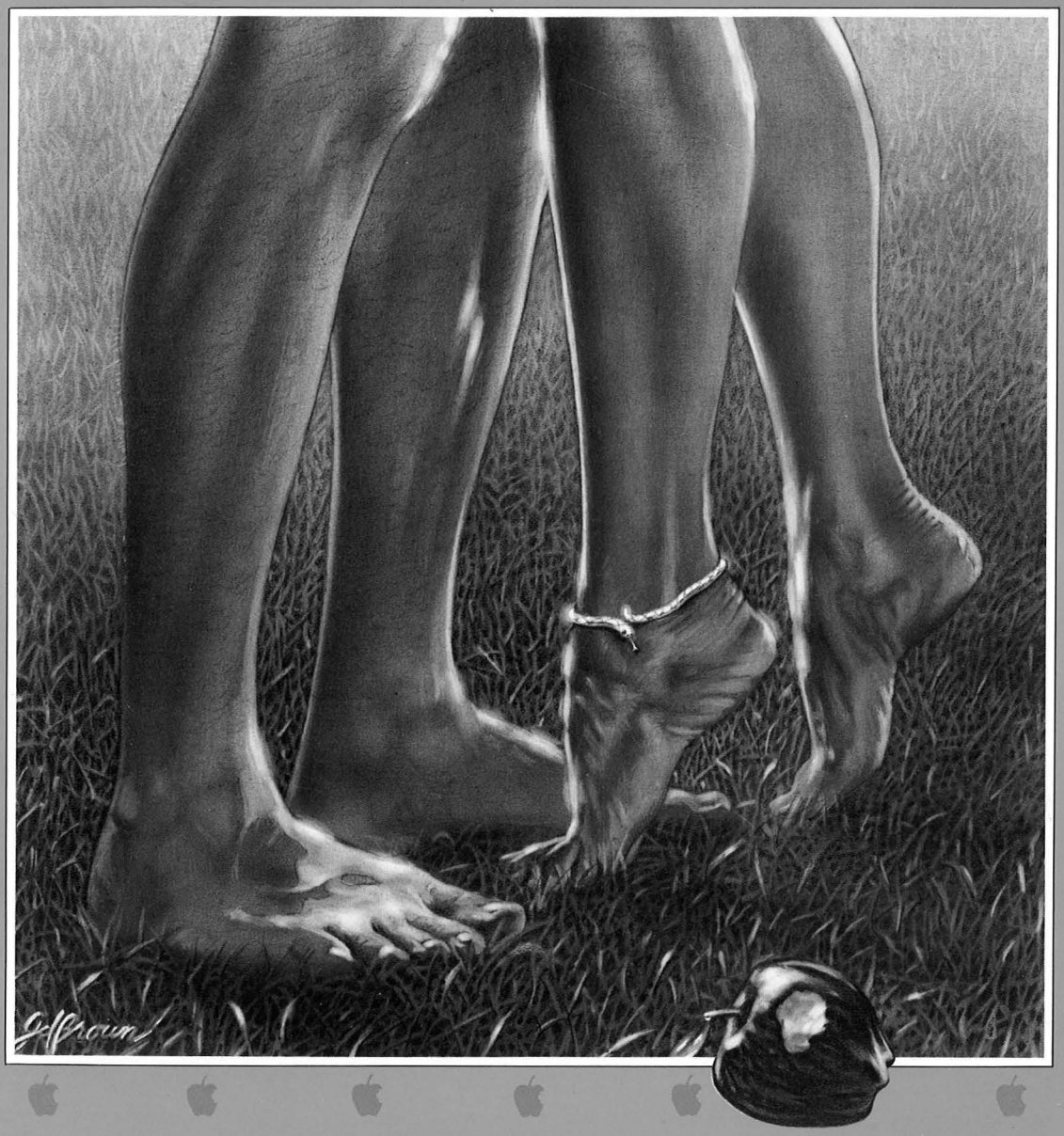
BIOLOGUE

The University of Texas Health Science Center at Dallas Spring 1984



Getting to the Core of Sex

Between the Covers

It is fascinating to speculate what sort of report an alien such as E.T. would give back home regarding the habits and mores of the human race.

The customs regarding sex would almost certainly provide a most bizarre part of the narrative.

"Would you believe," we can almost hear E.T. saying, "these beings pay money to witness movies about their own reproductive acts?

"Would you believe that until a few annums ago, it was socially unacceptable for them to even discuss reproduction – one of their most vital physiological functions?"

Had our alien come to Dallas he would have found sexually transmitted diseases rampant while myths and ignorance still held sway over a considerable portion of the citizenry.

"Humans have not yet decided what can and what cannot be transmitted via a toilet seat," E.T. might relate.

And he might further observe, "They're extremely afraid of a new sexual disease – acquired immune deficiency syndrome – AIDS – with some saying it's a punishment from their God for non-heterosexual behavior."

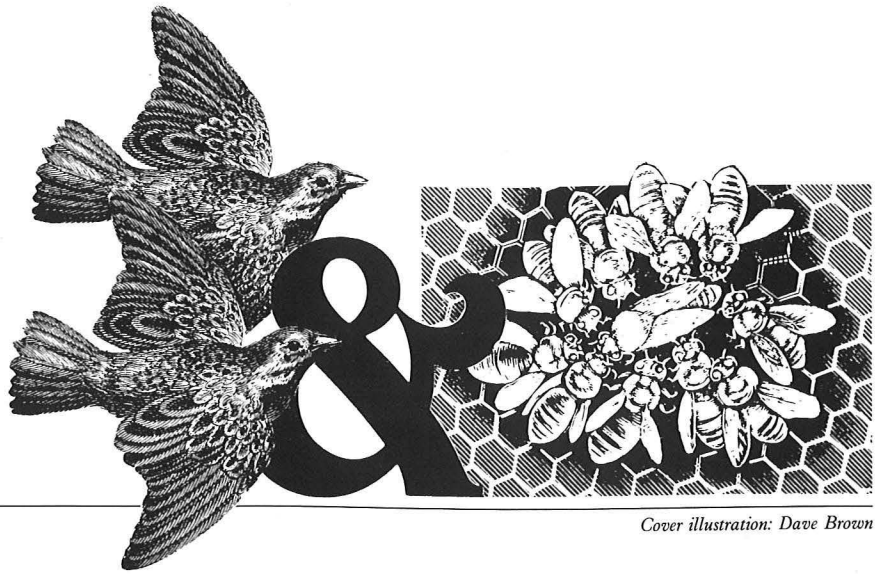
And this would be a report on the "civilized" world. What he would report from the Third World – where in some cultures the grisly practice of female circumcision still prevails – might be a longer chapter of inexplicable human behavior.

Perhaps this fantasy is objectivity overdone.

Details of other fantasies less objective but contributing to the creativity of the staff of *BioLogue* and the Office of Medical Information have been scrupulously culled from this issue devoted to sex.

But if *BioLogue* is able to pull the curtain of culture aside for a moment and report clearly and dispassionately on a topic that evokes the deepest of human feelings – if we shed new light – then we will have succeeded.

Bob Fenley, Director
Medical Information



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Cover illustration: Dave Brown

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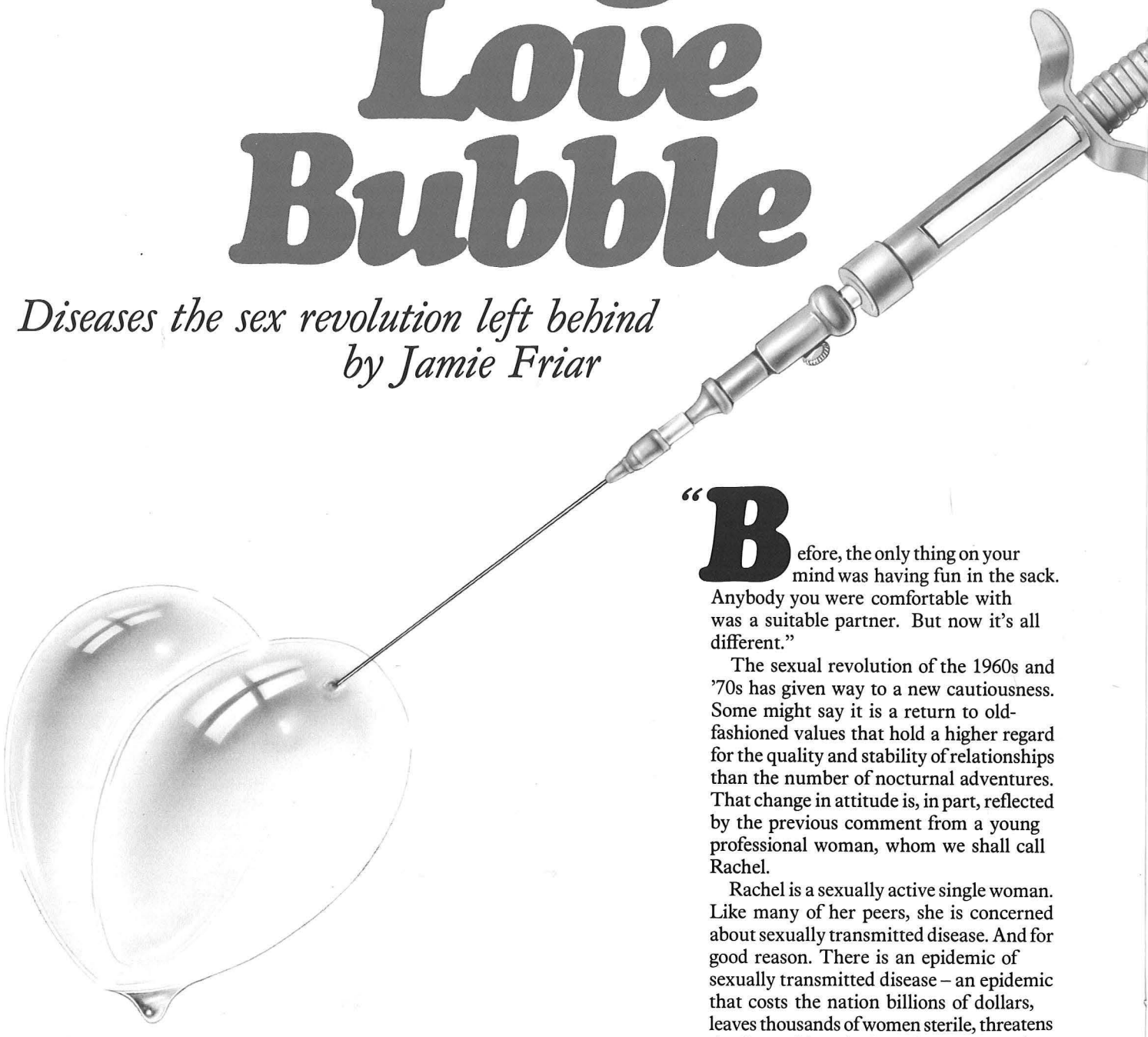
Bursting the Love Bubble

Diseases the sex revolution left behind

by Jamie Friar

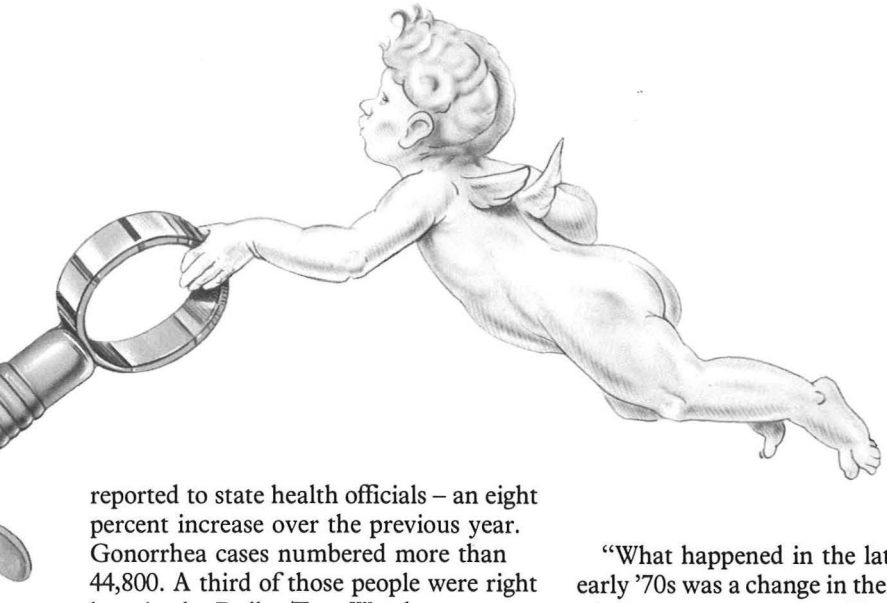


"Before, the only thing on your mind was having fun in the sack. Anybody you were comfortable with was a suitable partner. But now it's all different."

The sexual revolution of the 1960s and '70s has given way to a new cautiousness. Some might say it is a return to old-fashioned values that hold a higher regard for the quality and stability of relationships than the number of nocturnal adventures. That change in attitude is, in part, reflected by the previous comment from a young professional woman, whom we shall call Rachel.

Rachel is a sexually active single woman. Like many of her peers, she is concerned about sexually transmitted disease. And for good reason. There is an epidemic of sexually transmitted disease – an epidemic that costs the nation billions of dollars, leaves thousands of women sterile, threatens the lives of hundreds of newborns and raises the specter of becoming a sexual outcast for millions of sexually active people.

Texas has the dubious distinction of having one of the highest syphilis rates in the nation. In the first six months of 1983, more than 6,000 cases of the disease were



reported to state health officials – an eight percent increase over the previous year. Gonorrhea cases numbered more than 44,800. A third of those people were right here in the Dallas/Fort Worth area.

While syphilis and gonorrhea are what most people associate with venereal disease, the scope of sexually transmitted disease today includes more than two dozen disease entities.

Herpes, hepatitis, urethritis, vaginitis and AIDS are just some of the other diseases that are spread by sexual contact. The U.S. Department of Health and Human Services estimates the total cost to the nation for STDs is measured in the billions of dollars per year. And unfortunately, there is no light at the end of the tunnel. This wasn't always the case. A few decades ago public health officials thought venereal disease was on the verge of extinction. The rosy predictions did not come to pass.

Penicillin and complacency were the magic bullets that misfired. At the American Public Health Association's annual meeting in October 1943, the assembled professionals broke into cheers as they heard a paper detailing how penicillin cured four patients with syphilis. The long-sought treatment for VD was at hand. Wartime demands meant that penicillin could not be allocated for treatment of such mundane disorders as VD. But the public health experts knew it was just a matter of time before sufficient quantities would be available to wipe out syphilis and gonorrhea.

The false sense of security would cost the nation dearly. Sexually transmitted disease largely disappeared from medical school curricula. Public health departments closed their VD clinics or shifted their emphasis to other areas. Federal funding for VD control and research dried up. In 1955 federal appropriations for VD control amounted to just $3 million. When the bubble burst in the early 1970s, the nation was ill-prepared to deal with one of the most widespread epidemics in history.

"What happened in the late '60s and early '70s was a change in the demography of our society," says Dr. Kevin Murphy, clinical associate professor of Internal Medicine at The University of Texas Health Science Center at Dallas. "That change was a rapid expansion in the proportion of the population who were young, single adults." Murphy feels the continuing epidemic which began more than a decade ago, is due to several factors. "People began to postpone marriage until their late 20s and early 30s. People began getting divorced much more rapidly." Sexual mores changed. More people were sexually active, they became sexually active younger, they had more sex partners and their sexual encounters became more casual.

The '60s also saw a change in patterns of contraception. The pill eliminated the fear of pregnancy for sexually active women. The one truly effective method of VD prevention, condoms, lost favor.

One of Murphy's research interests has been herpes simplex. It is a virus that has been known for years but only recently moved from the virology textbooks to the front page. Discussion of herpes is tainted with emotion. It has been characterized as the new scarlet letter, branding the promiscuous with an incurable infection. Some herpes patients fear they will become sexual lepers and suffer great emotional trauma.

Hysteria aside, Murphy says, "It is the easiest of the STDs to get. One does not need to be promiscuous to get it, but it recurs and reminds you of whatever guilt you might have felt over the first episode. And it's sexually transmitted so a pall is sort of cast over sexual relations for those who have the disease."

Herpes can have serious consequences. But the disease itself does not warrant the emotional turmoil that surrounds it. "One could say there is a lot of unnecessary suffering." Murphy continues, "All the serious complications are at least theoretically preventable if one knows that he or she has herpes."

Murphy says if one has a number of sex partners, there may be little that he or she can do to avoid exposure to herpes. "The majority of people who are infected with genital herpes have no symptoms. But anyone with the virus, regardless of symptoms or lack of symptoms, is capable of secreting the herpes virus. And it is a very common virus, infecting as much as 40 percent of the population, according to some studies."

Consequently, herpes sufferers who put themselves through "excruciating self-flagellation over never being a worthy sexual partner are theoretically no greater a risk than the person who doesn't know he or she has herpes."

There are two main types of herpes simplex virus that are sexually communicable, HSV-1 and HSV-2. At one time it was thought that Type 1 was confined to the lips and mouth, typically a "cold sore." Type 2 caused genital lesions. Today the viruses do not consistently recognize anatomical boundaries, and both are considered to be capable of sexual transmission.

Much of the herpes phobia concerns the fact that it is "incurable." While herpes cannot yet be removed from the body, the serious consequences of the disease, particularly to the newborn can be controlled. Once the herpes virus enters the body through the skin, it can cause lesions. The body's immune system eventually brings the lesions in check, but the virus proves to be an elusive invader. It retreats to the ganglia, clusters of nerve fibers, at either end of the spinal cord. The virus, in its latent stage, can reawaken, causing new lesions. Herpes recurrences can flare up as frequently as every other week, as infrequently as once a year or never.

Recently the drug acyclovir was approved for use as a topical ointment for herpes sufferers. It has proven effective in lessening the severity of the initial outbreak. Research is now being conducted on using acycolvir in the form of oral or intravenous medication. While results appear promising, there is no indication the drug can prevent the virus from invading the ganglia or eliminate it

There is "more and more evidence that cytomegalovirus is transmitted sexually." Among some homosexual populations, antibody to the virus is almost universal.

once it enters the latent stage.

The eventual "cure" for herpes may be a long time in coming. Murphy says, "What patients really mean by a cure is eliminating the latent infection. There's not a glimmer of an idea on how to do that." The solution to the herpes problem resides in a basic understanding of how viruses work and how the body is affected. Murphy predicts it will be another decade before those fundamental questions are answered.

Herpes knows no demographic barriers. No one knows just how many Americans suffer from herpes infections. Hard numbers are difficult to come by. Herpes is not a reportable disease, and many cases are asymptomatic. It is estimated that some 20 million people in the U.S. have herpes, and that number is increasing by about half a million a year according to the Centers for Disease Control.

One of those suffering from herpes is Dr. A. He has two points of view toward the herpes problem – as patient and as physician. Ironically, today Dr. A. serves as the STD officer for a government agency. Like many millions of other herpes victims, Dr. A. has suffered the discomfort, both emotional and physical, of the disease.

Dr. A. and his wife keep the herpes infection in perspective. "I think it really becomes a concern in the period of pregnancy. That's the only time it will become a great concern to myself and my wife. The rest of the time it really doesn't play that big a role in our sex and personal life." As many herpes sufferers find, stress seems to exacerbate recurrences for Dr. A. "During times of stress we both tend to have herpes. Sex is either put off for a few days or is a little less comfortable." Dr. A says he has lesions only about one week out of every two months.

When Dr. A. was single and dating, he faced the problem that many herpes sufferers confront – what to tell his potential sex partners. "I had one situation where I told someone and she was quite taken aback. She decided she didn't want to continue the relationship. That was the one time that I really felt bad, like a sexual leper." Dr. A. says he felt compelled to reveal the nature of his infection. "I felt I had to tell her even though I didn't have any active lesions at the time – to let her make an informed decision about someone she may be sexual with. There are endless discussions about whether to tell or not to tell, but I think you are obligated to tell."

Limited testing of a herpes vaccine is being conducted at a few institutions. Dr. A. hopes that such a vaccine could prevent the spouse of a herpes victim from acquiring the disease. "It is a real problem in a relationship if you give your partner herpes. I think that's the main reason a vaccine would be important. If there is a lot of stress in a relationship and if one partner gives the other herpes, it can definitely ruin the relationship."

The herpes hysteria is partly the fault of the medical profession, says Dr. A. "Generally the physician-patient meeting is so rushed there is little time for emotional support. Herpes is considered to be relatively minor in a long list of medical problems so the physician might not help the patient with the psychological trauma that may accompany the infection." Dr. A. encourages herpes sufferers to join support groups such as those sponsored by the American Social Health Association's Herpes Resource Center. For information send a stamped, self-addressed envelope to HRC, P.O. Box #100, Palo Alto, CA 94302.

CMV

There is another strain of herpes virus that a person may carry and not know it.

Many people have cytomegalovirus with no apparent problems or visible symptoms. But there are two groups of people who are at risk from CMV, newborn babies and recipients of organ transplants.

There is a growing body of evidence that CMV is sexually transmitted and is the major known cause of virus-linked birth defects. Dr. James Luby, head of the Infectious Diseases Unit at the health science center, says CMV can be transmitted to the infant via a number of routes. The virus can make its way into the womb, birth canal or breast milk. While usually not life-threatening, CMV can cause hearing abnormalities and mental retardation.

About one percent of all newborns excrete CMV in urine. Of these about 10 percent will eventually show some hearing or neurological defect that is virus-related. Luby studied 58 babies with symptoms of CMV infection at Parkland Memorial Hospital and Children's Medical Center from 1970 through 1981.

No symptoms of CMV infection were found in the mothers of the infected children. Luby says his findings were similar to other studies suggesting, "The majority of primary (first) infections in normal hosts, at all stages of life, are asymptomatic."

Luby says there is "more and more evidence that CMV is transmitted sexually." Among some homosexual populations, antibody to the virus is almost universal, he explains.

Because of the high incidence of CMV infection in homosexuals, the virus is being investigated in relation to AIDS (acquired immune deficiency syndrome). Luby says the virus is not thought to cause AIDS. But it has been found in tumor tissues of a rare skin cancer that proves fatal to many AIDS victims.

CMV poses a particular threat to the recipients of organ transplants. They receive special drugs to suppress their immune systems. Unchecked by the body's natural defenses, CMV frequently causes potentially fatal pneumonia. Says Luby, "In these patients, because their immune systems are suppressed, infection is a major problem." He adds, "Pneumonia is the leading cause of death among bone marrow transplant recipients, and its chief cause is CMV. Since CMV is a herpes virus, it can cause persisting infection and remain latent for the lifetime of the individual."

Luby predicts that a vaccine against CMV will soon be perfected and drugs effective against CMV will be available in the near future.

AIDS

Medical sleuths are tracking a mysterious killer, acquired immune deficiency syndrome. AIDS has claimed nearly 800 lives and has infected 2,000 people in the United States. There is, as of yet, no known

cause nor cure for the disease which disables the body's immune system.

The news media dubbed AIDS the "gay plague" and raised fears that it could spread to the general population. In recent months the hysteria surrounding coverage of the AIDS story has given way to accuracy.

AIDS primarily strikes homosexuals. According to the Centers for Disease Control, 71 percent of AIDS victims are either homosexuals or bisexuals. Other high risk groups include: intravenous drug abusers, recipients of blood or blood products, infants born to infected mothers and Haitians.

"We know a great deal about its epidemiology," says Murphy. "We know who gets AIDS and where they are, but we don't know what the infectious agent is." Murphy says now the "smart money" on AIDS is that a virus is passed from person to person in a way similar to hepatitis B transmission. But there could be some surprises. Murphy points to the early phase of the CDC investigation of Legionnaire's disease. At the time it was thought that a virus most likely caused the infection. As it turned out, a common but then unidentified bacterium was the culprit. "Once again we all think the smart money on this disease is going to be on a virus, but we could be wrong."

AIDS victims lose their ability to fight off microscopic invaders. The AIDS patient frequently succumbs to a variety of infections. Kaposi's sarcoma (KS), a form of skin cancer, was rarely seen in this country and never in young patients before the onset of AIDS. Now KS and Pneumocystis carinii pneumonia (PCP) are common diseases that strike the AIDS patient.

The outlook for AIDS victims is bleak. No AIDS victim has had his or her immune system restored to normal function. The mortality rate is about 38 percent and the number of new diagnoses continues to spiral upward.

While the prognosis for AIDS victims is dim, current research should allay fears that the mysterious killer may be epidemic in the general population. There has not been a single instance of AIDS transmission due to casual or social contact. The only reported case among health care personnel that is suggestive of occupational transmission was in a surgical attendant who did not observe the standard precautions in handling human blood. The epidemiological thread that links AIDS victims is either sexual relations or blood contact. Murphy says that suggests that the causative agent is a virus found in body fluids, perhaps only in blood.

No country was immune, but many were blamed for the disease. It was called the "French disease" by the English and Italians while the French called it the "Italian disease."

Murphy says the ultimate solution to the AIDS puzzle would be a major scientific breakthrough. "Not just because it is an answer to this one epidemic, but because it would be a tool toward understanding how the immune system develops and how human cancer viruses function."

Syphilis

Columbus brought home more than just tales of a New World. Many historians credit him and his crew with introducing syphilis to Europe. It has been theorized that syphilis epidemics that ravaged Europe in the 15th and 16th centuries had their beginnings when Columbus' crew members freely mingled with the native population in the newly discovered lands.

Descriptions of syphilis abound in 15th century European literature but are curiously absent from writings previous to that time. Warfare, with its troop movements and accompanying camp followers, provided the ideal means for syphilis to spread throughout the continent. No country was immune, but many were blamed for the disease. It was called the "French disease" by the English and Italians while the French called it the "Italian disease." The Turks, Spanish, Neapolitans, Germans and Poles have all been blamed for syphilis.

Recent studies, however, have shown that even Neanderthals may have suffered from syphilis-like ailments. In any case, syphilis was one of the earliest documented and most studied diseases.

The advent of effective antibiotic therapy may have slowed research interest in syphilis, but did not kill it. Here at the health science center, the modern technique of genetic engineering is being used to study *Treponema pallidum,* the bacterial micro-organism that has been the bane of humanity for at least five centuries.

The major problem in syphilis research is the difficulty in culturing the offending organism. When *T. pallidum* is cultured *in vivo,* most often in rabbits, it grows poorly. When isolated, it is always heavily contaminated with tissue components from the host rabbits. Dr. Michael Norgard, assistant professor of Microbiology, is stripping DNA from *T. pallidum* and combining it with the easily cultured *E. coli* bacterium. The resulting "clones" can thereby synthesize unlimited quantities of "pure" *T. pallidum* antigens free of contaminating host tissue.

Norgard's group is one of the first in the country to use the genetic engineering techniques to isolate disease-producing antigens generated by *T. pallidum.* Another method being used by Norgard is to create monoclonal antibodies specific to the syphilis organism's antigens.

The body's immune response is, in part, an interplay between antigens and antibodies. Antigens are foreign substances that invade the body, such as viruses, bacteria or tissues from another person (i.e. transplants). Antibodies, circulating in the bloodstream, bind with the antigen and may kill an invading organism or act as a biochemical marker. Killer lymphocytes, small white blood cells, can then attack the antigens identified by the antibodies.

Antibodies will react only to specific antigens. Once an antigen is introduced into the body, via infection or vaccination, the needed antibody is produced. It takes much longer for the immune system to check an invader the first time a new antigen is introduced because there are no circulating antigen-specific antibodies and no immunological memory of the antigen.

An additional complication is that some antigens do not invoke a quick and strong antibody response. Such may be the case with syphilis. The disease can lie in a latent stage for years before causing very serious complications. Why *T. pallidum* is able to escape antibodies or the hunter/killer cells of the immune system is not known. In

order to find out why, a laboratory method of creating "pure" syphilis antigens was needed, and that's where Norgard's work comes in.

Genetic engineering is one way to generate the antigens; another is using monoclonal antibodies. A specific antibody-producing cell (called a B cell) is fused with an easily cultured mouse spleen tumor cell. The resulting antibody/tumor combination (called a hybridoma) is then cloned, creating thousands of identical antibody-producing cells.

The antibodies react only to a specific antigen. Thus the antibody from the monoclonal cells can be used as a biological filter. Pathogenic *T. pallidum* organisms can be introduced into a glass column containing monoclonal antibodies fixed in place. The desired antigen is bound by the antibodies with the unwanted biological material draining out of the bottom of the column. The antigen bound to the antibody can then be chemically stripped off, leaving isolated, pure antigens for research purposes.

Long-term benefits from the antigen research could be an improved understanding of the syphilis disease process, a new diagnostic test and a vaccine. The VDRL test now used for syphilis is effective but is negative some 30 percent of the time when the disease is in its earliest stages. And other ailments such as lupus or rheumatoid arthritis may cause false positives.

Gonorrhea

Of all the infectious diseases reported to the Centers for Disease Control, gonorrhea is by far the most widespread. Nearly a million cases a year are reported to public health officials. Many more are either untreated or unreported.

One particular concern is asymptomatic gonorrhea infections. Frequently seen in women, asymptomatic gonorrhea is now said to infect men as well. Gonorrhea can be particularly devastating to a woman. Left untreated, the infection can spread to the fallopian tubes, rendering the woman permanently sterile.

Today, as in Columbus' time, travel to far-off lands can spread new STDs. Now, with the advent of jet travel, introduction of new disease entities is a matter of hours instead of years.

Gonorrhea can be particularly devastating to a woman. Left untreated, the infection can spread to the fallopian tubes, rendering the woman permanently sterile.

One unwelcome returning veteran of the Vietnam war is penicillin-resistant gonorrhea. That particular strain was born in brothels and bred by indiscriminate use of antibiotic drugs since prostitutes and GIs had ready access to penicillin. They took the drug with expectations that it would protect them against venereal disease. It did, up to a point.

Mutant, penicillin-resistant strains of the gonorrhea developed and were brought home by returning veterans. The new resistant strain then began appearing in the civilian population.

Physicians treating patients at health science center clinics have an arsenal of antibiotic drugs. The penicillin-resistant strains may be impervious to some medicinal attacks, but they will succumb to others. There has yet to be a gonorrhea strain that proves resistant to all therapy.

Chancroid

Monoclonal antibody technology is being applied to one of the most common STDs in the Third World, chancroid. Dr. Eric Hansen, assistant professor of Microbiology, says little is known about the incidence and epidemiology of chancroid because there is no definitive diagnostic method. Chancroid symptoms often mimic other diseases. "A good clinician who has seen a lot of chancroid can usually recognize it although genital herpes can mimic chancroid."

Hansen explains that the offending organism, *Haemophilus ducreyi,* is very difficult to culture from clinical specimens under routine laboratory conditions. According to Hansen, his group has been able to produce monoclonal antibodies that will react to all tested strains of *H. ducreyi.* Eventually, Hansen feels the monoclonal technique will be perfected so that it can be applied to a simple-to-use diagnostic technique. "You would mix pus or tissue from the lesion with the monoclonal antibody solution. If the material has the chancroid organism, it will stick to the antibodies. Depending on the detection system used, the solution could either change color, or the antibodies and antigens would clump together and you would see the clumping effect."

The chancroid antigens recognized by these monoclonal antibodies might be useful in developing a vaccine for the disease, says Hansen. He predicts it will be another two years before the diagnostic chancroid test is ready for clinical trials. Hansen says it will be several years beyond that before a chancroid vaccine could possibly be developed.

Chlamydia trachomatis

As our knowledge about the disease process expands, and diagnostic techniques improve, the list of sexually transmitted diseases lengthens. Such is the case with a ubiquitous micro-organism, *Chlamydia trachomatis.*

The *Chlamydia* bug isn't so persistent as herpes, nor does it cause complications as serious as those of syphilis or gonorrhea. But it should not be easily dismissed. Chlamydial infections are now more prevalent than any other sexually transmitted disease, says Luby, with some three million new cases a year. In most instances, antibiotic therapy can rid the body of the bug, but detecting it is no easy matter. Chlamydial infection may mimic other diseases in its symptoms. And laboratories often have difficulty in culturing and isolating the bacterium.

Chlamydial infections manifest themselves in four primary ways:

- Genitourinary tract infections in adults. Non-gonococcal urethritis is by far the most frequently treated type of venereal infection. In many instances the specific micro-organism that causes the NGU is not known, but in about half the cases *Chlamydia trachomatis* is the culprit.
- Chronic eye inflammation, which may lead to permanent blindness. This type of infection occurs mainly in underdeveloped countries.
- A venereal infection called lymphogranuloma venereum. It can produce sores on the genitals, pain and swelling of the lymph nodes and extreme swelling (elephantiasis) of the genitals.

The herpes virus attacks the newborn in a number of ways. Herpes complications can range from isolated skin lesions to overwhelming shock and bleeding.

■ Complications in newborns. As with other STDs, chlamydial infections can pose a vastly more serious threat to infants than to adults. Acute eye inflammation and pneumonia are common chlamydial complications in newborns.

STDs and Children

In a very real sense, newborn babies are the innocent victims of the sexual revolution.

Herpes poses the greatest risk to newborns, according to Dr. Jane Siegel, assistant professor of Pediatrics. If untreated, 70 percent of infant herpes victims die, she says. The child acquires the disease from an infected mother as he or she travels down the birth canal. If delivered vaginally, about 50 percent of children born to mothers who have active lesions will get the herpes infection. Siegel says if physicians know the mother has herpes lesions, every effort is made to deliver the child via Cesarean section.

The herpes virus attacks the newborn in a number of ways. Herpes complications can range from isolated skin lesions to overwhelming shock and bleeding. Central nervous system involvement may also occur in infant herpes cases.

Some drugs – acyclovir on an investigational basis and Vidarabine – are available to the infant herpes victim, but the results are far from perfect. Says Siegel, "They have some effectiveness in decreasing mortality and morbidity but not as great an effect as we hoped."

Siegel's research interest is *Streptococcus* and its impact on the newborn. Strep is another disease entity that is now included on the list of STDs. It poses a particular risk to infants. Siegel says today, up to three out of every 1,000 children are born with group B strep infections. They face sepsis and meningitis as two possible complications of their infections. Siegel says 20 to 50 percent of newborns infected by group B strep will die.

The number of STDs that can be passed on to newborns is almost as large as the list that can infect adults. As with adults, some infections may be asymptomatic, but generally the complications in newborns are far more serious.

Some children acquire STDs as the result of sexual abuse. Often their abuse comes to the attention of authorities when the child is seen by a physician for treatment of urinary tract infections or even arthritis caused by STDs. "They seek attention for their medical problems," says Siegel. "Their chief complaint is not sexual abuse. It's pus in the eye, swollen and painful joints or a fever and rash. When the diagnosis is made, it is the responsibility of the physician to see that a full investigation is made."

Siegel says adults should be aware of the consequences that their sexual activities may have on future offspring. "This is something people should know about and make decisions accordingly."

PID

Motherhood is not an option for a growing number of women because of STDs. Pelvic inflammatory disease, a complication of many STDs, is the most common cause of female infertility, says Dr. Gary Cunningham, chairman of Obstetrics and Gynecology.

While commonly called PID, Cunningham prefers the more descriptive term "salpingitis" (inflammation of the fallopian tubes).

A variety of sexually transmitted microorganisms can migrate to the fallopian tubes. Scar tissue from the infection can block the tubes preventing pregnancy or causing an ectopic pregnancy. "In my opinion," says Cunningham, "salpingitis is the most important sexually transmitted disease because of its effects on fertility." In the last 10 years, the incidence has doubled. It is predicted that one in three women of child-bearing age will have at least one episode of salpingitis.

The key to treating salpingitis and preventing possible fertility problems is prompt care. Cunningham says there is no guarantee that early antibiotic therapy will eliminate the threat of fertility problems, but common sense dictates that the earlier the treatment, the better the chances of success. "Unfortunately many of these women don't come to see us soon enough. If we can treat women with early gonorrheal or chlamydial infections, we can avoid salpingitis."

One of the life-threatening complications of salpingitis is the ectopic pregnancy. In recent years the incidence of ectopic pregnancy has spiraled upward, and changing patterns of sexual behavior may be partly to blame.

An ectopic pregnancy occurs when the fertilized egg, or ovum, cannot reach the womb. Instead the embryo begins to develop and expand in the woman's ovary, fallopian tube or other location outside the uterus. The growing embryo can rupture the fallopian tube, resulting in internal bleeding.

Two studies published recently in the *Journal of the American Medical Association* outline the dramatic increase in ectopic pregnancy. Researchers found that nationwide the incidence of ectopic pregnancy doubled during the '70s.

The leading cause of ectopic pregnancy, says Cunningham, is salpingitis. The rise in ectopic pregnancies parallels the epidemic of sexually transmitted disease with 40,000 women a year developing ectopic pregnancies.

The emotional impact of infertility due to salpingitis is particularly heavy. "If you tell a woman she is infertile because of venereal disease she contracted while single, she is likely to feel very guilty about it," according to Cunningham.

The one common denominator among the sexually transmitted diseases is exposure. The experts repeated over and over, the greater the number of sex partners, the greater the chance of acquiring a sexually transmitted disease. Says Cunningham, "Talking with women who attend our clinics, I've seen a trend toward more stable monogamous relationships. They fear catching something, and they say, 'It's not worth it.' "

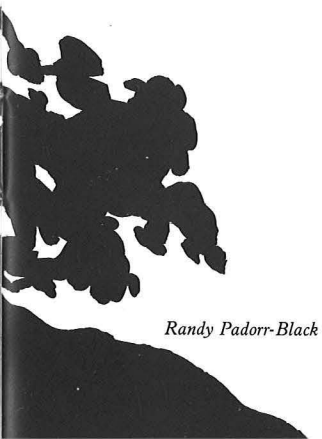
Rachel sees that sort of change in her own behavior. "I just want more out of relationships than I used to. More than just a sexual good time. In the past it was 'Hey! Let's go out and party and see what happens.' Now if I have a date, I know where it's going to end, and it's not going to end in my bedroom. I don't want to pay the consequences with some awful disease for the rest of my days."


Edward
Andrew
Anne
Charles
Queen Elizabeth II
Gouzolo of Spain
Rupert
Alfonso of Spain
Tsarevitch Alexis of Russia
Henry of Prussia
Waldemar of Prussia
George VI
Leopold of Battenburg
Maurice
George V
Leopold of Albany
Edward VII
Affected Male
Carrier
Queen Victoria

X Marks the Spot

By Carol Floyd

The X chromosome in males is the weakest link for genetic disorders



Randy Padorr-Black

A small boy thrashes about on the floor, his twisted body out of control as he bites off his lips and fingertips. His self-abusive, compulsive behavior is the result of a progressive disease that will eventually kill him.

Another child is born who appears to be a normal female. She will have normal female genitalia and breast development and think of herself as a woman. Yet she will never have menstrual periods or reproduce because she is genetically male.

Each of these children is a product of imperfect genetic coding, victims of inherited diseases known as X-linked recessive conditions. Either they received a defective gene from their mothers, or they developed from an egg or sperm that underwent a new mutation. This group of disorders primarily strikes males. Females are protected against inherited disorders by their genetic make-up. X-linked disorders cut across the disease spectrum ranging from trivial ones like color blindness to devastating conditions like Lesch-Nyhan syndrome, characterized by self-mutilation such as lip-biting.

At conception a child gets a complete set of 46 chromosomes, half from the mother and half from the father. In genetic terms, the basic difference between males and females is in their sex chromosomes. Females have a matching pair, two X's, and males have a mismatched pair, an X and a Y. There are few genes located on the Y chromosome, and the only one scientists are certain of is a gene that causes the development of testes. However, there are many genes located on the X chromosome and these may be the cause of any of hundreds of X-linked recessive disorders. Inheritance of these diseases is governed by the inheritance of the X chromosome. A daughter receives an X chromosome from each parent; a son receives one from his mother only.

"Conditions that are so-called sex-linked are really X-linked because the gene is on the X chromosome. They are linked to sex in the sense that they appear in males who have the X chromosome that has the abnormal gene on it, and the Y doesn't have the normal genes that can counteract the effect," says Dr. Mary Jo Harrod, associate professor of Obstetrics and Gynecology at The University of Texas Health Science Center at Dallas. "A female who has a single abnormal gene on the X chromosome but has another X with a corresponding normal gene, generally won't display any effects of it, although she is a carrier."

In the last 25 years, medical genetics has evolved into a science dedicated to diagnosing and treating genetic abnormalities. Medical tools are now available to detect defects in developing fetuses, provide alternatives to parents who fear giving birth to deformed or diseased children and treat a wide range of disorders.

Any disease having a genetic cause will belong to one of three groups:

- single gene defects called autosomal dominant, autosomal recessive, X-linked dominant or X-linked recessive;
- multigenic or polygenic defects involving two or more genes;
- chromosomal abnormalities.

About five percent of all births involve mental retardation and/or physical defects, many of which have genetic causes. One-fifth of all birth defects are due to single gene abnormalities. Of these, about seven percent are X-linked recessive, according to Dr. Jan Friedman, chief of Clinical Genetics, Department of Obstetrics and Gynecology.

"There really aren't examples yet (of genetic diseases) where we can take out the abnormal gene and put in a good gene," says Friedman. "There are some examples where we can put in good gene products. Hemophilia is a perfect example. People with hemophilia lack factor VIII, one of the proteins involved in blood clotting so the treatment is to give them what they lack.

"The hope for this kind of disease lies in treatment and counseling, not in a cure. There are very few things doctors cure anyway, most of what we do is treat. Some genetic diseases are treatable, and counseling may prevent recurrence of a problem in families."

Genetic counseling offers options to couples once a diagnosis has been made. If a woman is known to be a carrier of an X-linked disorder or if an affected man plans to reproduce, counselors calculate the chances of their having affected offspring. "We don't tell anybody not to reproduce. We tell them what the risks are," says Friedman.

Carrier women will transmit the X chromosome bearing the abnormal gene to half their daughters, who will be carriers, and to half their sons, who will be affected. However, not all affected males have carrier mothers; some are the victims of new mutations.

"If an affected male is able to reproduce, the only chromosome he can give his daughter that's going to make her a daughter is his X," explains Harrod. "One characteristic of X-linked inheritance is that males never transmit the condition to a son. But if a male is affected, all his daughters would be carriers."

X-linked recessive diseases occur rarely in females. Females with Turner syndrome are born with one X chromosome and no Y; this condition may predispose them to

Duchenne muscular dystrophy or hemophilia if their single X is abnormal since they lack the second counterbalancing X.

Another explanation for occasionally finding women with these diseases is X-inactivation or Lyonization (named after Dr. Mary Lyon who discovered it) whereby one of the two X chromosomes is inactivated in a cell (either the paternal or maternal X chromosome). That sort of inactivation doesn't occur with any of the other chromosomes. Since both X's are necessary for development of the ova, both are active in the ovaries.

"X-inactivation acts in the individual cell. For instance, if a woman is a carrier, she has one normal X chromosome and another chromosome that has an abnormal gene for muscular dystrophy or hemophilia," explains Friedman. "Each individual cell expresses only one of these two X chromosomes. If by chance the majority of her cells in the tissue that makes factor VIII are switched off and the abnormal chromosome is switched on, then that woman will have hemophilia. So, it's possible, although rare, for a woman to have an X-linked disease. On the average 50 percent of her cells are turned off, and 50 percent are turned on for either gene.

"If it weren't for X-inactivation, females would have double doses of all the enzymes and all the other products that are coded on the X but regular doses of products produced by genes carried on all the other chromosomes. Metabolically there would be an imbalance. So early in embryogenesis each cell in the female chooses one X chromosome to activate, and all the other X chromosomes get turned off."

Some of the more common X-linked conditions are hemophilia, Duchenne muscular dystrophy, color blindness and a form of mental retardation. Less common are cases of sexual ambiguity accompanied by a variety of defects ranging from normal male genitalia but lack of sperm to testicular feminization in which the genitalia are female but the genotype is male.

Hemophilia is a blood disease in which the blood fails to clot and abnormal bleeding occurs. Patients now receive frequent low doses of factor VIII at home, reducing hospitalization substantially.

Duchenne muscular dystrophy, a condition characterized by the wasting away of muscles, is usually fatal in the teen years.

X-linked mental retardation is as common as Down syndrome in males and may account for 25 percent of the retarded male population according to Dr. Patricia Howard-Peebles, associate professor of Pathology, director of the Cytogenetics Laboratory at Southwestern and a researcher in the field of X-linked mental retardation for 10 years.

"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, one of the world authorities on fragile X chromosome. "The problem is being sure the fragile X will be expressed (in the laboratory) if present. Each lab must follow a procedure that will give reliable results each time it is used."

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."

The researcher has studied 25 families with the fragile X chromosome.

"If a female is a carrier, you would expect half her sons to get the disorder and half not," says Howard-Peebles. "However, initial segregation analysis in these families indicates only about 0.4 of males have it and about 0.6 do not. Two-tenths of the unaffected males got the gene but do not express it. Their daughters would then become carriers with half a chance of passing it to their sons. All sons of a carrier male are free of it – they are the only ones we can be sure are free of it.

X-linked mental retardation is as common as Down syndrome in males and may account for 25 percent of the retarded male population.

"With most X-linked recessive disorders, you tell non-affected males they're free of it. Apparently, the fragile X syndrome doesn't follow that criteria – nonaffected males may actually be carriers. But when you test these males in the lab, they don't express or show the fragile site, just like some carrier females who are normal and do not express the fragile X."

Carrier testing in females is not completely accurate. It is estimated two-thirds of female carriers are normal; the remaining one-third have some mental disability.

"The interesting thing when comparing mildly affected and normal females is that in the mildly affected you can usually show the fragile site on the X chromosome. In normal females you may or may not show it," says Howard-Peebles.

Testicular feminization is perhaps the best example of an X-linked recessive condition that involves sexual differentiation, says Friedman. People affected with this disorder look like normal females although they don't have much pubic hair or have menstrual periods. Breasts and external female genitalia develop. Internally, they have no ovaries or uterus and only a partial vagina.

"What they do have is testes," says Friedman. "They're genetic males, gonadal males; but phenotypically their body is female. Many have a very exuberant female phenotype – very large breasts and extremely feminine physiques. Some are beauty queens."

This condition is due to lack of a cell receptor for a specific androgen, a male hormone that makes the body assume a male phenotype. The gene for receptors is carried on the X chromosome. Drs. Jean Wilson and James Griffin in the Department of Internal Medicine were responsible for finding this receptor defect.

"The genitalia in the early embryo are indifferent. Unless stimulated in a certain way, they will become female genitalia. To be stimulated to become male genitalia, there has to be a message for labial-scrotal folds to fuse into a scrotum and for the phallus to grow into a penis. That message comes through a cell receptor. If the receptor isn't there, the message isn't received, the genitalia remain female, and they become girls," explains Friedman.

Part of the treatment is to remove the internal gonads. Otherwise there is a high risk of cancer. These patients must also receive estrogen therapy for life.

Reifenstein syndrome produces individuals with less severe manifestations of sexual ambiguity. Instead of being completely non-functional, the receptor is partially functional so that the male genitalia don't differentiate completely.

"These people are incompletely masculinized. Externally, the penis may be small and the urethra doesn't open on the end, it opens in the middle, halfway between what you would expect for a male and what you would expect for a female," says Friedman.

The treatment for these problems is usually urological surgery. "These cases are much more difficult than testicular feminization because with that, you don't have to do anything with the genitalia. They think of themselves as females and

are perfectly functioning females. With Reifenstein syndrome, they may not be able to function normally as males but the genitalia are more male than female, and they think of themselves as male," says Friedman.

If a baby is born with ambiguous genitalia, it is usually easier to reconstruct the genitalia so that the baby is raised female, says Harrod.

"Sometimes a baby's penis is so small you can't tell what it is, and surgical urologists aren't that successful in making a penis. It is not that difficult to surgically construct a vagina that will function perfectly normally.

"You could take a perfectly normal XY male individual and make a functional female out of him. She would not be able to reproduce; but as far as functioning sexually, she would not know the difference nor would her partner," Harrod continues.

"It is much more difficult to take a male with abnormal genitalia and make him a functional male. Even though the identification may be male, if he can't function physically, he usually ends up an unhappy person." Even so, ethical beliefs may make the decision difficult for some families.

Probably one of the most distressing situations parents can face is not knowing what sex their child is, she says.

"The first question they want an answer to is 'Is it a boy or a girl?' If the doctor hedges, you know you've got a problem."

Carrier testing is possible to determine whether a female carries an abnormal gene for some X-linked recessive disorders. Yet the inaccuracy of testing makes it impossible to detect all carriers.

"There are always families who have no way of knowing whether a gene is present in the family," says Harrod. "Most of the families we see where a child is diagnosed with hemophilia or Duchenne muscular dystrophy have no family history."

The carrier test for hemophilia, for example, checks the blood for factor VIII, one of the proteins involved in blood clotting, which is what hemophiliacs lack. This test is roughly 75 percent accurate. Normal individuals produce 100 percent of the factor VIII they need whereas hemophiliacs produce zero.

In the case of Duchenne muscular dystrophy, doctors test blood to detect an enzyme that indicates muscle damage. Yet false results can occur making the test only 75 percent accurate.

"One problem with most carrier testing is you are not really looking at the gene, you're looking at some effect of the person having the gene," says Harrod.

Since males with Duchenne muscular dystrophy usually die before reproductive age, they cannot pass the abnormal gene on to the next generation. So new mutations continue to occur in the sperm or ovum, otherwise the gene (and the disease) would soon die out.

When a new mutation occurs in the X chromosome, a male can be affected even though his mother is not a carrier, or a female becomes a carrier even though no one in her family was. "The parents' genes can be normal, yet in the formation of either the egg or sperm, an alteration in one of the genes occurred, and now it is abnormal. This is rather common in a number of X-linked recessives. With Duchenne muscular dystrophy, about one-third of the cases are due to a new mutation," says Friedman.

Making an accurate diagnosis is critical to providing counseling for all genetic disorders.

Some patients the clinical geneticists work with are pregnant women who have already had a child with an X-linked inherited disease. Often the pregnancy was unplanned, and under such circumstances many women fear continuing the pregnancy without some assurance the baby will be normal.

"You could take a perfectly normal XY male individual and make a functional female out of him. She would not know the difference."

Amniocentesis (withdrawing fluid containing fetal cells from the uterus for testing) tells the parents the baby's sex. Knowing whether the baby is male may influence them to abort if the mother is known to be a carrier for a particular X-linked condition.

The major problem in prenatal diagnosis of X-linked conditions is that even if a woman is known to be a carrier for Duchenne muscular dystrophy, there is no way to determine whether the fetus is affected. "If it's a male, there's a 50/50 chance it's affected. A woman then has the option of terminating the pregnancy. But it's a horrible decision to make because you still have a 50/50 chance that it's a normal child," she continues.

Adds Friedman: "This is a circumstance in which people frequently change their minds about abortion because of the uncertainty. We've had patients who have brothers with muscular dystrophy and go into the pregnancy saying, 'There's no doubt if I have a boy, I will terminate the pregnancy.' Then they can't do it, knowing there's a 50 percent or greater chance the boy might be normal.

"And there are women who say they don't like abortion and want the test hoping it will reassure them. They find out it's a boy and can't continue the pregnancy."

In the case of hemophilia, once the baby's sex is determined through amniocentesis, a woman may be referred for further prenatal diagnosis to determine whether a male fetus is affected. Fetoscopy, a relatively risky procedure, allows doctors to obtain a fetal blood sample, which can be tested for the clotting factor involved in hemophilia.

One problem with amniocentesis is the length of time required to determine results.

"Technically the earliest we can do amniocentesis is the 16th week of pregnancy, and it takes another three weeks to get the results. By that time, a woman is half-way through her pregnancy," says Harrod.

Researchers at the medical school and elsewhere throughout the country are working to develop a prenatal test – chorion biopsy – that could be done earlier in a woman's pregnancy. The procedure involves inserting a catheter through the cervix and taking a tiny piece of tissue from the chorion (one of the outer membranes around the embryo). Cells are then cultured from that sample, or tests could be made directly on the tissue sample.

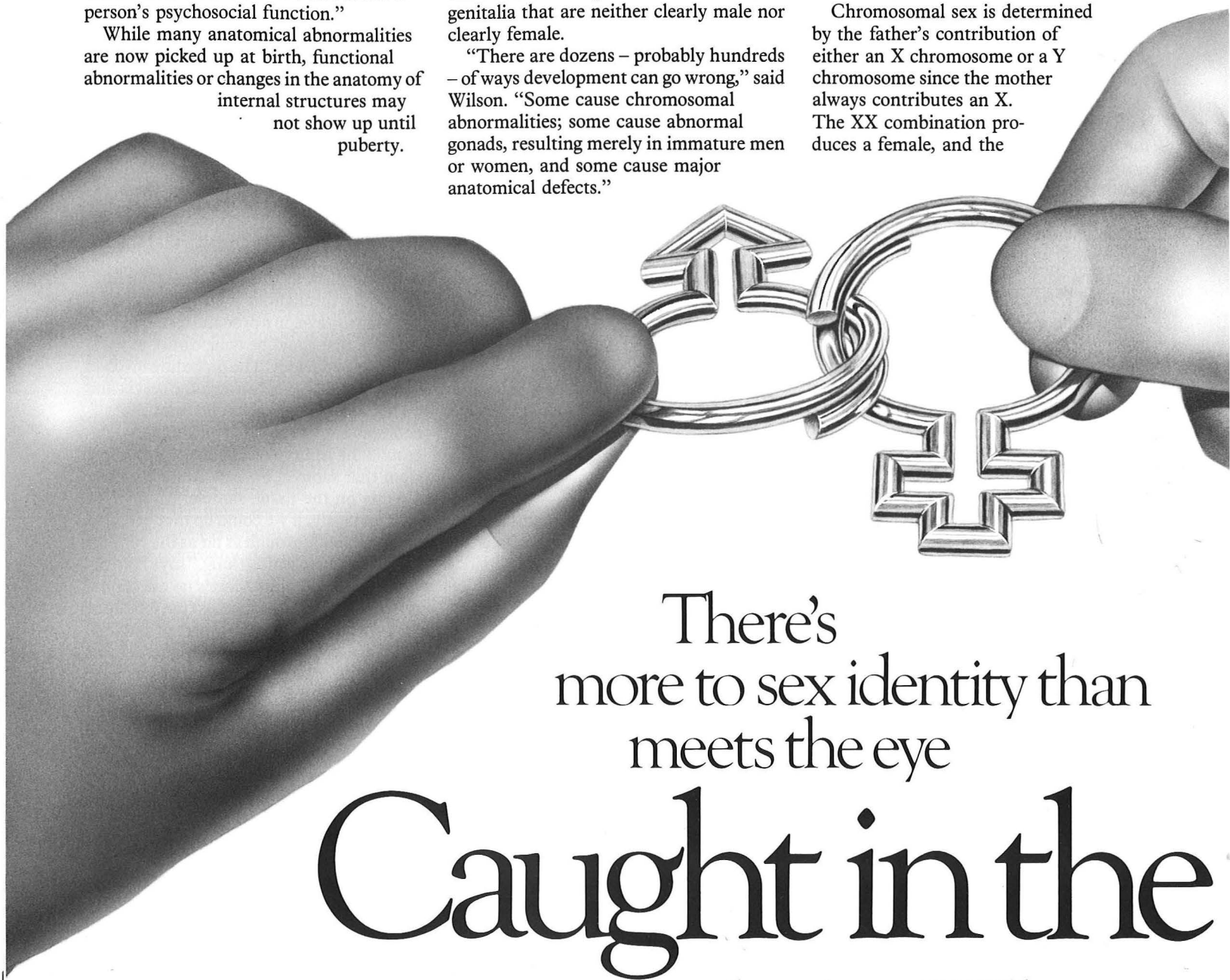
"Obviously, if we could do that, it would be a real breakthrough as far as the concern about having to wait so long," says Harrod. "Technically, I think there's no question it can be done. The question is 'Can it be done safely?' You are sampling part of the fetal structure, the part that is going to become part of the placenta. Most of the testing so far has been on pregnancies that weren't going to continue. So the question is 'Can you do this on someone who wants her pregnancy to continue and not interfere with it?'"

Prenatal diagnosis, abortion, adoption and perhaps even egg donors are options a woman has if she is a carrier of an X-linked disorder. Of course, the couple can also choose to have no children. "The risk is 50 percent for any pregnancy that is going to produce a male child. And at this point we do not know of any way to influence prior to conception or at the time of conception whether the baby is going to be male or female," says Harrod.

Caught in the

There's more to sex identity than meets the eye

by Ann Williams



"Is it a boy or a girl?"

The first question the parents ask is usually easy to answer. But sometimes the answer is, "I don't know. Additional testing will have to be done before I can say."

About four in 1,000 newborns have some degree of incomplete sexual development. At Parkland Memorial Hospital among 10,000 newborns each year, two to four infants with severe abnormalities are seen. These are abnormalities of the external genitalia.

"There are two kinds of sex – anatomical sex and functional sex," said Dr. Jean D. Wilson, professor of Internal Medicine at The University of Texas Health Science Center at Dallas. "Minor anatomical abnormalities in function don't affect a person's psychosocial function."

While many anatomical abnormalities are now picked up at birth, functional abnormalities or changes in the anatomy of internal structures may not show up until puberty.

One of Wilson's intersex patients was raised as a woman but became virilized as an adult. She now has a normal size phallus and would like to live as a man. But she's worried about losing her job and her retirement benefits if she were to change her gender role and consequently continues to live as a woman. "It is a tragic situation," said Wilson. "That's why sexual abnormalities should be detected as early in life as possible."

If a newborn has a major abnormality of the genitalia, it may not be obvious whether the baby has a very small penis or a very large clitoris. Since the external genitalia of both males and females evolve from the same fetal structures, disorders of anatomical development can result in genitalia that are neither clearly male nor clearly female.

"There are dozens – probably hundreds – of ways development can go wrong," said Wilson. "Some cause chromosomal abnormalities; some cause abnormal gonads, resulting merely in immature men or women, and some cause major anatomical defects."

Some of the abnormalities are inherited. Disorders involving the sex chromosomes may be caused by viruses, drugs, virilizing agents or environmental factors. Some birth defects are caused by several factors.

Fetal Development

"The model we use for normal sex development is that described by Alfred Jost," said Dr. James Griffin, associate professor of Internal Medicine. "Normally, chromosomal sex, which is established at conception, determines gonadal sex. Gonadal sex in turn causes the development of phenotypic sex (sex as it appears physically). A disturbance of any step in this process of fetal development may result in a disorder of sexual differentiation."

Chromosomal sex is determined by the father's contribution of either an X chromosome or a Y chromosome since the mother always contributes an X. The XX combination produces a female, and the

XY causes male development. For the first 40 days after fertilization, male and female develop identically.

The second stage of differentiation involves the conversion of the "neutral" gonad into either a testis or an ovary. A gene on the Y chromosome is necessary to produce a testis; and the hormones produced by a testis are necessary for male development. If an ovary is produced or there is no gonad, the anatomical development will be female.

In fact, at any stage of development, if there is no male hormone present and active, female development follows.

Once differentiated, the testis or the ovary starts producing hormones that enable further sexual development.

Normal internal "plumbing" is essential to fertility, and fetal hormones determine which kind of plumbing develops.

There are two sets of ducts that exist side by side in the early embryos of both sexes, said Wilson. In the male, one set of ducts develops into the system responsible for the transport and ejaculation of sperm. In the female, the other set of ducts develops into the structures responsible for the nurture of the fertilized ovum.

In contrast, the external genitalia and urethra develop from structures common to both sexes.

Development of the male anatomy requires the action of three hormones. Two of the three – mullerian-inhibiting substance and testosterone – are secreted by the fetal testis.

Mullerian-inhibiting substance causes the degeneration of the female ducts while testosterone promotes virilization in two ways. It stimulates the differentiation of the internal duct system, and it is changed into the third fetal hormone – dihydrotestosterone – which causes formation of the external male genitalia.

Wilson; Dr. Frederick George, research assistant professor of Cell Biology and Internal Medicine, and Dr. P. K. Siiteri (now at University of California, San Francisco) were first to describe the secretion of testosterone by the fetal testis. Wilson also characterized the enzyme 5 alpha-reductase, which is responsible for the conversion of testosterone into dihydrotestosterone.

Secretion of testosterone by the fetal testis and of estrogen by the fetal ovary peaks by the eighth to tenth week. And both the male and female phenotypes are largely completed by the end of the first trimester.

In addition to physical development, there is another type of sexual development, said Wilson. "Hormones probably play a role in the development of gender identity and role. There's more controversy over this. Some think everything is learned. Most think male hormones are necessary to male behavior."

Lewis Calver

Gender Trap

The endocrinologist defines *gender identity* as "the experience of oneself as male, female or ambivalent." *Gender role* is composed of "behavior that indicates to others the degree to which one is male, female or ambivalent." The patterns of gender role behavior vary from one society to another.

There is no evidence that abnormal sexual development is related to sexual preference – heterosexuality, homosexuality or bisexuality. And people who choose to have "sex change" operations usually do so for psychological reasons, not because their chromosomal and phenotypic sex differ.

Many genetic disorders related to testosterone synthesis and action have been discovered, but until now no such disorders involving estrogen have been found. "This implies that estrogen action is essential to life itself," said Wilson. If there are defects in estrogen formation or action, they may block the implantation of the embryo and thus be lethal. "In contrast, androgen action is not necessary for survival of the embryo."

"Normal sexual development is essential to the survival of the species but not to the life of individuals," said Griffin. "In contrast, developmental defects in organ systems essential to life frequently result in abortion or early death. Individuals with even the most serious abnormalities of sexual development survive and usually come to the attention of physicians."

At Parkland when the neonatologist sees an abnormality of the genitals in a newborn, he or she calls on the gender assignment group to aid in decisions regarding treatment. The group includes Griffin; Wilson; Dr. Jan Friedman and Dr. Mary Jo Harrod (genetic counselors); Dr. James Marks, pediatric endocrinologist; a pediatric urologist and a pediatric gynecologist. The specialists work with the parents in making a decision about how the child will be reared – whether as a boy or as a girl.

"We try to deal with this decision as much as possible while the baby is still in the newborn nursery. We want to present the parents with as normal a baby as possible to take home," said Wilson. "After the relatives have been informed about the baby's sex, it is very, very difficult to change the gender assignment. We have seen older children wrongly assigned in other hospitals, and even as young as 18 months old, it is exceedingly difficult to change.

"A couple came to us from Baja California with a baby mistakenly assigned as a boy. He had been evaluated in Mexico City by a very good group who told the parents it would be more appropriate to rear the child as a girl. The parents spent every penny they had to come here for a second opinion. They literally rode seven days on the bus.

"We agreed with the opinion of the Mexico City group. The parents were heartbroken. Dr. (Terry) Allen wisely refused to do the surgery until after they had changed the gender assignment – told everyone, changed the clothes, the toys and so forth. That was a year ago. We haven't heard from them."

Gender assignment of babies with ambiguous genitals is based on physical examination, hormone levels, radiological studies of internal organs and chromosome studies.

"In general, since functioning as a male requires the presence of a phallus, if there is not enough tissue there, the child will probably be raised as a female," said Griffin. "The decision is largely based on anatomy. And the decision should be made before the baby is taken home from the hospital. If the decision is postponed, it causes confusion among relatives and in the patients themselves. We may have more information for genetic counseling later if the abnormality is hereditary, but we usually obtain enough information to make an immediate decision about the baby's gender assignment."

"Molecular defects can be propagated in tissue culture and studied from skin biopsy. It's not necessary in every instance to study the patient."

In addition to the need for an immediate decision to aid normal psychosocial development for the baby, the physicians need to identify ahead of time any hormone treatments that will be needed at puberty. They also need to plan any necessary surgery. "This should be done before children start to school so they won't be embarrassed to urinate in front of others," said Wilson.

Disorders at Puberty

Some sexual abnormalities do not show up until later in life.

At puberty a girl may not begin to menstruate nor develop breasts. Or a boy might experience breast development and have no facial hair.

Klinefelter syndrome is the most common major abnormality of sex development, occurring in about one in 500 men. Boys with this chromosomal disorder appear normal except for small testes.

After puberty men with Klinefelter syndrome are usually infertile and undervirilized and experience breast enlargement. However, they function sexually as normal men.

Another chromosomal disorder is the most common abnormality that occurs with failure to menstruate – gonadal dysgenesis (Turner syndrome). This disorder is sometimes identified at birth because of other associated abnormalities – webbing of the neck, low-set or deformed ears and low birth weight. Incidence is estimated at one in 2,500 newborn females.

At the time of expected puberty, the patient experiences amenorrhea (failure to menstruate) and lack of breast development and is short in stature. Estrogen replacement therapy induces maturation of the breasts, labia, vagina, uterus and fallopian tubes. The growth rate usually doubles within the first year of estrogen therapy, but the woman never reaches her predicted height.

The second most common cause of amenorrhea is congenital absence of the vagina. Most of these patients are diagnosed at time of puberty when they fail to start menstruation. They appear to be developing as normal females with the growth of breasts and axillary (under the arms) and pubic hair. Height and intelligence are normal. The uterus may vary from almost normal to absent. The condition may occur sporadically or in families.

The third most common cause of amenorrhea is a form of intersex in which genetic males do not develop as normal men. Several defects can result in this problem.

Research work at the health science center focuses on the latter group of patients, most of whom have single gene defects. "It's easier to study genetic defects," said Wilson. "Molecular defects can be propagated in tissue culture and studied from skin biopsy. It's not necessary in every instance to study the patient. We have studied biopsies from all over the world."

Fibroblasts grown from a piece of genital skin three or four millimeters in diameter can be studied for several years. The samples are kept frozen, and when a new test is developed, they are thawed and tested again.

The group has been sent skin biopsies to test for 5 alpha-reductase and androgen receptor deficiencies from patients in Australia, the United Kingdom, Cyprus, the Dominican Republic, Malta, Egypt, Jordan, Pakistan, and many areas of North America.

Testicular feminization is one disorder that results from a lack of cell receptors for androgens (male hormones). Patients with this disorder are chromosomally male and have testes and normal male hormones. But due to a lack or abnormality of cell receptors, androgens cannot affect the fetal cells to cause male development of the genitalia. Therefore, affected individuals develop as phenotypic females. This occurs once in every 20,000 to 64,000 male births.

Patients with testicular feminization tend to be rather tall, and bone age and intelligence are normal. Behavior is unmistakably female, and patients may be voluptuous due to over-production of estrogen.

Since the testes are similar to undescended testes, they frequently develop tumors after puberty.

"We tell these women that there is something wrong with their gonads, which will never be normal and should be removed because they tend to cause tumors," said Wilson. "Also they will need replacement hormone therapy for the rest of their lives. They look like women, they adjust beautifully, and they make wonderful adoptive mothers."

Wilson never tells the patient that she is genetically male because he feels that would be devastating. She has been reared as a female, and her gender identity and gender role are female.

Most androgen resistance disorders result from the mutation of a single gene. Disorders that occur because of a lack of cell receptors for androgen are X-linked, that is, the gene is a part of the sex-determining chromosome contributed by the mother. In those resulting from an enzyme deficiency, the gene is "autosomal recessive," that is, the gene is a part of a chromosome that occurs in pairs in both sexes. To have this abnormality, the individual would have to receive the gene from both parents.

"We started with testicular feminization," said Wilson. "With more and more subtle techniques, we found more and more subtle defects. These range from testicular feminization to infertile men."

Griffin and Dr. James Aiman (now at Medical College of Wisconsin) found that an androgen receptor deficiency accounted for infertility in more than 40 percent of the men seeking treatment for infertility who had an absence of sperm for no previously known reason. This makes infertility the most common receptor disorder.

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For receptor disorders there is currently no treatment although they could possibly be overcome by high levels of the hormone.

In families with Reifenstein syndrome, another cell receptor disorder, individuals can vary from men with large breasts and no sperm to women with pseudovaginas. The most common phenotype is a man with a hypospadias (urethral opening on the underside of the penis) and gynecomastia (abnormally large breasts). Since the psychological development in most is male, the hypospadias should be corrected surgically. If the testes are in the abdominal cavity, they should be either brought down into the scrotum or removed. The only successful form of treatment of the gynecomastia is surgical removal.

A deficiency in the enzyme 5 alpha-reductase results in similar clinical manifestations but a different kind of problem of gender identity at puberty when girls suddenly develop penises.

From studies in animals and embryos, Wilson had predicted this abnormality in humans when in 1974 he and Dr. P.C. Walsh were presented with two Dallas sisters with the problem. The same year Dr. J. Imperato-McGinley of Cornell described a large family in the Dominican Republic with 5 alpha-reductase deficiency. Occurring much more commonly in societies in which close relatives marry, the disorder is so common in the Dominican Republic that there is a word for the syndrome that translates "penis at 12."

These individuals have the appearance of females but with a blind-ending vagina. They have well-developed testes and normal male internal organs. This disorder would be expected in a male with normal testosterone production, normal cell receptors and an enzyme deficiency because the abnormalities occur in the structures created by the action of dihydrotestosterone on fetal structures. Wilson had predicted this disorder would occur if an individual lacked the 5 alpha-reductase required to convert testosterone to dihydrotestosterone.

Studies have been done at the health science center on different types of 5 alpha-reductase mutations. Dr. Mark Leshin, assistant professor of Internal Medicine, working with Griffin and Wilson, has found that some affected individuals have a normal amount of 5 alpha-reductase, but the enzyme has a subtle defect that keeps it from working.

Since estrogen production is related to testosterone levels, and the testosterone levels are normal for men, the estrogen levels are also normal for men. So no breast development occurs.

The formation and function of the sexual phenotype is exceedingly complicated, says Wilson. Sometimes sex is a question of definition.

With so many physical variations possible, how do the experts define male and female?

"My definition is that it depends on the predominant phenotype," says Griffin. "We talk of *women* with testicular feminization, knowing they are chromosomally and gonadally males. But they are *women*, not *females*."

"In most instances, gender identity and gender role correspond to the predominant anatomic sex. But there are exceptions that make it impossible to define a single set of criteria for such a designation," says Wilson.

Gender may be in the eye of the beholder, he says. However, the gender the world sees may differ from that in the individual's own mind, that seen under the microscope or that determined by hormones. "It's complicated."

It is for this reason that he has opposed the use of chomosome tests at the Olympic Games.

"Some people misidentified (at birth) are revealed to the world – and themselves – as something other than what they thought they were. A Polish woman runner at Munich was identified as a 'man.' Her fiance broke their engagement. She didn't know she was genetically male.

"People who favor these tests believe that the Communist block countries were entering a lot of men as women. I think anybody who cares enough to compete as whatever sex should be allowed to do so. I'd rather let a few abuse the games than cause the pain that is inflicted on those who have been misidentified. It has a shattering psychological impact."

READY, WILLING BUT UNABLE

Specialists bring sexual problems in out of the cold

by Ann Harrell

"Most of sex is in the mind: the act itself is just a little friction with rather basic equipment," says Dr. Kenneth Altshuler. But when something goes wrong – something with the mind, something with the body, or, as in most cases of sexual dysfunction, something with both – the result is unhappiness.

Sexual dysfunction can be a problem for anyone at any age, says Altshuler, professor and chairman of the Department of Psychiatry at The University of Texas Health Science Center at Dallas. In either sex it can range from a simple lack of sexual desire to inability to reach orgasm. A woman might find intercourse painful or without pleasure while a man could be plagued with a broad spectrum of sexual complaints. These may include premature ejaculation, retarded ejaculation and impotence, which seems often to be the most frightening possibility of all.

Unfortunately, just naming these dysfunctions brings either comical or cruel stereotypes to

Dave Gresham

In the past experts would say that sexual dysfunction from organic causes was as little as 10 percent, but it is often difficult to separate the organic from the non-organic causes and one should always be aware of the interplay that often exists between the organic and the functional causes.

mind: The uptight, frigid bride perched on the side of the bed, ankles locked. The pathetic old man who can't "get it up." The young, inept lover who gets so excited he never makes it. The woman who starts screaming the minute a man makes a move. Someone's granny who couldn't possibly be interested. The serious heart patient.

Not only are these stereotypes not funny, but neither do they fit the reality of the situation. Sexual dysfunctions are not limited to the young and inexperienced nor to adults of the older generation. Anyone can develop a sexual problem at any stage of life. In fact, some experts say that at least 50 percent of the population will have a sexual dysfunction at some time in his or her life. And the other side of the coin is that the "stereotype" people may be laughing at – or feeling sorry for – may have a great sex life.

In fact, the causes of most sexual dysfunction – barring major psychiatric problems and physical illnesses – are anxiety and hostility, say many experts. Add a communication block, and the result may be a problem with sexual dysfunction for either or both partners.

"When a couple comes in for sex therapy," says Dr. Gerald A. Melchiode, associate professor of Psychiatry, "first look at the relationship." Melchiode reserves a few hours for consultation for sexual disorders as a part of his therapeutic practice at the health science center. He uses what he calls a "modified Masters and Johnson approach" with most of the patients he sees for sexual dysfunction.

This approach includes couple therapy plus the basic exercises in human sexuality pioneered by these therapists in the '60s. The exercises are used mainly to raise the levels of a couple's sexual responses to each other so that they begin to enjoy sexual intercourse together, either for the first time or to resurrect a sexual closeness that may have been lost.

This kind of therapy, he says, works best with couples who are essentially healthy. It also works best when there is only one problem between them causing a lack of communication.

An example is Laura, a young married woman who left college to support the couple while her husband attended law school. The agreement was that as soon as he finished, she would be free to pursue her own goals. Graduation's coming up, but now Tom tells her that because he's starting his own law office, he needs her to work with him as a secretary since he can't afford to hire one. She's furious with him, but she feels dependent, both emotionally and financially. Although they previously have had a very satisfying relationship, now she can't stand sex with him.

If there seem to be more serious underlying problems between a couple, says Melchiode, he suggests more intensive counseling. And in cases of a serious psychiatric disturbance with one or both of the couple, psychotherapy and often medication are indicated. Of course, if the patient or couple have not been referred by a physician who has already checked out possible physical illness, the therapist should be alert to any symptoms. This is particularly true when the problem is related to impotence.

Medical conditions that can cause or contribute to impotence include vascular, neurologic and hormonal diseases, diabetes, medications such as some anti-hypertensive medications, alcohol and invasive surgical procedures.

Sexual dysfunctions affecting the male include impotence, or erectile dysfunction as it is sometimes called, premature ejaculation and retarded ejaculation. When the man has never been able to maintain an effective erection, according to medical definition, it is called primary erectile dysfunction. When a man has once had the ability to have intercourse and then lost it, he is said to have a secondary erectile dysfunction. Masters and Johnson define secondary impotence as about a 25 percent failure rate at "coital connection."

They define premature ejaculation as the condition in which a man ejaculates before satisfying his partner at least half the time. This definition is a bit vague because it supposes that the partner is generally sexually responsive, orgasmic and cooperating. This many not be the case.

Retarded ejaculation exists when a man can't ejaculate within the vagina.

Dyspareunia, or painful intercourse, rare in a man, is generally considered a woman's sexual problem. Women also may be troubled with vaginismus, an involuntary contraction of the muscles in the outer third of the vagina. Both conditions can be treated medically.

Sexual apathy, defined as a lack of sexual desire or sex drive, is seen in both men and women.

In the past experts would say that sexual dysfunction from organic causes were as little as 10 percent, but Melchiode says that it is often difficult to separate the organic from the non-organic causes and one should always be aware of the interplay that often exists between the organic and the functional causes. For example, Paul, 34, was drinking heavily. After he stopped drinking alcohol, which had interfered with his sexual activity, he remained impotent. Anxiety about his performance caused him to be so afraid of failure that he could not achieve an erection although there was no longer any functional cause for his impotence.

Certain dysfunctions are known to be non-organic. These include premature ejaculation, retarded ejaculation and vaginismus when there is no pain. And there are certain clues to the origin of the problem. For example, does the patient have the dysfunction with only one

Most patients who come for help with non-organic dysfunctions are not suffering from depression but are having interpersonal problems. Often impotence, premature ejaculation, absence of orgasm or lack or sexual desire is an expression of buried anger or hostility toward the partner.

particular partner?

In addition, there are certain tests that can be used to decide whether a dysfunction is organic or non-organic. This is especially true in the case of impotence. Besides a urological exam, the patient may be given a workup to see if his circulation and pituitary/gonadal functions are normal. Sophisticated neurological, urological and sleep labs may play a part in the diagnosis. The recent knowledge that men normally experience erections as a part of the sleep cycle has been a boon to making a determination of organic dysfunction. If a man does not have an erection during sleep, it means he is physically incapable of erection. Unfortunately, science has no such development in studies of women, says Melchiode. There are no similar tests that can be used with the same degree of accuracy to identify physiological causes for female sexual dysfunctions.

When the cause is non-organic, the easiest problems to deal with are those that find their roots in sexual ignorance. Fortunately, few women today believe that sexual enjoyment is something for men only, but this has been common in the past. Sometimes older couples need assurance that sex may continue to be a normal, healthy part of their lives. And if they are having some physical difficulties, some "coaching" may solve the problem.

Melchiode terms some sexual difficulties "situational." Ron, 26, came to see the therapist, complaining of impotence. He reported that the first time he had a problem, he and his bride were spending the night with his in-laws. He was too tense to have sexual intercourse, and that episode led to doubts about his masculinity. The more doubts, the less sex. A session discussing the first episode was all that was needed to solve Ron's problem.

Sophia represents another kind of case, one the psychiatrist calls "learned-social." Sophia did not marry until she was 36. She had lived in a very repressed household with her parents and an older brother and sister, neither married. Kissing had been her only sexual experience before her wedding. Treatment centered on sex education and helping the patient get in touch with her sexual feelings. While women with primary orgasmic dysfunction make up the majority of patients with this disorder, "learned-social" dysfunction is not limited to the female sex. Men, too, may suffer from problems related to their upbringing.

Some impotence is strongly related to depression and is a symptom rather than an illness. The therapist must carefully look at the patient presenting problems of sexual dysfunction, such as apathy or impotence, and make sure they are not a part of a serious depression. Other depression symptoms include increased feelings of guilt and suicidal thinking; difficulty in concentration coupled with decreased energy, weight, appetite, sleep and a sad, depressed or anxious mood.

Most patients who come for help with non-organic dysfunctions are not suffering from depression but are having interpersonal problems. Often impotence, premature ejaculation, absence of orgasm or lack of sexual desire is an expression of buried anger or hostility toward the partner.

The most difficult cases, both to diagnose and treat, says Melchiode, are those in which the problems come from intrapsychic conflicts. In these patients either the sexual acts or the sex organs take on a hidden meaning that he or she doesn't realize. This kind of problem often comes from unresolved conflicts in childhood. Robert's wife complained that her young husband wouldn't have intercourse with her. Together the doctor and patient found that rather than being angry with his wife, Robert was subconsciously afraid of hurting her during intercourse. His fear dated back to a childhood misunderstanding.

Melchiode says that he's seeing fewer young people today than in the past. "And I don't see the simple problems I saw 10 years ago, such as premature ejaculation." This condition, he says, can be treated rather easily.

The reason he doesn't see many of the simple problems?

"I think there are many people out there treating themselves. There are lots of good books available, and the media has made them more acceptable."

However, the psychiatrist does caution against seeking help for sexual problems from "just anyone." "I would never go for treatment to anyone billed as a 'sex therapist'."

Melchiode says one should see a traditional therapist (psychiatrist, psychologist or social worker who has a master's degree and has had special training in psychotherapy) who has had special post-graduate work in dealing with sexual problems. In Texas, he says, the laws on who can practice therapy, including sexual therapy, are loose, "and just about anybody can call him- or herself a 'sex therapist'."

The psychiatrist is one of the founders of the Association for Sex Therapy, Education and Research, an association of sex therapists and sex researchers connected with medical schools, which sets high qualifications.

In the case of certain impotence problems, science, medicine and psychiatry work together. Many patients with medical problems related to impotency choose implant surgery. Melchiode does psychiatric evaluations for Dr. Paul Peters, chairman of Urology, who has done more than 200 penile implants in the last 11 years. Most of his patients are referred by other physicians.

The surgeon believes that many patients who come to him for penile implant surgery can also benefit from psychotherapy. On

Some researchers in implant surgery have reported that some patients have begun having normal erections around the implant following surgery, thus showing that the operation was an expensive placebo. In other cases where the operation is a success but the patient does not resume intercourse, it is obvious that there are also other problems.

the other hand, an implant could help some patients in psychotherapy for impotency problems gain confidence during the course of their therapy and thus help the progress of that treatment. "It is my hope that by combining physiological and psychotherapeutic techniques, many patients may be rehabilitated," says Peters.

Many patients come to Peters because of problems stemming from organic conditions. Others first undergo a number of sophisticated medical tests to make sure that the problem is not caused by an organic disease. Then if he has any question about underlying psychiatric problems that may make proceeding with the surgery undesirable, he sends the patient to Melchiode for evaluation.

"What we want to avoid is finding that the implant treats only a symptom. If surgery is done and anxiety and hostility are the problems, we have done the patient a disservice," he says.

Nor can the patient count on the new implant's working if there are certain kinds of unresolved conflicts going on. Sometimes the sexual partner will refuse intercourse with the patient following the surgery. In this type of case, even though the wife's complaint was sexual before the operation, it becomes obvious that there is some other problem between the couple. Some researchers in implant surgery have reported that some patients have begun having normal erections around the implant following surgery, thus showing that the operation was an expensive placebo. In other cases where the operation is a success but the patient does not resume intercourse, it is obvious that there are also other problems.

Most of the time, says Peters, this kind of situation can be avoided by proper psychiatric examination before the surgery. Unfortunately, not all physicians use psychiatric screening as a part of their patient review process.

If the decision is made to proceed with the operation, the patient is informed about a number of different kinds of implants. These implants may be either solid or inflatable. And they range in cost from $300 to $4,000. Insurance rarely covers the implants, because companies usually consider the surgery cosmetic – a classification Peters finds abhorrent. "Who has the right to say who has intercourse? This procedure should be considered rehabilitation," he says.

The Jonas prosthesis, which Peters says he uses most often, is a malleable rod of silicone with a 99.94 percent silver bar inside. Solid, non-malleable silicone models are less expensive.

The Scott, an inflatable prosthesis developed by Dr. Brantley Scott of Baylor College of Medicine in 1973, is the most lifelike implant. The implant and the surgery and hospitalization together can cost as much as $8,000, making it out of the price range for many. Since there are 11 working parts in the device, further surgery is often necessary. However, the patients who have the Scott are generally pleased with them because of their naturalness.

In general, the body accepts these silicone implants well. However, in cases of infection, the body may attempt to extrude the foreign object. Overall though, Peters says there are few problems. And to give a 22-year-old diabetic patient a chance at a normal sex life – or to revive the sex life of an older devoted couple can be a really positive thing, says Peters. Another type of patient who might profit from this surgery is the spinal cord injury victim.

Less enthusiastic about implants is psychologist Dr. Bob Dain. Dain, clinical assistant professor of Psychiatry, believes that sexual conflicts are only a part of what's going on with the whole person or within a whole relationship.

"Just about all the patients I see have sexual conflicts," says Dain.

"Many of them are related to a low self-concept." Like Melchiode, he thinks that anger is at the bottom of many couples' sex problems.

In addition, Dain thinks our culture places too much emphasis on sexual intercourse rather than developing our natural sexuality.

"Much of the problem of performance comes from anxiety. A man has been conditioned to think he must have a rock-hard organ and maintain it for an incredible amount of time. And the woman may think 'I've got to turn him on so he will get a rock-hard organ and maintain it for a long time, or I'm not a real woman.'

"This is sex like in the porno movies: it's not real life."

People, he believes, do themselves a disservice when they accept this kind of behavior as the standard. Instead, the emphasis in a sexual relationship should be on pleasure, not a fixation on a male erection.

He says working with people on their personal conflicts and opening communication are the best ways to help with sexual problems. "At the root of much sexual disturbance is the belief that we must have love and approval from many people and exclusive love and approval from one particular person," he says. Add problems of low self-esteem, a sense of inadequacy and trouble establishing and maintaining the kinds of relationships people want – these make up the conflicts Dain deals with on a daily basis. Other patients play out their sex problems in the context of the whole relationship, such as making silent demands for certain kinds of sexual communication and then being upset when they don't get what they want.

The psychologist says sex problems are usually secondary.

"I try to help a couple develop positive loving feelings toward each other through the expression of caring behaviors."

Counselor assists handicapped in developing sensuality

SEX: NOT JUST A ONE-ACT PLAY

By Ann Harrell

Ignorance, outdated attitudes and simple lack of information about sex create additional handicaps for the ill and the physically disabled, says a rehabilitation counselor at The University of Texas Health Science Center at Dallas.

Dr. Eugene Swenson, whose areas of expertise include the psychological aspects of disability and sexuality, is associate professor of Rehabilitation Science in the center's School of Allied Health Sciences and of Rehabilitation Counseling in the Southwestern Graduate School of Biomedical Sciences.

Many good rehabilitation programs in hospitals and specialized facilities around the country are adding seminars in sexuality as a part of their total patient program, says the psychologist. However, many more institutions are doing nothing to help patients with physical problems and crippling illnesses maintain healthy sex lives.

"Each individual has to re-learn his or her own sexuality following illness or disability," he says. "The key is helping that patient to broaden his or her personal definition of sexuality.

"Unfortunately in our society, feelings about sex are generally focused on genitalia, intercourse and orgasm. And so much of our sex is connected to our body image. You've seen the billboards with the girls in bikinis – they're saying if you're not one of these perfect bodies, you're less than acceptable."

Instead, Swenson says we should consider sexuality as a dynamic process starting at birth and continuing until death. It is comprised of genetic drive and learning experiences and incorporated into our self-concepts.

"For me, sexuality is expressed through the senses," says the educator.

"Sensuality, or enjoyment of our senses, is a vehicle through which you can express your sexuality. It's personal and individual.

"Intercourse may not always be an option, especially for the handicapped, but you can be sensual in many ways other than having intercourse," says Swenson. "Sometimes a romantic evening with dinner and holding hands can be a satisfying experience in itself. And there are other ways of making love."

Among the problems of patients who may be helped by sexual counseling, says Swenson, are the following:

Spinal cord injuries – Patients may have loss of sensation or altered sensation in various areas of the body. Males may also

lose or have diminished erectile ability. Sometimes penile implants are performed on men who are impotent because of spinal cord injuries and while the operation may enhance the quality of some patients' sex lives, it is not necessary for sexuality.

Arthritis – The arthritis patient may find sexual intercourse painful or may have trouble getting interested in sex because of the pain. Learning when to have intercourse, what positions may be most comfortable and how to coordinate medication and leisure time may prove helpful.

Cancer – Men who have had prostate cancer, which can be sexually as well as psychologically debilitating, may profit from counseling. Some of these patients may opt for penile implants. Women cancer patients who have had one or both breasts removed also have similar psychological problems linked to their body image and sexuality. Those who have had uterine or vaginal cancer may feel loss of their femininity and sexuality. In addition, counseling may prove beneficial to other cancer patients.

Cardiovascular problems – Patients often fear that intercourse will bring on another heart attack. However, those fears can usually be allayed by the patient's personal physician.

Stroke victims – Even though the victim of a stroke may be incapacitated in many ways, love, caring and tenderness can be expressed by touching and talking to the person in a warm voice and by just being near.

Victims of sensory deprivation – This classification includes persons who are blind, deaf or have a loss of feeling from various causes. It is important to remember, the psychologist says, that sensory deprivation doesn't cancel out a person's ability to be sexual, but it does alter it. "In order to understand what it might be like, think of yourself making love without hearing the sounds of love or seeing the person you are making love with or not feeling touch in some parts of your body."

Multiple sclerosis – Swenson calls MS a "teasing" illness. Sometimes the patient is just fine, sometimes the loss of motor control is extreme. Sometimes making love is a lovely, sensual experience; sometimes the sensations are overwhelming.

Myasthenia gravis – Chronic fatigue is a major factor in this disabling disease, and often patients don't feel sexual because of feelings of fatigue.

Victims of bad burns – Often these unfortunate people may have crippling resulting from their burns, loss of sensation in heavily scarred areas and special problems because of altered appearance.

Although serious illness or major disability puts a strain on nearly any marriage, Swenson stresses that it's not just the physical condition that causes problems. Psychologically these problems can be devastating to people. Each partner in a relationship must remember that it's important to work toward not letting the condition – physiological or psychological – ruin what they already have.

"Often the needs of the spouse or partner are not being met in this kind of situation. It is ideal if that person can be included in counseling sessions, too," he says.

Sometimes the able-bodied partner considers, like Ruby in the country and western song, taking her love to town. What does the psychologist think of this kind of solution?

The movie "Coming Home" did a lot for many disabled patients, especially spinal cord injuries. "Lots of the guys got charged up and started wheeling around in their chairs, sometimes getting out for the first time. A few, however, got really depressed. They said they knew someone like Jane Fonda wasn't going to really be available to them."

Swenson thought the movie did a sensitive and realistic job presenting the problems of the disabled veteran, played by Jon Voit.

When talking with a spouse who is considering an outside affair as an option to solving personal sexual problems caused by the partner's dysfunction, Swenson's advice is to stop and take a look at the consequences. How are you going to feel afterward? How will it affect the relationship in the home? Would you tell your partner or live with anxiety and secrecy? How will your mate handle it if you discuss it?

In some cases it may seem that the disabled partner is pushing the other to have an affair. He or she may say, "It's okay; go out – I understand."

"That's bullshit!" says Swenson. "The concept of 'open marriage' made a nice book – but there aren't many people who can do it. It seems to me it's a more healthy adjustment to redefine sex inside marriage."

Again the key is redefining sex and realizing that even if one can't have an orgasm, there are many ways of experiencing pleasure – the process of sexuality doesn't have to be lost.

"Our whole culture is 'fast-food' oriented," he says. "As we grow past the teenage stage, instead of a 'fast-food' experience, sex should become a banquet de-emphasizing orgasm and emphasizing process.

"Part of the rehabilitation process is helping the person interact in the real world." And beginning and maintaining relationships are part of that world.

Of course, it's tough. People who do not have disabilities tend to look at the obviously handicapped as non-sexual people. This, in turn, makes the person with a disability begin to feel non-sexual. It's really easy to get into that kind of negative spiral.

"A young man may meet two young women at once. One is in a wheelchair, and one is not. He may never look into the eyes of the lovely person in the wheelchair and will never know she might be the right person for him."

The movie "Coming Home" did a lot for many disabled patients, especially spinal cord injuries, says the counselor. "Lots of the guys got charged up and started wheeling around in their chairs, sometimes getting out for the first time. A few, however, got really depressed. They said they knew someone like Jane Fonda wasn't going to really be available to them."

Swenson thought the movie did a sensitive and realistic job presenting the problems of the disabled veteran, played by Jon Voit. Ironically, he said, the theater where he saw the film wasn't equipped for persons in wheelchairs.

Overall, Swenson thinks the situation is getting better.

The faculty member is involved in teaching rehabilitation students, counseling, consulting and presenting group seminars. More and more groups and agencies are looking for help in working with patients and their sexuality. Also, he says, good reading materials are now available. All these things are helping to dispel ignorance, outdated attitudes and lack of information. This skirmish in the "sex revolution" can contribute to the handicapped or seriously ill person's living as full and normal a life as possible.

'Tis better to nurture with care just one child Than produce half a dozen and let 'em run wild...

Valentin, "Le Franc Bourgeois," 1706

Any preventive means, to be satisfactory, must be used by the woman, as it spoils the passion and impulsiveness of the venereal act, if the man have to think of them.

Dr. George Drysdale, 1854, England

Fruitless and Fancy-free

Hormones provide long-sought solutions to unwanted pregnancy. What next?

by Susan Rutherford

Contraception is not new. In former times it was blamed for nymphomania and madness leading to suicide, among other things. Even today some consider it "immoral" or "unnatural" – "not to have a baby is to kill a baby." But how many could tolerate paying for pleasure and intimacy with non-stop pregnancy?

Practically speaking, the risk of pregnancy from unprotected intercourse ranges from two to 30 percent through mid-cycle.

Past cultures devised countless novel if misguided methods for avoiding the consequences of sexual enjoyment. Women jumped backwards and did "physical jerks" after intercourse. Or they drank themselves sterile with the mysterious "cup of roots." Substances such as elephant dung, cabbage, animals' earwax, tar, sour oil, honey, cedar gum, rock salt or vinegar have been used at various times.

Withdrawal for husbands and the sponge for wives was "diabolically" recommended in 19th century England by one contraception advocate. The sponge should not "diminish the enjoyment of either party," according to Shirley Green's *The Curious History of Contraception.*

The sponge, says Green, was also used by the Hebrews at the time of Christ. Hebrew men were told to increase and

Some feminists have cried "discrimination" to researchers and those granting money for research. With this charge has come a push for some desirable, effective form of male contraceptive. Females are chosen over males as those responsible for contraception because "it intuitively seems easier to prevent the production of only one ovum per month in the female than to prevent the production of billions of sperm in the male."

multiply and were prohibited from practicing contraception. Nothing was said of the women, however.

The men often kept two wives. One wife was for procreation. The other, kept for enjoyment, drank the cup of root, a concoction of Alexandrian gum, liquid alum and garden crocus, to become sterile.

Infanticide and abortion were so heavily relied upon by the ancient Greeks and Romans that contraception was ignored. Court women of Greece had their ovaries removed, primarily to ensure a trim figure but also to avoid what some have called the "big belly and squalling brat."

The condom, invented just prior to 1706, has always been a source of complaint. Men have lamented that the sheath blunted sensation, whether the material was of the original linen, animal membrane, tortoise shell, vulcanized rubber or latex.

Oral contraceptives, too, have been around for centuries. The Chinese made potions of oil and quicksilver to produce sterility. They also concocted a broth of ingredients that were first marinated in a child's urine.

Twentieth century contraception includes many holdovers from ancient times – spermicidal creams, condoms, the rhythm method, withdrawal.

It wasn't until the middle of this century that two leaders of the feminist movement, Margaret Sanger and her friend Mrs. Stanley McCormack, encouraged the development of the almost foolproof birth control pill for women.

This was the beginning of the use of hormones for birth control.

In the United States the pill gained rapidly in popularity, especially from 1965 until 1975 when its easy-to-use, effective qualities revolutionized contraception. Due to widespread publicity on potentially serious side effects, sales have fallen off in recent years.

The pill's widespread use and subsequent side effects prompted protests from women's groups. They began to ask why they, and not men, should largely bear the responsibility for avoiding pregnancy. Some feminists have cried "discrimination" to researchers and those granting money for research. With this charge has come a push for some desirable, effective form of male contraceptive.

Females are chosen over males as those responsible for contraception, according to Dr. James Griffin, associate professor of Internal Medicine at The University of Texas Health Science Center at Dallas, because "it intuitively seems easier to prevent the production of only one ovum per month in the female than to prevent the production of billions of sperm in the male. Even an 80 to 90 percent reduction in sperm density may not be sufficient to cause infertility."

The one effective, available method of male contraception – vasectomy – is unfortunately difficult to undo, says Griffin.

Reports indicate that men often experience increased sexual enjoyment and frequency of intercourse after vasectomy. "This is probably because men become less inhibited and less concerned about intercourse resulting in pregnancy," says the researcher.

Two major scares have threatened public acceptance of the vasectomy within the past few years. Both are unfounded, according to Griffin. First came a realization that the procedure causes an increase in sperm antibodies beginning seven to 11 days after surgery. This raised the question as to whether there might be a life-threatening reaction in which antibodies would attack the body itself. Two studies involving more than 1,000 men could not show that antibodies were directed at anything other than sperm.

Next came a report showing atherosclerosis (fat deposits in the arteries) in rhesus monkeys that were vasectomized nine to 14 years earlier. While reasons for this are not clear, human studies have not found any increase in heart disease.

According to Griffin, most male contraceptives now being tested produce unacceptable side effects, including decreased sex drive. Some do cause sterility, but some are completely ineffective. Ideally, Griffin says, an acceptable male contraceptive would be something taken by mouth with a rapid onset of action, would not interfere with hormone balance and would have its effect on sperm development, prohibiting sperm maturation or motility. It should also be free from toxic side effects.

For women, particularly those who are young and don't smoke, Dr. Bruce Carr, assistant professor of Obstetrics and Gynecology, favors the pill. The birth control pill, composed of two synthetic hormones, an estrogen and a progestogen, works on the brain and indirectly on the ovaries, preventing ovulation. It is possible that changes at the cervix make the cervical mucus hostile to spermatozoa.

The pill causes transient side effects, which can include those typical of pregnancy – nausea, vomiting, tender breasts, weight gain – as well as nervousness and depression.

There were major health risks when the pill was first placed on pharmacy shelves in the mid-'50s. At the time it was composed of hormones at dangerously high levels. Estrogen was blamed for causing blood clots while both estrogen and progestogen

may have been responsible for an increase in blood fat. This increase of fatty substances in the blood was believed responsible for strokes and cardiovascular disease.

However, the hormone contents of the pill have been decreased and refined. With this change, the mortality rate has dropped. Carr also attributes the lower mortality level to better patient evaluation and knowing when to give another form of birth control to someone at risk.

Today the pill can be used safely by many young women, according to Carr. Findings indicate that the age of menopause is not affected by oral contraceptive use as some had feared.

The pill is not safe, however, for those who smoke or are not in good health. Pill users should not have known or suspected breast cancer, hypertension, thromboembolic disease (as in severe diabetes) or heart disease, active liver disease or undiagnosed vaginal bleeding. They should be sure they aren't pregnant because two studies have indicated that taking steroid hormones during pregnancy can cause cardiovascular and limb defects in the fetus. (Other studies have not observed an increase in such abnormalities, however.)

Carr would not prescribe birth control pills to anyone over 40, but some gynecologists won't give them to women over 35. He advocates follow-up exams every six months to a year for those taking the pill.

The pill has numerous beneficial effects, says Carr. "Benefits associated with oral contraceptives include effectiveness in preventing pregnancy, more so than any other present form of birth control; help in regulating menstruation when cycles are irregular or bleeding is excessive; decrease in incidence of pelvic inflammatory disease; protection against ovarian cysts and a decrease in incidence of fibrocystic disease in the breast, endometrial cancer and cancer of the ovaries."

There are a variety of drugs that may decrease the efficacy of oral contraceptives. Some reports show an increased incidence of pregnancy when antibiotics are used with oral contraceptives. Other studies, however, do not report increased pregnancy in rats. To be on the safe side, some recommend that women using low-dose oral contraceptive pills should use additional protection during antibiotic treatment.

Alternatives to the pill include injectables of progesterone, which have not been approved by the Food and Drug Administration but are widely used in Third World countries. They have been found to induce benign breast tumors in dogs.

There are hormone-releasing implants surgically placed under the skin of forearm or abdomen. They are removed after the hormones have been released with effects lasting from six months to six years. Tests with the implants report bothersome breakthrough bleeding between periods and, at times, a lack of menstruation.

Vaginal rings are a relatively new method for delivery of hormones. Silastic rings are impregnated with hormones – mostly estrogen and progestogens. These are placed in the vagina and fitted like a diaphragm. A ring is used for three weeks and removed for one week to allow for withdrawal bleeding before being reinserted. Now undergoing clinical trials, the ring is not yet available commercially. Problems include expulsion, interference with coitus, odor, difficulty with insertion and occasionally breakthrough bleeding. Rings that can be left in for longer periods of time are also being evaluated.

Then there are steroid-releasing IUDs, developed to avoid "systemic effects of steriods and to increase the effectiveness of IUDs."

Post-coital contraception is appropriate most often in cases of rape. In the past women used douching and intravaginal placement of a variety of drugs and other substances. Modern post-hormonal interception began in the '60s with high-dose estrogens, which caused nausea and vomiting as well as menstrual disturbances. Now a smaller dosage has proved to be as effective and causes fewer side effects.

The brain peptide luteinizing hormone-releasing hormone (LHRH) is being used experimentally in both men and women to reduce levels of sex hormones. Subsequently, the use of LHRH as a contraceptive in men and women is gaining interest. LHRH analogs have various sites of action as potential contraceptive agents, but the primary site is the pituitary. During continuous administration of LHRH, there is a decrease in sex hormones after an initial period of release. Daily nasal administration and also injections of LHRH have been used effectively to inhibit ovulation in women and provide effective contraception.

There are problems associated with the use of LHRH as a contraceptive, however. Since the primary site of action is in the pituitary, LHRH shuts off sex hormone release. In men this causes a diminished libido and decrease in sexual function. Weekly injections of the male hormone testosterone must accompany LHRH. In women the action of LHRH on the pituitary causes a decrease in the ovarian secretion of estrogen. Without estrogen a woman is at risk of osteoporosis (thinning of bones).

Today the pill can be used safely by many young women. Findings indicate that the age of menopause is not affected by oral contraceptive use as some had feared. The pill is not safe, however, for those who smoke or are not in good health. Pill users should not have known or suspected breast cancer, hypertension, thromboembolic disease or heart disease, active liver disease or undiagnosed vaginal bleeding.

Randy Padorr-Black

THE TIE THAT BINDS?

Surgeons gain success in reversing sterilizations

By Liz Willding

The best-laid schemes o' mice an' men
Gang aft agley,
An' lea'e us nought but grief an' pain,
For promis'd joy!
– Robert Burns, "To a Mouse"

Even the feelings and decisions we are most certain about can become altered over the course of time and life changes. Medical professionals now recognize that such is often the case with elective sterility. More and more patients who have chosen to have vasectomies or tubal ligations are changing their minds and wanting to have children. Microsurgical techniques now make it possible for at least some of these people to reverse their decisions.

By far the most common request for a reversal comes from the person who already has children but, having been divorced or widowed and remarried, finds he or she would like to have more, says Dr. Paul Peters, chairman of Urology at The University of Texas Health Science Center at Dallas.

Consider the case of a man in his early 40s, says Peters. The man is divorced but has several children by his previous marriage. At the time he and his wife chose permanent sterilization, divorce may not have been imminent in their relationship. But in the course of time, they parted ways and he remarried, this time to a younger woman in her 20s. His new wife may never have had children and longs to have this experience.

The other side of the coin is the young woman who had her tubes tied in her late teens or early 20s following several pregnancies. Four or five years later she marries a man who has never been a father. They want to share the experience of raising a child they have produced together.

Others may just find that they don't feel the same as when they opted for sterilization. And Peters says there are always cases where a man will submit to a vasectomy when pregnancy may be detrimental or life-threatening to his wife.

Whatever the situation, Peters says the main issue is that "we live in a temporary society. The divorce rate in Dallas is 62 percent. It is over 50 percent in many major metropolitan areas.

"That is something to bear in mind when one is considering a vasectomy or a tubal ligation. Patients should advise their doctors that they firmly feel that they never want to have children again. And that should be the philosophy of the doctor who does the vasectomy. We now advise doctors to do the procedures in ways that lend themselves to reversals, but that doesn't mean it shouldn't be done with permanency as the main objective."

Despite the encouraging percentages of successful vasectomy and tubal ligation reversals, Peters says there are failures. "Even if you do everything right, the couple may never be able to conceive a child." He remembers the case of a young, widowed man who, upon remarrying, wanted to have his vasectomy reversed so

he and his new wife could begin a family. Peters reversed his vasectomy only to have the vas deferens tubes (ductal system that carries the sperm) shut down about six months later. He reoperated and reopened the tubes. Although the patient has since shown promising sperm counts, a pregnancy has yet to be achieved.

"The point of any vasectomy or tubal ligation is to ensure that the individual can never father or conceive a child again. And those are usually the circumstances under which it is done. From a medical standpoint, it is safer to sterilize the male rather than the female because there are less risks from the vasectomy procedure," says Peters. "In either case reversals can sometimes be achieved, but there are certainly no guarantees."

He says that much of what will determine whether or not a tubal ligation or a vasectomy can be reversed depends on how the operation was done and how long it has been since the original surgery was performed.

Tubal Ligation and Reattachment

"Tubal ligations have been done for a long, long time," says Dr. Bruce Carr, assistant professor of Obstetrics and Gynecology. "Tubal reversals have become more popular in the last eight to nine years. There are a whole variety of ways to do both procedures."

At Parkland Memorial Hospital, patients are screened and counseled before being accepted as tubal ligation candidates.

Tubal ligations are not paid for under a federally granted program unless the patient is at least 21, says Carr. Exceptions are made when there are severe medical problems. Examples might be women who have had two or three C-section deliveries, a serious disease or a malignancy."

Carr says that the recommended age for a tubal ligation is 35 and over. But despite this recommendation, he admits that the surgery is usually patient-dictated and the average age is mid-to-late 20s. Parkland averages around 10 tubal ligations a day. Reversals are much less frequent; on the average they are done once a month.

Most of the people who come to Parkland for a tubal ligation are first seen in a family planning clinic. They are evaluated by nurses or doctors and told about other birth control options. Tubal ligation is the last resort – they are told it is permanent and not readily reversible.

Tubal ligations at Parkland are primarily done by ligation (tying off) and resection (removing a section) of the tubes. Carr says some doctors bury the tube endings into the side of the uterus, but this opens up more chance for post-operative adhesions. Many tubals are done postpartum (immediately after a woman gives birth) when the uterus rises high in the abdomen. The tubes are carried up by the enlarging uterus and are easily accessible through a small incision.

Ligating the tubes through an abdominal incision is the preferred method, but Carr says the operation can be done vaginally. "You make an incision through the vagina, grasp the tubes and cut and ligate them just like you can from above. We prefer not to do them this way though because we believe more infections occur."

A common tool that is now used both in tubal ligations and in evaluating women for reversals is the laparoscope. The laparoscope gives a magnified view. "We fill the abdomen with CO_2 and place a large trocar or scope through a small incision in the abdominal area. Then we make another incision or use the same scope to go down and grasp the tubes. We can either burn the tubes or put clips or bands on them to tie them off. It has been thought that clips and bands would make a later reversal easier, but we haven't done enough yet to know."

Tubal ligations usually require a hospital stay of one and one-half to two days. Tubal reversals require five to six days of hospitalization.

Carr says that tubal ligations usually require a hospital stay of one and one-half to two days. Tubal reversals require five to six days of hospitalization. Both procedures are usually done under general anesthesia when the patient is completely asleep.

"With the reversal we have to make a bigger incision and this opens up more possibilities for infection," Carr explains.

He says the success rate for reversing tubals has been reported to be as high as 80 percent. Average is 50 to 60 percent.

"If the woman has less than four centimeters of tube or the fimbria (the fringelike extremity of the fallopian tube) has been removed, the tubal cannot be reversed. If the tubes have been burned, this also decreases the chances of successful pregnancy."

Reversals can be done without loupes (low magnification) or a microscope, but Carr says most studies show that microsurgery techniques do improve pregnancy rates. This is further improved by careful technique.

"We don't use clamps or gauze sponges when we are operating," Carr explains. "We rest the tubes on a Kerlix sponge (a special sponge used in microsurgery) that is soaked in heparinized saline and irrigate the field continuously rather than blotting the area. Very fine suture (sewing) material is used along with microsurgery operating equipment.

"We also inject dye into the uterus to know where the tubal opening is. The number one thing that probably improves the technique is the use of dye."

In the last year Carr has done five reversals.

"Although the chances of having a tubal reversed are better today, I still would not advise anyone to use this as an excuse for having a tubal. Something anyone considering a tubal should also understand is that, as with any form of birth control, there is a failure rate. One in 200 cases of pregnancy still occur after tubal ligation. Probably these failures are due to fistula formation (breaks in the tissue often due to abcess)."

Along with this he cautions that the operation is not risk-free. The death rate is one in 10,000 for those having surgery.

Expense may also be a factor influencing a person's decision. "The average tubal costs $500; a reanastomosis (reconnection) is around $2,500. Most insurance companies will pay for a tubal ligation, but they often consider a reversal to be elective plastic surgery and the patient has to personally bear the expense."

Vasectomies and Reversals

Because tubal ligations present considerably more operative risk, physicians have long recommended vasectomy to couples considering a permanent form of contraception. However, Peters says 35 to 50 percent of all men who have had a vasectomy ask, within 30 years, to have it hooked back up again. Because of this he encourages more conservative operative techniques so those who "want to be rehooked" can be.

The expense of vasectomy is around $500. A reversal can go as high as $3,500. As with the tubal reversals, vasectomy reanastomosis is considered plastic surgery and may not be covered by many insurance policies. Vasectomy reversals are now 90 percent successful with a pregnancy occurring in 50 to 70 percent of the cases.

Both vasectomies and vasectomy reversals can be done as day surgery procedures. A vasectomy takes about 30 to 40 minutes; a

reversal takes two and one-half to three hours. While infection in the genitalia can occur, there are fewer risks in these operations than in a tubal ligation or tubal reanastomosis. "Tubals require invasion of the peritoneal cavity," Peters explains, "which is considered more of a major procedure. The complications in the tubals may be more serious."

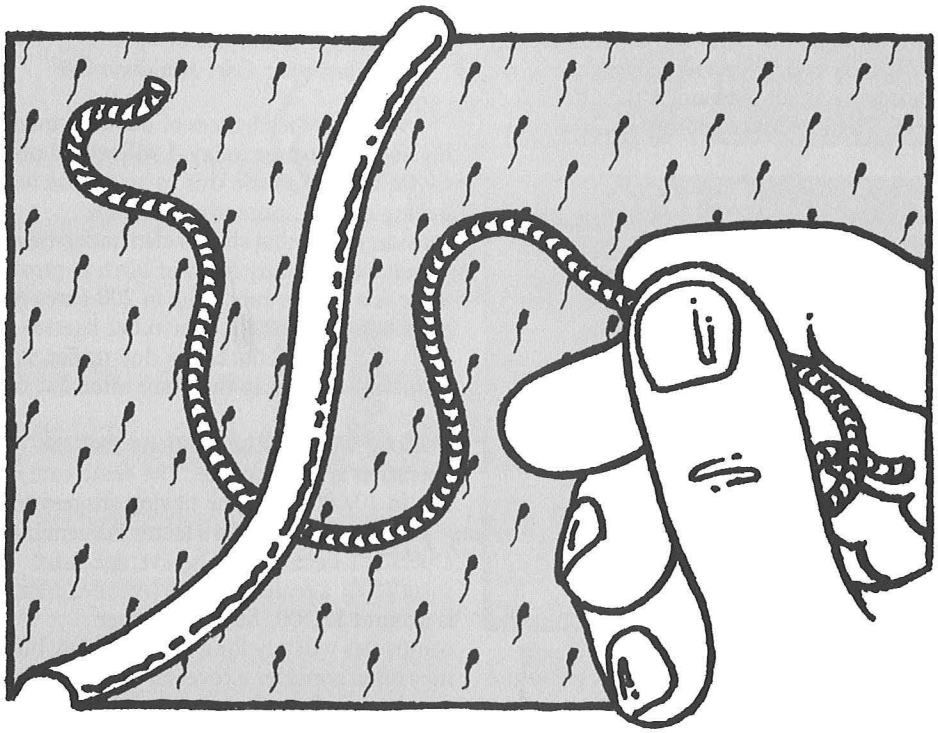
Vasectomies are done by removing a portion of the vas deferens and tying off the remaining ends. The vas deferens originates high in the scrotal sac as a muscular, straight tube; lower in the scrotum it becomes convoluted or twisted and is much smaller in diameter. "We recommend to doctors who are tying off and removing a segment that they do it high in the scrotum where the vas is straight." If the vasectomy is done in this straight portion, Peters says the chances for a reversal are much better.

When reversing a vasectomy, he explained that the vas deferens ends are rejoined first by inserting a stent (support). This stent is made with a small piece of suture material and provides alignment between the severed ends. The suture is inserted through the wall of one end of the vas deferens, threaded through its duct and out its opening, then run through the opening of the other end, and threaded back up and out.

After the stent is in place, the two ends are sewn together along the outside. The patient comes back in two weeks, and the stents are removed. Once the stents are removed, the vas deferens should again be clear and able to provide a passageway for the sperm.

"Vasectomy reversals are generally done with the help of an operating microscope. The procedure becomes more difficult if we've got to try to join a segment of straight vas deferens to a convoluted segment because the convoluted segment has a smaller opening and diameter.

"One of the major problems is that it is much more difficult to put a stent in to provide alignment," he explains. "Sewing the vas in the straight portion is like sewing two pieces of spaghetti together. Sewing a straight portion of the vas to a convoluted portion is like sewing a piece of spaghetti to a string."



Peters says the patient is allowed to go home the same day if he is awake and ambulatory. Pain from the operation can usually be managed with aspirin or an ice bag and doesn't generally last more than 24 hours. "We usually tell them to take the weekend off and rest. I advise individuals who do heavy labor to take a week to 10 days off."

Three months following the surgery the patient returns for his first sperm count measurement. "We usually wait three months since the lifecycle of the spermatozoon is about 90 days – 75 days, plus or minus five days, in the testis; 14 days, plus or minus five days, in the vas deferens." In patients whose vasectomies are reversed after 10 years, Peters says restoration of sperm count is not so good. However, it is still possible in some cases.

"Before 10 years – and there is nothing magical about 10 years, that's just kind of a statistical point in the curve when the range of success begins to diminish – one would be optimistic about restoring continuity of the vas deferens and the sperm count. The motility of the sperm doesn't always come back as good, but it is usually good enough. Realistically it takes about one sperm in 3,000 to reach the cervix and one in 14 million to reach the fallopian tube where the ovum is usually fertilized.

"Men who have counts much below 30 million per cubic centimeter are considered borderline as far as fertility is concerned although many with lower counts than that, 11-12,000 per cc, have fathered children."

When either a woman who has had a tubal ligation or a man who has had a vasectomy begins to consider a reversal, Peters urges that the spouse be thoroughly tested for fertility. "I insist that the wife be examined by a gynecologist and be determined reasonably capable of having an egg fertilized before I perform a reversal. She needs to be able to positively answer, "yes," to three questions: Do you have regular periods? Do you have discomfort or pain midway between periods? Do you have mucous show?

"If she can answer 'yes' to these questions, that puts her in the 95th percentile. She should also be willing to submit to a medical history, a pelvic exam and X-ray studies of the fallopian tubes before asking her husband to undergo a vasectomy reversal. In the same way, a husband should submit to a sperm count test before asking his wife to undergo tubal reanastomosis."

If a couple has difficulty conceiving a child following a vasectomy reversal, Peters has several recommendations for the husband:

- Eat more bananas – bananas contain fructose, the sugar that nourishes sperm.
- Wear boxer shorts – this keeps the scrotal temperature down.
- Avoid hot baths – soaking in a hot tub is an old Japanese trick for contraception. When a Japanese boy is going out on a date, he takes a hot bath. The increased temperature kills sperm.
- Blue ice – sleeping with blue ice in your shorts cools the sperm and preserves it.

While all of these methods may seem farfetched, Peters says heeding these tips has been known to speed up the conception process. "Sometimes when we do a vasectomy reversal, the wife gets pregnant before the husband's first sperm count. Sometimes, even though everything seems to be right, she never gets pregnant. The child is the ultimate result. We can't guarantee that what we do will work every time, but I've got a file full of baby pictures that shows that it just might."

NOT THIS MILLENIUM– I HAVE A HEADACHE

BY BOB FENLEY

Amoebas at the start
Were not complex;
They tore themselves apart
And started Sex.
-Arthur Guiterman, "The Light Guitar"

Sex. Do we really need it?

It is complicated but exciting, frustrating, sometimes painful, pleasurable, often ecstatic and occasionally boring. Why was sex invented anyway?

The most widely held theory is that sex allows a much wider variety of offspring and thereby speeds the process of evolution and the ability of a species to survive. According to noted geneticist Theodosius Dobzhansky, there are at least 20,000genes in the human sex cell.

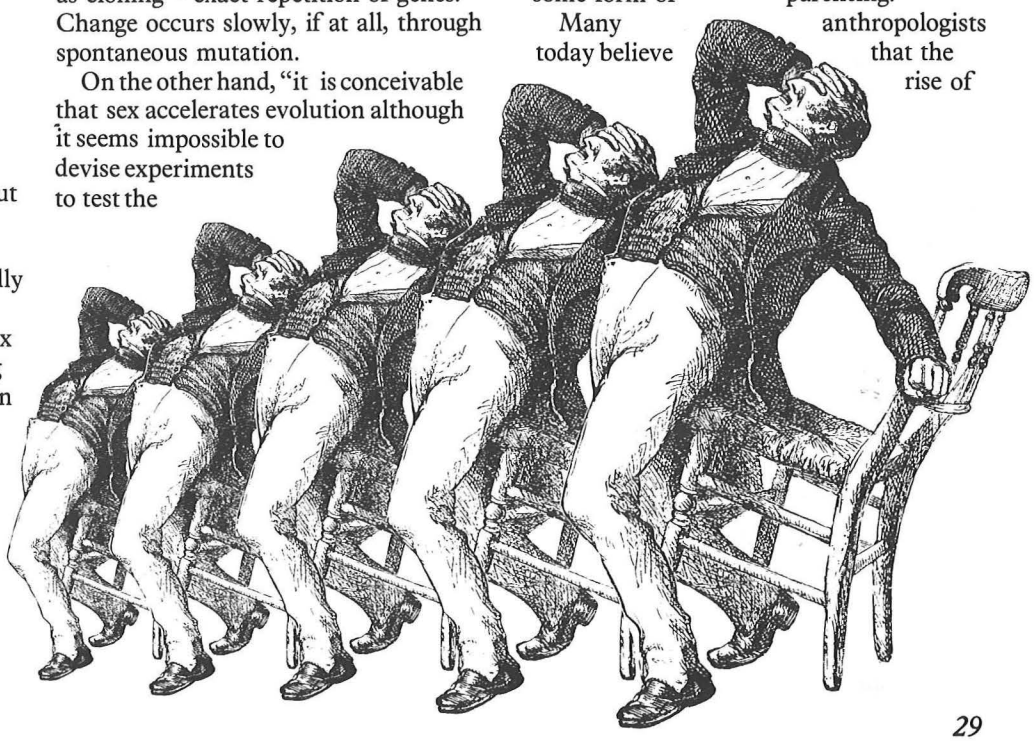
Although all genes are available for combination, it is the polymorphic genes – averaging about 3,200 – whose combination promotes diversity most strikingly.

This means the number of human genetic types possible is represented by a three or a four followed by 3,200 zeros – a number greater than the atoms in the observable universe. Without sex, reproduction occurs as cloning – exact repetition of genes. Change occurs slowly, if at all, through spontaneous mutation.

On the other hand, "it is conceivable that sex accelerates evolution although it seems impossible to devise experiments to test the concept," says Dr. Jean Wilson, professor of Internal Medicine at The University of Texas Health Science Center at Dallas and noted authority on sex mechanisms.

"But you can construct alternate theories as to the need for sex," he adds. "One of these has become fairly attractive recently: As you get to higher and higher animals in which the nurturing of the young takes longer and longer, it's quite clear that parenting becomes so complicated that it has to be shared by two individuals. The female has to be protected for a period of time as do the offspring. There is some thought that in several higher animals, evolution could not have gone so far without some form of parenting."

Many anthropologists today believe that the rise of



intelligence in higher animals is directly linked to the time the young spends with parents.

And long nurturing periods may require some form of social organization or adaptation:

"In hyenas, the baby has to be nurtured for about three years. This means that the males and some of the females not involved in infant care have to hunt to provide for the mothers and infants," says Wilson.

In some creatures, sex seems to be an option. One species of lizard found in New Mexico is both sexual and parthenogenic – that is, the females can either mate with a male lizard or alone they can produce another female that is a clone or exact copy.

In more bizarre attempts to use sex to cope with environmental survival, there are many fish that are hermaphroditic and others that can actually change sex. Recently scientists at the University of Hawaii determined that the female saddleback wrasse (Thalassoma duperrey) can change to male. Surprisingly, this switch is based on relative size – the larger fish in a school tending to become male. The philosophical implication is that a social situation dictates sexual adaptation.

Biologists consider there are two major but seemingly opposite strategies for sexual survival – one, the production of a great many eggs or ova in a relatively hostile environment with the hope that a reasonable percentage of offspring would survive the attrition, and the production of very few ova but in a well-protected environment.

The oyster typifies the many-egg strategy while the human produces relatively few ova in a highly protected environment. The latter strategy seems to have demanded a corollary response in the male:

"Men produce about 200,000,000 sperm per day. Thus, from puberty to age 50, each male produces upwards of a trillion sperm," observes Wilson.

"This means that each man theoretically could impregnate every woman who lived from time immemorial. That's an enormous over-production.

"It is, incidentally, that fundamental difference in production between women and men that makes it unlikely in my opinion that we'll have a safe birth control pill for men any time soon."

Humans may have developed other evolutionary sex strategies.

"I feel that in humans, socialization plays a very large part in the development of sex roles," says Dr. Christine de Lacoste, a neuroanthropologist in the Department of Cell Biology at UTHSCD. "Both 'nature and nurture' are involved. As we go up the evolutionary scale, environment becomes more and more important."

In the nature area, de Lacoste recently discovered that human and primate females have a larger corpus callosum than males. This brain structure is thought to mediate messages between right and left hemispheres. The significance of this physical difference between male and female is not yet understood, says the researcher.

She does feel that the contemporary environment and the long nurturing period characteristic of *Homo sapiens* can downplay nature by either emphasizing or de-emphasizing differences in sexual behavior. If differences are de-emphasized, humans could promote an equality of sexes resembling the marmoset in the animal world.

She notes that sexual dimorphism (a difference in body size between male and female) seems to make a difference in whether nonhuman primates mate for life.

"At one end of the scale, the marmoset male and female are very close in body size and are close in behavior and parental duties. Their monogamous behavior and pair bonding may last through adult life. The gibbon ape in Asia also is monogamous, and there is an absence of sexual dimorphism."

Socialization plays a very large part in the development of sex roles."

At the other end of the scale are a number of species, including the gorilla, in which the male is nearly twice the size of the female. Gorillas choose many different mates during their lifetime.

In many instances in the primate world, the degree of monogamous pair bonding seems related to the degree of bi-parental offspring care.

These behavior patterns seem reasonably clear for the vast majority of primates, but sometimes in the case of humans, there are confusing anatomical and psychological complications.

Sometimes nature itself does not clearly define sex in an individual. Reported cases of sexual ambiguity in humans have been the subject of sensation and prurient interest.

Wilson cites the case of Herculine Barbin, a hermaphrodite raised as a girl in a Catholic orphanage in France in the 19th century. Redesignated a male at 22, Barbin committed suicide eight years later. Barbin's life inspired *A Scandal At The Convent,* as an example of literary treatment of such subjects.

Equally astonishing are current-day cases in which "girls" change to "boys" at puberty. Wilson described such an affliction, "familial incomplete male pseudohermaphroditism," in two Dallas sisters in 1974. They had been reared as female, but the older sister began to masculinize at 13 with deepened voice, growth of phallic structure and absence of breasts. Although the person had a short, blind-ending vagina, doctors discovered testes and a hormone makeup within male limits. This was categorized as a genetically derived deficiency involving an enzyme called 5 alpha-reductase.

Later, other scientists described the disorder in families from the Dominican Republic where the process was dubbed "penis at 12" but was considered a more or less acceptable occurrence.

The cases illustrate the fact that sex is not always clear – it can occur in many shades of status between what is considered male or female.

Although most humans are programmed for male if they have XY chromosomes and female if they have XX chromosomes, the subsequently issuing hormones play a most powerful role in the development of sexual types – both from the same basic fetal structures.

"In all species, including man, gonadal steroid hormones are involved in the conversion of the sexually indifferent embryo into the male phenotype, in sexual maturation of males and females during postnatal life and, in the male at least, the development of a basic sexual drive at the time of sexual maturation," wrote Wilson in *Clinical Neuroendrocrinology.*

Oddly, sex drive of the female does not seem dependent on ovarian hormones, he observed.

While animals seem to have more or less stereotyped reaction to genetic and hormonal influences, the case for such cause and effect in humans is much less clear.

The question of hormonal influence before birth on gender identity – one which includes possible mechanisms of homosexuality – is far from settled, according to Wilson.

Perhaps the unhappy Barbin best expressed in his/her memoirs the plight of a human caught in an anatomical trap between male and female:

"What strange blindness was it that made me hold on to this absurd role until the end? I would be unable to explain it to myself. Perhaps it was that thirst for the unknown, which is so natural to man."

CAPSULES

Labor trigger

Amniotic fluid – composed primarily of fetal urine – may hold the key to the mysterious unnamed substance that triggers labor in the human female, say researchers in the Cecil H. and Ida Green Center for Reproductive Biology Sciences.

The group has recently published an article, "Stimulation of Prostaglandin Biosynthesis of the Human Fetus May Serve as a Trigger for Parturition" in *Science.* They are Drs. Daniel M. Strickland, fellow in Obstetrics and Gynecology; Sheikh A. Saeed, visiting assistant professor in Obstetrics and Gynecology; M. Linette Casey, assistant professor in Biochemistry and Obstetrics and Gynecology, and Murray D. Mitchell, research associate professor in Biochemistry and Obstetrics and Gynecology. Since the mid-1970s researchers in the Green Center, under the direction of Dr. Paul MacDonald, center director and professor of Obstetrics and Gynecology and Biochemistry, have been working on the mystery of the initiation and maintenance of labor until the fetus is ejected from the mother's birth canal.

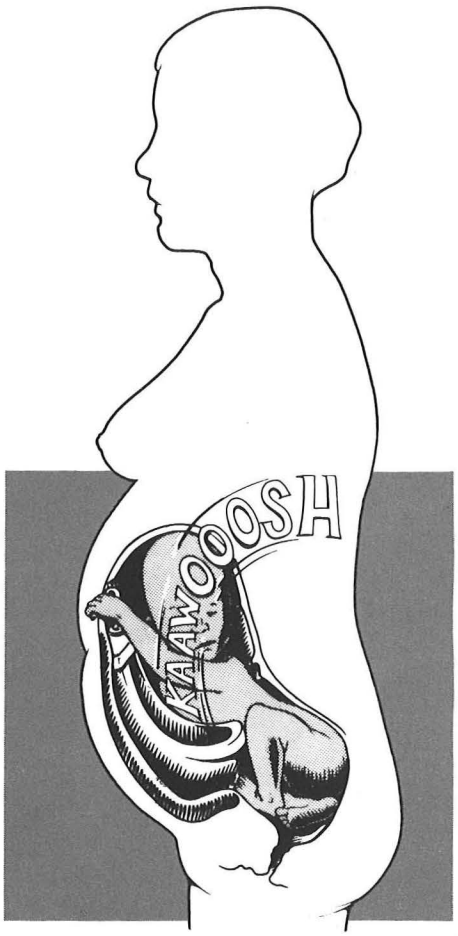
MacDonald says there is much evidence to support the proposition that prostaglandins (fatty acids that stimulate contractions in the uterus) are the substances that cause the initiation of labor. But where does the signal or "trigger" that starts the process come from?

"We believe that the beginning of labor in humans is caused by the maternal musculature, but that the fetus 'calls' for it to begin, working through an 'organ communication system' from child to mother," says Mitchell.

"It looks like the initial signal enters amniotic fluid in fetal urine, moves out into the amnion (the inner membrane of the bag of amniotic fluid) and stimulates the synthesis of prostaglandin E_2. The prostaglandin E_2 diffuses to the decidua, or inner lining of the uterus. There transformation takes place, forming PGF_2 alpha, another prostaglandin that acts on the smooth muscles in the uterus walls to start contractions."

Mitchell, who worked on labor onset for eight years with Alec Turnbull at Oxford, says that researchers in the Green Center are also looking at the effect of fetal urine on whole cells. They want to learn whether stimulation of prostaglandins can be accomplished in the test tube, the subject of the *Science* report. The researchers compared the urine from 10 infants born following normal labor with 10 delivered by Caesarean section before labor began. It was found that urine from the infants delivered vaginally caused a greater increase in the formation of prostaglandins than did urine from the infants delivered by Caesarean.

In addition to looking for "stimulators" of labor, says MacDonald, Green researchers are also looking at nature's "handbrake" system. It is known that there are inhibitors, such as cortisol, an adrenal steroid that acts to inhibit prostaglandin synthesis. During labor there is an increased level of cortisol in the blood, probably in response to pain and fear. However, UT studies show that unlike other tissues, the inner membrane of the bag of amniotic fluid and the lining of the uterus are immune to cortisol's inhibiting action on prostaglandins. So while the cortisol levels rise during labor, there is no reduction in the rate of synthesis of the prostaglandins causing uterine contraction.



L. Sadler

Sleep and eye movements

"Dreaming is the experienced portion of a mind-body event," says Dr. John Herman, co-director of sleep research at the health science center.

"Most people think that the function of dreaming must have to do with the material that's recalled. But as we study dreaming, we become more aware that it's related to a very complex state of the nervous system. The recollected dream is just one layer. It seems as if there are both encoding and playback structures," says the researcher.

His new findings shed light on how the waking experience affects not just dreaming but also the eye movements during the regularly occurring periods of rapid eye movement (REM) sleep.

Herman restricted his subjects' eye movements when they were awake by having them wear "tunnel vision" goggles that made everything appear smaller and limited the vision to a five-degree field. The small eye movements in the awake state resulted in increased size and frequency of eye movements during REM sleep. The number and length of REM sleep periods were unaffected.

It has long been observed that the waking experience influences dream content. But Herman's report marks the first time an experimentally induced physiological effect in the waking environment has produced a measurable change in REM sleep.

Herman's studies are aimed at showing how the dream content and physiology occurring at the same time are related.

Danger in pregnancy

Protection of the fetus – in many cases before the mother is aware of its existence – has been the thrust of Dr. Mary Esther Gaulden's work. The first two weeks after conception is the "most sensitive part of the whole life cycle," says the radiation biologist.

Gaulden is associate professor of Radiology and chairman of the Graduate Program in Radiological Sciences at the health science center. In addition, she serves as adjunct professor of Environmental Sciences at The University of Texas at Dallas.

"The first two weeks of pregnancy, when the mother doesn't know she is pregnant, is the worst possible time for low-dose radiation," she says. "If you produce with a small amount of radiation a viable change in one chromosome, a mutation that is a small deletion of part of a chromosome, there is a good probability of knocking out genes that affect the central nervous system. And the earlier you produce a mutant cell, the more cells in the baby are derived from that mutant cell.

"People fear radiation because they don't know anything about it, can't see it, taste it, hear it, smell it...Some chemicals may be more dangerous than a small amount of radiation, but there's no mystique – you can see them and smell them," says Gaulden.

She is now studying the effects of chemicals on the neuroblasts from grasshopper eggs, which respond to mutagens in similar ways to the mammalian embryo. While many carcinogens (cancer-causing agents) have been studied, the researcher laments the fact that there has been much less study of the effects of chemicals on the fetus.

Gaulden now does a lot of consultation with physicians on the use of X-ray during pregnancy. "Every week I get calls from several women. They have had a chest X-ray. Should they get an abortion? I tell them 'No.' Or they have had a couple of bite-wing films at the dentist. There is no way that could affect the fetus if the machine is working properly," she says. The fetus must receive direct beam X-ray to be affected.

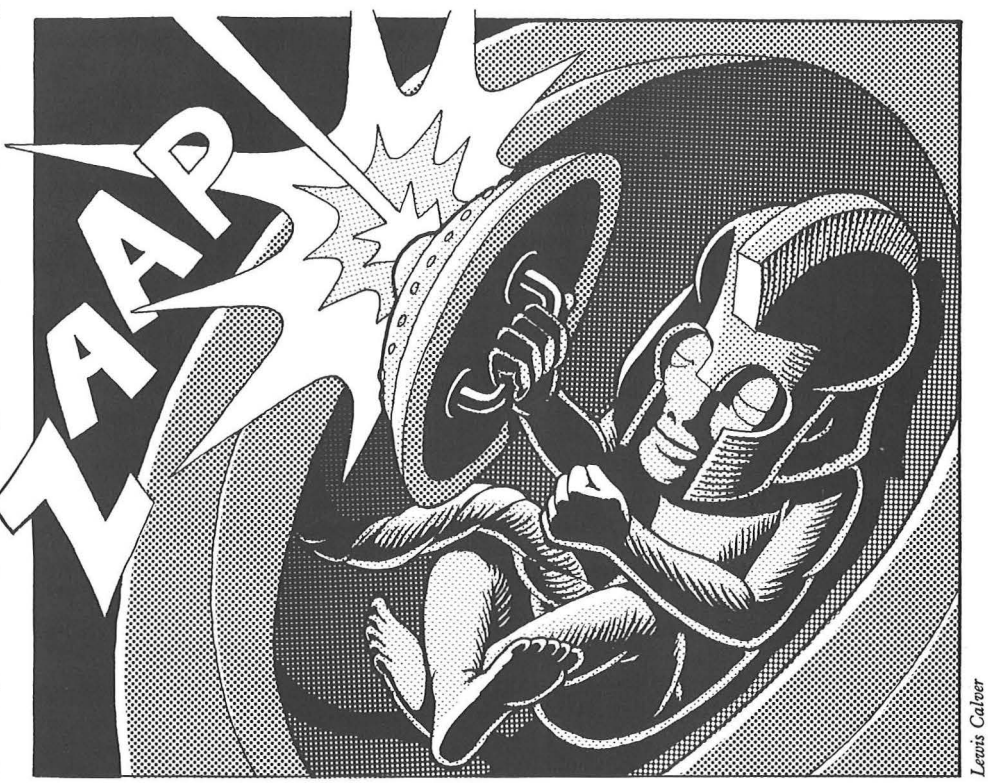
Together with the late Dr. Ed Christensen, radiologist at Parkland Memorial Hospital and professor of Radiology at UTHSCD, she began a pre-X-ray screening program at Parkland for women of child-bearing age that has become the prototype for such screening nationwide.

They began postponing elective abdominal X-rays or nuclear medicine procedures in any girl or woman who could possibly be pregnant. If emergency X-rays were essential, they often did one film instead of a series.

In a follow-up of 500 women whose X-rays were postponed, they found that five percent of the women were indeed pregnant at the time. The researchers also concluded that the quality of medical care was not adversely affected by the delay.

When they presented their findings at the Radiological Society of North America, the question was raised whether this type of screening was cost-effective. "My answer was 'If you're going to prevent some abnormality in these children – even just a few – it is cost-effective.' The mentally defective cost money, not to mention the emotional cost to the family. Screening may also prevent a malpractice suit against the physician," says Gaulden.

For her work in the protection of children from the effects of radiation and for her efforts in encouraging women in medical careers and in women's rights, Gaulden was presented a Women Helping Women Award by the Women's Center of Dallas.



Lewis Calver

Lactation

Breastfeeding mothers know that a psychological cue can create great discomfort from breast engorgement, especially when the mother is away from her baby or when the baby refuses to nurse.

This phenomenon of the lactation response is being studied by a research team at the health science center.

Findings reveal that two hormones known to act in the breast – oxytocin and prolactin – interact in the brain's pituitary gland to cause lactation. At UTHSCD, scientists in the field of neuroendocrinology are conducting precise tests for chemicals in the brain that initiate or inhibit this and other mind-body relationships.

"Before now it was thought that the two hormones worked in the breasts but were not related in the pituitary gland," says Dr. Michael Lumpkin, a postdoctoral fellow in the Department of Physiology.

Whether the stimulus comes from a psychological cue or from a suckling reflex, the researcher's findings suggest oxytocin is released from the hypothalamus (part of the brain over the pituitary) to stimulate prolactin cells within the pituitary. The oxytocin then may be carried to the pituitary gland by the bloodstream and there stimulate the release of prolactin. The suckling reflex can cause a signal to travel nerve pathways from the breast to stimulate the release of oxytocin by nerve cells in the brain.

Cherish the children

Today angry moralists blame the increase in teenage sexual activity on the pill and complain about increased sexual stimulation in movies, and "swinging singles" behavior among young people. But a Dallas obstetrician-gynecologist says that neither the development of better birth control methods nor our more permissive society is the major reason for the increasing and earlier sexual activity of adolescents in this country.

Dr. Norman Gant, professor of Obstetrics and Gynecology at the health science center says, "Taking all the pills in the world won't make a person sexually active. You've got to remember that in order to get a biological system going, you've got to turn it on."

That's where the problem begins: kids are "turning on" earlier today. And too often, there's no one to prepare the new adolescent for the very real physiological and emotional change in his or her body caused by what Gant calls "the most powerful biologic drive in the world."

"If you care for your child, you have to talk to that child," he says. "You have to explain what the young person is going through intellectually and emotionally – if you don't, you starve them. You have no other choice."

Today young women in the United States are experiencing their menarche, or first menstrual period, at an earlier age than ever before. The average is now around 12, but the average is even a little younger for blacks. In 1847 in Norway, the first country to survey this information, the average age of menarche was 17. At that time young ladies were expected to finish their schooling and marry soon after. When a similar study was first done in the U.S. in 1900, the average age of beginning menstruation was 15. Usually the teenagers finished school, married and began their families.

When a 12-year-old experiences the beginning of the monthly cycle that will permit her to bear children, she's a long way from finishing her education. She also is not necessarily expected to marry and have babies soon after.

"When the young woman of 1900 picked up her diploma, she had no expectations of becoming a doctor or a lawyer or an accountant – and certainly not a telephone repair-person," says Gant.

Why are our young women developing sexually and reproductively younger and younger?

The answer is nutrition, says Gant.

"We're feeding kids better and it's been established that the advent of menstruation is related to body weight, not body height.

"Turning kids loose with their new bodies and no emotional preparation or warning is like giving them the keys to a new Ferrari, parking it in the driveway and telling them they can't drive it. Meanwhile, they're seeing how much fun it is to drive a Ferrari in the movies, in pictures, in magazines and on TV.

"Sometimes they see that Mom and Dad have separated – and each is off chasing new Ferraris of their own."

The problems of teen pregnancy are not going to go away, says the physician. Today 40 percent of young women have had intercourse by the time they're 16. The percentage for young men is 60 percent.

"What it means is that anyone can estimate that four out of 10 girls on their street have had sex. Unfortunately, almost all think it's not their daughter."

This is the kind of attitude that leads to ignoring the problems of teenage sexuality, as well as the problems of teenage pregnancy.

"It's difficult taking care of a baby when you're not through being the baby in your family yet," says Gant.

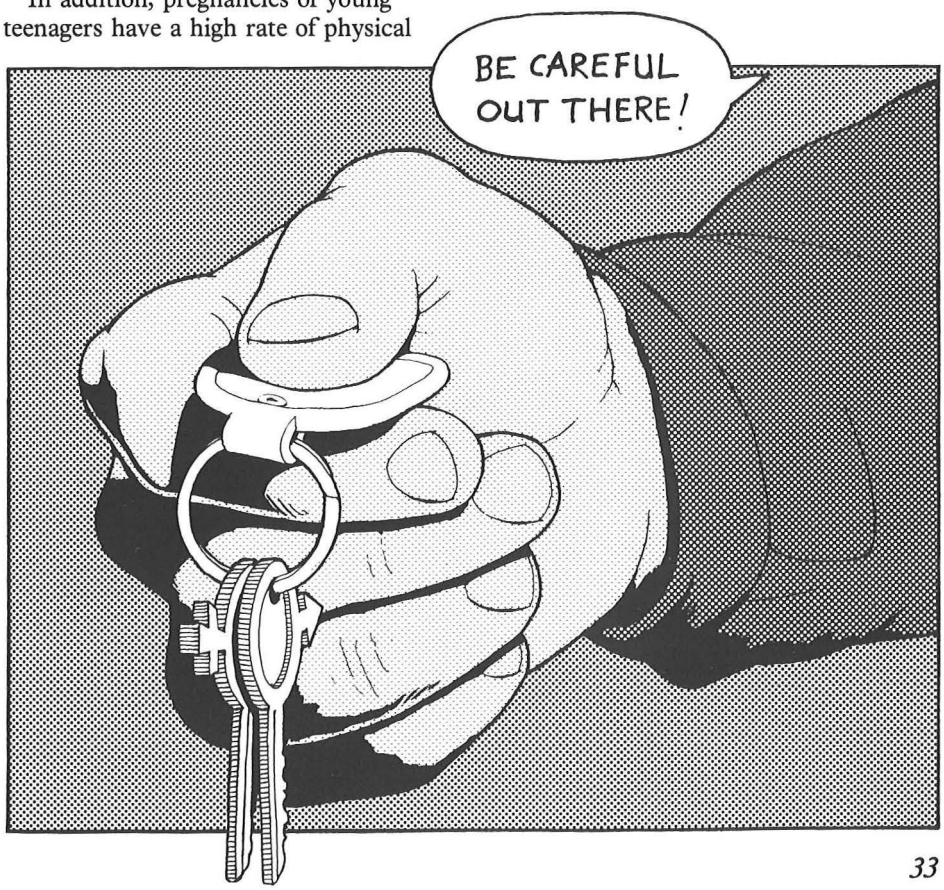
In addition, pregnancies of young teenagers have a high rate of physical problems, such as high blood pressure, and often are associated with such conditions as neurological injuries, brain damage and mental retardation in the child. There is also a higher death rate associated with both very young mothers and their babies, and child abuse is too frequently seen in the homes where "children had children" before growing up themselves.

If the parents are not able to confront their children on the sensitive subject of their sexuality, says the physician, someone must be responsible.

"I believe education is the only way. Too many times the homes, the churches and the physicians have all failed. There is one melting pot where young people can be reached, however: the schools."

Gant is a big supporter of the program in parenting education in the Dallas Independent School District. Currently 57 schools, most at the ninth grade level, are offering parenting education to teenagers who have their parents' permission.

The course is for both boys and girls. And that's the way it should be, the physician says. Too often we have been educating young women and leaving the young men out. Boys in our society need to have readily available information, and appropriate counseling as well. In fact, good parenting education should stress that sex is a joint responsibility whether the decision is to become a parent, to be sexually involved without having a child or to refrain from sexual intercourse.



Lewis Calver

Radioactive implants

Small radioactive implants targeting the tumor site offer some women with early breast cancer an alternative to the mutilation of radical or modified mastectomy.

The implant acts as a "booster dose" of radiation, that, when combined with limited surgery, shows a local control rate equal to mastectomy, according to doctors at the health science center.

In 1982, 120,000 new cases of breast cancer were discovered, making it the most common type of cancer in women.

Mammography and breast self-examination are aiding women in early discovery of breast cancer when the tumor is small and before it spreads to the nearby lymph nodes. In these cases, radical surgery may not provide the only hope for a cure, says radiation oncologist Dr. Phuc Dinh Nguyen, assistant professor of Radiology.

"Surgeons are trained to do surgery and some do not have faith that removal of the tumor and radiation can do the proper job," he says. "Yet, we do have a lot of information from long term follow-up of five, 10 and 15 years that for early breast cancer, 'lumpectomy' (surgical removal of the tumor) and radiation can bring results as good as those from radical mastectomies."

Dr. Daniel Flynn, assistant professor of Radiology, who performs the procedure with Nguyen, says women do not always have to sacrifice a breast for the treatment of some early breast cancers. "Why do a mastectomy in 100 patients when only 10 need it? Approximately 90 patients will live 10 years without recurrence or evidence of disease using radiotherapy, and the cosmetic results compared to conventional surgery are excellent. Often you can't tell which breast was irradiated and implanted. There's no sense using a cannon to kill a fly."

The implant follows surgical removal of the tumor, axillary sampling to determine lymph node status and 20 to 25 external radiation treatments given over a four- to five-week period. Once the implant site is determined, hollow tubes are inserted into breast tissue.

The patient is then transferred from the operating room to her hospital room where tiny grains of a radioactive isotope sealed in thin plastic rods are inserted into the tubes.

The implant stays in place two to three days, depending on the tumor characteristics.

"I never expected it to be so easy," says Adrienne Christie, one of Nguyen's patients who received the implant in April. "The implant was left in for 28 hours and I felt no pain."

"The radiation we offer is only for local control in the breast and axilla (armpit) where lymph nodes are located," says Nguyen. "The aim of mastectomy is about the same. These treatments have no effect in distant areas if the disease has already spread."

To screen out women whose cancers are too large or advanced to benefit from two-step radiation, certain guidelines are followed. The primary tumor should be no larger than approximately three centimeters (a little over an inch) in diameter. A mammogram must show only one area of cancer in the breast and the breast should be small to medium in size.

"Breast cancer is known to be multifocal. Instead of having one tumor, we can find others as well. If a mammogram shows multifocal disease or if we can feel it clinically, the patient may not be amenable to conservative management. In such cases, we're dealing with too much disease for the radiation to take care of," says Nguyen.

Mevinolin

An experimental drug called mevinolin has been shown effective in treating people with dangerously high levels of blood cholesterol.

The mevinolin study was conducted by a team at the health science center including Dr. Scott Grundy, director of the Center for Human Nutrition; Dr. David Bilheimer, head of the Lipid Metabolism Unit and associate dean for Clinical Affairs at Parkland; Dr. Joseph Goldstein, chairman of the Department of Molecular Genetics, and Dr. Michael Brown, director of the Center for Genetic Diseases.

Grundy calls the drug "a significant step forward," comparing mevinolin treatment for high blood cholesterol to insulin treatment for diabetes. "The basic defect in cholesterol metabolism still exists in the patients studied. But treatment with the drug alone or in combination with another drug can bring blood cholesterol levels to about normal." Two kinds of lipoprotein carry cholesterol in the blood. HDL (high-density lipoprotein), the type that increases with exercise and alcohol consumption, seems to be beneficial. The other type is LDL (low-density lipoprotein). "This is the culprit in atherosclerosis," says Bilheimer. And mevinolin lowers LDL without affecting the level of HDL.

The drug, like the Japanese drug compactin, works by blocking the manufacture of cholesterol in the bloodstream.

Six patients with severe forms of an inherited disorder called "familial hypercholesterolemia" (FH) were chosen for the study.

FH, affecting about one in 500 individuals in this country, causes a retention of abnormally large amounts of cholesterol in the blood. Frequently it leads to premature arteriosclerosis (accumulations of cholesterol on artery walls). Left untreated, heart attacks and strokes occur prematurely.

The defect in FH, first identified by Goldstein and Brown, is a lack of cell receptors for LDL. These receptors normally draw cholesterol from the blood into cells. Once inside the cell, the LDL is degraded, and the cholesterol is freed for cellular use. This process removes LDL from the blood and reduces the threat of arteriosclerosis.

Normal cells produce enough receptors to bind the LDL they need. When cellular cholesterol needs are satisfied, they turn off receptor production. This maintains a constant level of cholesterol within the cell. When cells cannot collect enough circulating cholesterol, they use a back-up capability and produce their own.

By blocking the cell's capability to produce cholesterol, mevinolin stimulates the cells to produce more LDL-receptors. By taking cholesterol from the blood, the additional receptors bring cholesterol to a safer level.

Bilheimer also expects that mevinolin may improve patient compliance. Current therapy has unpleasant side effects and is not always effective in reducing the blood cholesterol to the desired level. Mevinolin appears to be highly effective in reducing the cholesterol level. It was tolerated well by all patients studied, and no toxicity nor abnormalities were noted.

The health science center team plans further studies of patients with FH. However, drugs like mevinolin will not be available to patients who have high cholesterol levels for other reasons until long-term studies for safety have been completed and Food and Drug Administration approval has been granted.

Glaucoma surgery

Laser surgery is a useful tool in the treatment of glaucoma, but there may be complications if it's overdone or patients are not properly selected. Now, says Dr. Robert Weinreb, associate professor of Ophthalmology, those problems can be reduced with better patient screening and by making only half as many laser burns in the eye as previously thought necessary.

Glaucoma is a blinding disease affecting more than 1.2 million Americans. An eye with glaucoma is like a sink with a clogged drain. Drainage in the eye becomes inadequate, and fluid backs up. The eye pressure then rises, leading to optic nerve damage and, if untreated, blindness. The disease is dangerously symptom-free until the latest stages, so patients generally aren't aware that they have it.

Weinreb says that laser surgery is a promising alternative to conventional surgery. "This technique is exciting because it appears to be as effective in most cases as conventional surgery but doesn't require hospitalization and operating room time. It can be done in an outpatient setting using a topical anesthetic."

He explains that the patient is awake throughout the procedure, which takes about five to 10 minutes and is painless. In contrast, conventional surgery takes an hour to an hour and a half and requires more general or local anesthesia and several days of hospitalization.

Weinreb says laser surgery done through the UTHSCD Glaucoma Service is currently reserved for patients whose medications are not effectively lowering their eye pressure. "This is an important point. Many people feel that because they have glaucoma, they should have laser surgery. At the current time, we believe that it should be reserved only for those patients whose eye pressure is too high or whose medications are associated with too many side effects.

"In some patients, the laser may have made their condition worse. We do not understand why it works in some cases, does not work in others and in some actually makes their condition worse. We think that, in those cases that worsened, the laser intensity might have been set too high or that the burns were improperly placed. These patients develop a great amount of inflammation following the treatment. This inflammation can even lead to higher eye pressure than before laser treatment."

Weinreb is conducting clinical as well as laboratory investigations at UTHSCD to understand better the problems of the laser surgery.

Male and female brain

A physical difference between the male and female brain has been discovered by a physical anthropologist working at the health science center.

The corpus callosum, a bundle of fibers connecting the right brain with the left brain, is larger in human females than in males even in the fetus, says Dr. Christine de Lacoste, neuroanthropologist in Cell Biology.

She has found a larger corpus callosum in females in studies of human adults, human fetuses at 26 weeks and older and adult nonhuman primates from gorillas to prosimians (small primates related to monkeys).

The corpus callosum is involved in communications between the hemispheres of the brain although its specific function is unknown.

"We do know some things that happen if a person doesn't have a corpus callosum. It is sometimes severed to control epilepsy," said de Lacoste. "The left hemisphere is responsible for verbal ability. The two sides of the brain must communicate.

"For example, if a person has a severed corpus callosum, you can blindfold him and put a pencil in his left hand, which is

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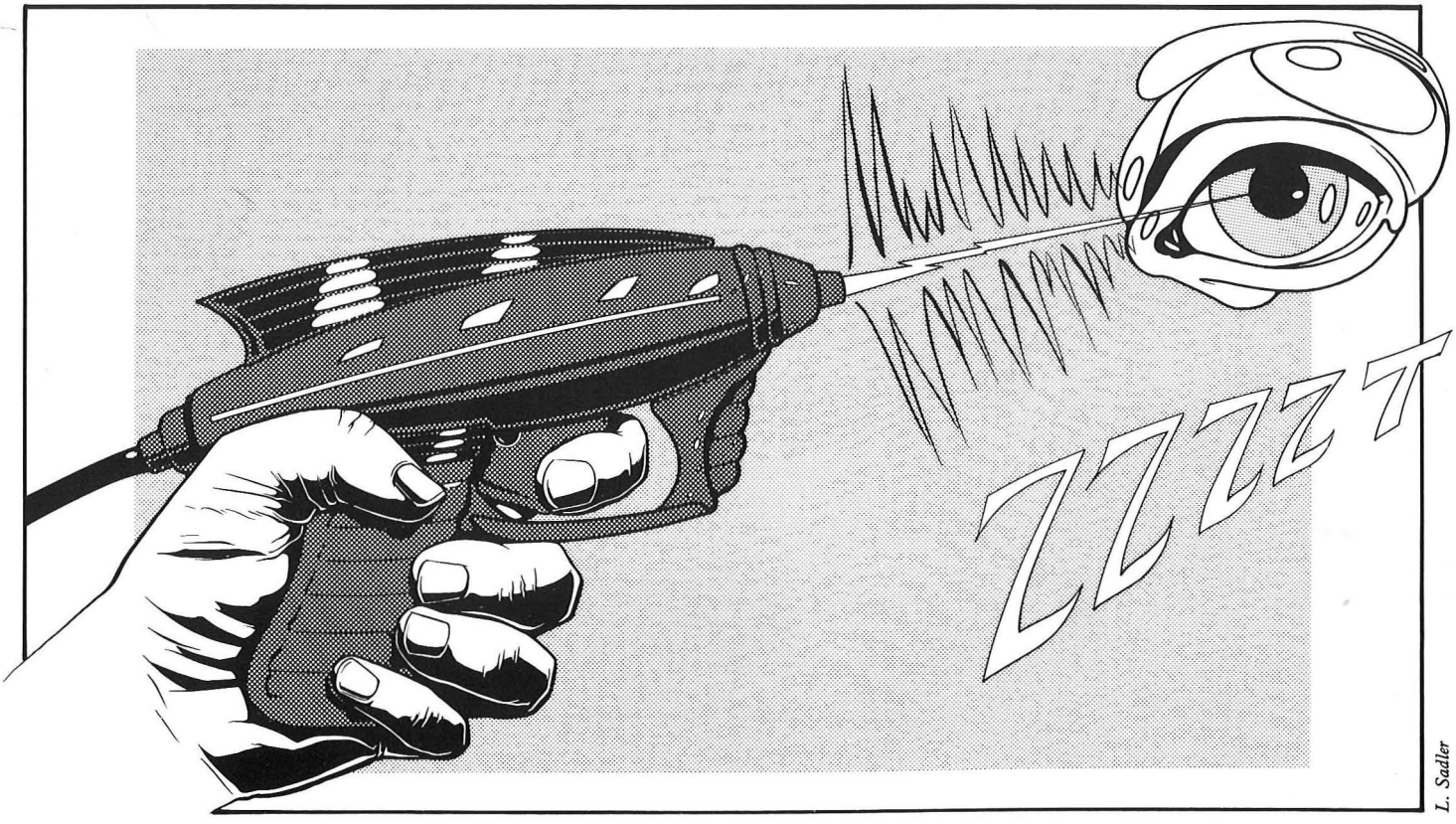

L. Sadler

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controlled by the right hemisphere. He knows in the right side of the brain that he is holding a pencil and how to use it, but he can't verbally tell you that it's a pencil. If he holds the pencil so that he can't see it and you show him slides of objects, he can point to a pencil and thus identify the object. He just can't say that he is holding a pencil. It's the corpus callosum that makes consciousness into one."

The researcher does not know what the brain difference may mean in behavior. "Anatomy is fact. However, at this point we can only speculate on the functional implications of these findings. They may mean that the two hemispheres interact differently in males and females. But I'm just reporting the fact of a physical difference," she said.

She is also interested in the evolution of the brain. The female brain is, on the average, smaller than the male, but that difference is relative to height, not to sex. "In the hunting and gathering days, there may have been a selection pressure for a larger male. But with women providing 80 percent of the food and nurturing the kids, it doesn't make sense to select for less intelligent women. It's possible that with hunting skills needed, men's visuospatial function improved while women evolved better verbal and symbolic skills."

Capillary reversal

For the first time a reversal in the thickening of capillaries in insulin pump patients has been recorded. Dr. Philip Raskin and associates reported their findings in an article published Dec. 22 in *The New England Journal of Medicine.*

In their two-year study 13 pump patients achieved normal or near-normal levels of blood sugar using an experimental treatment program combining constant infusion of insulin by portable pump, dietary management and self monitoring of blood glucose. These patients experienced a reversal in the width of skeletal-muscle capillary basement membranes in the thigh. The capillary basement membrane is the inside layer of the capillary wall.

There was no change in the basement membrane in 10 other diabetic patients receiving a more conventional diabetic treatment that included insulin injections, generally twice daily, and dietary advice. Their diabetic condition, however, remained stable.

Other researchers participating in the reported study are Drs. W. Allen Shannon Jr., Angel O. Pietri and Roger H. Unger.

Fire deaths

Many experts believe burning plastics, which release toxic gases, are the culprit in the case of smoke inhalation. But it doesn't matter what's burning according to a UTHSCD toxicologist. Toxicity leading to death from smoke inhalation is due instead to the rate of burning and the heat intensity, says Dr. William Lowry, associate professor of Pathology.

Slow-burning, smoldering fires of whatever material are often the most dangerous, says Lowry, because the first step in combustion seems to be the most deadly.

Lowry explains it this way: For materials to burn, they must be coverted to a gaseous state. The first breakdown of burning material into gas involves the release of tiny organic molecules. Floating free into the surrounding atmosphere, these molecules search for something with which to bind. Called "free radicals," the high-energy molecules may cause suffocation by reacting with the substance covering the inside of the lungs. Or they may react by binding with molecules of oxygen in the lung. The reaction of free radicals with "surfactant" covering the lungs or with the oxygen itself would reduce oxygen uptake into the bloodstream and cause asphyxiation.

"We know that people die in minor fires. On autopsy their lungs are clear and their blood usually shows sub-lethal levels of toxic substances. It's known that people die quickly in these fires."

Yet in a series of 100 fires studied by Lowry, a member of the Dallas County medical examiner's team, 90 percent of the fires produced toxic gas amounts that were insufficient to kill.

As he explains it, there is controversy about the toxicity of burning plastics. But there have been no studies to prove that plastics are responsible for more deaths than natural organics.

Plastics may be hazardous, but so is everything else that burns, says Lowry. What should people do in case of fire? "Regardless, get out of the building as soon as possible. If you can't see because of smoke, crawl on the ground to get out. But if you can see, crawling on the ground can impair movement and waste precious time. Carbon monoxide, lighter than air, can be avoided by crawling, but free radicals, which are not lighter than air, cannot be avoided by crawling. A moist cloth can be very beneficial by capturing the free radicals."

Capsules were compiled by Jamie Friar.