

BIOLOGUE

Fall 1982



*As time goes by –
not the same old story*



Editor's Message

This first issue of *BioLogue* was a long time in the birthin' process, and one of the longest-enduring pains had to do with naming our new creation. After months of playing around with words and their meanings and realizing that some of the best names—*Discover* and *Life*—had already been taken, the name *BioLogue* sprang fully formed from the arcane brain of our director Bob Fenley.

Bio, of course, means “life,” and - *logue* means “discourse, talk; performance, recital; student, specialist.”

We have taken our newly coined word apart and looked at it from different angles, and every time we analyze it, we like it better as a name for this new publication.

BioLogue will feature research at The University of Texas Health Science Center at Dallas but will also include trends in medical care and education from time to time.

Readers are invited to send ideas for future stories and general comments on *BioLogue* to the editor.

Ann Williams

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Editor

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Altered States

Researchers relate events of aging to hormone changes

by Ann Williams

Aging is not a healthy state. But unlike cancer and heart disease, it happens to everybody.

With age, the body's production of hormones changes. Sometimes it's hard to tell the aging process from a disease process. Sometimes the changes actually result in disease.

Research into hormone changes with aging at The University of Texas Health Science Center at Dallas has already contributed greatly to the knowledge of these mechanisms even though research on aging is relatively new, most of it having been done within the last 10 years.



There are more than 40 million women in the United States who are more than 50 years old. "One-third of a woman's life is spent after menopause," says Dr. Paul MacDonald.

"We need to understand the physiological changes that accompany menopause so that we can address the health problems that women experience during this time of their lives," says MacDonald, director of the Cecil H. and Ida Green Center for Reproductive Biology Sciences and holder of the Green Chair in Reproductive Biology Sciences.

Recognized internationally for their work on estrogen production in women after menopause, MacDonald and his co-workers were first to show that postmenopausal events are not due to total estrogen deprivation but to a different type of estrogen produced.

MacDonald relates that he got into research on postmenopausal women "by accident." He had found that in pregnant women, male-type hormones were converted to estrogen in the placenta. He recruited men, young women and postmenopausal women for a control group to show that androgens (male hormones) were not converted into estrogen in them. He was wrong. The hormone conversion took place in all groups. And in postmenopausal women, it was even higher than in men

and in young women who were not pregnant.

He went on to describe the changes in estrogen production that occur after menopause.

It was already known that the ovaries stop making estrogen after menopause. MacDonald found that even though the ovaries stop making estradiol, the potent form of estrogen, the body becomes more efficient in producing a weaker form—estrone—in the tissues.

In fact, after about age 50 the efficiency of conversion of plasma androstenedione to estrone increases with age in both men and women. The conversion takes place in many tissues including bone, brain, hair follicles and skin. But most estrone is produced in fat tissue.

As both men and women become obese, more estrone is produced. In morbidly obese postmenopausal women, those who weigh 50 percent more than their normal weight, there may be enough estrone made to prevent hot flashes, says MacDonald.

It has puzzled researchers for a long time why obese people should be able to make more estrogen than normal weight people. Some thought that the answer was simply larger tissue mass. Fat cells (adipocytes) increase in size by storing lipids (fats), but they don't increase in number. At least this was the thought until recent work done at the health science center by Dr. Evan Simpson, associate professor of Obstetrics and Gynecology and Biochemistry, and Dr. Carole Mendelson, assistant professor of Biochemistry.

Building on MacDonald's clinical research, the biochemists found in working with adipose (fat) tissue removed surgically from obese patients that estrone is made in the stromal cells, the supporting cells of fat tissue. These stromal cells, they found, do increase in number with obesity, and they may possibly develop into fat cells.

This probably explains why when obese people lose weight, the efficiency

in estrone production doesn't decrease—there is no decrease in the number of stromal cells.

Glucocorticosteroids, hormones that protect against stress and affect protein and carbohydrate metabolism, are found in obese people in higher levels than in normal weight people. Simpson and Mendelson found that glucocorticosteroids stimulate a conversion of androstenedione to estrone 60 times that found in fat tissue untreated with any hormone.

At first glance, it would seem highly desirable to produce estrone efficiently. Perhaps a woman could get through menopause with no hot flashes. But MacDonald has also found that an increase in estrone production is linked to endometrial cancer (cancer of the uterus lining).

Women at high risk for endometrial cancer are aging women, obese women and women with liver disease, ovarian tumors or polycystic ovarian disease. Also in all these groups, estrone production is above normal. And aging and obesity act synergistically on estrone production. An aging, morbidly obese woman may produce 10 times the estrone that a young normal woman produces.

Even low-dose estrogen therapy for postmenopausal women is linked with an increased risk of endometrial cancer. (See story on page 6.) Recent work at other institutions has been done on cyclic administration of progestin to counteract the effects of estrogen on the endometrium.

In the Dec. 31 issue of the *New England Journal*, MacDonald called for caution in the use of progestin. Estrogen and progestin used in cycle are similar to the "pill," which, used for contraception, has been linked to heart disease and stroke. He calls for more studies of the risks and benefits before advocating the use of progestin in post-menopausal women because the risk of using progestin may not outweigh the risk of low-estrogen therapy.

"The risk of endometrial cancer is

low and the cure rate of early diagnosed appropriately treated endometrial cancer is high," says MacDonald.



While aging women suffer from a lack of the active estrogen, aging men are plagued with a disease that results from an excess of a male hormone—dihydrotestosterone. Non-cancerous enlargement of the prostate gland is an almost universal feature of the aging man and dog, says Dr. Jean Wilson, professor of Internal Medicine. Wilson found that accumulation of dihydrotestosterone in the prostate gland causes the abnormal growth and that it develops only in males with intact testes.

They have also learned that an azosteroid drug that blocks the formation of dihydrotestosterone reverses the gland enlargement in dogs, virtually "melting the prostate away," says Wilson. The drug decreases a 20-gram gland to less than six grams without affecting the plasma testosterone or the sex drive.

Merck Sharp & Dohme is considering clinical studies of the drug in human subjects. If azosteroid proves effective in men, it will allow treatment of patients who are poor surgery risks without having to subject them to "chemical castration." Eventually, it may make it possible to prevent this disease process so common in aging men.

found that prolactin also stimulates the secretion of dopamine in the brain of rats. So, at least in the young rat, dopamine and prolactin form a self-regulating cycle. In old rats, this regulation is lost or weakened.

The word "hormone" comes from the Greek word that means "to stir up" or "to excite." In the classical definition, hormones are secreted by endocrine glands, such as the ovary or the pituitary gland. They are carried by the bloodstream to other tissues where they produce an effect.

Neurons (certain nerve cells) secrete neurotransmitters. A molecule of a chemical such as dopamine is secreted by one cell. It interacts with the next cell, stimulating or inhibiting secretion, and so on throughout the nervous system. "So the neuron is the ultimate reduction of the endocrine gland," says Porter.

As people age, their production of dopamine decreases. Even in relatively young people, a dopamine deficiency results in Parkinson's disease, one of the most crippling of the central nervous system disorders. Many elderly people eventually develop symptoms of Parkinson's disease such as tremor, muscle stiffness, slowness of movement or impaired balance.

Porter is using the rat model to study the decline of dopamine production with aging and the effects of drugs on dopamine secretion.

He and his group have measured the secretion of dopamine by neurons in the hypothalamus, a small gland in the brain that controls the body's autonomic (involuntary) function. They have found that the secretion decreases with age. But they do not yet know whether the decreased production is due to the cells' loss of ability to secrete the hormone, the death of secreting cells or both.

The secreting neurons have cell bodies that lie in the hypothalamus with their axonal endings feeding the dopamine into the capillaries that lead into the portal vessels to the pituitary gland. By tapping into these portal vessels, the researchers obtain the highest concentration of dopamine in the blood supply. "At this time these are the only neurons in the brain in which true secretion of a neurotransmitter can be measured," says Porter.

He has narrowed the problem of decreased dopamine production to one specific reaction in the neuron cell body. In this cell, tyrosine is changed into L-dopa, which is then changed into dopamine. (Tyrosine is an amino acid obtained from dietary protein.) Giving

If azosteroid proves effective in men, it will allow treatment of patients who are poor surgery risks without having to subject them to "chemical castration."

The condition, called "benign prostatic hyperplasia" or BPH, produces discomfort and significantly decreases the quality of life for a large number of older men. In about 75 percent of men age 75 and older, the prostate growth results in symptoms of urethral obstruction, which include lack of bladder control, increased urinary frequency and urgency, excessive urination at night and, eventually, retention of urine that can lead to urinary tract infection and even kidney failure. Surgery is an effective treatment for BPH, but some elderly patients are poor surgical risks because of heart disease or other problems.

Drugs currently used to treat the condition block the body's production of testosterone and consequently interfere with the man's sex drive.

Wilson and his group have discovered in their work with dogs that BPH results from the conversion of testosterone to dihydrotestosterone in the prostate gland itself. They have confirmed this in humans, finding a striking increase in dihydrotestosterone in enlarged glands and in normal glands as they start to enlarge.

While MacDonald and Wilson have worked with elderly human subjects, most medical research in the past was done with young people and young animals.

"It's no accident that most animal research is done on the young," says Dr. John Porter, professor of Obstetrics and Gynecology and Physiology in the Green Center. "Aging research is expensive. You have to keep animals a long time—until they are aged. For a rat, that's two or three years. A three-year-old rat is senile, and the number of rats in a colony still alive at two years is greatly reduced."

Porter is interested in what happens to the aged rat's secretion of dopamine, a hormone that carries messages throughout the nervous system to ensure coordinated movements of the muscles. Dopamine may also be involved in thought processes, and it is known to affect the pituitary gland by suppressing the secretion of prolactin.

Prolactin is a hormone that stimulates milk production. Porter has recently

an aged animal L-dopa increases the production of dopamine, but giving tyrosine does not. Since both the enzyme tyrosine hydroxylase and the

from pro-opiocortin, which looks like the "granddaddy" hormone for several other peptide hormones when charted family-tree style. Pro-opiocortin con-

tives of pro-opiocortin accumulate in these regions of the brain in the same proportion, regardless of age. (The peptide hormone beta-endorphin has been reported by other researchers in the brain of old rats at half the concentration found in young ones.)

Based on her studies, she theorizes that the cause of the decreased levels of α -MSH and ACTH in the brain of aging animals is a decrease in the supply of the "raw material" pro-opiocortin.

Surprisingly, not all peptide hormones are produced in smaller quantities in the aged brain.

Barnea and others have found no decrease in the concentration of some peptide hormones in the hypothalamus of aging female rats. She believes, therefore, that aging has a specific effect on neurons that produce pro-opiocortin and that aging thereby affects the production of ACTH, α -MSH and beta-endorphin. "It is tempting to speculate that the changes in these neurons are related to the altered function of the brain of the aged," says Barnea.

People today are worried about deterioration of brain function with aging. "The life-span is longer. We are confronted with health problems that we didn't see before," she says. "If a biochemical process is faulty in the aged, it could eventually be corrected if we had knowledge of how this process operates in the young, healthy person. If

"It's no accident that most animal research is done on the young. Aging research is expensive. You have to keep animals a long time—until they are aged."

co-factor tetrahydrobiopterin are necessary for the conversion of tyrosine into L-dopa, a deficiency in the enzyme or the co-factor or both may be the cause of reduced dopamine secretion.

This work by Porter and his group increases the possibility of treating nervous disorders with the specific biochemical the body is lacking.



Aging rats and their hormones are also being studied by Dr. Ayalla Barnea, associate professor of Obstetrics and Gynecology and Physiology. She has studied the biochemistry of the aging process in the brain with emphasis on peptide hormones: peptides are known to affect memory and learning in animals and in humans.

These peptides, produced in the brain, may also regulate important biological activities of the brain. "They may affect how we learn, how we think, how we remember, how we perceive pain, how we adjust to cold," says Barnea. "If we know how these peptides are produced and secreted, we may understand some processes regulating brain function and know what to do when something goes wrong."

In rats, alpha-melanocyte stimulating hormone (α -MSH) and adrenocorticotrophic hormone (ACTH) may have "profound effects" on memory and learning. These brain functions are known to deteriorate markedly in aging animals and humans. Therefore, she and her co-workers want to learn whether the aging process is associated with a decline in the amounts of ACTH and α -MSH produced by the brain.

ACTH and α -MSH are derived

sists basically of a chain of amino acids, and the order of the amino acids is unchanged from "generation to generation."

A molecule of pro-opiocortin is literally broken into pieces that form new hormones, which in turn are broken down again and again until there are three or four generations of peptide hormones, each of which affects the body in a different way.

The important peptide hormones derived from pro-opiocortin are ACTH and beta-endorphin. Beta-endorphin


"If a biochemical process is faulty in the aged, it could eventually be corrected if we had knowledge of how this process operates in the young, healthy person."

has recently been touted as the body's own anesthetic and is also important in memory and learning. ACTH is further broken down into α -MSH.

Using radioimmunoassay techniques, Barnea has measured the content of α -MSH, ACTH and their precursors in the rat hypothalamus and thalamus at different ages. She has found that although the concentrations of these peptides are lower in old rats than in young ones, the various deriva-

we didn't know the biosynthetic process for dopamine, we couldn't treat Parkinson's disease. In the biosynthesis of peptide hormones, we just have to start from scratch and see what is related."

In the Heat of the Night



Hot flashes are not caused by a lack of estrogen. Rather they are apparently the result of "estrogen withdrawal."

"Women who have never produced estrogen do not experience hot flashes," says Dr. Paul MacDonald, director of the Cecil H. and Ida Green Center for Reproductive Biology Sciences.

Those undergoing estrogen withdrawal may experience vasomotor instability (characterized by hot flashes) and vaginitis, the known physical symptoms of menopause. MacDonald recommends low-dose estrogen therapy for women suffering severely from these symptoms. Therapy should be carried out for a limited period of time, and the patient should see her physician for a checkup every six months.

Other symptoms attributed to menopause, such as depression and loss of recent memory, may be psychological symptoms due to the stage of life the woman is going through, says MacDonald.

Usually at menopausal age, the children are leaving home; the woman's husband may be experiencing a career or identity crisis—he realizes he is not going to be quarterback of the professional football team or president of the bank; her own parents are aging.

These circumstances are enough to cause depression and other psychological symptoms. But it has not been proven that estrogen is helpful for a woman's emotional health, says MacDonald, although it may alleviate sleeplessness caused by hot flashes.

Another physical symptom often attributed to estrogen loss is osteo-

porosis. This condition, caused by calcium loss in the bones and characterized by easily broken bones, may be due more to aging itself rather than to the amount of estrogen produced by the body.

MacDonald recommends estrogen replacement therapy in women who undergo an early menopause, either naturally or surgically, to reduce the risk of osteoporosis.

Estrogen therapy may help prevent osteoporosis in other women also. He feels that this therapy may be indicated for small, frail white women, whose bone density is known to be less at menopause than that of larger women. Osteoporosis also occurs less frequently in men and in black women.

Until estrogen therapy has been proven effective for preventing osteoporosis, MacDonald recommends regular physical exercise, such as walking or tennis, in which the weight is put on the bones, and adequate calcium in the diet. And he says an inexpensive, low-calorie way to get enough calcium is to take two Tums every day.

Risks related to estrogen therapy include endometrial cancer (cancer of the uterus lining) and gallbladder disease. Because of these increased risks, the patient needs to see her physician every six months.

Many women worry about estrogen causing breast cancer. MacDonald says that estrogen therapy neither causes nor prevents breast cancer. If a patient develops a benign breast tumor during therapy, she may have an increased risk for breast cancer.

Estrogen therapy may help in treating menopausal symptoms

Ann Williams

Growing old in America: a question of quality

“Young old” or “old old”?

Attitudes of society and of older people themselves affect health care

by Ann Harrell

George Burns is fond of telling the story about the young reporter who couldn't resist the temptation to ask him about his behavior that many consider improper—especially in an older person.

“Mr. Burns, is it true that you go out with young girls?”

He told her it was.

“Is it true that you smoke between 15 and 20 cigars a day?”

“Yes, it's true,” replied America's most popular senior citizen.

“Is it true that you drink between four and five martinis a day?”

Again his reply was in the affirmative.

“Well, what does your doctor say about that?” she asked, a scolding note creeping into her voice.

“My doctor's dead.”

◆

The beloved comedian, who may well be the youngest 86-year-old man in the world, was chosen last year by the American Academy of Family Practice to be their spokesman for an emphasis on attention to the problems of aging. Burns, whose career in show business began nearly eight decades ago, was feature performer for the annual AAFP meeting last fall, which preceded the White House Conference on Aging. In addition, he and AAFP president-elect Dr. Gerald R. Gehringer, director of the Louisiana State University family practice residency in New Orleans, met with national media to discuss the problems of aging in America.

Throughout the meeting Burns's stories reflected a serious concern with the problems of discrimination against the aged and the fact that our society stacks the cards against older citizens and then discriminates against them. He also addressed remarks to our elderly citizens, imploring them not to take the stereotypes lying down—to get up and do something about the quality of their lives. And the showman means it quite literally.

“You can't help getting older, but you don't have to get old. You have to get out of that bed,” he admonished.

One of the ironies of our society is that while we are living longer these days as a nation, the quality of the lives of many of our elderly citizens has gone down. Many of these problems are intertwined with all the other problems of urbanization.

No longer do most of us live in small towns with close family units or continue to farm the old home place for generations. Rather we are transferred around the country by large corporations or choose lifestyles more compatible with a jet plane than with a Model T. Our parents are often left alone except for holiday visits.

Dr. Bruce Jacobson, director of The UT Southwestern Medical School family practice residency at John Peter Smith Hospital in Fort Worth, says that in his clinic program it is rare to see a family group of more than two when the mother and father are over 45.

We are living longer, and our life expectancy is expected to continue rising. In 1950 the expected life span in this country was 68.2. Last year it had risen to 73.3. Yet this life span increase is not accompanied by an increase in income to take care of these added years. Most elderly Americans are trapped in fixed incomes, and in many cases these incomes are from the federal government, that is, welfare funds or Social Security, which many believe is an endangered species. Nor do Medicare/Medicaid payments cover the costs of the elderly ill.

Today 11 percent of our population is over 65, the figure that is most often used as the demarcation point into the “valley of the shadow of death” as many old and young alike view it. And at the time of their lives when they probably have fewer funds available than ever before, health problems add to their financial burdens. In fact, 33 percent of all health care dollars go for medical/hospital care for these senior citizens, and health economists are looking with

alarm to the year 2020 when the post-World War II baby boom population reaches the “magic number.” At that time projections show that one out of every five Americans will be among this group. Since today 59 percent of all catastrophic health care costs are for the elderly, that statistic can only increase.

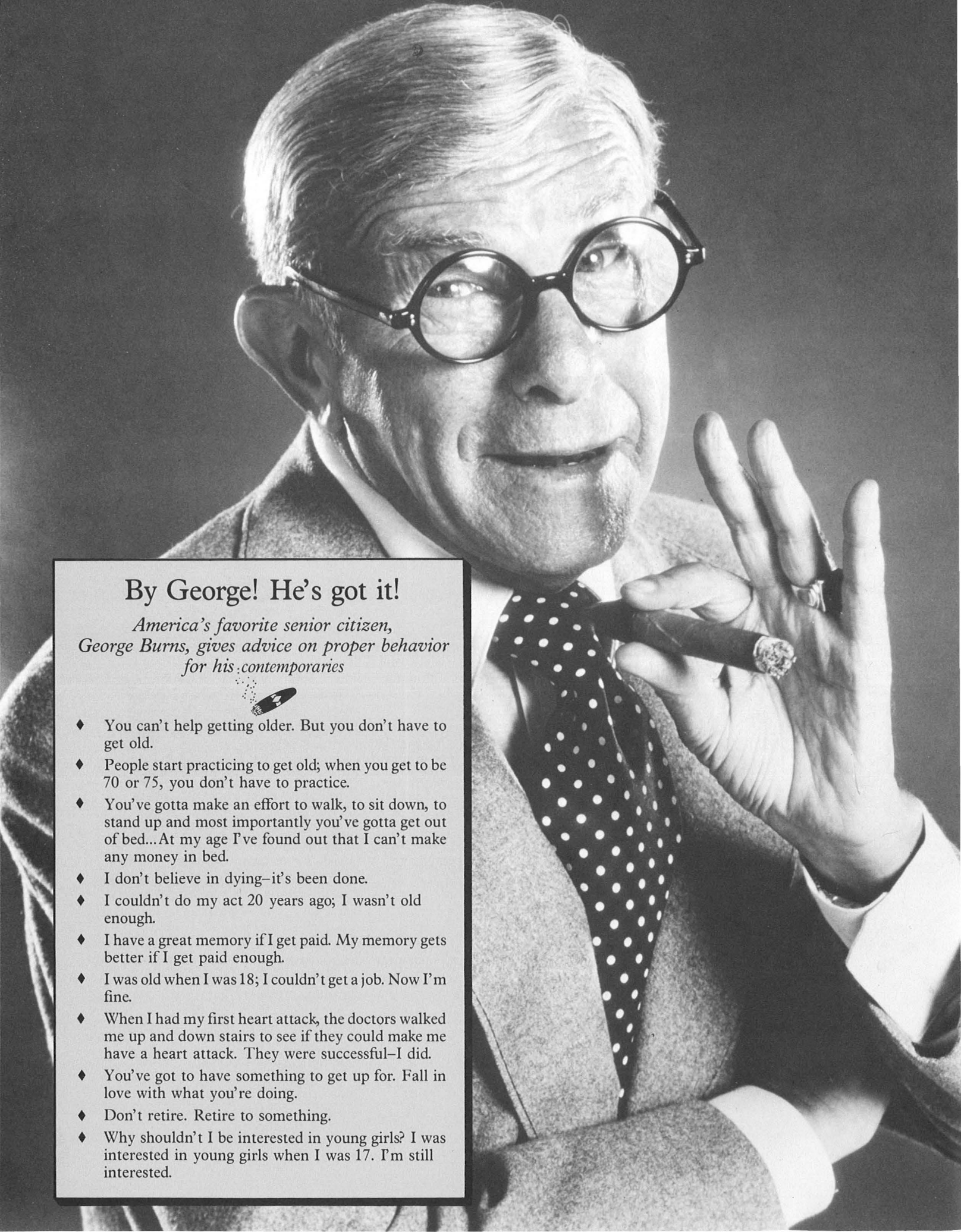
Part of the problem, of course, is that expectations of quality medical care are held by a far larger segment of our population today than ever before. “Twenty-five years ago a large percentage of the elderly didn't even go to the doctor until they thought they were dying,” said Jacobson. “That's not the case today.”

In fact, the medical care available today is one of the major reasons that many in our population seem so young and vital after 65 and for many more years.

“Many people over 65 today lead active lives and don't think of themselves as old. And they're not!” said Dr. Laura Wilson, gerontologist who heads the health science center program. The School of Allied Health Sciences program in Gerontology is designed to train professionals to work in nutrition and recreation programs with older people as well as to train administrators of nursing homes.

Dr. Bill Ross, who heads up the medical school's Family Practice Division after being in private practice for many years in the state, looks at it a little differently. “Old people are not so old as they were 20 years ago,” he says about his former patients. “That's because I'm getting old myself and am beginning to understand how they feel.”

Both comments, however, point up one of the problems that people over 65 in our society face. Too often they are stereotyped, and then they are discriminated against, say health professionals who work with older people. These professionals—a group that includes family practice physicians, geriatric specialists in internal medicine, gerontologists, psychiatrists interested in the problems of the elderly and others—



By George! He's got it!

*America's favorite senior citizen,
George Burns, gives advice on proper behavior
for his contemporaries*

- ◆ You can't help getting older. But you don't have to get old.
- ◆ People start practicing to get old; when you get to be 70 or 75, you don't have to practice.
- ◆ You've gotta make an effort to walk, to sit down, to stand up and most importantly you've gotta get out of bed...At my age I've found out that I can't make any money in bed.
- ◆ I don't believe in dying—it's been done.
- ◆ I couldn't do my act 20 years ago; I wasn't old enough.
- ◆ I have a great memory if I get paid. My memory gets better if I get paid enough.
- ◆ I was old when I was 18; I couldn't get a job. Now I'm fine.
- ◆ When I had my first heart attack, the doctors walked me up and down stairs to see if they could make me have a heart attack. They were successful—I did.
- ◆ You've got to have something to get up for. Fall in love with what you're doing.
- ◆ Don't retire. Retire to something.
- ◆ Why shouldn't I be interested in young girls? I was interested in young girls when I was 17. I'm still interested.

speak of the "healthy aged" and "young old" or the "elderly elderly" and the "old old." They agree that one can belong to either group at any age.

The stereotype is one of "helplessness and weakness" because of the loss of capabilities, says Dr. Kenneth Altshuler, chairman of Psychiatry at UTHSCD, who has worked for many years with older people in a nursing home setting in New York. Gehringer put it more bluntly at the Las Vegas media briefing: "We think they can't see, can't hear and smell bad."

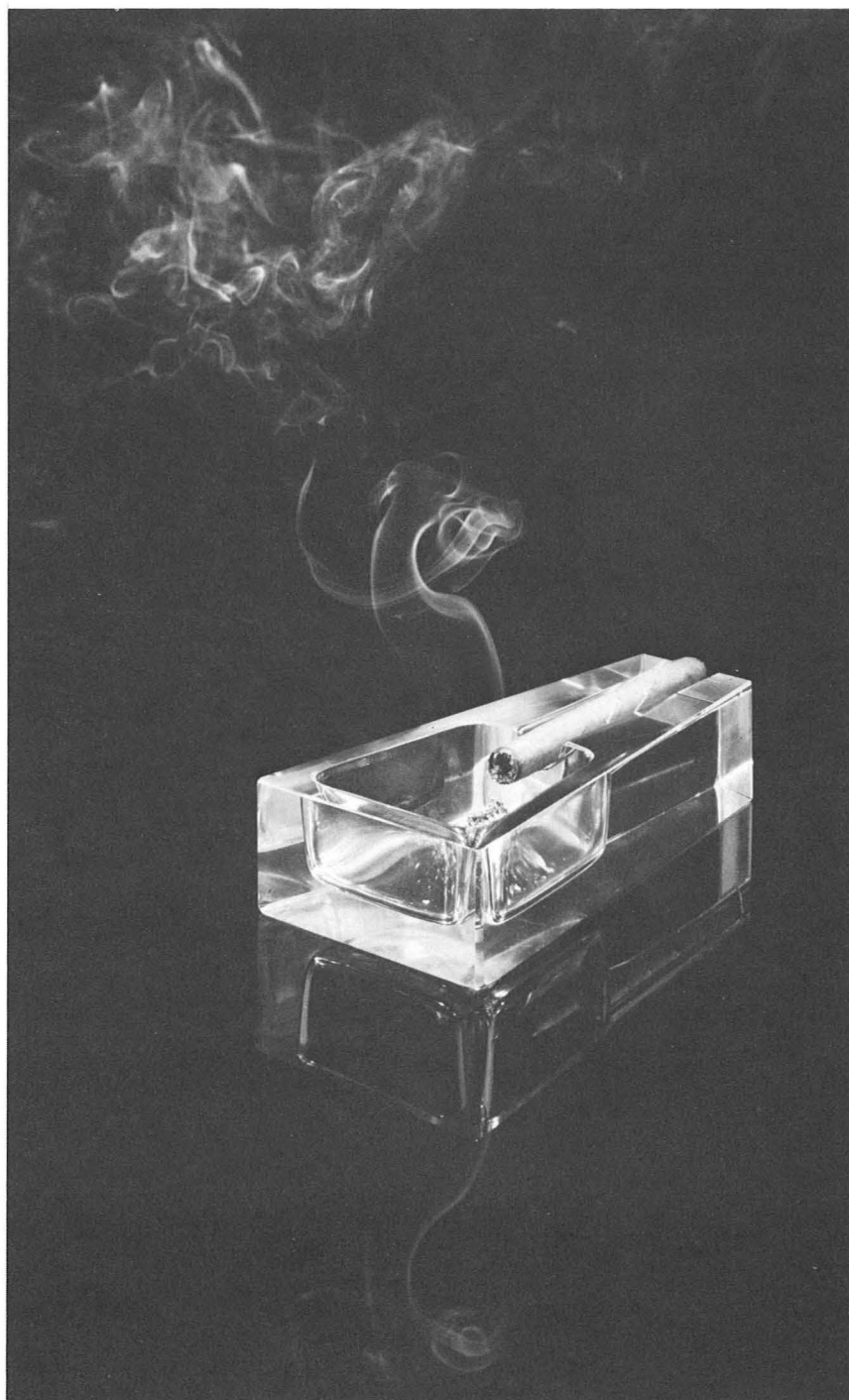
What is elderly anyway? Fifty-five? Sixty-five? Seventy-five? Someone with bad health and failing capacities can be old at a young chronological age. Others are young at 90.

"After all, there's a '10' for all seasons," pointed out Dr. Seymour Eisenberg, chairman of the school's new Geriatric Unit in Internal Medicine. Eisenberg, a geriatrics specialist, said his goal is to help the elderly maintain not just life, but "life with vigor." Besides working with internal medicine residents at Dallas Veterans Administration Medical Center, he lectures to medical students on the aspects of aging in such areas as biochemistry, pharmacology, anatomy and cell biology. He was an official observer at the White House conference, representing the health science center and the Texas Medical Association.

Altshuler pointed to his own parents as good examples of vital elderly people. "They had good health, an extended family for support, and they were fortunate aging into their 80s. They didn't feel old.

"After all," he quoted the old joke, "old age is when you realize that the old lady you helped across the street is your wife or when you wake up feeling like the 'morning after' when nothing happened the night before."

Probably the most important element in the quality of our lives is good health, both mental and physical. And it is the loss of their mental and physical capabilities that most often leads to the stereotyping of the elderly. Because there are physiological changes as we grow older, it is true that the human being suffers what Eisenberg calls a generalized "slowing down." Examples include our kidneys' getting smaller, their loss of function and the shrinking of the brain, which has some correlation to our mental processes but is not fully understood. Also, older people have a decrease in reserve, said Eisenberg, which makes them more vulnerable to disease and to drug reactions. This is



not to say that nothing can be done.

"Future generations of elderly will be healthier if they can be educated now to use good judgment in drinking alcohol, smoking and exercising. And older women especially should be told to drink milk to strengthen their bones."

Eisenberg himself takes to the stairs in the hospital, climbing 15 to 20 stories a day "to build my muscle mass while I still can."

Some of the common diseases associated with aging include senile dementia (or senility); osteoporosis, a

softening of the bone that lends itself to easy breaks; temporal arteritis, a swelling and inflammation in the temporal artery of the brain that may lead to blindness; and prostatic hyperplasia, an enlargement of the prostate gland that often requires surgery. Others are a disease of the shoulder muscles; vascular diseases with gangrene problems; adult-onset diabetes, coming from a high glucose level; sudden drops in body temperature that can lead to death; thyroid abnormalities and high incidence of congestive heart disease;

strokes and hypertension as well as back pain; and depression, which is often confused with dementia.

Easily the most feared of the diseases associated with old age is dementia, which comes from the Latin *dementare*,

"Most drugs are handled by the liver or kidney, and these organs age a lot. Smaller doses must be given to the elderly because of changes in metabolism and kidney function. Other problems are related to the absorption of drugs in the gastrointestinal tract, the percentage of body fat and a failure on the part of the older person to learn how to take the drug."

to make insane. Old people with organic deterioration of the brain can literally resemble the insane: confused and out of touch with the reality around them.

Unfortunately there is not much that can be done for these patients medically at this time, Eisenberg said. But there is hope for the future. Perhaps new methods of forestalling the progression of this disease may be discovered.

There is hope today for the elderly patient whose depression is often confused with dementia. "This," said Eisenberg, "is one of the great leaps forward in the treatment of the elderly."

Some of the clues that help physicians differentiate between depression and dementia, said Altshuler, include the following:

- ♦ Is there more confusion at night when "cues" are less evident? The patient whose depression is masquerading as dementia is more likely to be confused all the time.
- ♦ How does the patient do on cognitive tests with increasing difficulty? The patient with dementia does less well as the test gets harder. The pseudo-demented, or depressed, patient is more likely to fail all the time.
- ♦ Does the patient try to hide his or her confusion? The senile patient will try to cover up while the deeply depressed patient is more willing to display helplessness

and give up.

- ♦ Was the onset of the disability sudden or slow? Depression is more likely to appear suddenly.

Even with these guidelines, it is often difficult for the psychiatrist to distinguish between the two conditions. Another indicator is whether the patient has suffered a previous depression. The doctor may also want to try anti-depressant medication to see if this makes any difference in the patient's condition. In addition, the physician looks for symptoms such as weight loss, sleep difficulty, hopelessness and failure to find pleasure in anything, symptoms common to depression that are most likely to respond to medication. In addition, the patient may be given the dexamethasone hormone test that indicates the depressed patient who responds well to drug therapy.

The psychiatrist also looks at the psychological aspects of the case for indicators: Does the person have social support? Are there real problems of finance? Is the person suffering from loss of role in his or her life?

Dr. Elliott Snyder, assistant professor of Psychiatry at the health science center, acts as consulting psychiatrist at Golden Acres, a local care facility for the elderly. The mean age at Golden Acres is 86. Most of the patients are in the facility's nursing home and suffer from dementia or psychiatric problems, Snyder said.

"Many of these residents are depressed and unhappy and have reason to be." The young psychiatrist, who is popular at the home, is using transcendental meditation as one method of fighting depression with a group of residents. A great number of the patients he is seeing often can't remember what has been happening to them over a period of time and cannot discuss their symptoms. Obviously, guidelines for discriminating between the depressed patient and the demented patient often can't be used in these cases.

Even if his elderly patients can communicate with Snyder, they often have symptoms easily confused with depression. Loss of vision, hearing and the sense of taste may add to the patient's confusion and give both patient and physician the impression that "I don't enjoy things like I used to."

Another value of giving the dexamethasone test to patients is that anti-depressant medications are not prescribed to them routinely. The success rate in patients who the test indicates will be

responsive to drugs is as much as 97 percent, but only about one-third would respond to drug therapy if it were given prophylactically to all patients, said Snyder. These medications, which scientists theorize help the nerve cells communicate through neurotransmitters, have some dire side effects in some patients. These include hypertension, which may lead to falls and delirium.

Even common drugs are implicated in other health problems of the elderly. The metabolism of the older person changes as he or she gets older, and often drugs become as much a part of the problem as a help in the health care of the older person. In fact, Eisenberg estimates that 20 percent of geropsychiatric admissions are due to drug reactions, another syndrome commonly associated with senile dementia.

"Most drugs are handled by the liver or kidney," he explained, "and these organs age a lot. Smaller doses must be given to the elderly because of changes in metabolism and kidney function." Other problems are related to the absorption of drugs in the gastrointestinal tract, the percentage of body fat



and a failure on the part of the older person to learn how to take the drug.

Dr. John Schermerhorn, dean of SAHS, lectures gerontology students on the problems of drugs and the aging. Schermerhorn, who is also a pharmacist, talks about the kinds of drugs

commonly taken by the aged, including laxatives, tranquilizers, antacids and vasoconstrictors and the conditions for which they're prescribed.

Many of the problems with old people and drugs, Eisenberg believes, is that they may see several doctors at once and be taking multiple medicines without letting the various physicians know they are seeing anyone else. This can lead to drug poisoning and even death. Others fail to stop taking medicine that they were given years ago. Some of the elderly ill remember how much better they felt a couple of years before on a certain medication and trot to the medicine cabinet for the remains of the old bottle. And many load up their systems with non-prescription drugs on top of those their doctors prescribe. Still others stop taking their medicine as soon as they feel better.

Drugs, depression, dementia, major illness, genteel and hard-core poverty—these are among the medical and medically related problems of the elderly. Probably no group in our society needs more help from health professionals. And no group has fewer specialists trained to help them. Why?

"I can tell you from my own experience I disliked nursing homes when I was a private practitioner," commented Jacobson. "It seemed as though when you put patients in, they were in a holding pattern waiting for death. And the feeling was there that you couldn't change the quality of their lives. Doctors tend to stay away from old people in droves."

Eisenberg agrees. "There is a bias against the elderly in medicine," he said. "This agism is a part of the bias against some kinds of patients that too often develops in medical school when the student is seeing patients in the hospital, particularly in a large community setting. Many of the people have become ill from self-abuse, drugs, alcoholism, massive obesity, and many are the elderly with multiple problems. These patients don't get well so quickly, are complicated to take care of and often very difficult to handle. But they can be very satisfying if the young doctors would only give them a chance."

Another problem, said Altshuler, is attitudinal. Medical students come into school with the idea that they are going to cure disease.

"What happens then is a revelation. Much of the acute illness, for example, infectious diseases, plays a lesser role in medicine today than in the past. In licking such problems, we have, however, lengthened the life cycle leaving

the elderly with a great deal of chronic disease such as diabetes and cardiac and pulmonary problems."

George Burns aside, Altshuler said that identification with these older patients and the fear of becoming like them may cause these young doctors to expect too much from their patients and to push them too hard.

"Sometimes what an old person wants to do is just sit on the front porch in the sun in a rocking chair. The young



health professionals may urge exercise and greater involvement in other activities. But there's a lot to be said for sitting in a rocking chair if you're comfortable there."

Another part of the problem of getting physicians to treat the elderly lies in the selection process for medical school, said a well-known medical educator.

"Medical students have been chosen for their youth, their aggression, their competitiveness. Spartans, they stay up all night and still manage to be brilliant, dazzling, superhuman. In the hospital they see clinging, helpless patients who are probably whining and not grateful.

"Competitive pressures involved in the obstacle course of becoming a physician fosters in the medical student a need for a sense of victory at all times. Thus the stereotype arises: the elderly ill are losers."

The picture, thankfully, is not all grim.

"The problem is not new: old people have been with us a long time," said Ross, whose family practice philosophy espouses treating family members "from womb to tomb."

"But now medical schools are get-

ting more responsive." So is the medical establishment. Fellowships in geriatrics are being established, and the AAFP is putting an emphasis on continuing education in geriatrics for family doctors.

Family practice residents in Southwestern's programs have practices in which approximately 20 percent of their patients are over 65. That's about the national average, says Jacobson.

Dallas VAMC will soon be opening an outpatient clinic and beginning construction of a nursing home. "I must say that our residents do a superb job with the elderly in our hospital. They see it as a real challenge," said Eisenberg. "But the new facilities will bring new dimensions to training for work with the elderly."

Snyder is also interested in teaching medical students about work with the elderly. As director of the undergraduate education in psychiatry at Southwestern, he has incorporated a visit by sophomore medical students to area nursing homes as a part of the psychiatry course. On the visit the students talk with administrators, visit with patients and tour the facilities. He is also working on a study on the impact of a geriatric curriculum on medical students' attitudes with Dr. Larry Kimsey at The UT Health Science Center at Houston.

Contrasting with the youth of the medical students and residents is the average age of the gerontology students in the allied health school's program. The average age is 42, and most students are women who are making career changes, preparing to rejoin the job market or people who are already in "helping" fields, such as nursing, who want new skills.

The program graduates 15 to 20 students a year. These professionals are proving to be an excellent resource to physicians and families of the elderly as they bring their training into the "aging network" of agencies and nursing homes. Faculty members are looking into such problems as consumer issues specific to the elderly, the death rate in nursing homes, the burnout problem in work with the aging, big business and pre-retirement counseling and support of the aged in minority communities.

People are getting more sensitive to the elderly and their problems, as Ross pointed out. Physicians and other health professionals who work with the aged have a mutual goal: to give them something in their lives to look forward to besides death.

As George Burns says, "I don't believe in dying. It's been done."



*There's no business
like no business*

Fear of losing ability to cope triggers depression

Loss.

Loss of a beloved spouse.

Loss of role as a breadwinner or homemaker to busy family.

Loss of the home itself.

Loss of economic lifestyle that comes with loss of employment.

Loss of good health.

Loss of the mind's former keenness.

Loss of powers to cope with loss.

These losses may be experienced by anyone, but are "common and keenly felt" among the aging, says Dr. Kenneth Altshuler, chairman of the Department of Psychiatry. He has studied dreams of elderly patients in a nursing home and found that the primary concern exhibited in their dreams was the loss of their resources—physical and mental—that allowed them to cope with their lives. And more often than not the aged find themselves dealing with several "amputations" in their lives at one time, and so the causes of their depression may arise from multiple losses.

Thus the cycle begins. The more depressed and the less able to cope, the more "old old" the person becomes. The more "old old" he or she becomes, the less the person will be able to cope. Frightening? Yes. Even more frightening is the realization that even middle-aged people can be caught in the psychological quicksand.

Johnny Vacca says it nearly happened to him.

"I got canned Dec. 7, 1977," said Vacca. "Only later did I realize that it was Pearl Harbor Day."

Only 55 years old at the time, Vacca was one of three top company officers in Denver who were removed from their jobs in a corporate reorganization. Vacca and his family had left Dallas, their home for many years, only six months before when he was transferred to Denver.

Neither he nor his wife was prepared for the firing.

"Corporate officers—including me—are too egotistical to think that something like this can ever happen to them. Sure, I had read about this sort of thing in the *Wall Street Journal* and other business

publications, and I'd thought, 'Too bad, fella.'"

Vacca says his first reaction was anger; his second, self-pity.

"But after a couple of weeks job offers began coming to me and the frantic feeling lessened: my ego was fed."

The Vaccas were lucky. With early retirement, a cash settlement and excellent company benefits, there were no financial problems. They headed home to Dallas, and it wasn't long before the broadcast executive settled into a new career.

Vacca had held a real estate license in Texas for corporate purposes for many years. Now he began selling first residential, then commercial properties for the first time. Again, he found himself highly successful from a financial standpoint.

"But like J. Paul Getty said, I wasn't a successful person—I just made money."

When the company changed directions, the former broadcaster found himself frustrated and bored. The personal satisfaction he had found in his job was gone.

"I walked away from a guaranteed income. But the job wasn't giving me what I wanted any more. What was that? Simple: satisfaction."

Johnny Vacca had been without a job before—even fired at the height of his career—so being jobless was no big deal. However, something—he's not sure what—was different this time.

Although only a few years had passed and Vacca was still in his 50s, this time he didn't bounce back. Something in him snapped, and paralyzing depression stepped in.

"I was settling down to a life of quiet desperation. Fortunately, I have a strong

wife and practical children. I think they would have ultimately prevented me from falling into the gates of hell."

Vacca says it was his son, John III, partner in a Dallas media service company, who essentially "got me to get up off my can."

"Dad," he said, "you've got more voice talent than anybody in this town. Why don't you get an agent and get back into the business?" In the meantime he put me on a project for his company, and I placed the Dallas Cowboy show in 42 radio stations."

Vacca took his son's advice and started auditioning for commercials and training films. On his first audition he froze, forgot his lines and blew it.

"I really screwed it all up," he says. "No excuse—they weren't getting a virgin. I'd spent 18 years in front of the camera on local and national TV."

But it was okay. Vacca got his first job portraying a convenience store clerk in a training film—after only four auditions. Getting one job in 10 is good for a talent, he explained.

His wife Isabelle had another suggestion. "While you're waiting around to be rediscovered, why don't you go to work?"

A personnel position with a local department store opened up. Management agreed to let Vacca work flexible hours so he could continue part-time media work. Now he's not only working in the field he has loved best all his life, but he's learning new skills in the business world.

A few months ago Johnny Vacca was on his way to a premature old-age at 59. Today he's a happy man.

"The future for me today holds as much promise as when I was 20."

Ann Harrell



HOMING IN

Contingency planning assists families in search for surrogate homes for the elderly

by Ann Harrell

The decision has finally been made. It's going to be hard on everyone, but Grandma is just too much to handle in the home. And she can't make it living alone. The family hates to do it, but it looks as though a nursing home is the only answer.

Although this situation is common in many families today, the people involved rarely know anything about institutional care for older people in general. In fact, "few even know the names of homes in the area where they live," says Dr. Helen West, UTHSCD gerontologist who has been working with nursing homes for 10 years and acting as a consultant to families who

have had to make this kind of decision. A faculty member at the School of Allied Health Sciences, she has been concerned with the level of care, training of personnel and professional "burnout" in these fields. She has worked with biofeedback in relation to treating and preventing chronic illness as well as avoiding overmedication and is interested in the use of stress intervention techniques as a way of reducing the death rate in nursing homes.

"Of course, contingency planning is always best," says the gerontologist. "There is no substitute for planning ahead before the need arises."

She recommends getting a copy of

You and Your Aging Parent: The Modern Family's Guide to Emotional, Physical and Financial Problems by Barbara Silverstone and Helen Hyman. (This book, published by Pantheon, is available for \$15.95 in hardback and \$8.95 in paperback.)

Another good resource is a booklet, "Nursing Homes: A Guide for the Family Before and After Placement," available from Senior Citizens of Greater Dallas and Dallas Mental Health Association, 712 N. Washington, Suite 202, Dallas, TX 75246; phone: 214/823-5700. Cost of the booklet is \$1.50. A postage and handling charge varies depending on location.

Whether your family is pre-planning for possible future needs or whether you have an immediate problem, West has some suggestions for finding the best possible surrogate home for your parent or grandparent. "Take it on as a challenge," she says. "Try thinking of yourself as a bit of a detective spotting out clues."

Here are her suggestions:

1 Decide what level of care is needed. Families too often think that nursing homes are the only kind of institutionalization for elderly parents. Nursing homes are for people who need nursing care and/or supervision all the time. There are also homes that provide independent living quarters with such individual features as communal dining rooms or intercom systems in the rooms. They may have separate cottages, or they may be assigned to different floors according to their level of independence. Your family physician will be glad to discuss the level of care needed with you.

2 Does the institution have Superior Certification from the State of Texas? This certification is given by the State Department of Health. (Other states have their own licensing system.) Don't lean too heavily on certification as a guideline, however. Although it is called "superior," what it actually means is that there were no deficiencies at last inspection. Maintaining this rating means that the home passed with at least minimal standards. Certification is given for all levels of residency care.

3 Does the home participate in Medicare? Except for a few wealthy people, anyone can run out of money quickly in a nursing home. Even if medical care is not needed at this time, the family will want to consider the impact of change on Grandpa in case he has to be moved at a later time, so they may want to consider institutional housing that includes a nursing home on the same site.

4 Talk with some of the residents. Ask them how they like it there. Ask them about how they spend their time.

5 Talk with the staff. Find out how many of the patients are able to go back into the community. This will give you an indication as to how rehabilitative the care in a particular home is.

6 Check on the staffing. Are there adequate nursing personnel available? Are there physical or occupational therapists on staff or coming in on a part-time basis? This will also be an indicator as to how rehabilitative the care is at that institution.

7 Sense from the staff how welcome your visit and your questions are. If staff members don't spend much time with you, try to decide whether it's because they are busy or whether they are avoiding you.

8 Is there much hustle and bustle? Too much silence indicates what West calls the "Rust in Peace" syndrome. Lots of moving around may indicate lots of recreational and therapeutic activity for the residents. Lots of visitors indicate a place family and friends like to come to.

9 Ask if there's an extra place for lunch. That's a good way to check out the quality of the food. Don't bother asking the residents, says West. "They'll always tell you it's horrible!"

10 Is there a calendar of events? Study it. This is another indication of the quality of life for the residents.

11 Is there a newsletter? Pick up several issues. The newsletter will also give you an insight into the recreational activities at the home. In addition, they usually run obituaries of the residents. This is a good indicator of the death rate in a particular home.

12 Pay attention to the way the place smells. Bad odors are "awfully tough" to avoid in nursing homes, says West. But it can be done. Don't pay any attention if an administrator tells you, "You can't help it." There are ways: bladder training can be given to patients, enough aides to take care of the incontinent patients can be hired and professional cleaning compounds for this specific problem can be obtained. Also, foul odors may be an indication that PTs and OTs should be hired or called in more regularly. The strong odors may be a hint that "maybe those patients don't have to be lying down all the time."

Another thing that lack of strong odors does is encourage families to visit. Since older people lose much of their sense of smell, the unpleasant odors may not bother them. But it certainly will act as a deterrent to guests. The more visitors a resident has, generally the happier he or she will be.

13 If the institution does not have several levels of care, what kind of referral arrangements does it have? Even though the older person does not need nursing care now, a fall—or even simply a worsening condition like failing eyesight—can change the situation quickly. Does the institution have a relationship with others? Is it part of a chain? Does it give referrals? Can you get these names in advance so you can do some contingency planning?

14 Does the home honor Patients' Rights, including the right to privacy in entertaining friends in the resident's own quarters or in a specially designated area of the home? Remember, following these federally prescribed Patients' Rights is required in all nursing homes receiving Medicare funds. And respecting individual privacy is an important factor to be considered in evaluating any home, whether it is required or not.

15 Talk with a minister or rabbi who visits the home on a regular basis. Most churches or synagogues have someone on staff who spends a great deal of time visiting with older members of the congregation. They usually have excellent insights into the quality of care in the homes they visit. Ask for their opinions and discuss what you learned about the homes you visited from applying these "tips" to see if they are in agreement with you about the homes they are familiar with.

Even after the decision has been made and the new resident is settled in, guilt about abandoning a parent is often a problem to be dealt with within the family. Sometimes, also, there may be resentment and hostility toward the older person who is now in a dependent role.

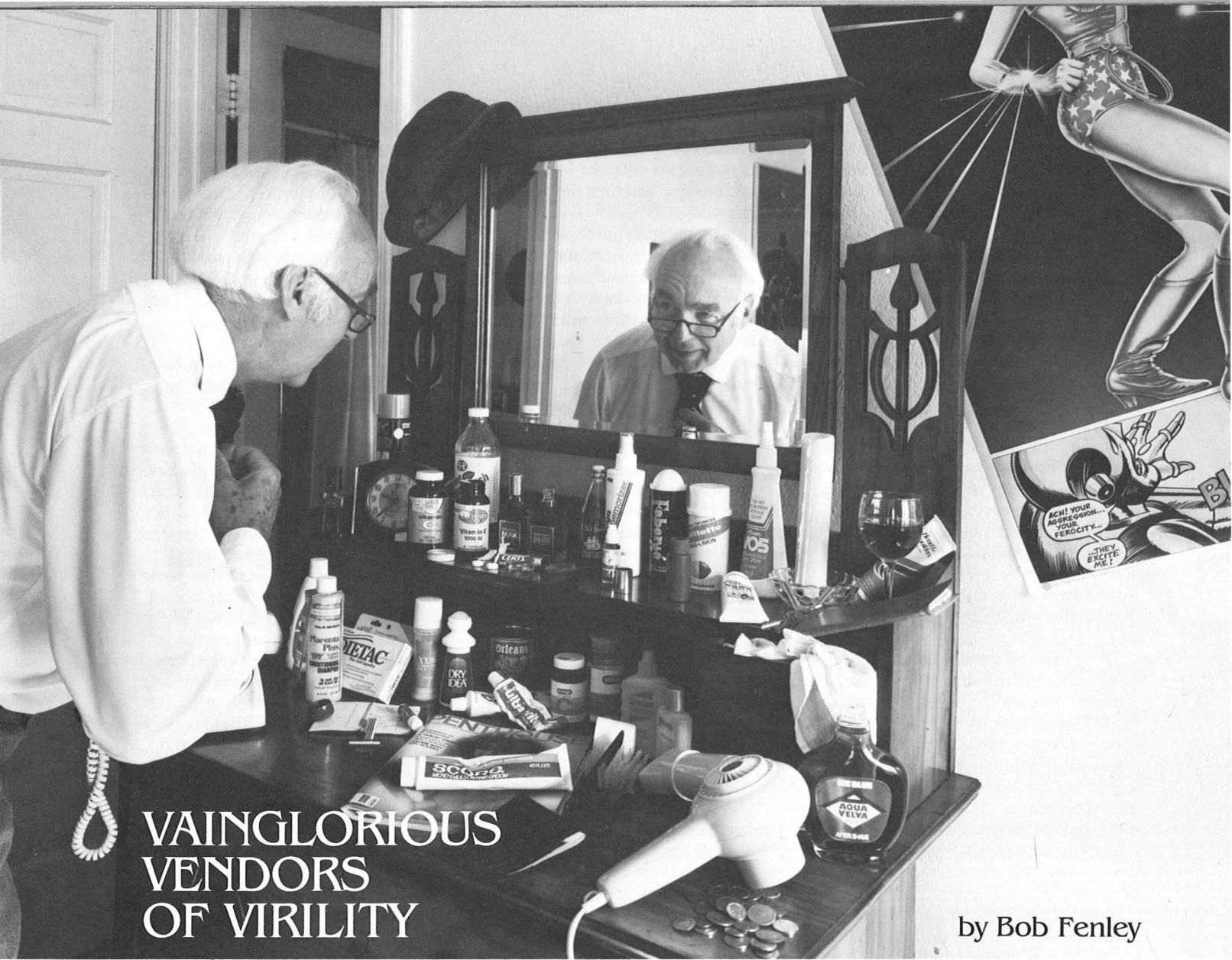
"I've had a lot of people tell me, 'My mother practically disowned me when I married. Now she's seriously ill and wants to live with me. I can't take care of her and my family, too.'"

Sometimes when "the children" go home for their annual visit to see Father, they are shocked at how he has aged. Their first impulse may be to rush him into a home to assuage their feelings of guilt when they realize he's "slipping." Actually, Father may be doing fine in the little town where he lives and should not be rushed prematurely into a nursing home.

In other cases, guilt may keep a family from putting an older member into a nursing home when he or she would be better off under full-time medical supervision. The family physician can be of great help by making a medical judgment about the parent's condition.

Guilt feelings, which in their own way can incapacitate family members, are another reason that "what if" planning should be done in advance. And it's even better if the older members of the family can take part in making these contingency plans, too.





VAINGLORIOUS VENDORS OF VIRILITY

by Bob Fenley

MR. BONES: Mr. Interlocutor, what's the fastest thing on earth?

MR. INTERLOCUTOR: Well, I don't know, Mr. Bones. What is the fastest thing in this whole wide world?

MR. BONES: It's a goat . . . going past Doctor Brinkley's clinic. (a short slide trombone fanfare)

During the 1920s and '30s Dr. (?) John Romulus/Richard Brinkley transplanted goat testes into aging men who were longing for restored sexual vigor. And as he cut a raucous and racy swath across middle American medicine, the "Goat Gland Doctor" wrote another chapter in the male Homo sapiens' seemingly endless search for eternal potency.

Nature seems to have been both efficient and inscrutable in designing the male reproductive system and behavior. The aggressiveness and lust of the male is associated with a hormone called testosterone that is manufactured by Leydig cells in the testicles.

This hormone is found in highest levels in male Indian elephants who

conduct unmanageable rampages during sexual cycles and in the Kenyan hyrax during a two-month period during which the males fight viciously among themselves and mate with females, according to Dr. William Neaves, who has researched the physiology of reproduction in Africa and in laboratories of The University of Texas Health Science Center at Dallas.

But in studies of the impala, Neaves concluded that high testosterone levels might be the result of territorial behavior and accompanying sexual activity rather than the cause.

Whether Brinkley was ever able to transfer true sexual drive or simply suggestion to his patients is a matter of some dispute. All the cross-species

transplants were rejected as far as is known.

What Brinkley may have done unwittingly was perform a transplant of pheromones (sexual odors): the slivers of goat testicle used in the early operations also transferred a characteristic goat musk odor to its recipient. Alas, this sexual attractant apparently did not work with the female of the human species, so Brinkley switched to the non-odorous Toggenberg breed of goat.

With or without musk, men have long sought to reverse the inexorable process of nature.

"After a peak of sexuality occurring sometime late in the teens or early in the 20s, the average human loses 10,000 Leydig cells per testis per day," says

Neaves, dean of the Graduate School of Biomedical Sciences at UTHSCD. Although Neaves and Lawrence Kaler of the Cell Biology Department reported decline in Leydig cells, the question of whether this reduces testosterone is rather clouded.

Many researchers have contended there is a loss of testosterone with advancing age. Seemingly shoring up this contention is the fact that injections of testosterone can sometimes relieve some symptoms of what has been termed the male climacteric or "male menopause."

But scientists with the National Institute of Aging recently have reported that healthy old men maintain their production of sex hormones at levels found in younger men. This finding is at odds with many published reports that, in men, production of testosterone decreases and female sex hormones increase with age.

In reasonably healthy men, production of sperm sometimes continues to 70, 80 and even 90 years of age. There are well-accepted instances of men fathering children at those ages.

"There is no firm end-point for germ cell production in the human life span," says Neaves. "The variable limiting factor is most likely involved with hormones."

Whether biochemical or psychological—or more likely, a mixture of both—declining sexual performance has driven men to drink strange elixirs like ground rhinoceros horn.

When Mme. de Maintenon perceived that Louis XIV was beginning to have amorous flameouts, she brewed up a potion of distilled spirits, sugar and orange water spiked with perfumes.

For the poorer folk of Paris, the street vendors were peddling "artichokes, artichokes...heat the body, the spirit and the genitals."

Spanish fly, or cantharides, long has had the folk reputation of being a potent aphrodisiac but this strange concoction of ground beetles is dangerously toxic and irritating.

The search for amorous amplifiers has ranged from myrtle leaves to Bura Gookeroo seeds. Even today, advertisements aimed at the older male invite him to try the product and "ENJOY SEX WITH ANYONE, ANYTIME..."

It was once thought that injections of testosterone might be the long sought road to rejuvenation.

"In fact," says Neaves, "administering testosterone in moderate amounts can actually suppress male fertility." If the brain senses normal amounts of

testosterone from an external source, it may signal the testes to cease production of testosterone hence depriving the young germ cells of the high local levels of this hormone that are required for their development into sperm.

In recent years, with the discovery of the so-called neuropeptides—"executive" hormones that originate in the brain's hypothalamic region—experiments have been carried out by Dr. Robert Moss at UTHSCD and others with "luteinizing hormone releasing hormone." LHRH initiates a chain of hormonal events through the pituitary down to the gonads of both males and females. In females, luteinizing hormone stimulates ovulation...in males, spermatogenesis.

While LHRH sends rats into mating frenzies, its effect on human males is not so clear. "In fact, it actually is a contraceptive, also," Neaves declares.

A variation of LHRH, called LHRHa, also has been reported to have "turnoff" and contraceptive effects when administered by injection. Of course, the natural hormone plays an important role in reproduction when it is produced within the body.

If this appears complex, it is. "During the past two years, scientists have found that control of Leydig cells and testosterone production is a lot more complex than had been thought," Neaves relates.

When luteinizing hormone (LH) is bound to receptors on Leydig cells, it turns on production of testosterone. But when LHRH (that causes the pituitary gland to secrete LH) is itself bound by specific receptors on the Leydig cell membrane, it turns testosterone production off, Neaves said. Other specific receptors, which bind a substance like epidermal growth factor, inhibit testosterone synthesis.

There is another testosterone turnoff mechanism: Leydig cells also have receptors for estrogen, a female hormone, and this will suppress production of the male hormone.

The estrogen comes from testicular Sertoli cells, which have produced it from testosterone, and from an ultra-short feedback loop within the Leydig cells themselves.

Why all this fine tuning? It may well be connected to behavioral integration of basic reproductive functions.

In Africa, Neaves discovered dominant and breeding male impala had testosterone levels twice as high as males in the bachelor herd during the 38 to 46 hours they defended their turf and mated with females.

"During this period they do not eat or drink," says Neaves, and afterwards the male impala is exhausted and he retires to the bachelor herd while another male takes his place.

There is good evidence that social cues influence endocrine status. In mice, the smell of a female will raise male testosterone levels and, conversely, an extremely small amount of male mouse urine on filter paper can start a cascade of LH in the female mouse.

And, although humans douse themselves with deodorant, then sometimes confuse things with a synthetic musk perfume or cologne, there is some indication that people have some pheromone activity. Pheromones are the special chemical signals produced by an animal which, detected by the sense of smell, cause a certain behavioral response in another animal.

Maybe Brinkley missed a bet when he switched to the Toggenbergs.

Although he netted at least \$12 million from 16,000 goat gland transplantations, Brinkley wasn't the first to try. Neaves and Dr. Rupert Billingham, chairman of Cell Biology, point out that in the late 19th century Brown-Sequard, the founder of modern endocrinology, inoculated himself with extracts of guinea pig and dog testes and claimed improvement in strength, vigor and mental activity. Others tried various transplanting throughout the years.

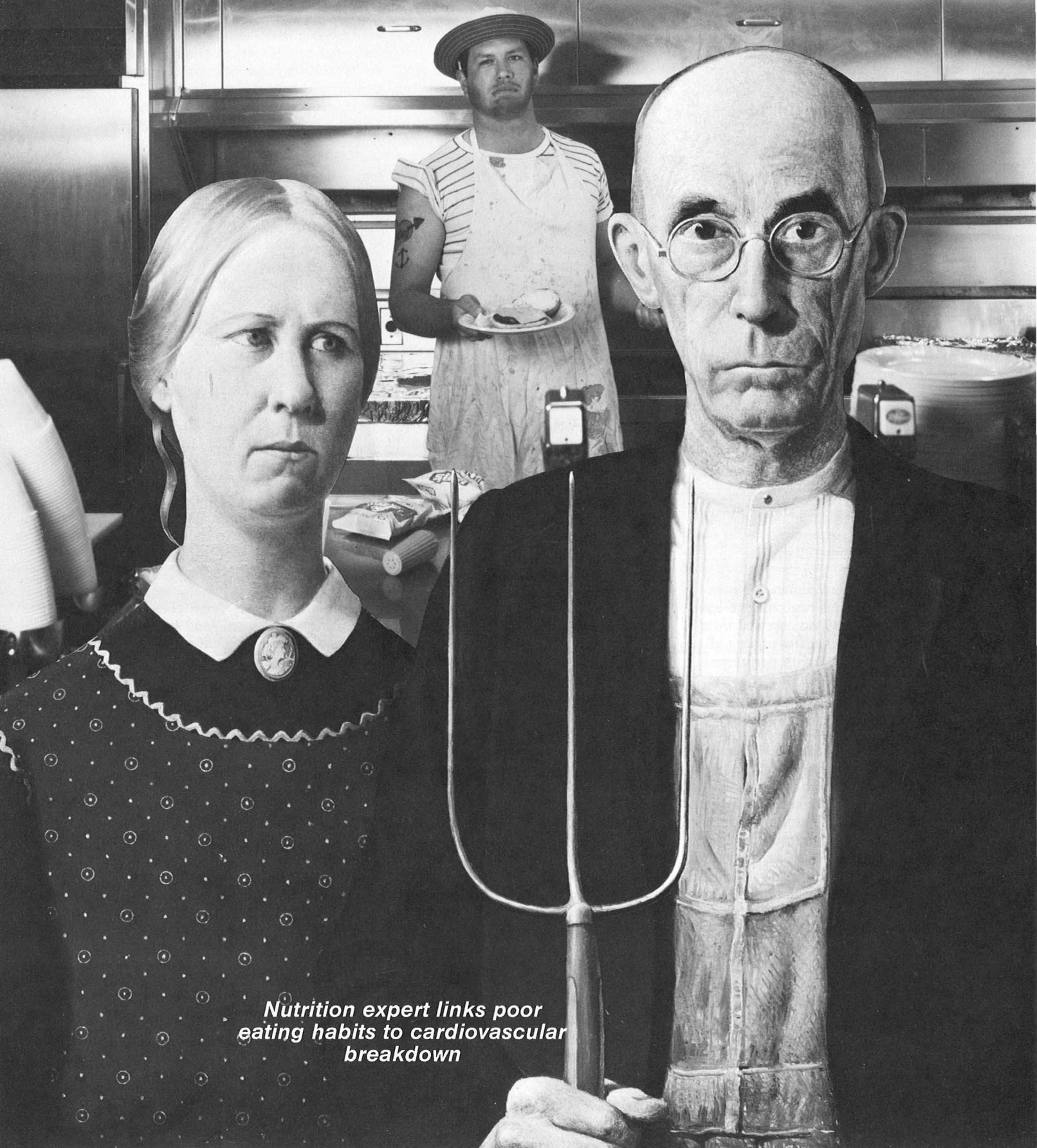
But only one absolutely documented testicle transplant has been known to work. This was done in the case of twins who were identical except that one was born without testicles. A carefully done transplant was effected "and soon after the operation the recipient achieved an acceptable testosterone level and went on in the ensuing months to father a child," related Neaves.

"Clearly, the potential of testicular transplantation to contribute to biomedical science has not been exhausted," wrote Billingham and Neaves in the journal *Transplantation*.

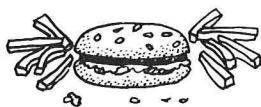
"The extent to which this potential is realized must depend on recognition and appreciation of previous legitimate applications of testis grafting, as well as dissociation of these creditable accomplishments from the highly publicized and tainted history of its exploitation in the hands of so-called rejuvenators."



BASEBALL, HOT DOGS AND ATHEROSCLEROSIS



***Nutrition expert links poor
eating habits to cardiovascular
breakdown***



Yellow, waxy build-up on artery walls is too often a by-product of the aging process.

Cholesterol deposits are not usually a problem during childhood. But atherosclerosis, an accumulation of cholesterol on artery walls, tends to accelerate around age 50.

When blood cholesterol becomes excessive, cells on walls of major arteries get force-fed the fatty substance. Bloated cells, described as "foam cells," are filled with cholesterol and gradually replace normal tissue. Eventually, scar tissue forms, hardening and narrowing the vessels with connective tissue and calcium. This reduces blood flow to heart or brain and results can be devastating.

A lifetime of poor diet coupled with a little-understood aging component may be a major factor in atherosclerosis, says Dr. Scott Grundy, head of the Center for Human Nutrition at the health science center. "If there is a tendency toward atherosclerosis, time is also a factor. Cholesterol accumulation is a continuous process throughout life."

Years of eating food high in cholesterol and saturated fats—food such as dairy fats, fat-rich meats and egg yolks—contribute to making more than half the U.S. adult population at risk for heart attack and stroke. Studies suggest that modification of the diet can reduce the risk of coronary heart disease, says Grundy, who also chairs the American Heart Association's Committee on Nutrition. And some trials even suggest a reduction of recurrence rates of heart attacks by switching to a cholesterol-lowering diet.

"Unless the eating habits in our society are widely changed, people in the higher risk categories probably will not alter their eating patterns," says Grundy. "The popular American diet with its quantities of total calories—fast foods, 'junk' foods and fried foods—can be changed. It's a matter of public education and the individual taking responsibility for health." Currently the "norm" for an American adult is a blood cholesterol level between 200 and 275 milligrams per deciliter while desirable levels probably are below 200.

Grundy recommends widespread dietary changes to a low-cholesterol, low-saturated-fat diet of skim milk, chicken, fish, egg whites, fruits, vegetables, whole grains, legumes and

moderate increases in polyunsaturated oils.

Polyunsaturated fats lower the level of the body's cholesterol by aiding in its removal. The mechanism of this process is unknown.

Diet studies of Japanese people living in Japan, Hawaii and San Francisco illustrate the effects on a basically homogeneous people as their diet becomes more "Americanized." Serum cholesterol levels were 12 percent greater among Japanese in Hawaii and 21 percent greater in San Francisco than in Japan. Saturated fat calories for the three groups were about seven percent of total calories in Japan, 12 percent in Hawaii and 14 percent in San Francisco. And deaths from coronary heart disease were 1.7 times higher in Hawaii and 2.8 times higher in San Francisco than in Japan.

Life expectancy in Japan exceeds that in the U.S. at every age. A somewhat better life expectancy than ours can also be found among Italians who eat less saturated fat and cholesterol than Americans and whose diet contains large amounts of a monounsaturated, olive oil. (Monounsaturates have a plasma cholesterol-lowering capability that is slightly less effective than polyunsaturates.) Incidence of coronary heart disease in Italy and the rest of the Mediterranean region is relatively low compared to countries where ingestion of saturated fat is high.

"The popular American diet with its quantities of total calories—fast foods, 'junk' foods and fried foods—can be changed."

Coronary heart disease within any group is a selective process, says Grundy. Even within the desirable cholesterol range, individuals may be at increased risk from smoking, hypertension or diabetes mellitus. Also, genetic tendencies for developing atherosclerosis in some people make modification of diet futile in reversing the disease process.

Determining individual risk and treatment is further complicated by an aging component. "When a person reaches the age of 70 with a history of high cholesterol and has not had a heart attack, he or she may have a natural defense against coronary heart disease.

"Cholesterol levels usually do rise with age, however, as does the risk of heart disease. And neither future cholesterol levels nor their effects in any

one person can be predicted with accuracy. Adherence to a diet low in cholesterol and saturated fats may help the elderly by diminishing the increase in plasma cholesterol that occurs commonly with aging."

Elevated concentrations of cholesterol accumulate in people whose bodies have high circulating levels of the fatty substance or have an inability to rid themselves of it. Cholesterol is mainly transported within water-soluble molecular complexes, usually a lipoprotein called "low-density lipoprotein" (LDL). LDL acts as a vehicle to deliver cholesterol to body cells. Traveling together through the bloodstream, LDL binds to special receptors on the surface of cells needing more cholesterol. Once the LDL-cholesterol is attached to the cell, it is drawn into the cell where the LDL complex is degraded and the cholesterol is freed.

As an active researcher with a metabolic ward at the Veterans Administration Medical Center, Grundy has found that some people with normal or mildly elevated cholesterol levels can suffer heart attacks when their blood contains too much LDL-protein.

The protein of LDL is called the B protein. This protein directs the uptake of LDL into cells, and it may promote deposition of cholesterol into the artery wall. In most people with high cholesterol, the major cause of excessive cholesterol levels seems to be overproduction of LDL by the liver. However, decreased removal may play an important role in some people.

One major example of decreased removal of LDL is found in the disease "familial hypercholesterolemia," the cause of which was first described by scientists at the health science center, Drs. Joseph Goldstein and Michael Brown. In this disease, cells are lacking a receptor for the B-protein of LDL, and they therefore have an inability to remove cholesterol from the bloodstream. People receiving defective genes for the LDL receptor from both parents are destined to die from coronary heart disease by the age of 10. Those inheriting the gene from one parent, which happens to as many as one in 500 people, may die of a heart attack in later life.

Grundy foresees the day when tests for measuring protein B in LDL will replace cholesterol measurement for more accurately assessing those at risk for heart disease.

"We'd like to facilitate a way of measuring protein B so that someday the test will become routine."

Susan Rutherford

Manic-depressive illness and Huntington's disease

Cell membrane abnormalities may provide the link needed to identify manic-depressive patients and those with Huntington's disease.

Using fluorescence spectroscopy and nuclear magnetic resonance, Dr. Jay Pettegrew, assistant professor of Neurology and Pediatrics, has been 100 percent successful in identifying patients with the two neuro-psychiatric diseases. Future use of these tools may provide detection of these inherited illnesses long before patients develop symptoms.

Manic-depressive illness, affecting about one percent of the population, is the form of depression most often fatal. Suicide results in 15 percent of the cases. The prevalence of manic-depressive illness is about 100 times greater than that of Huntington's disease.

Since both diseases are genetic, cells outside the brain carry the abnormal gene. Therefore, easily accessible blood or skin cells are being used to study the presence of the brain disorders.

In blind studies using coded samples, Pettegrew has been able to distinguish cells containing the molecular defects relating to the two diseases. Of 40 persons tested in the manic-depressive illness study—with 20 patients known to have the disease and 20 normal subjects—the methods picked out the 20 who had previously been diagnosed as having manic-depressive illness. Likewise, with approximately 100 persons as test subjects for the Huntington's study, the methods determined the known Huntington's cases from the same number of normal control subjects.

Pettegrew made his identifications by monitoring the motion of molecules within the cell membranes. Abnormal movement showed the presence of a defect. Findings indicated that neither medication, severity of symptoms nor age had an effect on the membrane defects.

Pettegrew has also segregated an "at risk" group of 23 young adults for long-term Huntington's studies. If indeed his findings are linked to the defect, these

people will begin to show symptoms in 10 to 20 years.

The unique aspect of Pettegrew's studies, allowing him success where others have failed, is that he is using intact living cells. Cells are analyzed less than an hour after being taken from the patient. By monitoring molecular motion in the living cells, an abnormality of molecular movement can be detected. For a cell to function normally, the dynamic qualities must be kept under control, by the body or artificially. In the studies, temperature and chemical environment are designed to avoid disturbing the molecular motion of the cells so that abnormal dynamic properties become evident.

In the fluorescence spectroscopy studies, fluorescent chemicals are applied to the cells and penetrate layers to certain depths. Polarized beams of light strike the membrane molecules and their emitted light allows measurement of excitation and emission energies and rotational rates of the molecules. Sensitive instruments monitor this movement and produce graphs of the dynamics on paper.

Abnormalities in cells can also be detected by superconducting magnets. Placing a blood or tissue sample within a magnetic field, radio frequency energy can be applied to identify the kinds and amounts of molecules and their dynamic properties.

"With these two research techniques, it's possible to elegantly and accurately measure the dynamic properties of intact, living cellular membranes and the dynamic properties of their metabolism," explains Pettegrew.

Depression experts Drs. John Rush and Michael Schlessor collaborate with Pettegrew by providing carefully evaluated psychiatric patients, patients' family members and normal controls for study. Says Rush, "If we succeed in finding a molecular marker for this disease, psychiatry will be in a position for the first time ever to prevent an illness before it is clinically apparent. For example, in some children and adolescents who may have inherited this illness, we find dysfunctional be-

havior. The molecular marker may help us distinguish those whose behavior can be explained by manic-depressive disease from those who are troubled for other reasons."

Part of the equipment used in Pettegrew's research was provided by the Southwestern Medical Foundation.

Hemorrhage may be caused by life-saving procedures

Controlling intracranial hemorrhage in pre-term infants (the condition is called stroke in adults), is the subject of a new study by Drs. Charles R. Rosenfeld and Billy S. Arant Jr. and a group of their associates at the health science center. Rosenfeld is professor of Pediatrics and Obstetrics and Gynecology, and Arant is associate professor of Pediatrics.

Dallas' Charity Ball has donated about \$300,000 to support the three-year project. Equipment purchased for the study will include a system for monitoring every premature infant with a birth weight of 1,500 grams (three pounds) or less admitted to the neonatal intensive care nursery at Parkland Memorial Hospital.

Babies 1,500 grams and under have a 50-90 percent chance of suffering intracranial hemorrhaging. About 40 percent of these babies die in the hospital; another 25 percent develop conditions such as cerebral palsy, mental retardation, hydrocephaly (commonly called "water on the brain") and/or seizure disorders. Others may possibly suffer from more subtle neurologic handicaps, such as learning disabilities or behavior problems.

Rosenfeld says hemorrhaging in the brain of the low birthweight infant may start before, during or after delivery. The exact causes of this hemorrhaging in individual cases may be multiple and hard to pinpoint, says the physician. Neonatologists are beginning to suspect that some of the medical procedures commonly used to save the infant's life may actually cause hemorrhaging in the brain, leading to death or disability.

Headaches are treated with non-drug therapies

Everyone has a headache now and then. But for some, headaches can become constant, chronic companions.

It is for the latter sufferers that scientists at the health science center have been working with visualization along with a battery of other psychological techniques. Some of these use electronic devices.

Dr. James Lipton, physiologist and psychologist, has been working with a number of other "non-drug" treatments, including muscle relaxation exercises and individual patient control of skin temperature through use of biofeedback techniques. Biofeedback machines help the patients learn how to raise skin surface temperature, which is believed to influence blood flow in the head, and to relax muscles of the head, neck, shoulders and upper back. Another device being used in the Anesthesiology Pain Clinic is an electrical stimulator.

Also, some patients are taught to find relief by placing small-gauge hypodermic needles on their "ho-ku points," a term used in acupuncture for an area beneath the skin near the top of the fold of skin that forms when the thumb and second finger of the same hand are pressed together.

Many of these techniques, used for either interfering with the duration of a headache already in progress or preventing one from starting, use hypnotic suggestion and/or visualization. For example, the patient who is being monitored by biofeedback equipment measuring the surface temperature of the little finger, must find a method of actually increasing the surface temperature of that finger. Lipton says this may be done by relaxing and thinking about warming hands beside the fire in the winter. Another patient may prefer to think of lying on the beach on a tropical island. Yet another may see him or herself riding a camel under the hot Sahara sun.

As the surface temperature of the skin begins to rise, the patient can read success on the digital numbers of the

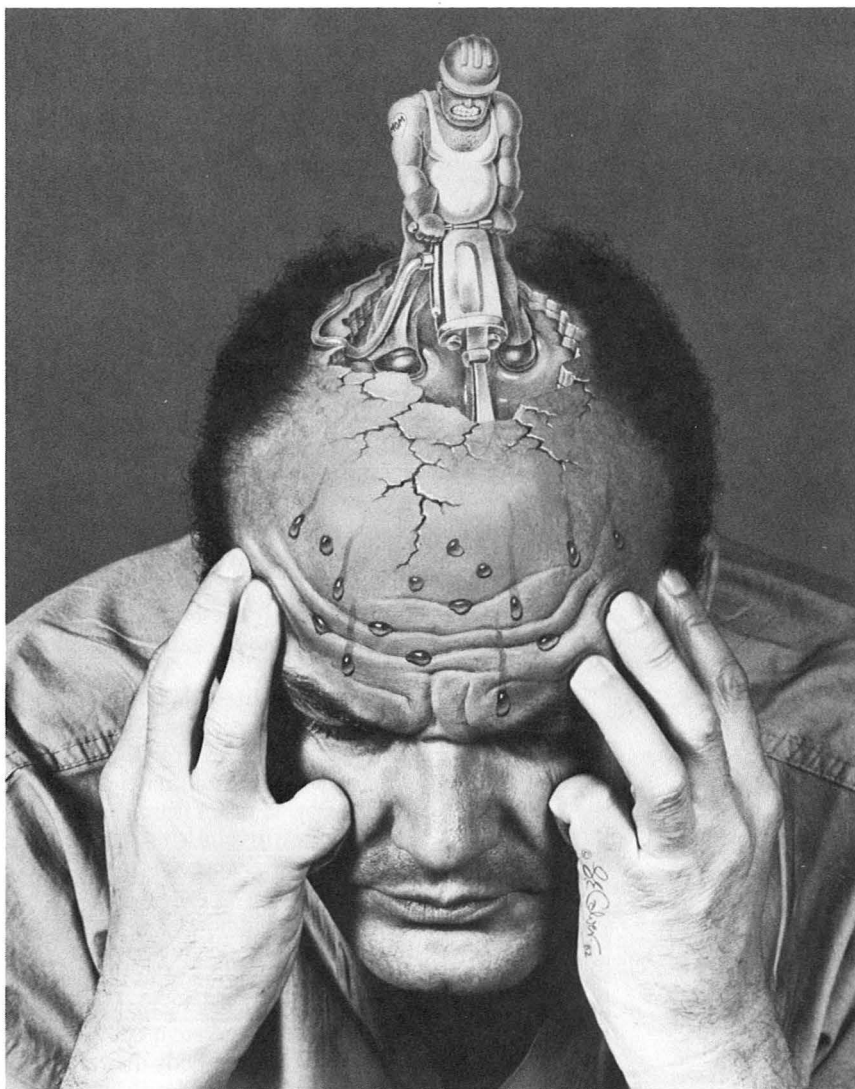
biofeedback equipment in the clinic.

No matter what kind of headache the patient is being treated for, muscle relaxation is basic. Lipton begins simply by instructing the person to tense the muscles of the lower extremities by drawing the feet, one at a time, as far back as possible without letting go. He then instructs the patient to "let the foot go," and if the patient is successful a feeling of relaxation floods that portion of the body. Slowly and speaking in a soothing voice, the physiologist guides the patient in applying this technique progressively until the neck and the

head are completely relaxed.

"This may sound simple—and it is—but many chronic headache patients don't know what 'relaxed' feels like," says Lipton.

"Pain treatment has traditionally been the province of the anesthesiologist in this country," says Dr. Adolph Giesecke, chairman of the Department of Anesthesiology. "Now we are also very excited about our efforts in attacking the debilitating pain of chronic headache, both with treatment for its victims and research for the future."



Selective therapy may prevent kidney stones

The pain is excruciating. Some people say it is worse than childbirth. Many people live in constant dread of passing their next kidney stone.

Dr. C.Y. Pak, director of the General Clinical Research Center and professor of Internal Medicine, has reported success in suppressing formation of the stones through careful diagnosis and selective therapy tailored to the various causes of kidney stone formation.

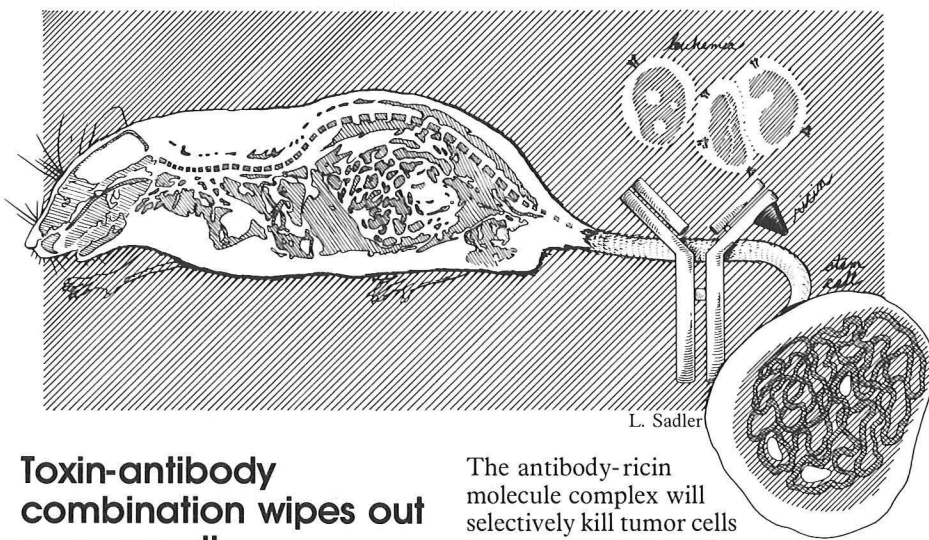
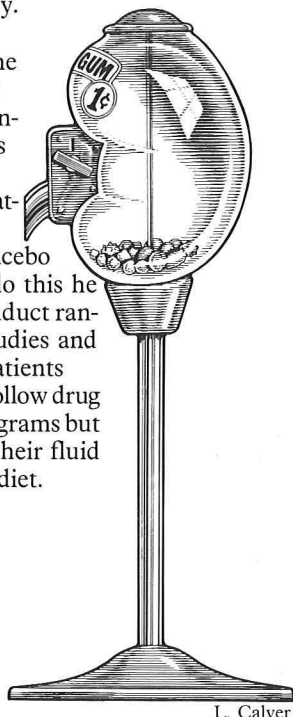
He has been able to prevent stone formation in 70 to 91 percent of patients and reduce stone formation in 88 to 100 percent of patients.

Effective treatment has been slow in coming and Pak says, even today, persons undergoing traditional treatments for kidney stones can expect about a 70 percent recurrence rate.

Helping to reduce this 70 percent rate has been the goal of the ongoing study Pak started at the National Institutes of Health in 1968. He has continued the study at the health science center since 1972, supported by NIH's Special Center of Research (SCOR) project and the General Clinical Research Center.

Working with 241 patients, the scientist has found that most patients can be categorized by the mineral make-up of the stones they suffer from. Once their type of stone is identified, the problem can usually be corrected by modifying the diet and, in some cases, the use of drug therapy.

For research in the future, Pak hopes to conduct studies to separate effective treatment from possible placebo effect. To do this he plans to conduct randomized studies and to follow patients who don't follow drug therapy programs but do modify their fluid intake and diet.



Toxin-antibody combination wipes out cancer cells

Using deadly toxin attached to a cancer-seeking antibody, researchers at the health science center have successfully eradicated cancer cells from the bone marrow of leukemic mice.

Drs. Jonathan Uhr, professor and chairman of Microbiology; Ellen Vitetta, professor of Microbiology, and Keith Krolick, instructor in Microbiology, have documented that their technique will eradicate at least 99 percent of tumor cells from diseased mouse marrow. A report on their work was published in the Feb. 18 issue of "Nature" magazine.

The technique may someday be useful for humans in combination with currently used therapy and bone marrow transplantation. The concept of bone marrow transplantation treatment is actually a rescue technique: patients with certain advanced cancers are given supralethal doses of radiation and drugs to wipe out their rapidly reproducing cells. To replace the normal cells, the patient is then given a bone marrow transplant.

It is in this marrow that all of the cells necessary to repopulate the patient's blood are made.

Because of tissue incompatibility problems, the trend has been to give patients their own marrow back instead of marrow from an unmatched donor. The marrow is taken from the patients while they are in remission but there is a danger of reintroducing some of the cancerous cells.

The researchers say they came upon their "cleansing" technique after first discovering an antibody in a mouse model that would react with tumor cells but not the delicate stem cells of the marrow. To this antibody they attached a modified form of the deadly drug ricin.

The antibody-ricin molecule complex will selectively kill tumor cells in a test tube, leaving the normal cells alone.

"It's a kind of guided missile approach," Vitetta explained. "There are a number of research groups currently developing this approach and all of us are beneficiaries of two decades of basic studies on how plant and animal toxins kill cells."

An extract of the castor bean, ricin in its purest form is quite deadly. Because as little as 100 micrograms (barely visible) is needed to kill a human, it has gained notoriety as an assassin's drug.

The powerful chemical received world-wide media attention in 1978 when an unidentified agent murdered a self-exiled Bulgarian named Georgi Markoff by shooting a tiny bullet of the substance into his leg through the tip of an umbrella.

But the cancer researchers render the ricin harmless to the stem cells by removing its normal binding ability.

"Ricin has two peptide chains, A and B. A is the toxic element and inhibits protein synthesis. B acts as a binder. We've eliminated B from the ricin molecule and replaced it with our specific antibody," said Vitetta.

The researchers' mouse model, called BCL₁, mimics almost exactly the human cancer chronic lymphocytic leukemia (CLL) making it an excellent study guide for their work.

The new technique has yet to be tested in humans but, should human trials prove successful, it could help to achieve permanent remission for patients with some kinds of cancers. The researchers caution that studies with humans are just beginning and it will be several years before the results are known.

Cancer cells become drug-resistant

Dr. Fred Baskin, associate professor of Neurology, and his co-workers have recently identified an enzyme that is present in high quantities in many cancer cells resistant to a diverse group of commonly used chemotherapeutic drugs—vincristine, adriamycin and Baker's antifolate. This enzyme, alkaline phosphatase, is a product of "gene amplification" in many cases of drug-resistant cancer, says Baskin. He is now looking at ways of inhibiting alkaline phosphatase in the hope of making cancer cells less drug-resistant.

Initial doses of a cancer-killing agent are often relatively efficient. Solid tumor growth is slowed as some tumor cells are picked off by the toxic drug. Cancers of the blood, the leukemias, may also regress.

But cancer cells are capable of muta-

ting out of drug sensitivity with surprising speed. And they may remain drug-resistant long after the drug has been taken away.

Baskin is investigating the ways genetic alterations in cancer cells block the effects of drugs. According to Baskin, the answer to the chemotherapy problem is not in looking for another drug to kill cancer—millions of drugs have been screened for their cancer-killing effectiveness. The answer, he says, is to take the 100 drugs that almost work and make them work.

"It is commonly agreed that cancer cells are made resistant by the drugs, judging from the speed at which the cells become resistant and the frequency with which this happens," says Baskin, whose research is funded by a grant from the National Cancer Institute.

The gene amplification process appears to be the cancer cell's most common protective mechanism in block-

ing the effect of toxic drugs. Gene amplification involves an over-production of a particular gene and its neighbors in a chromosome. Where drug-sensitive cancer cells generally have only one gene for a particular purpose, a drug-resistant cancer cell would have hundreds or perhaps thousands of copies of that gene. These gene copies instruct the cancer cell to make proportionately more of their resistance-related protein, commonly a protein that blocks transport of the drugs into the cell.

Alkaline phosphatase could be such a protein. "Or it could just be the product of an innocent neighboring gene. The real culprit gene could be producing another protein not yet identified, but first alkaline phosphatase will be thoroughly investigated," says Baskin.

"An entire new approach to making chemotherapy work is being opened up by findings on gene amplification."

Psychotherapy aids children who set fires

In an overwhelming number of cases young fire-setters aren't just playing with matches—they know exactly what they are doing and their behavior is deliberate. But psychotherapists at the health science center say there is hope of altering the destructive behavior for some young "firebugs." Their studies show that behavior-modifying techniques can be successful for children and adolescents who use fire-setting to mask "bad feelings."

Dr. Eugene Bumpass, clinical associate professor of Psychiatry, and his

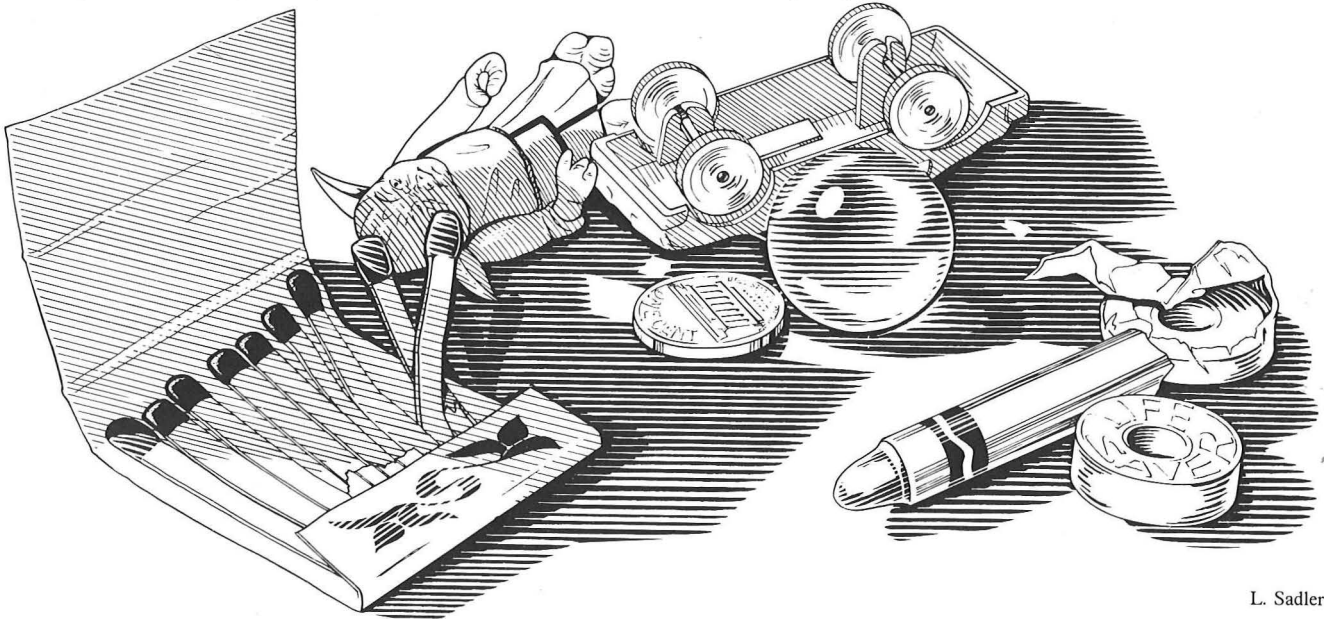
associates have developed a technique to help these children pinpoint the feelings that led to the fire-setting behavior and substitute a positive kind of activity leading to a change in mood.

For the past eight years, team members have seen 29 children and teenagers who had set fires—nearly all more than once—as a way of dealing with uncomfortable feelings. Twenty-five of the cases have been followed to see if there were any repetitions of the fire-setting behavior. Of this number only three have repeated the incidents, and none of the three is known to have set more than one fire since seeing members of the therapy team.

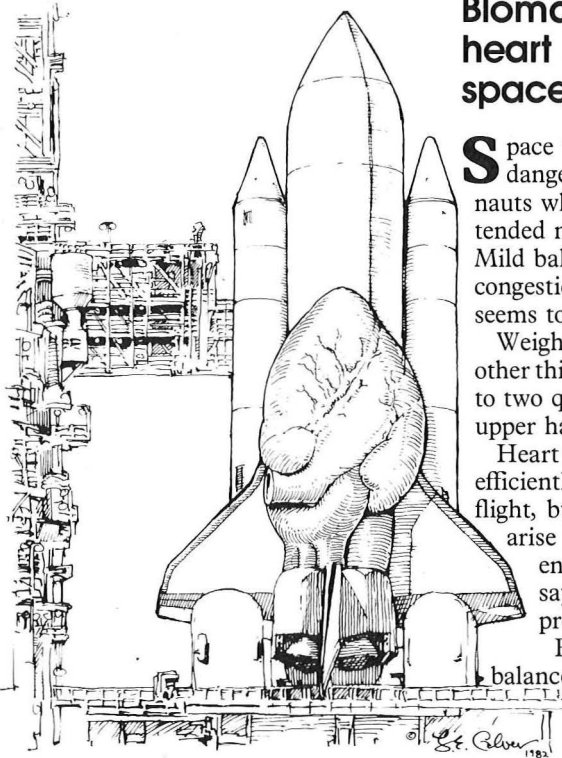
The children are almost always eager

to cooperate, says Bumpass. They don't like being out of control and generally are frightened of both their bad feelings and the compulsive fire-setting behavior. Recommendations for further sessions may be made whenever the psychotherapists feel it is appropriate.

The therapists have been working with the support services section of the Dallas Fire Department's prevention bureau in founding a city program. Officers in the division are trained by the UTHSCD psychotherapists to use their method for intervention in fire-setting behavior. Fire department counselors are now seeing about 100 juveniles a month in voluntary counseling sessions.



L. Sadler



Blomqvist to study heart circulation in space shuttle

Space travel creates potentially dangerous body changes for astronauts who must pass hours with distended neck veins and puffy faces. Mild ballooning of the heart with congestion of blood vessels in the lungs seems to be one consequence.

Weightlessness initiates, among other things, a shift of body fluids—one to two quarts—from the lower to the upper half of the body.

Heart and circulation can adapt efficiently within the first few hours of flight, but signs of heart abnormality arise during the early stages of re-entry into the earth's gravity, says Dr. Gunnar Blomqvist, professor in the Cardiology Unit.

Because of difficulties in fluid balance and nervous system control of blood pressure and flow, there is a tendency to faint

in the upright position.

Blomqvist, an M.D. with expertise in physiology, and a small group of scientists will get a firsthand chance to explore these problems when their experiments are conducted aboard a 1985 flight of the NASA space shuttle. Blomqvist hopes to find the regulatory changes involved in the body's adaptation to zero gravity and to re-entry.

Exercise and redistribution of blood are two avenues Blomqvist is exploring as countermeasures to cardiovascular deconditioning. Short-term body cooling using a special suit with cooling coils of water will be observed as a possible aid in redistributing blood from the skin to the heart.

Probably the most dramatic experiment to be performed by mission specialists in-flight will be the measurement of heart filling pressures using central venous catheters placed in the chest. The specialists will fly their first 12 hours with the catheters in place to record cardiac measurements during the early adaptation period.

Mental retardation may be due to fragile X chromosome

An elusive genetic abnormality may be responsible for 25 percent of the mental retardation found in males. Mental retardation due to this abnormality, called "fragile X chromosome," may be as common among males as Down's syndrome.

Women under 20 who have a family history of mental retardation, especially among the males, should be tested to see whether they are carriers of the fragile X chromosome, says Dr. Patricia Howard-Peebles, director of the Cytogenetics Laboratory and associate professor of Pathology.

"We like to test a retarded male family member first," says the clinical cytogeneticist. "If he is positive for fragile X, we say the family has it. If he is negative, we like to test another affected male before we rule it out. If both are negative, we conclude that the family doesn't have fragile X-linked retardation. I prefer to test males of two generations, such as a man and his nephew by his sister. If one is positive for fragile X, then we can test females in the family to see whether they are carriers."

Even though a woman has no immediate plans to have a child, she may want to be tested to know whether

she is a carrier because after age 20 to 25, the fragile X frequently does not show up in the test of a woman's chromosomes. An older woman may have mentally retarded sons who do show fragile X chromosomes and not show the abnormal chromosome herself.

This defect occurs most often in males with females as carriers of the defective chromosome. But it has recently been discovered that some female carriers are slightly retarded also.

Fragile X-linked mental retardation follows the pattern for other X-linked recessive genes with the family pedigree resembling the well-known pattern for hemophilia.

The X-X or X-Y pair of chromosomes determines a person's sex. The mother contributes an X chromosome to every child. The father contributes an X chromosome to females and a Y chromosome to males. So a female child with a defective X has a "back-up" normal X chromosome to provide normal function although she may pass the fragile X to her children. A male child with a defective X has no "back-up."

Affected males (those with mental retardation) and female carriers may be tested for the fragile X chromosome at UTHSCD and some other genetic counseling centers in the nation. Now a fetus can also be tested for fragile X although this is still experimental. Two *in utero* diagnoses of fragile X have been

made, but more testing will be necessary to assure that a test of cells obtained through amniocentesis is accurate for fragile X.

"At least we could tell the mother for sure whether it's a boy or girl," says Howard-Peebles. If the mother is a known carrier for fragile X chromosome, her child has a 50-50 chance of getting that chromosome. That means a son has a 50-50 chance of having mental retardation and a daughter has a 50-50 chance of being a carrier with possible slight retardation.

The researcher has studied 18 families with the fragile X chromosome. Although there are no consistent unusual physical symptoms with fragile X-linked mental retardation, the affected men have enlarged testes in more than 90 percent of the families studied.

"There is no problem recognizing the fragile X site, a 'constriction' near the end of the long arm of the X chromosome," says Howard-Peebles.

What is the fragile X site exactly? "We don't know," she says. The gene that causes the mental retardation may not be at the site—it may just be near the site. The fragile X site may occur as a defect in chromosome structure.

Fragile sites have been found on other chromosomes, but so far the fragile site on the X chromosome is the only one known to be associated with an inherited disorder.

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