever without finding that it has been enriched by Leo Loeb."

This same Dr. Loeb, 78-year-old emeritus professor of pathology at Washington University Medical School, is the grand old man of St. Louis scientists. He is a small, gentle man who was moulded in the German universities in which he received his early training and seems out of place away from them. He is not a man who would stand out in a crowd.

Some scientists in the relatively small group who are familiar with Dr. Loeb’s investigations think any of several of his accomplishments should have won a Nobel Prize for him long ago. One reason why the prize committee consistently has overlooked him may be that almost nobody knows of all of his contributions to medical knowledge. Few people outside of St. Louis even know his name.

In 53 years of research, he has delved into an enormous number of subjects, some directly concerned with the study of cancer, others far removed from the field. Two associates pooled their knowledge of his work to list the following major contributions which Dr. Loeb has made to man’s knowledge of cancer:

He was the first man to show that sex hormones, in certain circumstances, are a major cause of cancer.

He was the first man to demonstrate that susceptibility to cancer frequently is inherited.

He disproved a formerly widely-held belief that cancer is infectious.

He was a leader in developing a method of making living tissue grow in a test tube after removal from an animal’s body, and in transplanting cancer from animal to animal on a large scale.

He showed that eggs can develop in female guinea pigs without being fertilized. The unfertilized eggs sometimes develop into complex tumors of the reproductive organs. His brother, the late Jacques Loeb, did similar work with invertebrate animals.

He put together the work of himself and other men to formulate the complete mechanism of the sex cycle of mammals. In particular, he found the cause of the formation of the placenta, the structure by which an unborn child is nourished.

Sensitive and retiring almost to the latter, he has amassed a voluminous scrap book of newspaper clippings — letters to the editor, editorials and columnists’ opinion.

His philosophy is based on a passionate belief in democracy and in the dignity of the individual. Scientific and technological advances of the last 50 years, he says, have tended to lessen the value society attaches to the individual. Society, with the help of scientists and physicians, must find out how to restore the individual to his
The science of surgery is only about a hundred years old and it may not last another hundred years. Dr. Evarts A. Graham hopes the end may come sooner than that, although he is Bixby Professor of Surgery at Washington University School of Medicine, head of the department, and responsible for all the surgery in the Barnes Hospital group.

Destruction of the science of which Dr. Graham is one of the world's leading figures can come about when most of the conditions which today call for surgery can be prevented. Surgery now concerns itself with correcting conditions resulting from injuries, malformations, infections and cancer. A long step has been taken toward eliminating infections with the development of the sulfa drugs and penicillin; a cure for cancer remains to be found, outside the realm of surgery, except for X-ray treatment in a few instances.

It is conceivable, however, that in the not-too-distant future surgery will be left only with the correction of conditions due to accidents and malformations. The surgeon, then, would become less a scientist than an "applied anatomist," to use Dr. Graham's own phrase.

It is his suggestion, therefore, that surgery may well have reached its zenith — and may from this date decline in importance. If this notion fails to recommend itself to the rank and file of the medical profession it will not be the first such notion to be advanced by Dr. Graham.

His influence has done much to make the "research approach" to surgery the accepted dogma of the profession. A test for gall bladder disease devised by Dr. Graham, with the help of associates, has removed diagnosis from the realm of guesswork to a 98.5 per cent certainty.

He is the "father of modern chest surgery." He laid down the principles of chest surgery, then put them into practice by demonstrating that an entire lung could be removed in a one-step operation. Because of that operation sufferers from lung cancer, formerly faced with certain death, now have at least a 30 per cent chance to recover and an even better chance to recover if the disease is discovered in time.

No other living surgeon has had a greater influence on the profession as a whole in the opinion of Dr. Graham's associates. A dozen "Graham-trained" men now head departments of surgery at universities the world over, from Bangkok to Glasgow to the University of Iowa. The American Board of Surgery, for the founding of which Dr. Graham was chiefly responsible, has become the accepted measure of surgical competence.

Today the habit of success has become a part of the personality of Dr. Graham. He is tall, slender and upright. His eyes, behind rimless spectacles, are cold and gray. His hair is sparse and white. He speaks softly, but with the unconscious assumption of authority.

The first impression of the man is one of austerity. There is a kind of awesome dignity about him, the dignity of an old sea captain, of a man accustomed to responsibility, unshared. Such men have learned to feed on their own resources.

During World War I, the influenza epidemic was killing soldiers faster than enemy bullets. The Surgeon General, at wit's end, created a commission to try to discover the cause of the terrific death rate. Attention was directed to the young medical officer, Dr. Graham, because of his unusual scientific education. Besides his medical degree and his studies in chemistry, he had obtained a liberal arts degree from Princeton University, had interned for two years at Presbyterian Hospital in Chicago and had worked under a fellowship in pathology at Rush Medical College for two years.

Dr. Graham, therefore, was appointed a member of the commission; its specific task was to investigate a pleural cavity abscess, empyema, which in some camps was killing as high as 90 per cent of the soldiers who suffered from this form of post-influenza disease.

At Camp Lee, Virginia, Dr. Graham
watched the standard procedure, surgical operation, and watched the patients turn blue and die. Then he asked for several months' release from the Army, got it, went to Johns Hopkins University at Baltimore to conduct some experiments of his own on cadavers and on live dogs.

When he returned to Camp Lee he was ready to announce that the chief cause of death from empyema was not the disease — but too early surgical treatment. He advised that the operation be delayed until after the pneumonia had subsided.

The older surgeons were amused, at first, then indignant. They refused to change the "standard procedure." Dr. Graham, therefore, went to Washington, where the Surgeon General — after reviewing the evidence the young medic had amassed at Johns Hopkins — somewhat reluctantly agreed to let him take a group of empyema patients at Camp Lee and put them aside for treatment in accordance with his ideas.

In this group the mortality rate quickly dropped to around 4 per cent.

The reputation Dr. Graham made as a member of the empyema commission won him an appointment, after the war, as professor of surgery at Washington University, in 1919. There he developed the test for gall bladder disease, a method of making the gall bladder visible to the X-ray camera.

Often a critic of medical practice and of the economics of that practice, Dr. Graham has been the target of bitter abuse. Such abuse today, however, belongs to history, alongside the persecution of Galileo. Medals, awards, distinctions and eight honorary degrees have been showered on Dr. Graham from all quarters.

Dr. Edmund Vincent Cowdry

Microbe-hunting has led Dr. Edmund Vincent Cowdry, St. Louis' internationally known anatomist, from Nairobi, East Africa, to Peking, China. He is now concentrating his attention on cancer; his investigations in the past have ranged from tropical diseases to medical education in the Orient.

Dr. Cowdry, professor of anatomy at Washington University Medical School and director of research at Barnard Free Skin and Cancer Hospital, is a quiet man with an earnest manner, gray hair and a penchant for cigars. His expeditions to various remote corners of the earth have given him a considerable store of assorted anthropological knowledge and an unsatisfied taste for new sights and new places.

Dr. Cowdry became director of research at Barnard Hospital in 1937. Working with the advice and encouragement of Dr. Major G. Seelig, who retired recently and moved to California, he has organized and directed the experiments of a group of scientists who are trying to unravel the cancer problem by concentrating on a single type, that of the epidermis.

The researchers thus far have found many differences between normal epidermis and epidermis in which cancers will grow, including a sharp decrease in the amount of free calcium present in cancerous skin and a number of differences in protein content of the tissues. Assisted by a grant from the National Cancer Institute of the United States Public Health Service, the team is now trying to use that knowledge in experimental treatment of skin cancer.

Beginning next July 1, the work will be conducted at Washington so that Dr. Cowdry can concentrate his research and his teaching at one institution, giving him more time to devote to the study of cancer.

Since pointing out in 1944 that the results of cancer research have been "trifling," largely because of a lack of cooperation among leaders in the field, he has become the prophet of the scientists who are organizing a world-wide concentrated attack on cancer and who are attempting to obtain greatly-increased funds for cancer research.

He was president of the Fourth International Cancer Research Congress, which was held here last September, and is the United States representative on the International Cancer Research Commission, which was organized at that meeting.

"We should not delay attempts at cure until we learn the cause of cancer," he said recently. "We should remember that the cures for such things as malaria, scurvy and other devastating diseases were found before we knew what caused them."
I am in the position of having to say that the medical profession is less than perfect. If physicians do not see that there is a problem, the public does. Consider the results of a recent poll conducted by the American Medical Association. Only 29 percent of patients said their doctors spend enough time with them. Forty-three percent of respondents said the physician explained the patients' problem well. Fifty-seven percent said physicians do not care as much for their patients as physicians of the past.

The results of this dissatisfaction are tangible. In Missouri in 1990, 741 complaints were filed against physicians. This represents an increase of 51 percent over 1989. Forty percent could have been avoided if there had been better communication between physician and patient.

The plethora of medical columns in newspapers, self-help medical books and articles, and critical reports in Time and Newsweek are ample testimony to the dissatisfaction of a large percentage of the patient population. This dissatisfaction with the medical profession is growing and cannot simply be dismissed.

Some attempts to make students compassionate and sensitive have been based on certain myths. The first is the "Humanities versus Science" myth. The operating assumption is that students who read classic novels and poetry, who steep themselves in art and music, somehow become more compassionate and humane. But only 19 of the 126 medical schools in the U.S. offer courses directly addressing the patient/physician relationship.

I assume that every one in the audience is concerned, compassionate, and humane. It is my belief that this is in man's nature. However, I will argue that students and physicians don't know how to translate that concern for fellow humans to compassionate and humane care. Furthermore, there are forces at work to make the physician less compassionate and humane.

Ignorance is one of the most important factors accounting for the failure of the physician/patient relationship. While we understand a great deal about the biology of disease, we know very little of the emotional and psychological aspects of disease. What are the important issues? If we knew them as we know the issues of tremor and slowness of movement in Parkinson's disease, we could approach them scientifically and routinely. These issues could be studied as an integral part of the review systems. With such an emotional check list even the most obtuse physician could do much better.

Many medical students and physicians have a very narrow view of who the patient is and who is affected by the disease. Every disease affects not only the patients but all those who care about the patient. I was caring for an elderly man with Parkinson's disease who was not under good control. Neither he nor his wife was able to give enough information to help. I admitted the patient and was able to adjust his medications. A few weeks later, his wife called to complain that the situation was out of control. The patient...
was doing much better, but now he wanted to go places and do things, and his wife could not keep up.

This situation posed a difficult dilemma. Do you maintain the patient under good control while his support mechanisms are stressed to the breaking point, which would endanger his care? Eventually, we were able to get the patient's wife more help. They both did better. Some medical students believe that they must be "objective," although it is never clear what "objective" means. Most often, being "objective" is a way the medical student or physician protects himself from his own fears generated by the patient's illness. A dying patient reminds each of us of his own mortality. It is easy to identify which room in the hospital has the dying patient. It is the room nurses and doctors visit the least, and that is not because of risk of contamination or infection. A sick patient reminds us of our own frailties. Medical students are never taught how to deal with this fear. Many come to some silent understanding and acceptance. Others do not.

Medical information is not enough! Franz J. Ingelfinger was editor of the New England Journal of Medicine and primarily responsible for making this journal the foremost source of new medical knowledge. After his retirement, he became ill and wrote of his experiences. He described how physician after physician came into his room reciting fact after fact, when what he wanted most was for someone to tell him what he should do. The facts were never an issue. Every physician who visited him did not want the responsibility of making a decision and hoped that Franz J. Ingelfinger's sophisticated medical knowledge would relieve them of the responsibility. It did not!

The first and most overwhelming loss caused by disease is the sense of a loss of control. This control cannot be reestablished with an encyclopedic rendition of facts and figures. The sense of control is a subjective one found in the calm and reassuring voice of the physician. This loss of control causes fear, desperation, and panic, which themselves are perhaps the greatest source of suffering. It is important to make the patient feel that between him or her and the physician things are under control. This does not necessarily mean that the illness can be cured or its progression stopped. Rather, control may be the acceptance and preparation for what will eventually happen.

However, for the physician to be convincing, the physician must believe that while there are incurable diseases, there are no untreatable diseases. This will not happen if the physician narrowly defines treatment as meaning only medicines or surgery. Patients want some hope. If not hope for longer life, then at least a dignified and peaceful death. A survey of elderly people showed that what they feared most was not death but dying. Physicians may not be able to do much about death; they can and should manage dying.

Disease also causes a loss of self-esteem. Most of us define ourselves in terms of the roles we play in society, in our family and in our circle of friends. For many adults, the transition from caregiver to a carereceiver
changes the patient's perception of himself. Resistance to this change produces denial. Often, medications are not taken because the medicine reminds the patient of his illness, not because the medications taste bad or cause side effects. Insensitive physicians often wrongly attribute non-compliance to stupidity.

This may come as a shock, but internship and residency programs will teach you to hate your patients! Every new patient that comes into the hospital becomes another sleepless night. There is good news. New York State has passed a law which says that you cannot work more than 120 hours a week or 36 hours straight. It is no wonder that interns and residents develop a siege mentality in which it becomes us against them.

When I was an intern, the residents schemed so that only a certain number of patients could be discharged in any one day so as to limit the number of new patients that could be admitted. It was a matter of self-preservation.

My advice to medical students entering their internship comes from Dante's "Inferno." Over the gates of hell it is written "Give up hope all ye who enter here." I tell the students to plan never to leave the hospital. This way, when you do get to go home, it is an unexpected pleasure. If you plan to go out to a movie, then one of your patients is going to get very sick just before you get ready to leave.

I would not underestimate the stresses interns and residents experience. A great many of my friends who got married in medical school got divorced during their internship or residency. Not a small number of my fellow interns were on anti-depressants by the end of the internship.

Most physicians outgrow these problems during the internship, but some do not. These physicians remain resentful and jealously guard their time. I routinely give my patients my home phone number. This shocks some of my colleagues who fear that their patients will call them all the time. In all my years of practice, I cannot remember any case in which a patient has abused the privilege of calling me at home. Most patients are apologetic. There have been patients I have had to threaten because they did not call me at home when they needed to.

W. Somerset Maugham said: "I do not know a better training for a writer than to spend some years in the medical profession ... The doctor ... sees [human nature] bare. Reticences can generally be undermined; very often there are none. Fear for the most part will shatter every defense; even vanity is unnerved by it."

Sir John Parkinson said: "The common duty required of a physician lies in the recognition and treatment of disease. If he enlarges his study to cover life as affected by disease, and masters the psychology of the individual sick body, he will widen his usefulness and reach a fuller life himself as a physician. He will dare to enter into the mind of this patient with imaginative sympathy, proving himself a friend in need. To professional skill he will join human warmth and understanding. By so doing, and only by so doing, will he accept the whole burden and fill his destiny. If anyone seeks happiness, here it may prove to be. It is the second mile enjoined in the text, "And whosoever shall compel thee to go a mile, go with him twain." The good physician will accompany his patient on the second mile - and to the end of the road."

When I was in college and applying to medical school, I had to write an essay on why I wanted to be a physician. I wrote that I would like to integrate scientific curiosity with caring for people. I had no idea. I knew the science but I had no idea about people as patients. I became amazed at the trust patients place in me. They took me into their lives. They brought me pictures of their summer vacations and their grandchildren. They shared their thoughts, hopes and fears. They shared their lives with me, expanded mine and taught me things never written in any book. I have seen the human spirit struggle and survive, I have seen it give up and die. I have seen incredible bravery in the humblest patient. I have seen patients in great pain giving comfort to others. Though I may not be able to prove it, I feel that I have learned from them and that I am richer for it. I give this lecture as payment for what my patients, such as Harold Wade, and the families, such as Pam Grant, have given me. Finally, I would like to thank Dr. William Landau, my teacher whether either of us liked it or not.

Editor's Note: This article is a condensed version of The Harold Wade Memorial Lecture, presented at the School of Medicine by Erwin B. Montgomery, Jr., M.D., on March 15, 1991. The editors of Outlook thank Doctors Montgomery for his kind permission to reprint this abridged version of his opinions.
A year ago, the editors of the journal *Clinical Pediatrics* began a new series of landmark papers in pediatric research called, "From the Archives of Clinical Pediatrics," the first article they selected for reprint was a 1966 report on pediatric blood pressure by Sol Londe, M.D. '27.

The editors sought classic works published in previous issues that had, "offered major contributions to the pediatric literature for a variety of reasons. These articles either represent significant contributions in their own right, have stimulated significant other investigations, have served as a first report on a particular subject or illustrate an important aspect of the disease or the investigation of the disease."

Londe's paper meets all of those criteria. The clinical study was done on Londe's own time and largely without outside funding while he was on the clinical faculty at Washington University School of Medicine. It was the first work to establish clear criteria for normal standards of blood pressure in children — a lifelong interest that has sparked an outstanding career in medicine.

Before Londe's work appeared, pediatricians who took blood pressures had no criteria of normalcy to apply. In effect, the one paper — written entirely out of a clinician's interest — became the standard of medical practice. Done in Londe's private practice, at the St. Louis Labor Health Institute and St. Louis Children's Hospital, the study was meticulous. It involved 894 boys and 911 girls, all well children aged 4 to 15 years old. After the paper appeared, Londe says he found that children aged three are relaxed enough for accurate blood pressure measurement, and he added data on that age group in 1968.

He showed that blood pressure in children was related to age and weight but not to height. And he provided guidelines: the 90th percentile for a given age was to be considered suspicious, the 95th percentile was to be labeled hypertensive. Those values remain in use today, 25 years later. According to the research, about two percent of children are hypertensive and should be followed closely by their pediatricians.

Perhaps equally important is Londe's paper published in the *Journal of Pediatrics* in 1971 reporting 74 children with hypertension as previously defined by Londe. That study suggested a genetic component in more than half of the subjects and established that, in some, hypertension may begin during childhood.

Londe's research into the blood pressure of young people actually began long before, when an article he read substantiated something he'd observed in his own practice: that anxiety during a physical examination, as indicated by a rapid pulse rate, does not always cause an increase in blood pressure. Londe's groundbreaking research began in 1959, when the pediatrician was 55 years old. For seven years thereafter, he collected data in preparation of his own study with the guidance and help of David Goldring, M.D., then chief of pediatric cardiology.

By what Londe says is "coincidence," his very first publication, a 1932 paper in the *American Journal of Diseases of Children*, also dealt with blood pressure. In that piece, written during his residency and published just prior to his joining the Washington University faculty in 1933, he examined blood pressure in premature newborn infants. Londe took measurements with a specially designed instrument he describes as, "primitive by today's standards."

Completing the circle, a Londe commentary published in *Pediatrics* in 1987 also dealt with the topic of hypertension. His last clinical investigation — circa 1984 — detailed the effects of pressure on the head of the stethoscope in taking blood pressure. It showed that even slight pressure on the stethoscope artificially lowers the diastolic reading. That paper appeared in the year that Londe celebrated his 80th birthday.

Then, after 22 papers on the subject of blood pressure from the clinician's vantage point, Londe says it was, "time to quit." But he remains proud of what he has been able to accomplish. "I feel very good that in my lifetime I contributed something," he says. "Unfortunately, too often important observations or approaches to treatment by clinicians are not published and die with them."

(Continued on next page)
Today, at 87, Londe lives in Northridge CA, where he still passes along some of what he knows two mornings a week on behalf of the Los Angeles County Health Services and young people in the juvenile-detention system. It's a 28-mile drive to work, but Londe has no plans to quit. “Oh no,” he says, “I keep busy.”

The elder Doctor Londe has left a substantial legacy in other ways, too. Both of his children are M.D.s: daughter Helen is a researcher in virology, and son Stephen is a cardiothoracic surgeon.

Stephen Londe recalls that when he began medical school at Washington University (he graduated in 1963), he sometimes was referred to as “Doctor Londe’s son.” As he became known during his surgical training at Barnes Hospital, he said, “Doctor Londe’s father.”

Now that the senior physician is reaping the credit his dedication and contributions deserve, Stephen says that he is delighted to once again be known as “Doctor Londe’s son.”

For What It’s Worth

In May, 1991, Washington University medical school alumni from all parts of the country convened in St. Louis to re-establish contacts and revitalize memories. They brought with them the wisdom of their experiences. As a means of tapping into that wisdom, the staff of the alumni and development office asked all reunion registrants to respond to a few questions. Among those questions was: “What advice would you like to give to our current students?”

More of the responses than we have room for were instructive or entertaining. But here are a few of the suggestions, arranged by class. They appear in no particular order, for the protection of those brave enough to give free advice.

1931

Study and enjoy your work.

1936

It’s a great career. Don’t go into medicine to make a lot of money but to have a satisfying life.

Be more intimate with your patients. Get to know them physically, mentally and, if possible, socially. Don’t depend entirely on lab work and radiology.

Remember! The patient does not care how much the doctor knows until he or she knows how much the doctor cares.

1941

The wide world is out there. It’s waiting for you. My advice is: Don’t go.

None. In a changing world, today’s advice is meaningless tomorrow. Each must do his or her own thing as he or she sees it.

Because the magnitude of available knowledge exceeds the mental grasp of the individual mind, it is my opinion that speciali
zation in a group situation will more and more become the most satisfactory type of medical practice.

1946

Strive to maintain empathy and compassion in an increasingly technological science.

Expand your life beyond medicine! Do not let yourself become merely an interface between computers. Remember, the cemeteries are full of essential persons.

Carpe diem.

1951

Don't lose sight of the complicated person you see for the dysfunction of one system. Strange holistic disciplines have arisen because we have neglected the “whole patient” in order to expertly treat a specialized part.

Stay healthy -- you can't afford the expense of illness. True satisfaction: family, friends, service to patients.

Don't worry about getting practical experience while you are in medical school. You'll get all you need and more during your residencies. A sound theoretical background will serve you well in most situations.

1956

Learn that what we know is small compared to what we don't know. Learn to care for patients, not diseases.

Attend law school.

Aspire to be the best physician you can be. Never stop being a student of medicine. Get to like your patients -- spend a little time getting to know them. Don't let all the negative things you hear about medicine diminish the joy and the fun and the honor you've been awarded in being a doctor. There is no better profession.

1961

Stay away from drugs and alcohol; they are an occupational hazard in medicine, nursing, dentistry, pharmacy. Learn the principles and practice “CQI” - continuous quality improvement -- as it applies to health care institutions.

Don't panic about current economic and social problems affecting medicine. Solving them is offering us a great challenge now, and they will be solved. Then medicine will continue to be the satisfying and gratifying profession it has always been.

1966

Seriously consider another career until the government comes to its senses, or at least consider organizing in a meaningful fashion on the national level for maximum political leverage.

Take time to reflect, to get a bit of exercise, to laugh, to think and to be very careful to maintain close personal relationships.

1971

Take advantage of the facilities and the faculty that you have because there aren't any better opportunities to learn medicine anywhere else.

Be open to change.

1976

Cultivate your research interests both during and after medical school; obtain financial support from any possible source.

Remember, the ability to help people in need is the common denominator that makes it all worthwhile.

There is nothing trivial. Every bit of information received in medical school is important and will be used. Study hard, but make time for outside activities.

These can be the best years of your life -- enjoy them. You'll never learn everything you need to know, so set a pace that won't burn you out.
A. Raymond Eveloff, M.D. '33, retired in 1988 after 52 years of medical practice. He is a founding member of the Springfield Clinic that currently employs 84 physicians. A resident of Springfield, Ill., Eveloff was a clinical professor of pediatrics, past president of the medical staff at St. John's Hospital, and a past president of the Springfield Board of Education.

Ralph C. Green, M.D. '34, reports that he has recently published a book, *Medical Overkill*, and articles in *American Heritage* and *MD* magazines.

Alexander Ling, M.D. '34, reports that he has been happily retired for five years after 15 years as the senior partner in the largest and oldest neurosurgical group in northeastern Ohio.

Robert N. Webster, M.D. '34, retired from 36 years of active practice as a urologist on May 1, 1991, shortly after completing a year as the president of the Southeastern Section of the American Urological Association.

Marvin E. Levin, M.D. '51, professor of clinical medicine and associate director of the metabolism and diabetes clinic, was presented with the American Diabetes Association's Award for Outstanding Physician Educator in the Field of Diabetes in 1991. Levin serves as editor in chief of *Clinical Diabetes* and as an editor of *Diabetes Spectrum*, publications of the American Diabetes Association.

Harry R. Kimball, M.D. '62, has been named president of the American Board of Internal Medicine.

Gary Rachelefsky, M.D. '67, reports that he is a member of the Executive Committee of the American Academy of Allergy and Immunology and past chairman of the American Board of Allergy and Immunology. He and his wife, Gail, celebrated their 25th wedding anniversary in June. Two children are in college, a third is a sixth grader.

John Gumbelevicius, M.D. '70, was recently promoted to clinical professor of pediatrics at the University of California and is head of pediatric cardiology at Kaiser Medical Center in Sacramento. In his position as a colonel in the U.S. Air Force Reserve, he was activated to serve in Operation Desert Storm.

As of July 1, 1991, Joseph K. T. Lee, M.D. '73, has assumed the position of chairman of the Department of Radiology at the University of North Carolina Medical School at Chapel Hill.

Linda Christine Loney, M.D. '76, is now a clinical associate in the Clinical Genetics Program and Birth Defects Service at Boston Children's Hospital and an instructor in pediatrics at Harvard Medical School.

Her husband, Thomas W. Cooper, M.D. '76, is in the full-time private practice of dermatology in Dedham, MA.

Neil E. Sherman, M.D. '76, writes that he is back in private practice in Houston, TX, as the medical director of the Radiation Therapy Center at Memorial City Medical Center. Married for 14 years, he has two sons, ages six and 11.

Charles R. Carrasco, M.D. '77, practices radiology in Boise, ID. He and his wife, the former Millicent Haynie, have two daughters. Carrasco writes that he is a "self-declared 'golfaholic.'"

Jeffrey P. Cichon, M.D. '79, recently was inducted as a fellow of the American Academy of Orthopaedic Surgeons during the academy's 58th annual meeting. He was one of 675 new fellows named, bringing the number to 15,600.

C. James Holliman, M.D. '79, took a leave of absence from his position on the faculty of the Penn State University College of Medicine and volunteered to work at the Peace Sun Medical Clinic in Riyadh, Saudi Arabia, in January 1991. He was in Riyadh fort the start of Operation Desert Storm and witnessed the first few weeks of the war, including Scud missile attacks on the city. Back at Penn State, his faculty responsibilities include the clinical directorship of the Emergency Department and developing a new emergency medicine residency program.

Patrick King, M.D. '83, is assistant clinical professor of ophthalmology at the University of South Dakota School of Medicine and in private practice in Yankton, SD. He and his wife, Meredith, age 8 and Emily, age 5.

Robert Alan Cooper, M.D. '80, and his wife, Micki Dardick Cooper, became the proud parents of a son, David Alexander, in February 1991. David's sister, Jessica, is three years old. Cooper practices as an invasive cardiologist with Kaiser Permanente Medical Group in Oakland, CA.

Ira Tabas, M.D. '81, assistant professor of medicine and cell biology at Columbia University, received the 1990 Columbia University Lamport Award for excellence in research.

Sandra Lee Hofmann, M.D. '83, Ph.D., has been named a recipient of the Charles E. Culpeper Foundation Scholarships in Medical Science for 1991. Through this award, Hofmann will receive $100,000 per year for up to three years to fund her research at the University of Texas Southwestern Medical Center in Dallas. One of three researchers selected for the prestigious award, Hofmann investigates molecular biology techniques to study how transmitters...
outside of cells produce responses such as muscle contraction. The work is relevant to hypertension, heart and blood vessel diseases and muscular diseases.

In July, Thomas Chang, M.D. '85, became a staff radiologist at Magee Women's Hospital and Montefiore Hospital in the University of Pittsburgh medical system.

John C. Powell, M.D. '86, has recently finished a general surgery residency at Indiana University and begun a fellowship in cardiovascular and thoracic surgery. He writes that he is the proud father of two boys and that the family is, "doing great."

Richard Noren, M.D. '87, and his wife Amy Feigen Noren proudly announce the birth of their daughter, Rebecca Gabrielle, on April 5, 1991. The family, which also includes two-year-old Ian, lives in Atlanta, where Richard is in his final year of an anesthesiology residency at the Emory University Hospitals and Clinics.

Elizabeth Ella Puscheck, M.D. '87, completed her obstetrics and gynecology residency in June of 1991 and reports that she looks forward to a fellowship in reproductive endocrinology and infertility at the Medical College of Georgia in Augusta.

John N. Constantinou, M.D. '88, writes that his first book, A Poor Man's Proof for the Existence of God, is a philosophical novel based, in part, on the story of a cancer patient he cared for while a medical student at Washington University School of Medicine. The novel is due out in November from Paulist Press. Constantinou is in the fourth year of a five-year combined residency in pediatrics and child psychiatry at the Albert Einstein College of Medicine in New York.

Renee P. Graham Merlino, O.T. '86, was married to Robert J. Merlino in Boston in July 1990. She works as a pediatric occupational therapist; her husband is an entrepreneur. Both are involved in fundraising for local charities and the Special Olympics.

Marjorie McCown, P.T. '62, has assumed the new position of assistant program coordinator of P.T. O.T. and A.P.E. for the Special School District of St. Louis County. She reports that her Masters of Science in physical therapy (pediatrics) is almost complete at St. Louis University.

Ruth Rose Jacobs, P.T. '73, was recently appointed senior research associate in the Department of Neonatology at Boston City Hospital. She directs a developmental laboratory in a large study looking at the effects of illicit maternal drug use on the development of infants.

Louise A. Partin, P.T. '77, was married in August of 1979 and moved to Austin, TX, in 1982. Partin works in home health and public health.

IN MEMORIAM

Armin C. Hofsommer, M.D. '22, died on February 14, 1991, in Menlo Park, CA. A retired pediatrician, he attended medical school with his wife, the late Aphrodite J. Hofsommer, M.D. '23. An accomplished photographer, an enthusiastic fisherman and an avid student of nature, he practiced pediatrics in Webster Groves, MO for more than 40 years before he retired to California. Dr. Hofsommer is survived by a daughter, Helen C. Glaser, M.D. '47, a son, Armin C. Hofsommer, M.D. '54, three grandchildren and two great-grandchildren.

Elizabeth Lowenhaupt Lowe, M.D. '37, died at home in Kensington, CA on February 4, 1991 at the age of 79. She practiced pathology and, later, psychiatry for more than 30 years.

Charlie Ruggieri, for 38 years (beginning in 1931) the assistant house manager and much more at the Phi Beta Pi fraternity house on Forest Park Blvd., passed away Friday, May 17, 1991, shortly before his 92nd birthday. Ruggieri was a friend to all medical students and served scores of young physicians-in-training as a second father. Born in Italy, he came to this country as an orphan and later served in the Army's Ambulance Corps in World War I. The Charles Ruggieri Scholarship Fund was established in 1985 after the sale of the Phi Beta Pi house to honor Ruggieri and to assist deserving students enrolled at Washington University School of Medicine with the financing of their medical educations. Alumni of the fraternity and others may make contributions to that fund by sending them to the School of Medicine and designating them for the fund.
Mildred Trotter, Ph.D.

Mildred Trotter, Ph.D., professor emeritus of anatomy at Washington University School of Medicine, one of the nation’s foremost physical anthropologists and an eminent anatomist, died Friday, August 23, after a long illness. She was 92 and a resident of the Bethesda-Dilworth Memorial Home in Oakland, MO.

During 47 years of teaching, Trotter trained almost 4,000 students in human anatomy, the course of instruction that sets the tone for a medical student’s education more than any other single discipline. Among her students were two Nobel laureates, one of whom, Daniel Nathans, M.D., later described her as, “a very exciting teacher,” “absolutely thorough,” and a woman of “tremendous vitality.” She was a member of the faculty for 71 years.

The first woman to be named to a full professorship at the School of Medicine, Trotter made “the structure of man” her study, according to long-time colleague and friend, Roy R. Peterson, Ph.D. She contributed greatly to the understanding of bone as tissue and as the central locus of mineral mass in the body. Her methods of determining a person’s size in life from bones found after death remain the standard for forensic medicine.

“Trot,” as she was known to her colleagues and the many students who became her close friends, was raised a farm girl in Pennsylvania. She first developed an interest in science at Mount Holyoke College, where she majored in zoology. Among her many lifelong loyalties was the love she maintained for her alma mater. Upon graduation in 1920, she joined the faculty of Washington University, where she earned both a Master’s degree and a Ph.D.

Robert J. Terry, M.D., chairman of the anatomy department at the time Trotter arrived, urged his new employee to “study nature, not books,” a motto that guided Trotter. She once said: “Each human body is different; the ability to discern the differences is a crucial part of medicine,” and she steadfastly insisted on the importance of what the naked eye could see during an age in which anatomy reduced its scale more and more to the cellular.

One of the founders of the American Association of Physical Anthropologists, she published more than 100 papers and book chapters and was the first woman to be awarded the Viking Fund Medal given by the Wenner-Gren Foundation for Anthropological Research, preceding even Margaret Mead in that honor. In 1956, she received the first Globe-Democrat Woman of Achievement Award. In 1975, the Mildred Trotter Lectureship was established by the alumni association in her honor.

In the Spring of 1980, Trotter received an honorary doctorate from Washington University. The citation noted her 60 years of inspired teaching, scientific leadership, and most importantly, her qualities of enthusiasm, warmth and goodwill.

Trotter was a demanding instructor who expected excellence. “The mention of her name can still get a few clinical chiefs to quake,” according to colleague Glenn Conroy, Ph.D. Conroy was with Trotter in South Africa thousands of students.

“Everyone in the field considers her a trailblazer. We all feel strongly about her as one of the founders of physical anthropology,” says colleague Jane Phillips-Conroy, Ph.D. Peterson recalls that she embodied good science: “Her motivation was doing the job well, to the very best of her ability, knowing that the results were correct and would stand.”
In this photograph from 1990, autumn descends on the Medical Center.
Principal investigator Elizabeth M. Smith, Ph.D., conducts research into the best way to help homeless women and their families return to the mainstream. For more on Smith’s investigations, see the article, “Long Way Home.”