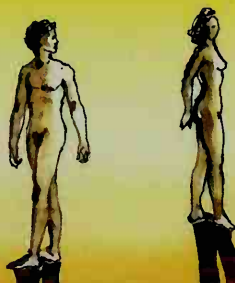
THE TRUTH ABOUT HERPES

What **everyone** should know.



- ☐ WILL THERE EVER BE A CURE?
- ☐ IS THERE A LINK BETWEEN HERPES & AIDS?
- ☐ WHAT SHOULD MOTHERS-TO-BE KNOW ABOUT HERPES?
- ☐ CAN A PERSON HAVE HERPES & NOT KNOW IT?
- ☐ IS SEXUAL FIDELITY THE ANSWER?
- ☐ ARE HOMOSEXUALS AT GREATER RISK?

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DIRECTOR OF THE UNIVERSITY OF BRITISH COLUMBIA HERPES CLINIC

THE TRUTH ABOUT **HERPES**

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For Anne and Leon
For Marika
For Adrian and Rebecca

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INTRODUCTION

If I have herpes, does that make me a sexual leper? Is herpes a sign of the Apocalypse? Is it the wrath of God? A modern day plague? Will I be able to have children if I get it? Will it give me cancer? Is it incurable? Should I become celibate? Should I see a divorce lawyer? Will I go blind? Is this the incurable social disease which deforms babies and causes cancer? These concerns, and many more, are very real ones for the thousands of people whose lives are touched by herpes. The questions are numerous, and they keep coming. Answers are essential.

At the University of British Columbia Herpes Clinic, one of only a handful of its kind in North America, we have seen hundreds of genital herpes sufferers. We have listened carefully to thousands of questions, and done our best to answer them with facts. A glance at the table of contents will give you an idea of what people are asking. The answers are based on current medical knowledge and day-by-day clinical experience.

There is no question that herpes is a growing problem. The number of people affected is increasing at an alarming rate. Unfortunately, misinformation has increased with the growth rate. We do not know just how many people are affected with herpes, but guesses of 500,000 to 1,000,000 *new* cases in North America per year have been made. These figures are generally based on the number of herpes sufferers who go to clinics which treat sexually transmitted diseases. However, all people with herpes do not necessarily go to such clinics. Family doctors, as well as specialists in dermatology, urology, gynecology, or infectious diseases, are diagnosing and treating herpes. Furthermore, because herpes is not always diagnosed with a standard lab test and because it is not, for physicians, a "notifiable" disease like syphilis or tuberculosis, there are no dependable statistics. During the last decade the number of people seeking medical attention for this problem has increased nearly tenfold. Along with the rise in incidence of genital herpes, there has been a parallel upswing in media attention. Some have suggested that the problem has grown more in print than in victims. While there is an element of

truth in this, herpes remains all too real to the person who has it. It is a serious concern to anyone who is or who plans to be sexually active in their life, whether those plans include one lifetime partner or a hundred. Coping with and living a normal life *around* herpes is a challenge which can be met. To meet the challenge, however, you have to arm yourself with the truth. Unfortunately, the dissemination of useful information has not always been the goal in the current media obsession with the disease. For television and the newspapers, herpes has become a major "news" event—from public affairs shows to the eleven o'clock news, from glossy magazines to hardcore newsmagazines. Such unrelenting public exposure to the problem has actually changed the disease itself. Herpes is no longer just a sexually transmitted infection which requires understanding—it has become a stigma which requires destigmatizing. We are subjected to flashy headlines and frightening stories; home remedies and personal tragedies. Herpes has good selling power but all too often, unfortunately, fear is transmitted in lieu of information.

Television, magazines, and even books wholly devoted to herpes have only rarely dealt with the subject with care. Whether it is the personal anecdotes told at cocktail parties or summarized in seventy printed words next to an ad for perfume, the issues surrounding this common infection have all too often been dealt with in a haphazard fashion. Even the medical profession has had a tough job of it. The time required to inform the patient fully about the problem, explain the details, and answer the questions is not always available in the doctor's office.

Several good organizations have been formed to help provide reliable information about herpes, but unless you're aware that they exist, they can't be of any help. Most of what's in print about herpes avoids the difficult questions, talking about the subject in a superficial way. This book is different. It will take you step by step through the plain facts. Your fears surrounding herpes will be honestly met—nothing, pleasant or unpleasant, is glossed over. Yet the truth has a way of placing fears into perspective. If you are reading this book to learn whether you have herpes—read on. It is important that you do find out, and this book will tell you how to do

just that. If you are reading it to find a method for prevention—read on. You may not find a simple answer to the question, but you will know enough to approach prevention intelligently. If you are a physician, you will find the book useful as a tool to help your patients cope with their herpes. It will show you what each person with herpes needs to know in order to live with it.

It is my hope that each person reading this book will realize that herpes is everyone's problem and everyone's concern. Whether you think you have herpes or think that you don't, you should be armed with the truth when you joke about herpes at a party or when you begin your next intimate relationship. You should know the facts before deciding you have never had or never will have this problem. You should know more than you do now before you agree or disagree that herpes may be "the wrath of God." You must learn more before you decide "it will never happen to me."

This book will give you new insight into a growing problem. It is my hope that the misconceptions which result from ignorance will cease to be the single, most important problem about herpes.

CHAPTER ONE

And you want to travel with her,
and you want to travel blind
and you know that she can trust you
because you've touched her perfect body
with your mind.

LEONARD COHEN, *Suzanne Takes You Down*

THE MOST IMPORTANT QUESTIONS FIRST

Am I contagious between recurrences? Do I have to give up sex?

Medical explanations will be detailed in the forthcoming chapters. For now, remember that **herpes simplex** can exist in two very different states: **active**, in which the virus is growing on the skin, often forming lesions, and **latent**, in which the virus is dormant within the nervous system, causing no harm. The latent period is a quiet period which persists for life. From the **latent** state, the herpes virus may seed a recurrence of an **active** skin infection.

When your herpes is in the latent state, and there is no infection on the skin, your sexual partner cannot contract the virus from you. Transmission can only occur when an **active** skin infection comes into *direct* contact with the skin of another individual. For this reason, people with herpes must learn to carefully avoid sore-to-skin contact when skin lesions

are **active**, but to resume normal activity when lesion areas are not active.

Often active herpes infections are mild. They are occasionally so mild that nothing is detected. Visible sores might not be present yet the herpes *is* active and can be grown in culture. This is very uncommon in people who know they have herpes. In other words, people who have experienced herpes symptoms once tend to know when they have herpes again. On the other hand, many thousands of people have genital herpes, but have never realized it. They may have an active skin infection and never know. This might seem unbelievable to someone with recognizable herpes symptons, but actually, most people who have herpes have never experienced any symptoms!

The chances of having a no-symptons, no-sores recurrence are probably low, however, if you've had symptoms before. It is impossible to know precise numbers. A recent study of pregnant women in Seattle suggests that **asymptomatic virus shedding** occurs less than one per cent of the time in 12% of sufferers. Other investigators think the likelihood of sufferers not realizing their herpes is **active** to be one to four per cent. Transmission will be less likely to occur from someone who knows they have herpes, who is careful to avoid sore to skin contact during active periods, than from the person who really has active herpes without ever having had symptoms. People in this latter group cannot take precautions against transmitting the disease, until they find out what they've got.

Herpes sufferers should get to know their own recurrence pattern. They can learn to identify the active periods when the virus is on the skin (see Chapter 3), and should acquire the skills necessary for self-examination. They will then adjust their sexual activity patterns around these times, avoiding sore-to-skin contact during the active phases. They must get to know and to understand the facts, so they can inform their partners and explain the risks. Limiting people with herpes to contact with others who have the same infection will accomplish nothing. Furthermore, celibacy will do the world no favor. Indeed, in the long run, these extreme measures will do a great deal of harm both to the herpes sufferer as an

individual, and to the social acceptance of the disease.

Herpes of the newborn is a deforming, blinding, often fatal disease—should I give up my plans to have children?

Now that you understand how herpes is spread—from **active** skin infection and not from **latent** infection—then you should understand that herpes in a newborn baby (**neonatal herpes**) may result if the baby is born while the virus is **active**. This generally occurs if the baby's skin becomes infected during the birth process. If herpes is **latent**, there is no virus along the birth canal to infect the baby. If herpes sores are present at the time of labor, then (and only then) a Cesarean section may be required so that the birth process skips the possibility of direct contact between the infection and the baby. Of course, the rupture of the mother's membranes (breaking the bag of waters) is also an important factor, because the membranes are a natural barrier against the virus travelling up from the mother's skin to the baby's skin. If the membranes rupture and a herpes sore is active, time is of the essence and a Cesarean section is performed as an emergency operation. If no sores are present, however, labor may proceed safely and normally.

In order to avoid giving herpes to your baby, you must tell your doctor that you have (or a previous partner had, or your present partner has) herpes; he or she will carefully inspect your genital area, especially the external area, for herpes sores during labor. You must take an active role and discuss the problem well in advance with your doctor. If possible, attend a special clinic where your herpes recurrence pattern can be mapped out and cultures taken regularly *before* delivery—starting when you are 32 weeks along in your pregnancy. You and the doctor should increase your awareness of your herpes outbreaks—what they feel like, what they look like, and so on. If possible, your doctor will take a herpes "culture" during labor, so that in the unlikely event that a sore is missed, there will be time to watch and treat the baby if necessary.

A different syndrome of infection of the fetus may also occur because of herpes infection *inside* the womb. In this situation, herpes could have an adverse effect on the fetus before birth. This syndrome of **congenital herpes** is very rare. Some physicians believe that **primary herpes** (the first bout of the virus) in the mother may lead to womb infection, especially if primary herpes occurs in early pregnancy. There is no evidence to support this belief. Indeed, most mothers who have herpes for the first time during pregnancy give birth to normal babies. Primary herpes in early pregnancy is not considered an "indication" for abortion, although some women choose to abort. Nothing specific can be done to prevent **congenital herpes**, but the risk is low. In fact some mothers with a proven herpes infection inside the womb have given birth to completely normal and unaffected babies. It would seem that most healthy babies born to women with herpes who are healthy and well-nourished are very unlikely to develop problems.

When you consider how many new mothers have had a genital herpes infection, it may seem surprising that herpes of the newborn remains an uncommon disease. Some physicians believe that **antibodies** account for this low incidence. Most mothers make plenty of herpes antibodies or chemicals which neutralize the virus (see chapter 2) on contact. The antibodies probably get into the amniotic fluid in which the baby floats, and coat the baby in a layer of protection. Antibodies may knock out the virus before (or after) it gets to the baby's skin. This is still a theory, but it fits with some of the facts—and the facts are that neonatal herpes is uncommon while genital herpes is common.

In the future, it may become possible to prevent herpes recurrences during labor by using medication near term. Furthermore, the extra protection offered by that careful medical examination will make the risk even lower. There is no reason, then, for herpes to affect your plans for a baby. It is, however, very important that you discuss your history of infection with your physician when you become pregnant.

I've heard that herpes can cause cancer. Does that mean it will eventually kill me?

Does herpes lead to cancer? The answer here is unknown. Several experiments have been performed which suggest that it *might*. Herpes viruses can "transform" cells in a test tube. This means that under special rigorous laboratory conditions the virus can cause a cell, which *normally* reproduces poorly or not at all, to live forever—i.e. to change into a "cancer" cell which reproduces and grows.

Several years ago, investigators noticed that people with more active sex lives had a statistically higher chance of getting cancer of the cervix. Celibacy, then, is one way to avoid cervical cancer. If we compare blood samples from women with cervical cancer and from women with none, we discover that samples from the group with cervical cancer are more likely to have herpes antibodies present. Does this prove that herpes caused the cancer—or does it only show that herpes relates to sexual activity and that something else about sexual activity relates to cervical cancer? In fact, there is no question that sex plays a part in cervical cancer. Several investigators believe, however, that it is not herpes—at least not herpes alone—that causes cervical cancer. It could be another sexually-transmitted disease, such as trichomoniasis or urethritis. Sperm itself might induce this cancer—several respected specialists believe exactly that. We just don't know. Whatever the reason, herpes sufferers do get cancer of the cervix about two to eight times as often as women without herpes. Therefore, the astute physician must *presume* that herpes can cause cancer in order to help prevent injury from this cancer in patients, while the researchers are working to find out whether herpes is the cause or not.

Happily, cervical cancer is a "good" cancer. It grows very slowly at first and is easy to detect in its early stages. Cure is virtually guaranteed if detected early, and major surgery is generally not required to halt the disease in the early stages. Detection is done by the Papanicoulou (Pap) smear, and I recommend one of these regularly for the herpes patient—not only for safety, but for peace of mind. The Pap test is a quick, simple and painless test which samples the coating

on the cervix (the mouth of the womb). Under the microscope cancer cells in the specimen can be detected in their earliest stage. This test should be done regularly in all women, but at least once a year in women with herpes. Beyond a regular Pap test no other precautions against cervical cancer are necessary for the woman with herpes.

My spouse is my only sexual partner. We've been together for months and I just got herpes. Is my spouse to blame? Has my spouse been unfaithful?

Genital herpes is a sexually-transmitted disease. There is a small theoretical possibility of obtaining the infection from another source—for instance from a warm, moist, shared towel. Practically speaking, however, for the virus to affect the genitals it must be inoculated *onto* the genitals, and the best way of doing that is via sex. But remember that herpes infections come and go. They are active, then latent, then active again. Also, remember that *most* people with genital herpes never have any symptoms which they can identify. Your partner could have been infected at some point in the past, yet perhaps it was only recently that you had sex at the exact moment that your partner had an *active* infection. There is also the possibility that you yourself have had genital herpes for several years and have only just now noticed or started having symptoms. There is no test which will tell the difference.

Furthermore, if you engage in oral sex, specifically with your partner's mouth in contact with your genitals, then you might get genital herpes if your partner had a cold sore, or fever blister, or canker sore of the gums (or no external sore at all) which *happened* to be caused by herpes. In fact, 50 to 80 per cent of us may harbor the virus in a latent state in our mouths, and shed the virus from time to time because of active infection. If you have oral sex at the right moment, in other words, genital herpes may result. The mouth type of herpes is usually called **Type 1**, and is most often spread from mouth to mouth (and often from parent to child). But herpes simplex is herpes simplex. While **Type 1** likes the mouth best and **Type 2** likes the genitals best, the site of

virus inoculation is much more important. (If the virus is on the toe and if the toe spends a lot of time in someone else's ear, an infection in their ear can result.) So your partner could have received herpes from a parent at age 3, have had no symptoms, and still transmit the virus to your genitals 30 years later!

Be careful, then, before calling the divorce lawyer. Talk the problem out with your partner. Don't let herpes alone come between you. Be honest and demand honesty. Possibly your partner was unfaithful—but maybe not. Herpes *may* bring you closer together.

A summary so far

In this chapter we have seen that herpes is able to cause a recurrent skin infection, and that often people never realize they have this infection. However, once herpes has been diagnosed its recurrence can be clearly recognized by the individual. Avoiding its transmission comes naturally once you understand the active phases of infection. Control of your infection comes gradually as your own army of immunity takes over and fights off each recurrence with efficient killing power. With time, the frequency of recurrences generally diminishes. The virus may cause a terrible infection in some newborn babies, but it is a highly preventable and uncommon syndrome—and almost always under the control of the sufferer and her physician—if she knows she has herpes and discusses the problem.

A form of cancer may or may not be related to herpes, but it can be easily detected, effectively dealt with, and is unlikely to occur—herpes or no herpes. Is herpes the incurable disease which kills babies and causes cervical cancer? On the contrary, herpes is an extremely common virus infection, poorly understood by many people and further sensationalized by the media. It is a nuisance, without doubt. It *can* be a problem when it recurs very frequently. There is no question that it can sometimes result in serious complications but, for the person who has a herpes infection, these complications become very preventable. Given the right information, herpes is a syndrome which can be under your control.

CHAPTER TWO

We live in a dancing matrix of viruses; they dart, rather like bees, from organism to organism . . . passing around heredity as though at a great party . . . If this is true, the odd virus disease, on which we must focus so much of our attention in medicine, may be looked on as an accident, something dropped.

LEWIS THOMAS, *The lives of a Cell (Notes of a Biology Watcher)*

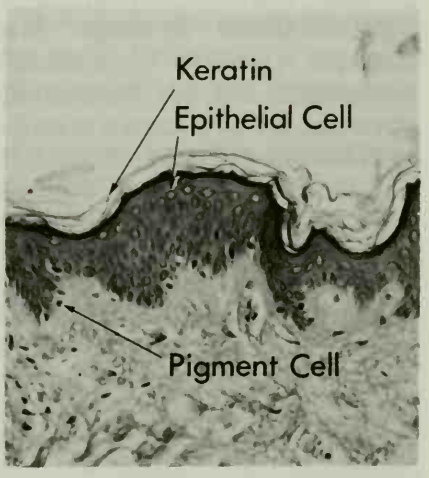
HERPES SIMPLEX: THE VIRUS

A short history of herpes

Herpes infections are not new. Over 25 centuries ago Hippocrates, the father of medicine, coined the word "herpes"—from the Greek "to creep." Medicine in his time was descriptive. Diseases were classified according to their appearance. In fact, the diseases called "herpes" by this ancient physician are now known to be several different skin maladies with several different names and causes.

During the first part of this century, scientists discovered the "filterable virus," a particle so small it could pass through a paper filter, so small it could not be seen with the microscope—yet fully capable of causing infection. It was not long before microbiologists had identified many different viruses which were capable of causing different diseases. Some examples are polio, hepatitis, influenza, rhinovirus (the common cold) and the herpes viruses. The cause of herpes infections became further understood and the types of viruses further classified.

A great step forward in our understanding of the problem was developing the technology to grow viruses outside the body, i.e. in the test tube. Since viruses are parasites of cells, the first advance in the field was the discovery that human cells could be stimulated to grow artificially by giving them the right nutrients and salts and keeping them at the right temperature. Cells are the "unit system" of the body. They contain all the parts necessary for reproduction and metabolism; that is, they can make new copies of themselves and eat in between. Furthermore, each type of cell in our body has a special function. It might specialize in movement (muscle cells); structure (bone cells); filtering poison (kidney cells); detoxification (liver cells); guarding the body surface (epithelial cells); killing foreign invaders (lymphocytes and leukocytes); or in carrying oxygen to other cells (erythrocytes). Pick any organ or functional system of the body—whether it be for pumping blood or for thinking. If you look at a slice of this tissue under the microscope, what you will see will be different cells each "doing its thing." Figure 1 is from a slice of normal skin. The cells can be seen lined up according to function, and each cell type has a name: the epithelial cells are the special targets of the herpes simplex virus. Note the thick layer of keratin, a waxy outer coating on skin that forms a natural physical barrier to ward off invasion by infection.



1. *A microscope view of a slice of skin. The waxy outer coating of keratin is apparent at the top of the picture. As long as the keratin stays unbroken, it helps to prevent herpes simplex virus from finding its target–the epithelial cells. The cells with the dark pigment (called melanin) give the skin its color.*

Viruses are grown in the laboratory by allowing them to parasitize cells like those in this diagram. Basically, a piece of tissue is placed into a test tube with chemicals and enzymes and gently chopped up. The separated cells are then given nutrients like sugar, amino acids and vitamins. If everything goes well, the cells will soon grow and multiply. The photograph below is an example of cells grown in culture. No longer specialized, these cells are all of the same type.

2. *Human fibroblast cells grown in tissue culture. This picture is taken through a microscope. Cells in the laboratory look like this if they are healthy–not affected by virus or anything else. Different viruses can be detected by the changes they induce in these cells.*

Once scientists were able to grow cells outside the body, getting viruses to do the same inside those cells became easier. Viruses were soon purified, analyzed and classified. Herpes simplex virus could be detected, on the genitals and elsewhere. At first it was not considered to be a sexually transmitted disease: it was later shown, however, that the greater the number of sexual experiences of an individual, the greater the risk of contracting herpes.

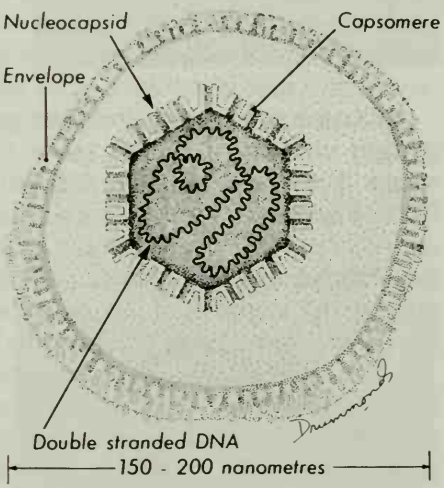
By the late 1960's the syndrome of herpes of the newborn had been analyzed and linked to active herpes infection in the mother at term. This marked the beginning of an explosive period of herpes research. Cervical cancer was connected with herpes. As more became known about the problem it became more widely publicized, and the public alarm made good press. More people with bothersome sores sought medical help. At the same time, our population became more sexually "active." We loosened many of our taboos. Sexual

contact often became casual. Oral sexual contact became more frequent. Possibly the most important factor in the growth of herpes, however, was the change of birth control methods. As we left behind condoms and foam for the convenience of the I.U.D. and the pill, we left behind these unnatural but effective barriers to infection.

Today we have come up against a reservoir of virus in the community which is so large that herpes has become, literally, almost unavoidable. Today, ten times as many people seek help from a physician for genital herpes as they did ten years ago. You don't have to be a statistician to see the problem we face, now or in the future.

What is a virus, anyway?

A virus is a very small living thing. It is so small that it can pass through something as fine as a coffee filter. It cannot live on its own. It contains either **DNA** or **RNA** (hereditary

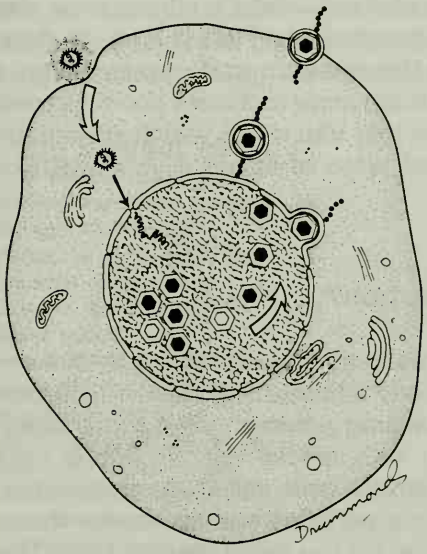


3. *This is an artist's drawing of herpes simplex virus. The virus is protected by its envelope which allows it to attach to cells. The envelope is made of fatty material and is therefore easily dissolved by organic solvents such as alcohol, ether, etc. It is also destroyed by soap. Without the envelope, the virus cannot attach to a cell. The virus core is surrounded by a shell called the nucleocapsid. This consists of 162 subunits called capsomeres which form a unique geometric shape called an icosahedron. Inside of the icosahedral nucleocapsid is the double stranded DNA coiled like a doughnut and weighing in at 100 million daltons. The whole particles measure about 150–200 nanometers (0.0000002 meters) across.*

material which passes on its characteristics to the next generation of viruses). This hereditary material is surrounded by a protective outer coat made of protein and sometimes another protective coat called an **envelope** which is made of fatty and protein-like material.

A virus lives according to all known laws of heredity and natural selection. Its job in life is to reproduce copies of itself. These are called **daughter particles** by virologists. A virus reproduces in a straightforward fashion. First, since it is a parasite, it seeks a host cell which provides a likable environment. Each virus has its own favorite cell type. In fact, which cell the virus likes best will determine which disease it might cause. For example, while a hepatitis virus likes liver cells, a herpes simplex virus likes skin and nerve cells.

After finding the right cell, the virus makes its presence known by attaching itself, probably to special receptor or receiving sites, on the outer layer of the cell—the **membrane**. It then undresses itself and injects its nucleocapsid into the



4. *The reproductive cycle of herpes in a cell is depicted by an artist here. The virus causing infection finds its way to the epithelial cell surface and attaches to the surface using its envelope (upper, left). There it begins the job of reproducing. Reproduction is herpes role in life. First, after attachment it injects itself without envelope into the cell, and then the capsid travels to the nucleus where it injects just its DNA. The DNA makes copies of itself, and these copies fill up newly formed capsids. The filled capsids pick up new envelopes on their way out of the nucleus and out of the cell itself.*

cell. This finds its way to the cell nucleus and then injects its hereditary material (DNA or RNA) into the nucleus, where the reproduction of new daughter particles takes place using the cell's own machinery. Usually, this reproductive process eventually stops the host cell from living for itself and so, after new virus particles are made, the cell bursts and dies, scattering daughter virus particles around to neighboring cells—where the cycle is repeated.

This parasitic relationship between viruses and cells is quite different from bacteria which can live all on their own. A virus survives by taking over the host cell machinery. That is why it is so hard to kill. Bacteria (like gonorrhea, for example) don't need a host cell to live and grow. They only need basic nutrients (like a good diet—a source of carbohydrate, protein and so forth). In fact, it is because bacteria can make so many of their own products that they are so easy to kill with drugs called antibiotics. These substances, such as penicillin, interrupt some manufacturing process vital to the bacteria, but irrelevant to the host. The virus needs its cell, however, and since the virus uses the host cell system for its own life cycle, many chemicals which kill the virus also interrupt the normal host metabolism. That is why, to date, we are without a cure for the common cold—and without a cure for herpes. We are learning more and more about viruses, however. As we find things that viruses do which are unique to the virus, so do we find ways of killing a virus without harming the host.

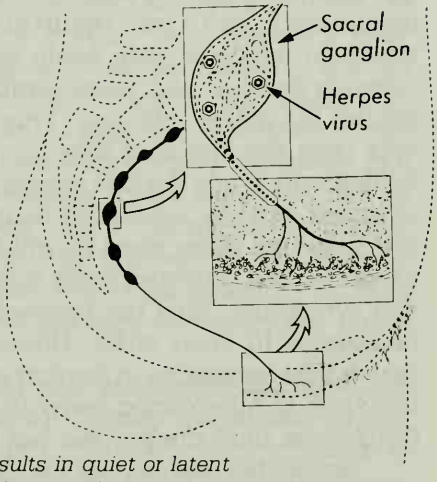
What stops a viral infection?

The growth cycle of a virus is eventually halted by the coordinated strategy of the body's immune system, which produces specific virus-neutralizing poisons called **antibodies**. These antibodies team up with special infantry fighter cells called **lymphocytes** and janitor cells called **macrophages**. Antibodies cling to the virus particles and inactivate them. Meanwhile, the lymphocytes kill the living few left over. The macrophages chew up and clean out the mess, leaving room for healthy unaffected cells to grow and replace the old.

Why don't we develop immunity to herpes? (The story of latent infection)

We really do develop immunity to herpes. In fact, as we've just discussed, this immunity is very effective at stopping a recurrence once it starts. But how, then, is it able to start at all? Herpes simplex has two special tricks up its sleeve to beat the system: one, a kind of hibernation, the other a unique method of travel. While most of the virus goes through the process just described only to be wiped out by our body defences, some of the virus finds its way up the nerve endings that give feeling to the affected areas of skin.

The body's sensory nervous network is everywhere, giving us feelings such as pain, temperature sensation, touch sensation and so on. Nerve fibres extend to all areas of skin like a branching network of phone cables supplying many thousands of homes with phone service. The first switching station which gathers up the electrical input from several areas into one "cable" for transmission to the "central clearing house"—the brain—is called a **ganglion**. The ganglia lie next to the spinal cord—the "main cable," and house the cell machinery for all those little nerve fibres. There are several ganglia running along the spinal cord from top to bottom.



5. *During active skin infection, while the infected epithelial cells are going through their active phases in battle with the immune system, it is thought that the nerve fibers which supply sensation to the affected areas of skin also become infected (lower box). The virus travels up the nerve fiber until it gets to the core of the cell inside the ganglion. There, it stops. Unlike the productive and explosive infection occurring on the skin, infection of the nerve cell results in quiet or latent infection which persists (upper box).*

The herpes virus stops when it gets to the ganglion. It comes to rest, for reasons we understand (survival), but by mechanisms we do not understand. This resting state is so quiet that the body's defences do not sense a problem. There is no damage to the nerve, but no fight from the body and so the virus enters a **latent** state. Exactly what it is doing in this state is unknown. Some scientists believe that the virus is growing inside the nerve cell, but that the infection is slow and "nonproductive." In other words, it has entered a state of hibernation where its growth processes slow down. Alternatively, the DNA of the herpes virus may have united with the DNA of the host cell, making them essentially one and the same. Other possibilities certainly exist. The only facts that are known for certain about latency are that the virus *can* be cultivated from ganglion cells removed at the time of autopsy under very special conditions of care called **cocultivation**; and that it is known that if a surgeon tampers with a latently infected ganglion, herpes will recur at the original skin site, apparently because tampering reactivates the virus.

For the most part, a latent virus will remain latent. If and when a trigger like a surgeon's scalpel stirs things up, the virus may change its character and decide to reactivate. It will then travel down the same nerve fiber it first went up and re-enter a healthy skin cell. At this point the active state begins again and a new **recurrent** infection takes place. The recurrent infection once again signals danger to the body's immune system, and those antibodies and cells go to work halting the active infection. This recurrence is often less severe than the first skin infection because neutralizing antibodies were made the first time and are already there, waiting to attack **virions** (emerging daughter particles). During the first infection there were no antibodies, and so lesions took longer to heal, affected more skin, and caused more blisters and symptoms. Now the immune system is able to halt the recurrence in short order. However, preventing the reactivation from beginning in the first place is not so easy, because the virus is hibernating away in a quiet state, sneaking by the system until the process has already reactivated.

Remember, herpes has *two* tricks. The second is its ability to go from one cell to another without ever leaving the

cell environment. Suppose you decided to rob other homes in your neighborhood by going from your house to your neighbor's house without ever going out of doors. In that way you could avoid the police. To go a step further, you could send a signal to a carpenter in your neighbor's house telling him to build a self-enclosed bridge until he is inside your house. In fact, this is exactly what the herpes simplex virus can do with relatively little effort. The host cell with virus can fuse with a neighboring cell by inducing **bridges**. In fact, so many cells may fuse that a giant cell is formed. (These giant cells are so specific to herpes, in fact, that they are one way the virologist can tell if a virus culture is growing herpes.)

Why is this bridging so important? With most viruses, antibodies are sufficient defense to prevent a recurrence. This is, indeed, the basis for preventive vaccines like polio and measles. The vaccine stimulates antibody production: when the virus comes along it is neutralized before it spawns a disease. Since antibody is a very good antivirus poison, and since most viruses grow inside cells and then release themselves into the **interstitial** (out-of-doors) environment when the cell bursts, disease cannot recur. Antibodies are waiting, and the infection is nipped in the bud. Herpes is different, however. Most infected cells do indeed burst and most virus is indeed neutralized. But antibodies cannot easily travel to the inside of a cell to attack a virus—and herpes is busy building bridges *before* its growth has progressed to the cell bursting stage. A few virions saunter happily to a neighboring cell, safely protected by their bridges from the reach of the antibodies. Other young virions will be killed effectively in a few hours when they break outside, but a select few live on and infect healthy neighboring cells. Quite a trick! Of course, the immune system can cut this process off by using its lymphocytes and macrophages—just as our imaginary scheme for robbing houses would not get very far before the police put a stop to it.

We can now understand why antibodies are helpful in limiting the severity of recurrent disease, yet useless in preventing the recurrence entirely. Herpes is very effective at hiding from its enemies. Hippocrates chose a remarkably apt name—"to creep."

What Is a Herpes Virus?

The herpes family of viruses includes a total of four different viruses which can effect human beings.

The **Epstein Barr virus** is the major cause of **Infectious Mononucleosis** ("mono," "kissing disease").

Cytomegalovirus may also cause mono. It may be sexually transmitted and may cause problems to newborns. It can cause hepatitis. Occasionally it is transmitted by blood transfusion. It is very common among homosexual men and is often associated with (but probably not the cause of) **A.I.D.S.**, the **Acquired Immuno-Deficiency Syndrome** we are hearing so much about. We have a lot to learn about this virus.

Herpes zoster (also called **Varicella zoster**) is the cause of **chickenpox**. Chickenpox results from the primary (first time) infection. The virus itself may recur. The recurrent form is known as "shingles."

Herpes simplex virus Type 1 and 2 is the subject of this book. Depending on the situation, it may cause **cold sores** and **genital herpes** or, less commonly, **herpes of the newborn** and **herpes encephalitis**.

These four viruses are similar in that they are large viruses. Their hereditary material is DNA rather than RNA. They all have a protective envelope. Under an electron microscope, they all look exactly alike. Each remains latent for life once the primary infection has occurred. (Yes, people who have had mononucleosis harbor the Epstein Barr virus all their life.) Each of these viruses will have infected most people before the age of 30, and most of them with no symptoms. Each infection may recur. Yet in a similar way to the latent state of the herpes simplex virus, each of these viruses does no harm during latency. Latency is *not* a disease. Recurrences of active infection may cause symptoms, however. For example, the elderly gentleman with a painful bout of shingles is having a recurrence of a virus infection he first caught in early childhood called chickenpox. For 80 years he has harbored the latent herpes zoster virus in his ganglia—the virus left him unaffected for 80 years until an active infection recurred as shingles.

Here the similarities end, however. These different herpes

viruses do not cause the same diseases. Infection with one does *not* make infection with another more likely. Nor does infection with one *prevent* infection with another.

Yes, your grandmother with shingles has "herpes," but because of its notoriety the word "herpes" has specifically come to mean herpes simplex, one of the four members of the family of herpes viruses (Herpesviridae) capable of affecting humans. Each herpes virus is unique. They should not be confused.

CHAPTER THREE

Yes, it is the exact location of the soul that I am after.
The smell of it is in my nostrils. I have caught glimpses
of it in the body diseased. If only I could tell it.
Is there no mathematical equation that can guide me?
So much pain and pus equals so much truth?

RICHARD SELZER, *Mortal Lessons, Notes on the Art of Surgery*

GENITAL HERPES: THE SYMPTOMS

What are the symptoms of genital herpes?

Any infection may cause a spectrum of disease symptoms from very mild to very severe. Herpes is no different. In other words, there are some people who suffer no symptoms whatsoever from the infection who can be proven by a lab test to *have* the infection while, on the other hand, there are people whose symptoms are so severe that they may result in severe disability or even death. An example of the latter would be a newborn baby who becomes infected with herpes which disseminates.

When it causes infection in a normal person, however, genital herpes almost never causes disease at the far end of the spectrum, that is it almost never results in severe disability or death. In fact, the majority of people with genital herpes find themselves at the opposite end of the spectrum. They have been exposed to genital herpes, developed latent infections and antibody, but deny ever having had symptoms of this infection! It is difficult, then, to paint any single picture

of a herpes sufferer. The symptoms depend not only on the severity of infection, but also on the site of the infection. The site of the infection is determined by the site of inoculation. In other words, where did the herpes virus find its easiest access to epithelial cells of the skin? For the most part, herpes simplex likes mucous membranes. Mucous membranes are areas where the skin is thin. These include areas like the **labia** (lips) of the vagina and the lips of the mouth. However, any area of the body may be fair territory for herpes. If a **finger** has a tiny crack, and such minor injuries are common, the virus sitting on the finger could easily find its way to an epithelial cell. In general, though, it will avoid places like the hand and other thick-skinned areas because it's more difficult to find a way in there. However, any time there is excessive moisture and especially if there is trauma or injury even to a protected area like the hands, the setting is ideal for herpes to be transmitted.

With genital herpes there are the three major classifications of outbreaks: **primary** infection; **non-primary** initial infection; and **recurrent** infection.

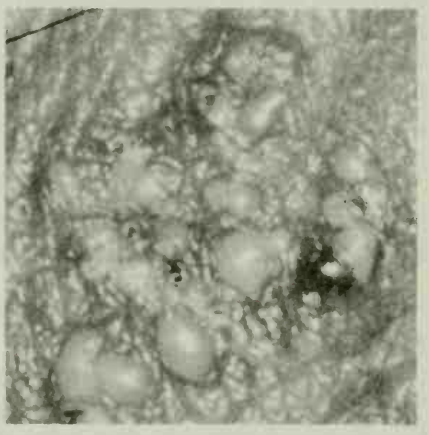
Primary Infection

The person who experiences a primary infection has never been exposed to any herpes simplex virus at any time. In other words, there is no history of cold sores, there is no history of exposure to cold sores, and he or she has developed no previous antibodies to herpes. The absence of antibodies is crucial. Antibodies, remember, are capable of neutralizing herpes quite effectively. The body, in defense of its first attack by the virus, has the job of making antibodies. It usually does so quite effectively. Once antibodies are present, herpes infections become very different.

During this first (primary) infection, however, the virus can be **inoculated** or transferred from one place to another. Infection may be much more severe because no antibodies are yet present. More sores may develop. In addition, there is a greater chance that a person will feel sick with his first infection. Usually this is a flu-like illness. It feels very much

like any other viral infection and can cause muscle aches and pains, and possibly fever and headaches. A primary infection can also fall into the herpes spectrum, however. In other words, for some people it may pass unnoticed, without a hint of a problem.

When genital sores erupt, they generally do so at the site of inoculation, which is usually on the external genitals. Sores will generally look like a cluster of small blisters which are filled with clear or whitish fluid. The classical herpes sore, seen in the figure below, is just this—a group of small blisters—**vesicles**—on a red base of inflamed skin.



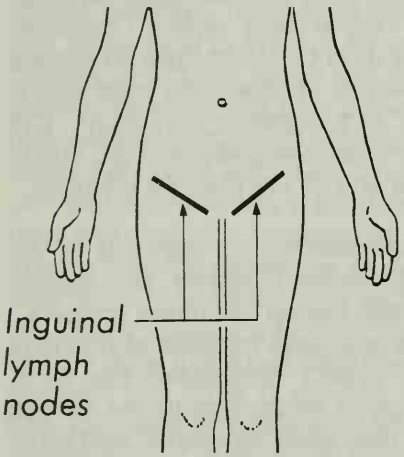
6. *A picture of a typical or classical recurrence of skin herpes. A cluster of fluid-filled vesicles are seen overlying a red base of inflamed skin. These sores are itchy and may be somewhat painful, especially if touched directly.*

Often, these blisters are never seen, and the first signs of infection are small erosions of the skin called ulcers. **Ulcers** also tend to come in clusters or groups.

In women, herpes sores or lesions are usually on the external genitalia, most commonly on the labia of the vagina. Another common site is the pubic hair. In men, they are usually on the foreskin or shaft or in the pubic hair, but the **glans** (tip) of the penis is also possible territory. Sores may vary in size from very small (one to two millimeters) to very large (one to two centimetres). Sores are usually quite superficial i.e. the infection is on the outermost layer of the skin. The skin becomes raw and painful, and itchiness is the rule. There is a lot of inflammation going on at this time because the body is attacking the virus. This is a healthy response,

but may lead to quite a bit of distress. If sores are present around the **urethral meatus**, the spot for the exit of urine, urination may become quite uncomfortable. People may complain of **external dysuria**, or the feeling that urine stings once it has exited, and has touched the sores. Sores might also appear on the thighs, on the buttocks, or around the anus. In addition, sores may be present in other areas, for example the mouth. If oral contact occurred in the same area as genital contact, there is a reasonably good chance that a mouth infection will result. Rare sites of infection—again depending upon the place and circumstances of virus inoculation—will be the fingers, the breasts, or the eyes.

Often the lymph nodes are swollen in the **inguinal** region. This means that the immune system is fighting off the virus. Lymph nodes are those "glands" that the doctor often feels for in the neck when you have a cold. Similar "glands" are present throughout the body, and those in the groin are the areas of **lymph** (internal body fluid) drainage from the genital area. With genital infection these groin lymph nodes may become swollen and tender to the touch.



7. *Location of the inguinal lymph nodes. These "glands" or lymph nodes may become swollen and/or tender during a bout of herpes. This swelling is most common during primary herpes, but may occur with recurrent herpes also.*

The urinary tract itself may become infected with herpes, resulting in discomfort on urination or even difficulty in passing urine. An unusual vaginal discharge may be present. However, when an atypical vaginal discharge is present—

every woman is different, and some type of discharge is normal for everyone—it may be caused either by herpes or some other infection going on at the same time. Discharge may also be a normal phenomenon. In fact, some discharge is normal for every woman. If a discharge is present, it is important to find out if some other cause such as trichomoniasis or a yeast infection is present *along with* the herpes. In fact, whether or not discharge is present, a physician or a specially trained paramedical person must examine you for other treatable infections which are not unlikely to occur at the same time as herpes. Internally, the cervix (the mouth of the womb) is infected about 80-90% of the time during primary infection. By itself, cervical infection causes little in the way of symptoms. It may produce a thin, watery vaginal discharge. Occasionally, the doctor can see herpes sores on the cervix. However, during primary herpes, herpes is usually on the cervix, whether there are sores to be seen or not.

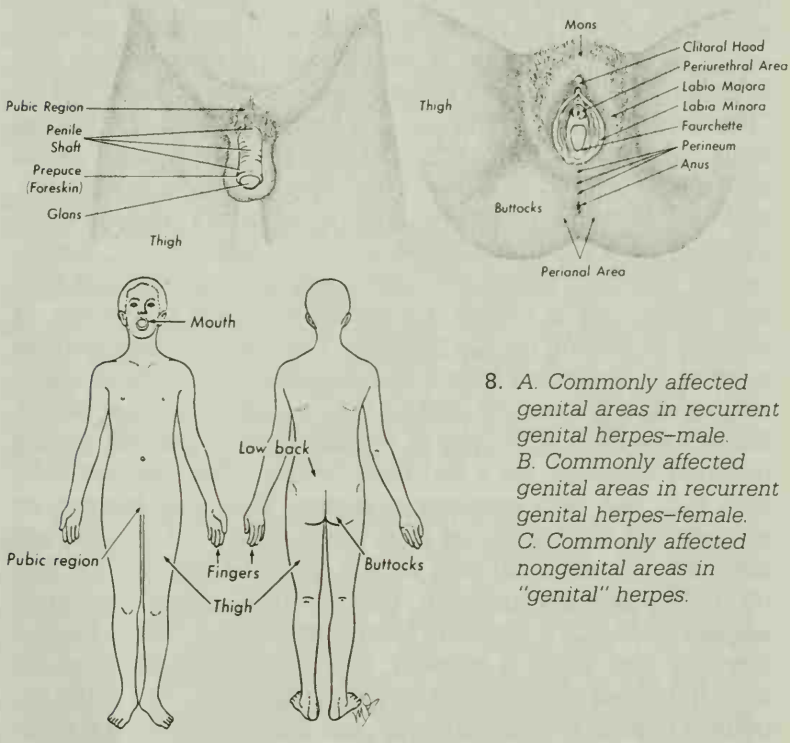
So, as you can see, primary herpes infections may cause anything from no symptoms to a couple of sores; from a sore throat to headache and muscle pains. It can cause any or all these symptoms. Symptoms will clear up and disappear completely, usually within about two to three weeks. Occasionally, people complain that they didn't feel just right for several weeks after their primary infection. There is no good explanation for this feeling, but it is a common complaint. The ulcer-like sores will eventually scab over and these dry crusts will fall off. This will mark the end of the primary infection.

Non-primary, initial infection means that this is the first episode of symptoms of herpes. However, the patient with non-primary, initial herpes, has an "immune memory" for herpes simplex virus. This is usually because of previous infection with herpes simplex Type 1. Remember, that 50 to 80% of people have some type of antibodies to the herpes simplex virus usually because they were exposed to cold sores in childhood. So, in fact, the first infection with herpes is commonly of the non-primary variety. Initial, non-primary herpes is very different from primary herpes, because of these antibodies. Other components of the immune system, lymphocytes, etc., have also already "learned" about herpes and

are ready to be quickly triggered. Since there is already a mechanism built into the human defense system to fight this infection, the body fights off the disease quite effectively and rapidly. The symptoms are essentially the same as for recurrent herpes. It has a special name only because it is the first episode.

Recurrent infection. Recurrent herpes is usually much milder than primary. In fact, people with recurrent herpes are often troubled very little in terms of their physical ailments during recurrences. Again, symptoms are the result of herpes infections of epithelial (skin) cells. However, recurrent infection begins when virus is inoculated into these cells by travelling back down the nerve pathway that it originally travelled up on its way to creating latent infection of the ganglion (see Chapter Two). This time there are antibodies present and an "immune memory". That is, the body has seen the herpes virus before and is quite effective at limiting its growth. Sores are usually limited to a few. They may be single or multiple, and tend to come in clusters. That is, sores are often grouped together on a small, reddened, inflamed base of skin. Recurrences will often begin with some sensation or warning sign that something is wrong, for example, a pain in the leg, or tingling or itching on the genitals. The warning sign may be present for anywhere from a few minutes to a few days. Sores may develop first as tiny blisters (also called vesicles) or ulcers. Blisters are filled with clear or whitish fluid. These are usually grouped together, on a red base of skin. The vesicles soon turn into wet skin erosions or ulcers. This may happen so quickly that the blister *per se* is never noticed. The ulcer will then dry out and scab over with a dry crust which soon falls off. Unlike primary infection, this recurrent herpes sequence usually takes just a few days from start to finish. Fewer lesions develop, less virus is present, and the discomfort is much less. Itchiness is extremely common, however. The sores are usually painful to touch directly, but often do not hurt a great deal if left alone. If, however, the sores are in a place which is rubbed or where urine hits them, pain may be more of a problem. That general feeling of sickness which comes with primary infection is usually absent. Sores are in the same

places as discussed in primary herpes, except that the cervix is usually not affected. In other words, genital herpes is an affliction, generally, of the external genitals (the parts you can see with your clothes off, holding a mirror and a light). The internal genitals are usually not affected (4–15% of the time depending on the study). As with primary herpes, the symptoms of recurrent herpes will depend upon the area affected. Generally, one small area of one of the sites noted below in the figure will be affected during one recurrence. The site may stay precisely the same at each recurrence for some people. It may move from place to place each time for another. It may itch only in one site and hurt more in another.



8. *A. Commonly affected genital areas in recurrent genital herpes–male. B. Commonly affected genital areas in recurrent genital herpes–female. C. Commonly affected nongenital areas in "genital" herpes.*

It is important to reiterate the wide range of severity here. Active recurrent sores may be obviously herpes when they come in clusters of little blisters. But genital herpes may never be more severe than one very small sore on the labia

or foreskin or around the anus or on the thigh. It may be the size of a pencil eraser or it may be as small as the sharpened lead point. The sore may, in fact, never be painful at all in some people. It may not even itch! It is not hard to imagine how people with a painless ulcer, the size of a pencil point, might serve as an excellent source of herpes for others. They, the unwitting reservoir, infect the unwitting victim. Most people who get herpes never get anything but mild unrecognized sores. They may never even notice the sore, and if they do, they may never seek the advice of a physician. Occasionally, however, people with recurrent herpes who know about the active phases of their virus fall into another trap. Imagine the following scenario:

- *"Is your herpes active today?"*
- *"No, doctor."*
- *"Do you notice any unusual or uncomfortable sensations in your genital area, around your anus, or on your thigh?"*
- *"As a matter of fact, Doc, now that you mention it, I have had a small cut which I got from this tight underwear. But this isn't herpes, because it* hurts. *My herpes sores just itch and they are over here on my leg."*
- *"This is actually herpes. It is in a spot you have never noticed before. Herpes may be mild once and less mild another time. It may itch on the buttock and hurt on the labia, or vice versa. The lesson to learn here is that any unusual break on the skin or sensation of an unusual feeling should be checked out with a mirror and a good light, or by a friend. Get to know your herpes and/or anything else of an unusual nature happening on your genitals."*

Over the years, I have heard herpes called a lot of things. The most common mistaken names for things that turn out to be genital herpes are: spider bite (especially on the leg or the buttocks); yeast infection; hemorrhoid; pimples (on the buttocks, labia, etc.); shingles; water blisters; cuts or slits of the vagina or lips.

The appearance and sequence of herpes sores are discussed in the coming pages. With each description, however, that wide herpes spectrum of severity must be kept in mind. The phases might all occur in obvious sequence. They can last a week or an hour. Some phases can be skipped. Some people need a hospital bed to recover from herpes. They usually know what they've got! Others will never notice anything unusual. When herpes phases are inactive there is generally no virus on the skin, so no symptoms occur, and transmission of infection does not take place. In any one person, an active recurrence may then occur never, once in a lifetime, once in a year, or as often as three to four times per month.

What are the phases of herpes infections?

The phases are very important to learn, because they determine when the living virus is on the skin. An active infection may be categorized in the following phases: **asymptomatic**; **prodrome** (warning); **early redness**; **vesicles**; **wet ulcers**; **crusts**; and a **healed** state.

During the **asymptomatic** phase, the virus is latent. It resides in the ganglion causing absolutely no harm. It is not on the skin. If you know what herpes feels like and know what it looks like (and you've looked), you can be nearly sure that no virus is there (see Chapter 5 for further details on transmission). Herpes cannot jump from your ganglion to the genitals of your sexual partner. It is only passed on when it is active on the skin. You can prevent this if you know what is active, you've looked carefully for herpes sores, and you've checked out any unusual feelings down there.

Furthermore, if virus is causing no symptoms, but is active, the amount of virus should be very small. Let us say for some reason you missed an active herpes because you just could not see it or feel it. You have had sexual contact anyway. Since there probably is an "inoculating dose", that is a minimum number of virus particles which must be contacted in order to get herpes, this period is probably still a low risk phase for transmitting the infection.

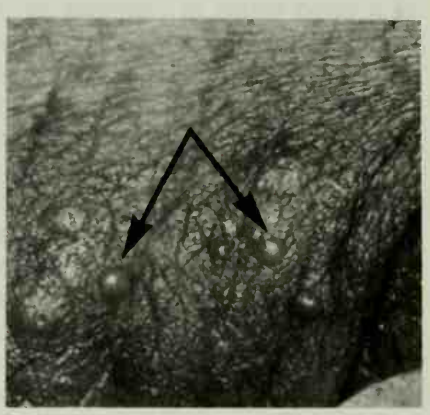
Most people who get recurrent herpes (but not all) will have a **prodrome**, or warning. This signifies that the virus has been reactivated and is on its way to the skin. As the virus activates, the nerve may react and symptoms may develop. The warning is different for everyone. In some it will be a pain in the leg or the buttocks. In others a feeling of numbness or coldness or itching or pain may develop right at the spot where the sores are going to soon appear. The most common prodromal is this itching at the site before the lesions appear. Occasionally, herpes starts with a special kind of headache or a fever. This prodromal phase may last five minutes or three days. Most commonly, it goes on for about 12 to 24 hours. It may be something you've never noticed. It is a good thing to pinpoint in yourself, and to think about and identify, if possible. It tells you that the active sequence has started. At this time some people will have virus present on the skin. Skin contact with genital areas or other areas where you usually get sores should stop until this recurrence is over. It is very common for this phase to come and go often without other phases following. Many people realize that they have had a warning after it is over. In other words, there will be a vague sensation that something is amiss—below the level of consciousness. Once a sore is there, there is the, "Oh yeah, I felt that all day.". This requires back-stepping in your mind. If you have warnings try to notice them as they occur. It will help you to learn to map out these active phases of infection.

Next, **early redness** can be detected in a small area of skin. It may feel itchy or painful to the touch, or just sensitive. At this point, the virus is beginning to grow inside the skin (epithelial) cells. The immune system of antibodies and lymphocytes is being called back to work. This ensuing battle between defences and virus causes inflammation or redness. Virus is in the skin. Sore contact is unwise.

Vesicles are the small blisters which form on top of the early red patch. They have clear or whitish fluid and are often grouped. There may be only one, or a few in a group, or so many that they run together. The tops of these are very thin and come off easily, often oozing a little of the fluid. The fluid is the product of sick, swollen skin cells which have been

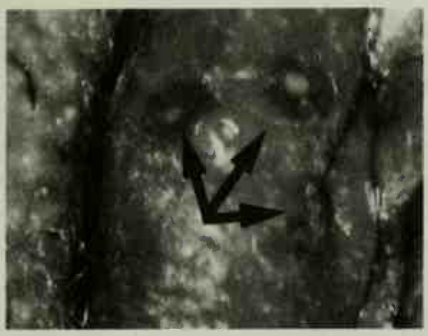
attacked by herpes. Inflammation continues. Itchiness and/or pain is usual, but not always there. Virus is virtually *always* present at this stage, making this a good time for diagnosis. This stage is commonly skipped, especially in women with labial sores and men with sores under the foreskin, since these wet areas quickly macerate the blister and rub off its top, leaving an ulcer underneath.

In fact, just touching these vesicles may cause them to break and leak fluid. A cotton swab or the blunt end of a toothpick poked at the bottom of one vesicle will be quite painful, even if they are not bothersome just sitting there. Avoid breaking them on purpose, since there is nothing to be gained by doing this.



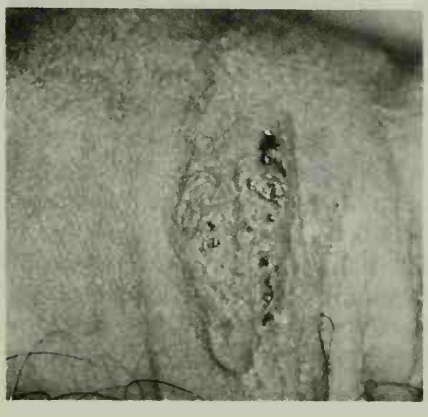
9. *A picture of a sore in the vesicle stage. These fluid-filled tiny blisters often come in clusters, but they may come one at a time. The fluid can be clear, white or red.*

The next stage is characterized by **wet ulcers**, which are vesicles with the tops off. They glisten with wetness and may feel raw to the touch. There may be one tiny sore which can only be seen with a magnifying lens, or there may be dozens of large and painful ulcers. They may group together to form larger ulcers. Herpes ulcers are superficial. That is, they are right at the skin surface. They are not deep and ragged, but rather round and wet. Painful to the touch is the rule, but there are exceptions. Virus is virtually *always* present at this point also. From as far away as the eye, they may look like a small cut. Spread away the pubic hair for a good look. Use a magnified mirror. Touch the sore with a blunt toothpick again to see if it is tender.



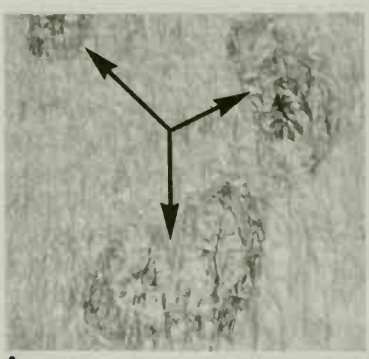
10. *A picture of a herpes sore in the wet ulcer stage.*

When the fluid in the ulcers begins to dry, the sores cover themselves with a **dry crust**. This marks the beginning of healing and virus begins to disappear. The scab covers the raw ulcer just as a scab grows over a cut from a knife. At first the scab is soft and wet and crumbly. If rubbed away a wet ulcer remains underneath. As the sore dries, however, the crust hardens. Underneath the skin grows anew. This is called re-epithelialization. While the crust is still there, virus is not always gone. Sexual contact within the area of the sore is still not advisable. The itch or pain may be leaving entirely, or the itch might just begin to worsen at this stage. The size of the lesion will generally determine the size of the scab. Commonly, small sores never have a crust stage. They just sort of melt away from ulcer to nothing. Others always get a dry crust.

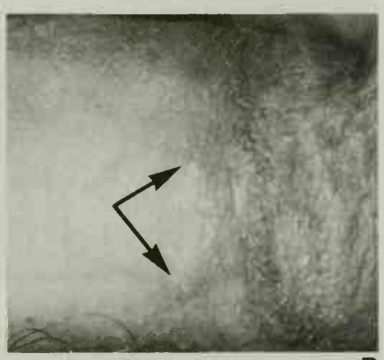


11. *A picture of a herpes sore in the crusted stage. Crusts can be wet (left) or dry (right).*

The sores are **healed** when the crust falls off and the active infection is over. This is the same as the asymptomatic phase. The healing may leave a red mark, just like a healed cut from a knife. These spots may also be whitish rather than red, or they may in some other way appear different from the unaffected skin. The marks may be slightly tender, but the surface is definitely healed with new skin. In some people this mark may last for weeks. In others the marks will be present for only a few days. Others will never get marks. The healed phase is an **inactive** phase. Virus growth is over; only healing is active. Skin contact with this area is now safe once again. This healed phase generally occurs five to ten days after the appearance of the vesicle stage in recurrent herpes. However, the time may be measured in hours, or occasionally (rarely) weeks. During primary herpes, however, the "natural history" of a single outbreak is quite a bit longer (approximately three weeks).



A 12. *Pictures of herpes sores in the healed phase. After healing, skin may appear totally normal or A) Healed sores might have increased color or B) decreased color.*



These color changes can persist for weeks or even months. They do not mean that herpes is active. This is an inactive phase. **B**

Remember that not every phase occurs in every person. One or several of the phases may be skipped. For example, warnings may occur and no sores develop. Ulcers may develop with no warning or blisters. Ulcers may heal with no crust stage. The stages are still important, however. Put sim-

ply, when no symptoms are present and when no sores are visible (and you've looked), or it is just residual redness left," the active infection is over.

What are the trigger factors?

Several studies suggest that latent herpes may reactivate *because* of certain trigger factors. These factors are poorly understood, however, and are for the most part, unavoidable. The "known" trigger factors include: **the menstrual cycle**; **emotional stress**; **another illness**, especially with fever; **sexual intercourse**; **surgery** or **injury**; **sunlight**; and certain **medications**.

Every person's trigger factor is different. For example, while many women will get herpes only during a certain part of the menstrual cycle, the trigger day of the cycle varies from woman to woman. One study suggests that more women develop recurrences five to 12 days before the onset of their next menstrual period than at other times. Unfortunately, birth control pills which stop the normal cycling hormones don't seem to affect herpes, but careful studies have not been performed.

Emotional stress may be important for some, but for others stress is unrelated to herpes outbreaks. I find that trying to force away stress in an attempt to rid oneself of herpes might succeed in making a lot of new stress. In fact, no one has ever proven that stress causes herpes to recur. Since herpes is stressful, how can we be sure "which is the chicken and which is the egg". This is a virus infection, not an episode of the jitters. Reactivation of latent infection in the nervous system is a very complex problem which remains poorly understood. Easy answers to tough questions like control of "triggers" may be misleading and create false hopes. That is not to say that getting rid of stress is not a good idea. Many people strongly believe that stress control can lead to herpes control. Indeed, a sizable proportion of persons who have herpes relate their outbreaks to stress. It is difficult to give general advice. I encourage anyone to take steps to reduce life's stresses. On the other hand, I encourage every-

one to avoid feeling a sense of failure or guilt if efforts at stress control do not reduce herpes outbreaks.

Some people say that sexual intercourse leads to sores. This is also a tough one. Most times I find that these are healed sores, usually in the early healed phase, which have a very thin layer of skin over them which tears easily during intercourse. This occurs mainly in people who have very frequent recurrences. They resume sex after healing, only to find a new sore in the morning. This is frustrating, indeed, but probably sex is not the trigger. Rather, sex is the innocent victim of unfortunate circumstance. If you feel that sex triggers recurrences, try waiting a few extra days after healing before resuming sexual contact. It may be the abrasion itself. Try gentler sex and lubricants. Make sure, by returning to your physician with a new sore, that your symptoms are really active herpes.

Surgery and injury and sunlight are just unavoidable. As far as medications go, make sure you need pills before you take them. That includes megavitamins. Never use cortisone creams or any of the derivatives of cortisone (ask your doctor or pharmacist) to treat herpes. If they must be used for another reason, make sure the reason is a good one. Nothing will help a herpes virus live a long, healthy and active life like cortisone will. In fact, any ointment other than specific antiviral medication may prolong the duration of sores.

If I've had primary (first-time) herpes, will I get a recurrence?

There is no way to predict who will get a recurrence and who will not. Most people will have at least a few. If your herpes simplex virus is a Type 2 (as opposed to Type 1) you might be more likely to have recurrences. In general, recurrences get milder and less frequent with time. This is true overall, but you should not keep a calendar and expect each recurrence to be shorter than the last, since the recurrence pattern and severity varies a lot. In fact, you can be sure that the recurrence pattern will change. One may have no problem for months or even years, and then suddenly have a flurry

of outbreaks right in a row. This may be the last flurry before recurrences stop. There is no way of knowing. There is no predicting the herpes virus.

Recurrences of herpes can start even as the primary infection heals. Recurrences may come one on top of the other so that one begins as another is ending. They may occur once on the labia and next on the thigh, or always in the same place. No treatment during the initial episode has yet been devised which will affect the pattern of future recurrences. The reasons for differences in recurrence patterns are poorly understood. Some people only get recurrences. In other words, their first symptoms occur months or years after their last sexual contact. The first infection was so mild that no symptoms occurred, yet latent infection was established. Something later triggered the recurrence.

Most often, recurrences are most frequent in the first several months after the primary infection, but months or years can pass between the two. It is safe to say that most people who develop recurrent herpes will suffer fewer or less severe recurrences with time, as the disease slowly "fizzles." Unfortunately, this "fizzle" phenomenon is not cast in stone for everyone. It is very variable, but holds as a general rule. There is nothing you can do to ensure your outbreaks will fizzle. It is also not a sign of failure if this fizzling does not occur.

Can I have herpes without any symptoms?

Several studies have shown that antibody directed against herpes can be found very frequently in the blood. Similarly, herpes can be found in the sacral ganglia of autopsy cases. Many of these people have no history of genital herpes, whatsoever. Furthermore, about half of herpes sufferers have not had contact with a herpes sore that they know of. Even in a private room with a physician listing symptoms, sexual contacts of persons with primary genital herpes very often deny any symptoms of herpes. This is not because they are lying. Rather, it reflects the fact that herpes commonly causes no symptoms.

The explanation for this is not clear. However, it is easy to see how a mild herpes blister, looking like a pimple or a tiny pinhole, might go unnoticed. Even a really severe infection on the cervix, if localized to the cervix or other internal genital area, may cause no symptoms whatsoever. An infinite number of scenarios to explain innocent transmission may be imagined. For example, a recurrent sore around the anus may cause recurrent rectal itching. This is a symptom which nearly everyone has at one time or another and could easily be passed off as insignificant. Can anyone reading this book honestly deny ever having had an itch in the rectum?

Must it always hurt?

Herpes often does not hurt per se. Even though we have heard elsewhere stories of terrible pain and so forth, these more severe symptoms are most prominent during the primary infection. Commonly, sores which are open and raw are tender or painful to touch. Push a blunt toothpick or a cotton swab on a sore and it will hurt. Urinate on a sore and it will hurt. Itching may be more common than pain during recurrences, however. Pain is a funny thing. People sense pain differently. Some people with recurrent herpes never feel anything and only know they are active by looking at the sores. Others are exquisitely aware of the slightest change in body chemistry. Regardless, pain is usually not the major problem in coping with recurrent herpes.

On the other hand, patients with strong primary infections may suffer extreme pain for a short time. It may be too painful to urinate, to sit or to walk. Hospitalization with intravenous therapy and painkillers may be required. It is very frightening to imagine this pain recurring every month for a lifetime. Happily it does not. If you are reading this during your primary, remember that herpes may recur, but it will never again do what it is doing now. Recurrent herpes is different from just recurring primary herpes. It is generally much milder. Sores are smaller and less painful. Generally, they are gone after several days and do not make you sick as they might have during primary herpes.

Can it cause other kinds of pain?

Because herpes likes nerves, it may cause irritation of the nerves. During reactivation (the prodrome phase) the virus is travelling down the nerve and may cause pain in other areas where the nerve runs. This is often leg or buttocks pain and is called a **sacral paresthesia**. It usually disappears when the prodrome phase is over. Headache may also be a warning sign. A rare patient will get reactivation of the virus travelling up the nerve instead of down. That is, the virus gets into the central nervous system and causes meningitis, or an inflammation of the sac around the brain. This is not harmful. It does not damage the nervous system, but if it happens it is quite distressing and results in headache, stiff neck, aversion to bright lights, and fever. It *does* get better. If these symptoms occur, seek the care of a physician so you can be sure it is just herpes. (Other causes of meningitis may require specific therapy.) An unusual, but not rare complaint after an active recurrence is residual pain in the area involved. The skin might be painful, or prickly, or it may feel as if it is drawn too tightly. Generally, this complaint fades with time. It is called postherpetic neuralgia. Postherpetic neuralgia happens very commonly following a herpes zoster skin infection (shingles). Note that it follows active infection and, therefore, does not represent active virus shedding. It would be an inactive phase. Happily, this is not usually a sequel to a bout of herpes simplex.

Can herpes make me sterile?

No, but a number of other sexually-transmitted infections can cause sterility. For example, **gonorrhea** and **Chlamydia**. These other infections are treatable. The most common warning signs are discharge, in males *and* females, painful urination, or a painful lower abdomen. These are internal genital infections which can cause enough inflammation around the ovaries and tubes in a woman to result in scarring, and thereby difficult passage of the egg to the womb, in other words, sterility. A culture test and examination will generally show

these internal genital infections. Many people, both male and female, have no symptoms whatsoever. The doctor who diagnoses herpes should also test for these infections, especially since they are easy to cure with certain antibiotics. In addition, herpes may be confused with syphilis and other diseases even by the most expert, most widely experienced physician. Only laboratory tests can distinguish the different sexually transmitted infections with 100% accuracy. Make sure you undergo these tests at least once.

Can herpes make me impotent?

Impotence means that a man is unable to obtain and sustain an erection when he feels like doing so. Commonly, herpes has a detrimental effect on feeling like it, especially during the period of anger after acquiring herpes. Anger, as well as depression and other emotional factors may commonly influence sexual urges in men and women with herpes. Usually such changes in urges are related to correctible things, such as getting over the fear of talking herpes over with your partner. Changes in sexual urges are normal and common. They should not stay for a long time.

Impotence is usually an emotional thing as well. Most times true impotence results from similar feelings which might potentially diminish sexual urges: anger, the feeling of having an "incurable" infection, etc. Severe primary herpes infections of males, especially homosexual males with proctitis (rectal-anal infection), may uncommonly result in physical impotence as a result of nerve inflammation. This inflammation leaves after the acute infection and generally does not recur. There are other physical causes for impotence, however, such as diabetes mellitus, certain drugs, and hormonal imbalances. If impotence or loss of sexual desire is sustained, you should seek specific medical attention for the problem.

Are cold sores (fever blisters) also herpes?

For the most part, yes. Fever blisters are generally caused by

herpes simplex. The virus is usually (not always) Type 1. Sores generally look like genital herpes, but they occur on the lip or the skin near the lip. The classic cold sore occurs at the vermilion border of the lip—the point where the thin mucous membrane of the mouth changes abruptly into the skin of the face (the outer edge of the lipstick). Ulcers in the side of the mouth may be herpes, but usually these are **aphthous** ulcers (not infectious). Mouth herpes—like genital herpes—is most often an external disease. Cracks in the corners of the mouth are usually not caused by herpes. True cold sores go through a similar sequence of active phases as already described. The ganglion for latency with the cold sore is called the trigeminal ganglion. It is located inside the skull. In fact, the mouth is the most common site for herpes recurrences. Sounds like genital herpes is just a cold sore in the genitals? That's almost exactly correct. In fact, a person with mouth herpes can readily give a sexual partner genital herpes by having direct oral to genital contact while infection is active. The nature of herpes sores and the sites affected simply depend upon what gets inoculated where.

Can I have received my infection months, or even years before my symptoms?

Yes. Primary herpes is often quite uncomfortable, but not necessarily. Remember that herpes infections form a spectrum from no symptoms to severe symptoms. Initial infection may pass unnoticed. At a later date recurrent herpes which does cause symptoms may begin.

A true primary infection, however, with its accompanying pain, numerous lesions, fever, etc. is unlikely to have been caused by a remote infection. The incubation period for primary herpes is probably between two and thirty days in general, and it is then that primary infection occurs. If your first outbreak is mild, this could be a non-primary, initial infection, or it could be the first recurrence after an asymptomatic primary infection which took place weeks, months or even years before. In this case, the incubation period is more difficult to pinpoint with certainty. An antibody test if

properly performed during the first episode will separate the primary from the non-primary initial infection. If you have a positive test (non-primary), however, you still will not know if the infection was just received from recent contact (and you already had antibody), or if it was long ago received from remote contact (you developed antibody then) with newly established symptoms.

I often get prodromal symptoms, but no sores: What does that mean?

It probably means reactivation. Most people who get warning symptoms with sores will also get them without sores. This means that the virus has reactivated. It may have travelled to the skin but, in some way, the body has stopped the infection before it could cause sores. This can be very common. We have recently found that twenty per cent of all prodromes will "abort" without further lesion development. While the prodromal is active, however, in order to be safest, herpes should be considered to be active. Examine yourself after the warning is over. Sometimes, people who feel they do not get sores after the prodrome are not looking closely enough. Women with herpes must learn to use a mirror. Preferably the mirror will have a well-magnified side. Use a flashlight or some other light source that can be brought near to the skin. Remember that sores can vary and they may be very small. They may not hurt much. If no signs of herpes occur on the skin, wait a couple of days and resume normal skin contact. If sores develop, follow the phases and wait until it is inactive. It may turn out that many of these "false prodromes" are just that—false. They may be more a symptom of fleeting neuralgia from the last episode.

Can herpes cause headaches?

Yes, indeed, there is a herpes headache. Having a headache is very common during a true genital herpes primary infection. Primary herpes occasionally may be complicated by a

syndrome called **meningitis**. The headache with meningitis is generally quite severe. It may be associated with other symptoms, such as stiff neck, nausea and pain from bright light and loud noises. If this occurs during primary herpes, your doctor may choose to perform a lumbar puncture (needle in the low back) so that a sample of spinal fluid may be examined. This is a very safe procedure and generally causes about the same amount of discomfort as a blood test. This will not be necessary in every case of primary herpes—only those where meningitis is considered a possibility. The test is important in some cases to make sure that other causes for meningitis are not present. Herpes meningitis is generally benign i.e. it gets better on its own without treatment and generally does not recur.

Alternatively, headache may be the symptom of a prodromal. In other words, it may herald the onset of a new recurrence. Generally, this headache is mild and has no known cause. In fact, most headaches have no known cause. Being sick with anything can give a headache. Fever can bring on a headache. Tension from herpes or *anything else* can bring on headaches. If headaches are very severe, whether you feel they are related to herpes or not, you should discuss it with your doctor. Herpes should not generally be called a cause for chronic headache.

What other symptoms can herpes cause?

Genital herpes is still a poorly understood disease. We do not know how many people have it, or how many know they have it. We do not know everything it can do. We do not know how often babies are affected and we do not know if it causes cancer. We probably only know some of the symptoms.

Once again, the symptoms of herpes are usually related to the sores. If they are near the urethra, it will hurt to urinate. If they are on the buttocks, it will hurt to sit. Sometimes, however, herpes causes invisible problems. Several of our patients complain of recurring leg pain. This is usually in the back, radiating down the back of one leg. It may occur in the thigh. It is probably related to herpes. Occasionally, this pain

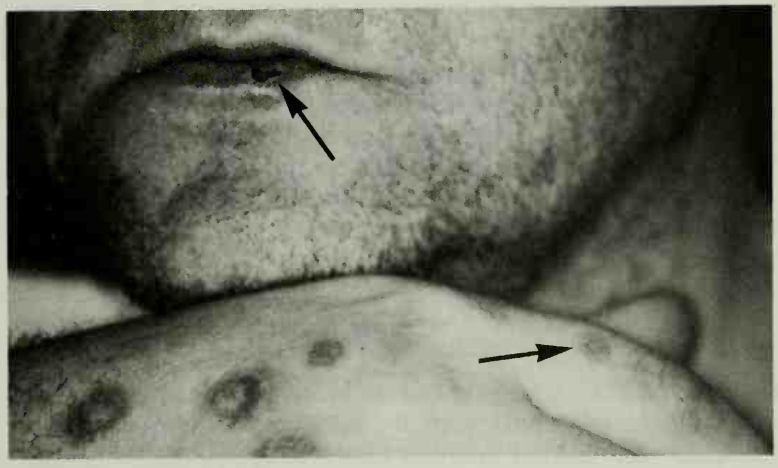
may occur without any sores like an "aborted" prodromal infection. If it is **episodic** (comes and goes) and is usually followed by sores on the skin, then it is likely a prodromal infection and should be considered a sign of active herpes. If the pain is **chronic** (always there or takes weeks to go away), chances are it will not be related to herpes. In the chronic situation, other causes for this type of pain must be ruled out by a physician, and the presence of pain will have very little to do with virus activity on the skin. Persistent pain may in unusual situations be one kind of **postherpetic neuralgia**.

During primary infection any number of unusual things may occur. Primary herpes is a whole body illness. Meningitis, as previously described, is common in primary illness. Other very rare severe consequences have resulted from herpes, including paralysis from a complication called **ascending myelitis**. This is so rare that only one or two cases in the world have ever been proven to be related to herpes.

Occasionally, a patient with herpes will get abdominal (stomach) pains from primary herpes. I have been told about patients who have actually undergone surgery looking for appendicitis, only to find out they have primary genital herpes. I should point out, however, that gonorrhea and Chlamydia are very common causes of a syndrome called **pelvic inflammatory disease** (PID) which often causes lower abdominal pain and often results in sterility. These are much more likely to cause abdominal pain than is herpes. In addition, they need to be treated by a trained person who must look and culture in order to find them.

Erythema multiforme is a curious disease. It causes a skin rash which may look like rings of redness with central color changes (target lesions). In addition, the mucous membranes of the mouth, eyes (conjunctiva) or genitals may ulcerate and get painful and raw. As opposed to the ulcers of active herpes phases, these ulcers are not infectious. They are generally thought to be a hyperimmune reaction. In other words, the immune system of the body has not only responded, but it has "overresponded" resulting in cessation of the active virus infection. A few normal cells are killed as well, resulting in a rash and ulcers. One of the many causes

of this unusual disease is herpes simplex. Any one individual with herpes is very unlikely to develop the problem. The treatment of this syndrome is sometimes simple and sometimes difficult. Because this is a problem of "too much" immunity, cortisone may be called for here. If so, it is usually taken by mouth rather than as a cream. The disease may relapse. It needs medical attention. Whether treatment with antiviral medication will alter erythema multiforme remains to be seen.



13. *A picture of the appearance of skin in a person with erythema multiforme. This is a "target" or "iris" lesion. The person has these sores which come and go from time to time when he gets a fever blister. These sores are not infectious.*

Now that I have herpes, am I especially prone to other infections?

Herpes infection does not make you more susceptible to anything. It was not long ago taught that secondary infection of the skin was a common complication of herpes, for example a **staph** infection or **impetigo**. This is now known to be not so. More than 99% of people with herpes have no other infection. Rarely, staph or strep (two common and easily treated bacteria) will invade the skin at the site broken by a herpes sore.

Because you have been affected by a sexually-transmitted disease, there is a small statistical risk that you will have acquired another infection at the same time. This has nothing to do with your susceptibility, but rather your statistical chances of having "caught" something else. This means that the other infections commonly sexually transmitted, and/or those easily confused with herpes by the way they look (syphilis, chancroid, shingles) should be ruled out. This is discussed in detail in Chapter 4.

Persons whose immunity is compromised from something unrelated, for example, patients with cancer, lymphoma, leukemia, transplantation or Acquired Immuno-Deficiency Syndrome (AIDS) may occasionally get herpes simplex infections which do not heal readily. This occurs because of their immunity problem, not because of herpes. Herpes itself does not make these people susceptible. Rather, their immunity makes them more susceptible to problematic herpes.

CHAPTER FOUR

Choice is future oriented and never fully expressed in present action. It requires what is most distinctive about human reasoning: intention—the capacity to envisage and to compare future possibilities, to make estimates, sometimes to take indirect routes to a goal or to wait.

SISSELA BOK, *Secrets*

GENITAL HERPES: THE DIAGNOSIS

How is the diagnosis made?

In some situations, genital herpes may be a simple diagnosis for the general practitioner. It may elude the specialist in others. When symptoms and signs of herpes are "classic," that is, when a known exposure has taken place and sores have developed which are painful, clustered vesicles (blisters) or ulcers on a red, inflamed base, the clinical diagnosis is clear. Recurrences further confirm the diagnosis. Tests for other diseases are taken—for syphilis, gonorrhea, a microscopic examination of the vaginal discharge for yeast and trichomoniasis—and one is pretty sure that herpes is there.

On the other hand, certain people with genital herpes have mild, intermittent symptoms. The only sore might be a pinpoint, single ulcer on the labia which lasts for a few days and comes every six months. It may not hurt at all. The diagnosis may not occur to the patient or the physician. The diagnosis will then not be made. If the possibility is considered, a test which shows virus to be present in the sore should be obtained. If the test is positive, herpes is the cause.

If the test is negative, however, herpes may or may not be the cause of the problem. Remember the discussion about the phases of herpes (chapter 3). Was the test obtained during an active period? If not, it can be expected to be negative even if herpes is the problem. Even if the period was an active one, sometimes herpes is not recoverable. How was the test obtained? Was the doctor's office far away from the laboratory? If so, the virus may not have survived the trip. How experienced is the laboratory? This may vary. Even under ideal circumstances, virus recovery in the laboratory after only one try may not always be possible.

If you suspect herpes and your doctor agrees, your best bet is to return again for virus culture at the *first* sign of recurrence. The earlier the specimen is obtained, the better is the chance of a positive test. In my experience, two visits will suffice, *if* the visits come early in your active phases. If we suspect herpes very strongly, however, we will keep culturing until we find it, and rarely 4 to 5 trips are necessary.

I have been exposed to herpes. Should I go to my doctor now for a test?

This is an increasingly more common story. It is also a difficult problem. If you have been exposed to someone with herpes, the person may have been in an active stage or an inactive stage.

If the stage is known to be inactive, your risk is very low. If no symptoms develop, do nothing and try to relax. Nothing will almost certainly be what continues to happen unless you become exposed, in the future, to an active infection.

If the infection was in an active stage, you may have been exposed. Whether you will develop herpes or not will depend upon several factors.

Was there virus present? The active stages are a good guess for when exposure risk is high, but often a sore may have no living virus in it. If sores were active, you may have been infected.

The inoculum is probably important. If the number of virus particles (inoculum) which have made contact is very high, then infection is more likely. If virus is present in very small amounts, infection is less likely.

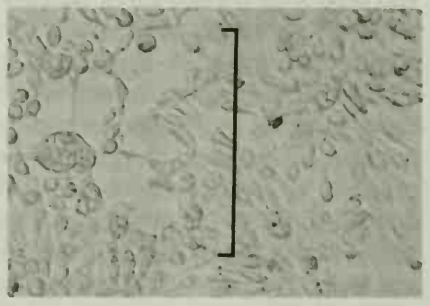
Where did inoculation take place? Was this contact through thin skin, for instance on the genitals? Were there cuts on the skin? Was contact prolonged? Did a long time elapse before washing the area? All of these things might increase the chance for any virus to transfer from one person to another.

Several other "host factors" also play a role. If you have developed antibodies to herpes a higher "dose" of the virus may be required to result in illness. The immune system may also be an important factor in other ways we do not understand. What really matters, however, is whether you develop symptoms of herpes, assuming you know what they are. If no symptoms are present, one trip to the doctor will *not* assure you that you do not have herpes. A doctor can only tell you if herpes sores are seen at the time you are examined, on the areas examined. If symptoms develop, e.g., vaginal discharge, sores, unexplained tenderness of the genitals, redness, pimples or swollen lymph nodes—then go to the doctor *without delay*. If no obvious other cause for the symptoms is present, and your exposure to herpes is likely, inform the doctor and ask for a herpes culture. Remember, seek diagnosis when the symptoms are present. Waiting it out does not help. Herpes will go away on its own temporarily, only to possibly return again. If you want to know (and it is your responsibility to know), go to the doctor when symptoms first appear.

How is the diagnosis proven?

The only way to prove that herpes is present, regardless of how sure it looks, is with a test that shows herpes simplex virus to be present in a sore. The most sensitive test (the most likely to show positive when it is herpes), is a culture test. This test requires that a sore be "scraped" with a cotton or dacron swab. Since virus lives inside cells, a few of those

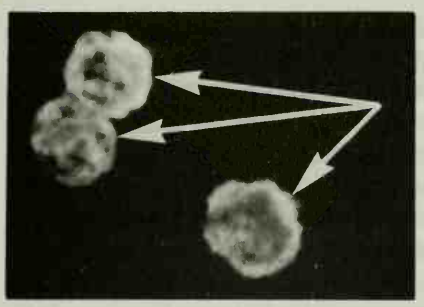
cells from a sore must be taken and sent for culture. This is easy to do by just rolling a wet swab into a sore. The swab is then placed into a salt solution and sent to the laboratory. Here, some of the fluid is removed and placed onto healthy human cells which are kept growing in tubes. The cells are called a tissue culture. Once virus is placed onto the cells, this is called a virus culture. The laboratory technologist will then keep the cells growing at 37° C in an incubator. During the next several days, the technologist removes the culture from the incubator and places the tube under the microscope. If the cells remain healthy, then the culture is negative. If the cells become sick from herpes, they will round up and group themselves together. This change in appearance is called the **cytopathic effect (C.P.E.)**. An area of herpes infection of cells called **fibroblasts** are shown below. Note the long, pointed wispy appearance of the normal cells. Compare this to the sick-appearing, swollen cells where the virus is growing.



14. *Microscopic appearance of cells affected by herpes simplex virus. Normal cells in culture are altered by the infection taking place in the test tube. Cells are swollen and fused. This is called cytopathic effect (or C.P.E.) and is suggestive of herpes simplex infection.*

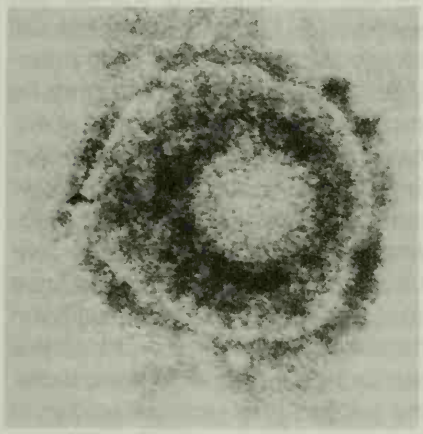
Once the CPE has occurred, a small number of cells are removed from the tube and placed onto a slide. The technician will then add a herpes simplex antibody to the slide. This antibody is usually attached to a chemical which will **fluoresce** (emit light) under ultraviolet (UV) light. If the cells fluoresce, the cytopathic effect must be certainly caused by herpes simplex: the positive culture test. A positive fluorescence test is shown below. The bright areas on the cells are fluorescing because herpes antibody is stuck to the virus on the cell.

Several other methods may also be used. If fluid is present, as inside a vesicle, the virus may be seen under the electron microscope. This is a very powerful (and very ex-



15. *Infected cells under the microscope are flooded with a herpes antibody attached to a fluorescent dye. Infected areas "shine" under the ultraviolet light.*

pensive) microscope which is about the size of a small car. An experienced and capable technician must operate the machine. Identification of "herpes-like particles" is truly an art. Interpretation may be very difficult and, unfortunately, occasionally misleading. Remember, all herpes viruses look the same under the electron microscope. Nobody can say if it is Type 1 or Type 2, or even if it is shingles, just from this test. Furthermore, even though the machine is powerful, it is not sensitive. One must have a lot of virus in a very carefully collected specimen in order to find a positive electron microscope test. One must have great faith in the talents of the microscopist. A picture of herpes simplex virus in the electron microscope is seen below.



16. *An electron microscope takes a picture of herpes directly. The regular microscope cannot see with such intense magnification. The electron microscope shows the enveloped virus. Its nucleocapsid within containing 162 capsomeres, shaped like an icosahedron can be detected if your imagination is good.*

The fluorescent antibody technique described above for cells in culture may also be attempted directly on clinical

specimens. A smear from the sore can also be placed onto a microscopic slide and examined directly—a Pap smear. Since herpes may result in the formation of giant cells, these may be seen in the microscope directly. Special stains can be done on these slides; the test is then called a Tzanck smear. These tests (fluorescence and electron microscopy) and others being developed are quick tests. In general, compared to culture tests, quick answer tests sacrifice a bit of accuracy for speed—or convenience. Which test to do depends on the situation. Sometimes it is necessary to do more than one test.

Each of these methods provides direct evidence of herpes infection and, if positive, proves that herpes is present. Remember, if a virus test is negative, this does not prove that herpes is not present. Proof that a negative finding means herpes is not causing a genital sore is always much more difficult (and sometimes impossible).

Is there a blood test for herpes?

Can I take a blood test to determine the presence of the herpes virus? Yes. Is it helpful? Not generally. What is the test? It is a test to measure herpes antibody and to say how much herpes antibody is present in the blood. This it will do, but herpes antibody is not type-specific. That is, it cannot tell the difference, with absolute accuracy, between past infection with Type 1 or Type 2. Antibody of some type may be present in fifty to eighty per cent of people by the age of 20. So what will a positive test tell you about herpes? Really very little. Sometimes people look for a rising amount of antibody to herpes from one time to another—termed acute and convalescent. Unfortunately, this does not work either. Conversely, some people with culture-proven genital herpes have negative antibody tests. Forget about herpes blood tests except in very unusual circumstances. A single blood test will *not* tell you if you have genital herpes. If two tests were done, the first was negative and the second was positive and your infection was your very first, it is suggestive. Someday—possibly soon—a blood test will become available which is specific. It is not here yet. In the proper setting, an antibody

test may offer useful extra information. A blood test cannot accurately determine if herpes is present or not.

What type of doctor should I go to?

If you have a good relationship with your family doctor you may wish to start there. Ask the questions you need to ask. Find out whether your symptoms are suggestive of herpes. If you need more detailed answers to your questions, you may ask to be sent to a sexually-transmitted diseases clinic or to a specialist in the area. Your physician should be able to guide you to a gynecologist, dermatologist, urologist, specialist in infectious diseases, or someone who has some special experience with herpes. It matters little how much or what type of special training the physician or other health practitioner has. It is information and accuracy that you need. You must work with your health practitioner. He or she is the only person who can help you find out if you have herpes using the proper tests. Only a trained professional can arrange for other tests you will need to be sure you have nothing else that requires specific treatment.

Does it matter if the herpes is Type 1 or Type 2?

As a general rule, herpes simplex is herpes simplex. Type 1 may cause genital herpes. In general in North America, however, 80 to 90 percent is caused by Type 2. Some infections are caused by mixtures of both types. Some scientists have observed that Type 1 genital herpes may recur less often after primary infection. This is not yet proven, but it is probably true.

In the near future, therapy will be available for treatment of herpes infections. Some (not all) therapy which is being developed is type-specific. If type-specific therapy becomes a clinical reality, then typing will become an obvious necessity. Some laboratories now do typing routinely. It has been a difficult thing to do well, but the methods for proper typing are rapidly becoming easier. Still, as of today, it is probably

not necessary for most people to know their "type".

Ways have now been devised for "fingerprinting" the virus. As a special research tool, it is possible to tell one person's virus from another by its "DNA fingerprint". This method has allowed us to trace outbreaks of infection to the source. It seems that the number of possible differences, in this virus, from strain to strain, are nearly infinite. These tools remain in the hands of the researchers for now, although typing for the clinical laboratory is becoming easier and more accurate. In a few years, virus laboratories may type virus routinely. It will depend on the need.

CHAPTER FIVE

Any disease that is treated as a mystery and acutely enough feared will be felt to be morally if not literally contagious.

SUSAN SONTAG, *Illness as a Metaphor*

GENITAL HERPES: TRANSMISSION

How does herpes spread from person to person?

In order to infect a new host, the herpes virus must attach itself to the epithelial (skin) cells of the body. It must use its envelope to hook on to the new cell. The virus will live only a very short time outside of a cell: as soon as it dries out, it is rendered "sterile." Furthermore, anything which might dissolve its envelope, such as soap or alcohol, will effectively neutralize the virus. It cannot be sent across open spaces (in a room by sneezing, for example) for it dries out quickly.

Probably a certain "quota" of virus particles must reach epithelial cells in the new host for infection to be successful. Using large numbers is nature's way of covering for the failure of most particles to set up successfully in their new host. How many herpes virus particles are needed for transmission? This is unknown and will probably remain unknown: one can easily imagine, however, that if a very small number of particles were to infect a cell, the reproduction process of the virus might lag behind the immunological defense network within the host prepared to halt the process. That network is much like an army with specialized units. These units have a certain starting force and reinforcements are always on the way,

capable of building up each battalion. If the invasion force (the virus) is very small, no reinforcements are needed and the invasion is squashed. If the invasion force is strong, there is a delay until reinforcements come. During the delay, disease occurs. Because of this numbers game and the fact that the virus dies upon drying, direct inoculation is generally required for herpes to spread. This direct inoculation occurs when infected epithelial cells from one person, preferably kept moist and warm at body temperature, helped by rubbing and best, even scratching, come in direct contact with the epithelial cells of another. Regular skin, like that on the hand, is protected against all but the most massive invasion because of a natural barrier on the skin called keratin. Keratin is waxy and strong. Just as it repels water, it repels herpes virus particles. Unless the keratin is torn, for instance in a fresh cut, the virus does not make it to an epithelial cell. In mucous membranes however—those lining the mouth, eye and genital area—the barrier is very thin. The epithelial cells are waiting, exposed, very near the skin surface. This, then, is where herpes tends to take up initial residence, for this is where access is easiest. It doesn't take much imagination, then, to see how herpes gets where it is going. An active lesion on one—herpes growing and alive; add friction for heat and for removal of infected cells from the surface of the donor; and moisture for easy travel to prevent drying; add exposed epithelial cells of another—and a new infection is the result.

Thus, genital herpes tends to be sexually transmitted. However, other types of transmission are possible—only not usual. One can imagine that most contact between two persons involving the genitals is going to be sexually oriented. This type of sexual transmission does not require penetration (penis into vagina). It could be mouth to vagina; mouth to penis; penis to mouth; finger to penis; penis to anus—or any other combination. The requirements are only infected cells and exposure to new cells, heat and moisture. Herpes does not care if there is sex happening. Sure, herpes likes sex, but it also likes kissing, and wrestling, and rugby, and anything else that gives it the new environmental opportunities it constantly seeks.

What can be done to prevent herpes from spreading?

For herpes to move from one person to another it must be active—*growing*—on the skin or mucous membrane. It does not jump from its latent site in the ganglion to the genitals of another. Protection when skin herpes is active is achieved by *avoiding* sore-to-skin contact—*not* by using condoms, or foam or avoiding vaginal penetration.

Anywhere herpes is *active* is a place to *avoid* having contact. If it is in the mouth, then avoid kissing, oral sex, and so on. If on the finger, keep your hand to yourself—while your infection is *active*. If it is on your thigh, watch what rubs against your partner (try bandaging it). If your herpes infection is on the genitals, *avoid genital contact*.

You need not avoid kissing with active herpes unless sores are in your mouth, just like people with cold sores on the mouth needn't avoid genital contact—just kissing. In other words, active herpes is a time to avoid contact with infectious areas, but *not a time to avoid contact altogether*. It is a time for creative contact. You have probably always had sexual contact during which you carefully avoided putting your finger into your partner's eye. This has never concerned you. Now, in somewhat the same way, you must learn to have contact with your partner while avoiding the area of skin *actively* affected with herpes. This is critical. Total abstinence is O.K. for a while, but it leads to changes in self-image which are not necessary or positive. They will be discussed later.

You think your active phases are over, but you're worried—you're not sure? Then use condoms and foam. There is no direct evidence that these precautions definitely prevent herpes, but logic dictates that they might. If your symptoms are over, chances are you've got no virus left on the skin. If you do, chances are it is a small amount. Vaginal contraceptive foams will effectively kill herpes in the test tube—they will probably help to get rid of the last little bits of virus on the skin.

Some people—though not all—find in the beginning, for the first several months after their primary herpes infection, that this business of telling one phase from the next is tricky

business. With careful attention to your body during this period, an awareness generally comes quite easily. One gets to know one's herpes. During this getting-to-know period, the condoms and foam might help your peace of mind. Do not, however, take this to mean that you can *prevent* transmission while sores are *active* simply by using condoms and foam.

Can I spread herpes from the genitals to my eyes? My fingers? My mouth? My brain?

This question is an extremely common and important one. The name for this is "autoinoculation." If one area on your body can be affected, why not everywhere? Can herpes move around?

The answer first requires some background information. If you broke a herpes vesicle (blister) during your active period with a needle, and stuck this needle into your arm, or your eye, or your lip or even your brain, for that matter, you would probably develop a new infection in that new site. Injection into the arm was actually tried on volunteers several years ago. Remember, however, that herpes very rarely gets into the blood or any other part of the person affected except for the *nerves* and the *skin*. It does not get tossed around from organ to organ. For the most part, it stays where it is.

However, if you held a finger with a good open cut directly onto a sore, and didn't wash your hands for some time, you could end up with an infection of the finger. Take these same dirty hands and scratch a piece of dust aggressively from your eye, and you might have trouble. In general, reasonable personal hygiene is a good rule—and since genital herpes is generally held within the confines of the underwear, the problem is minimal.

Time for a few examples. Robin has recurrent cold sores. He gets his herpes outbreaks twice a year—usually on the corner of his nose. This time his sores were on the nose. The month was August. The pollen was heavy in the air. Robin's hay fever was in full bloom along with the flowers. He sneezed and he sneezed, and he rubbed his itchy eyes and he rubbed some more. Later he noticed the appearance of herpes sores

on his eyelids. He has almost certainly autoinoculated herpes to the eyelid.

Often people ask if it's possible to contract genital herpes from oneself by rubbing a cold sore and then touching one's own genitals. This type of infection has never been documented, and for several reasons is very unlikely to occur. First, the dose required for autoinoculation is probably very high. Robin was able to infect himself by sneezing and rubbing repeatedly on an area right next to the original active one. Furthermore, it seems that autoinoculation with Type 1 herpes is tougher still. Thus, in cases reported to date, all persons who have developed genital herpes with herpes Type 1 have had no pre-existing antibody and no history of previous herpes.

Patricia has initial genital herpes. She notices the sores, but ignores them because they are only a little bit itchy. That night, she scratches and scratches some more. She has a new herpes on the finger she used. Again, the rule with herpes—there is no jumping from place to place. But put enough virus directly into a new place and new infection can occur. This autoinoculation business is much more likely to occur during the initial attack, especially if it is a true primary. At that time, the immune defences such as antibodies are not yet operating at full steam, and therefore little obstruction lies in the path of virus anxious to move on to new places. Antibody will prevent this spreading to some degree, so that once the primary episode is over, the amount of virus required for new sores to take root will be much higher. Antibody and immunity are not enough of a defense against a lot of virus, however.

Stick to good hygiene. Think about what you are doing when you touch your sores. Wash your hands afterwards. Keep contact lenses out of your mouth the same way you should keep them away from your genitals. If sores are active don't wipe your genitals and then rub your face with the same cloth. This is not generally something to fear. Transmission to your eyes from your genitals, for example, is talked about often, but seen almost never. I have seen only one patient with genital herpes who also had eye infection. It may have been inoculated there at the same it was inoculated onto the genitals. Autoinoculation in that situation is unlikely.

As you can see, genital herpes is not a blinding disease.

Genital herpes can affect the nervous system. It is not associated with herpes encephalitis in adults. Sometimes it causes an inflammation of the protective sac around the brain called "meninges." This is called aseptic meningitis. It will not damage the brain or you. It may cause one heck of a headache and has been discussed in more detail in Chapter 3. Encephalitis, or brain infection is no more (or less) likely to happen to the person with genital herpes than it is to anyone else. It is uncommon, confusing, difficult and dangerous, but not associated with genital herpes at all. Nongenital herpes infections are extensively discussed in Chapter 10.

Can I spread herpes without sexual intercourse, e.g. to my children?

At the risk of sounding repetitive, *direct* contact is required in order to contract herpes—not sexual contact. If your child's skin touches your herpes, then yes, of course it can spread. In fact, most herpes begins in childhood when the baby or child is kissed by a relative or friend with active herpes on his or her mouth.

Objects which pass quickly from one person to another are, theoretically, a possible source as well. For example, if you share a drinking cup or a cigarette while you have a cold sore, transmission is possible. How about a bath towel? I would suggest not using the same towel with the family or partner while lesions are active. That would logically go for underwear and other intimate articles. Simple washing of towels or other articles is sufficient to dissolve the herpes envelope and will kill the virus effectively. There is no evidence that these are a problem, but why risk it? Not sharing underwear seems like a small price to pay! Despite lots of headlines about towels, toilet seats, objects handled in doctors' offices, and even hot tubs and water slides, no evidence for transmission in these ways can be found. Children are not flocking to physicians with genital herpes. Patients with genital herpes generally avoid giving genital herpes to their

children because they are not in sexual contact with their children. It's that simple. That is not to imply that rare exceptions don't exist, because they do. You need do no more for prevention, however, than use reasonable personal hygiene.

What about toilet seats?

The toilet seat argument has been around since toilet seats were invented. Researchers have looked for gonorrhea, syphilis—you name it—on toilet seats. Herpes which gets onto a toilet seat, especially a wet warm one which has not been cleaned in a few days, can stay alive there for awhile. It does not stay very healthy. It begins to die as soon as it leaves the skin, but it takes a while. If dried or cleaned it disappears. If it stays wet it may take an hour or two to fizzle. Even if herpes were alive on the seat, transmission to the next person by this method would be unlikely. The back of the thigh and the buttocks are thick-skinned areas, relatively resistant to penetration by virus. The temperature and moisture settings are wrong for transmission. In fact, no cases of herpes from toilet seats or from any other inanimate object (swimming pools, saunas, water slides) have ever been proven. Experiments suggesting toilet seats as a source for herpes have never provided any evidence, whatsoever for transmission. Rather, they have concluded that toilet seats which are not disinfected do not actively kill the virus. Instead, the virus dies slowly on its own.

However, I have spent a lot of time on toilet seats in my life and have often wondered how a sexually transmissible virus could get onto the seat in the first place. Certainly if sores are present at the bottom of the buttocks, or if they reside on the back of the thigh, then they touch the seat. I do recommend that people with sores in those places use toilet paper on the seat or seat covers while the sores are in the active phase. They might consider drying off the seat for others, or using a pocket-sized wet napkin. If your sores are on the penis, the labia, the pubic hair or the mouth, the problem is avoided by keeping those areas away from contact with the seat. Now this seems straightforward to me. The

overwhelming majority of people with herpes never have contact with sores to seat unless they have unusual personal habits. An elder colleague of mine, upon reading about the toilet seat issue in the newspaper, suggested that herpes is transmitted in public toilets only when two people make love in the stall!

No, there should not be separate toilets for people with herpes. Yes, my personal bias and infectious disease background would suggest that daily disinfection of toilets is a good idea and that toilet seat covers are not a bad commodity. However, these suggestions will help to prevent infectious hepatitis and typhoid fever much more than syphilis or herpes. For herpes, the toilet seat issue is almost an academic one.

Can I spread herpes without having sores?

Not having sores means different things to different people. If a person has herpes enough times to recognize the phases; if these phases are very clearly understood; if healing is clearly recognized—then the risk of transmission is very small. Remember, herpes cannot jump from the latent ganglion site to the genitals of another. Occasionally, in some people, herpes is totally asymptomatic even after it has been symptomatic. For the most part, however, asymptomatic really means not recognized as herpes.

In other words, the hemorrhoid that suddenly swells up and itches is usually just a hemorrhoid. Occasionally, however, it is herpes. That intermittent pain in the leg could be a herpes prodromal. The itch in the pubic hair is probably a pimple or just an itch. It could be herpes. The sore throat you have may be a cold. It may be herpes. The list is endless. This all really means the same old thing; get to know your herpes. If you are aware of where it might be likely to bother you, avoid contact when an unusual symptom arises. Wait and see. Do blisters or ulcers (even very small ones) ever develop? If not, your itch is probably just an itch.

This risk is small—very small. In a recent study by Dr. Vontver and his coworkers in Seattle, the risk of having a no-symptoms, no-sores, culture-positive recurrence was studied

in pregnant women. In the absence of visible lesions, herpes was isolated in seven of 1,068 (0.66%) of cervical cultures and eight of 1,068 (0.75%) external genital cultures. Another study of a similar nature (in pregnancy) performed by Dr. J.H. Harger and coworkers in Pittsburgh suggested an asymptomatic rate of shedding of about 3%. Dr. J. Scher and coworkers from New York City feel it is about 4%. Numbers will depend upon the persons undergoing study (how well they know their herpes), the sensitivity of the laboratory (how much virus is necessary to get a positive test), and the care of the physician responsible for looking for sores (is this really asymptomatic or missed symptomatic?). The risk of transmission during inactive phases is small. It's probably smaller than the risk of sexual contact with someone who says they do not have herpes. They do not know what an itch may be and never consider herpes in themselves. This disease is so common that sexual contact with anyone in the 1980's is going to be a significant risk for herpes. The risk *within* the herpes group is no greater than the rest depending upon the people involved. It just requires care and mostly learning about yourself. Ironically, the person with herpes who is educated about the active phases of infection may, in some ways, be at an advantage since there is a clear course of action for avoiding transmission. On the other hand, the person who thinks he or she has no herpes (and is mistaken) will be a likely source of infection. The careful, informed individual who has symptomatic herpes is very unlikely to spread the infection.

If I have herpes, am I immune to a second infection from someone else?

No. In 1980, a study done in Atlanta, Georgia, offered proof that genital herpes can recur with more than one strain of the virus, suggesting that patients with one herpes can get another. Since immunity is important, it is generally thought that getting your second herpes is a little more difficult than the first. The antibody makes it more difficult and protects somewhat, but sex during active herpes can give a second infection.

It is a painstaking effort to tell one herpes strain from another. But, it can be done. This test is not something your family doctor can perform simply. In order to tell the herpes of Mr. Jones from the herpes of Ms. Smith, a "DNA fingerprint" is performed. The virus is grown in large amounts in the laboratory, purified and the DNA (see Chapter 1) extracted with chemicals. Then special enzymes called restriction endonucleases are added which cut the DNA in several special places. These small pieces which are left are then placed into a "gel" which is much like unflavoured gelatin—wobbly, but firm. An electric charge is added and the pieces travel inside the gel. Since small pieces travel faster than large ones, the gel makes a "fingerprint." Then, subtle differences between one virus strain and another can be detected. Using this method, several investigators have shown differences in the fingerprints between virus strains. Dual infections occurring with two strains at the same time, or two strains on separate recurrences in the same individual have been demonstrated.

How could this happen to me?

Herpes infection can happen to anyone. Several studies have proven this. In fact, you as a sufferer of herpes are in good "company." The Herpes Resource Center, an organization devoted to helping victims of herpes, recently completed a study of over 3,000 affected persons in their organization. They found that these people came generally from a high socioeconomic level (56% earned over $20,000 per year in 1981) and are highly educated (53% completed four years of college).

Sexual habits may or may not correlate, in any one individual, to the acquisition of this infection. Obviously, since herpes is almost always sexually transmitted, some type of sexual contact is usual. By statistical chances alone, anyone with more sexual contacts is more likely to acquire this virus. However, herpes has become so universal that often a history of just one or two sexual contacts is given. Since this is usually an external disease, that contact does not have to be vaginal

penetration. Several well documented cases of herpes in women who are virgins have been described, almost always the result of an oral to genital encounter.

As a society, we have subjected ourselves to a high chance of running into herpes by giving up condoms and foam as contraception for the convenience of the Intra-Uterine Device (IUD) and the pill. We run into it more often because sex has become less and less forbidden over the last few years. Oral-to-genital sex has also become commonplace, making the likelihood of oral to genital transmission of herpes more likely.

Sexual transmission is only required as the last event in genital herpes. Since herpes infection of some type is found in most people on this earth, we are talking about obtaining an infection which is almost more normal to have than to not have. When sores occur on the genitals, however, the emotional impact is greater than the same infection on the mouth. Realize that this stigma is mainly a media phenomenon and not an affliction unique to you. Herpes is a nuisance skin affliction which comes and goes. It has unusual complications which are preventable and unlikely to occur.

It has been suggested by some that the growth of herpes is a new demonstration of the "wrath of God." In response to this, I would point out that elimination of all but monogamous sexual contact would cut down the overall incidence of this infection, but monogamy would not eliminate herpes. A monogamous individual and even a sexually inactive individual could get genital herpes. It is, in fact, scientifically accurate to state that increasing the numbers of sexual partners statistically increases the chances of getting any sexually transmitted disease. From the prevention point of view, it is, and always was wise to be selective, to know your partner, to avoid casual sex, etc. Religious preference does not correlate whatsoever to susceptibility to infection, however. Herpes is no more a sign of punishment from God than Legionnaire's Disease was a sign of punishment from God inflicted upon the American Legion. Ascribing any new disease or affliction, or any old disease or affliction to the plagues of God is rewriting the Bible. In the case of herpes, it is also the product and the result of misinformation.

I had sex last night and awoke with a sore. Did I spread it to my partner?

Almost certainly not, if you had no symptoms of active infection when you had genital contact. Awakening with a sore seems to happen frequently to people with herpes. It is probably not significant. Such a circumstance obviously depends upon the frequency with which you have sex. If sexual contact is a daily occurrence, then every time you awake with herpes you will probably have had sex the night before. There is no reason to believe that herpes shedding starts before an outbreak. This is a common myth that probably has no basis in fact. This is, of course, another of those unanswerable questions, since scientists cannot travel from bedroom to bedroom taking random samples.

Can I have a long-term relationship with one person and never transmit my herpes to them?

Yes, such relationships are very common. In general, of course, the chances of missing an active sore have got to be higher as the number of encounters between any two people increases. It is often the case, however, that the couple who transmit herpes after several years together with only one partner affected remember an event during which the barrier to active infection broke down. Nobody denies that transmission can rarely occur in the absence of sores, so it would be misleading to say that transmission is 100% preventable. Nothing in biology is 100%.

Some unusual situations arise. For example, a couple who recently came to visit the clinic explained that extreme care had been taken for five years when suddenly the wife got herpes from the husband. They were unaware that a recurrence on the buttocks could also be infectious and had snuggled side to side, though carefully avoiding intercourse during this recurrence. The wife contracted herpes on the buttocks as well. Other examples include many partners who have stopped caring about transmission after awhile because it just does not seem to be worth the hassle. These types of

choices must be left up to the individual couple. A break in the barrier to active infection can occur because of mistake or because of choice, or less commonly, because of asymptomatic virus shedding.

CHAPTER SIX

Every mother entertains the idea that her child will be a hero, thus showing her wonderment at the thought of engendering a being with consciousness and freedom; but she is also in dread of giving birth to a defective or a monster, because she is aware to what a frightening extent the welfare of the flesh is contingent upon circumstances—and this embryo dwelling within her is only flesh.

SIMONE DE BEAUVOIR, *The Second Sex*

HERPES OF THE NEWBORN

What is it?

Despite dramatic breakthroughs in knowledge, our understanding of immunology (the defence network of the body) leaves a lot unexplained. The immunology of the newborn baby is especially confusing. At birth, an overwhelming number of changes take place in the infant. The heart begins pumping blood in a different direction, the lungs inflate with air for the first time, and the baby becomes a free-living organism facing the external environment. For reasons that are only partially understood, most babies thrive in this new environment. Others are highly susceptible to infection. Many different infectious agents can cause infections in newborns under the right circumstances. Most of these agents would be entirely tolerable to an adult. They may even be "normal flora"—a part of the normal (indeed, necessary) colony of bacteria or fungi that cause absolutely no disease in the adult who harbors the organism. One example of normal flora would be a bacteria called **Escherichia coli**. These bacteria inhabit

the gut of nearly everyone. Commonly, a woman will get some of these bacteria into her bladder—often the consequence of minor trauma from sexual contact—and a urinary tract infection (cystitis) will result.

Most babies tolerate this organism, as well. Nine hundred and ninety-eight of 1,000 babies who are born in its presence could not care less. However, an unfortunate one or two of the thousand will develop severe, overwhelming infection—even meningitis—with this agent. These infants may even die or suffer severe damage from this infection with a "normal" agent. In some of these babies the reason for infection is obvious, for example, prolonged rupture of the membranes where exposure of baby to bacteria may be very intense and sustained over a long period. In other cases the reasons for infection remain unknown.

Why should a newborn baby be so susceptible to infection? The possibilities are numerous. In every baby the immune system is somewhat "immature." Immune experience is nearly as undeveloped as the baby's job experience at birth—except that mother can give some immune experience to the baby by passing along some antibodies which filter across the placenta from the mother's blood. In this way newborns are born possessing many of the same antibodies as the mother—antibodies passed from the mother to the blood of the fetus.

While inside the uterus, the fetus is essentially protected from most infection by the filtering capabilities of the placenta which effectively exclude almost all infecting agents. This means that at the time of birth the newborn has never before had to respond with immunity to infection. All those lymphocytes and macrophages and so forth which do the majority of immune fighting against foreign invaders have never been stimulated before. Just as the newborn has never seen the light of day, so his white blood cells have never seen a bacterium. The cells are just beginning to learn how the system works. Thus, occasionally, a baby will succumb to an infection which would cause a mild illness or no problem at all in you or me.

Herpes of the newborn is one example of this problem. Herpes simplex, which causes a mild skin infection in the adult, may, under particular circumstances, overcome the

immature immune system of a newborn baby and lead to overwhelming infection which can disseminate throughout the body, result in encephalitis (brain infection) with consequent brain damage, or result in eye infection and eye damage. This type of problem is very unlikely to occur in any individual newborn. It is even unlikely to occur in any one individual born to a mother with genital herpes. Curiously, more than half of the babies born with this disease come from mothers who have never known they have herpes. In fact, once the mother knows she has genital herpes, newborn herpes becomes preventable. It needs to be considered so that the pregnancy can be properly guided. Herpes is not a reason to avoid having children, however, since the baby of a mother with genital herpes is unlikely to have any problems with neonatal (newborn) infection.

What are the signs?

Just as the symptoms of genital herpes vary depending on the location of the infection, so do the signs of neonatal herpes vary with the location. In unusual cases, herpes may already be present at birth. Since infection usually begins at the time of birth, however, it most commonly takes several days to a few weeks to become evident. The most common herpes infection in newborns is probably on the skin. The skin sore looks much like that on an adult, i.e., a single vesicle (blister) or cluster of vesicles. Occasionally, herpes may begin as a red rash or a purplish rash. Because many very mild skin rashes of infancy can mimic herpes, it is important to obtain a medical opinion when a skin rash develops in a newborn—especially if a sore develops which is similar to those pictured in Chapter 3. It is also important to remember that almost every baby has some type of skin rash at some point in the first few weeks of life. Normal things called **milia**, for example, which look like little pimples, may be frightening to the mother with genital herpes who thinks her baby has the infection. These are very, very common. Several babies in every nursery will have milia. Expect to see a skin rash in your baby just because it is a baby. Talk it over with your doctor. Genuine herpes sores may be found anywhere on the skin, but es-

pecially on the head of a baby delivered the usual way (head first), the buttocks of a baby delivered by breech (rear first) and so on. The mouth is a common site also, as is anywhere in the scalp that the baby was in contact with a fetal scalp monitor, if one was used.

Another common site of involvement with herpes of the newborn is the eyes. Again, most babies have red and swollen eyes unrelated to herpes because of the silver nitrate placed there at birth to prevent infection. Generally, this redness and discharge fades quickly over the first few days of life. Herpes in the eye most often presents as redness—"conjunctivitis"—with or without discharge of pus from the eye. This is often detectable only by special examinations done by an eye specialist (ophthalmologist).

The more severe neonatal herpes syndromes are infection of the central nervous system (the brain) and infection which disseminates (virus infection which is blood-born and thus distributed in many parts of the body). Brain infection tends to present late (from one to four weeks of age). An affected baby may suddenly lose his or her early very active behaviour (lethargy). He or she might stop caring about such things as feeding—or might do just the opposite, becoming very irritable. This, of course, is a very common thing in normal babies as well, but an irritable baby should be assessed to make *sure* it is "just colic." Shaking or twitching or fits (like epileptic fits) in an infant should be checked out by a physician without delay. Babies with herpes infection of the nervous system may have skin sores, but very often a baby with serious herpes infection will show no skin problem whatsoever.

The same is true for dissemination, i.e., skin sores may be present, but lack of skin sores is also very common. This syndrome presents a bit earlier, often within the first seven days of life. Rarely, herpes may be present at birth, implying that in very rare circumstances herpes may infect the baby inside the womb. This is so unusual that there is little need for concern. There is no known specific method for prevention of womb infection. Most babies with herpes dissemination have **nonspecific** symptoms. These include lethargy, going off feeding, vomiting, and so on. An affected baby may become gravely ill very rapidly. **Jaundice** (yellow skin) is a very

common thing in infants. When associated with actual liver enlargement and abnormal liver blood tests, jaundice may be the result of herpes or it may be caused by many other things. Sometimes the infant with herpes gets **pneumonia**, or has **difficulty breathing** or spells with no breathing at all. These are obviously serious problems that require intensive investigation in hospital. If the mother has herpes, the pediatrician needs to know, in order to consider herpes as a possible cause.

All of the scenarios discussed above, with the possible exception of skin sores, are nonspecific symptoms. This is the problem. So many things—some infectious, some noninfectious; some very serious, some very minor—can present themselves in exactly the same way. Herpes can cause many different things during the newborn period. Reading this section is frightening, but reading the list of symptoms from any disease can be frightening. You must realize that neonatal herpes is exceedingly unlikely to occur. It is highly preventable if you know you have herpes. Furthermore, in the unhappy event that it happens in spite of prevention, it is treatable. In fact, the problem we have with treatment is less the difficulty of finding a useful drug and *more* the delay that often occurs before the diagnosis is made. When the first sign of something serious is nonspecific it may take days to find the correct diagnosis. Treatment is made more difficult because of the delay. If your infant becomes ill, get medical attention. You can help by making sure the physician thinks of herpes as a possibility by telling him your history. You should not use this section to make your own diagnosis. In fact, even if your baby gets all of these symptoms, herpes is unlikely. Yet, it can be diagnosed only if it is specifically looked for. You can work with your physician so that the diagnosis of herpes is considered if the situation arises.

Is direct contact during delivery the only way of giving herpes to a baby?

No, but direct contact is by far the most common way of transmitting the infection. Most often, newborn herpes in-

fection results from a lack of awareness by everyone concerned. Remember, most people (that includes pregnant women) with herpes are never aware that they have this infection. Once recurrent herpes has been diagnosed, many things can be done to prevent transmission. When it is not diagnosed, however, prevention is not possible. Take for example the case of the woman who develops primary herpes (first time ever) during the last few days to weeks of pregnancy. It is common for the primary infection to begin with nonspecific symptoms, e.g., vaginal discharge or fever or urinary discomfort. It may not show up with obvious external sores early on. The mother does not realize what is going on, and cannot warn the physician. Furthermore, a visual search for herpes may not be routine during labor and delivery. The exam for herpes is a visual one and includes a search for uncomfortable sores on the vaginal lips, in the perineum, around the anus, in the pubic hair, and on the cervix. The usual obstetric exam during labor, however, is a manual one—a search for the progress of labor, using the fingers, to feel the cervix. Feeling with the fingers does not detect herpes sores. The eyes detect herpes.

What can be done to prevent transmission? People in general must learn to think about herpes when vaginal discomfort or other symptoms appear during the latter part of pregnancy. Physicians who deliver babies need to make the eyes an important part of their medical tool kits during labor. When herpes is strongly suspected in the mother, or in her sexual contacts, she may be closely watched for sores toward the end of pregnancy and during labor.

Another type of neonatal herpes is thought to result from infection after birth. This could come from the kiss of the parent with an active cold sore or from a nursery attendant who has a **whitlow**—herpes of the finger—and does not know, or from another baby in the nursery with herpes who gets handled by a nurse just before handling the baby in the next bassinette, without washing the hands.

A third type of infection mentioned previously, is the one inside the womb. Happily, this occurs rarely. Probably, most babies who get this infection early in gestation (their time inside the womb) will not survive and will be miscarried. Near

term, however, it is possible (though unlikely) for little holes in the amnion (the mother's sac of waters) to open and reseal, allowing infection. Fortunately, this is unlikely to lead to herpes infection. Herpes infection in the newborn generally occurs *during the birthing process itself*. The congenital herpes syndrome (inside the womb) does exist, however. There is, of course, nothing than can be specifically done to prevent this which follows infection in the womb. It cannot be predicted on the basis of the type of infection or by special tests. For example, there is no greater risk for this occurring in someone with five outbreaks per month than it is for someone with one outbreak per year. Why it ever happens is poorly understood.

Could I transmit herpes by kissing my baby?

The answer is "yes," as described above. Remember the rules. Herpes simplex is herpes simplex. Neonatal herpes can happen with Type 1 or Type 2. Approximately one-fourth of neonatal infections are caused by Type 1. It is not actually *proven* that kissing after birth is an important source for herpes. Despite academic argument to the contrary, it is prudent to assume that kissing and other nongenital contact can cause this syndrome. We use this assumption in deciding on the safest precautions for prevention. Think of the obvious. A cold sore is herpes. A kiss from a herpes-infected mouth may be as important as a delivery through a herpes infected vagina. This does not mean that someone with genital herpes needs to avoid kissing their newborn. You and your baby need those kisses and they are a wonderful thing. Genital herpes will not jump from your genitals to your mouth to your baby. On the other hand, if you have sores on your mouth just after the baby is born, this is a risk to be carefully dealt with during contact with the baby.

So what is done to prevent transmission after birth? First, if herpes is not active in the mother, nothing special is done. Delivery is completed normally and the baby is treated exactly like any other baby. He or she might room-in, or stay in the nursery, or both. Whatever you want to arrange with the doctor and the hospital is just fine. If herpes is active on the

genitals when labor begins, a cesarean section is performed (more on that later). After this delivery, the baby usually should room-in with the mother or be placed in a special area of the nursery where personnel are especially reminded to wash their hands. Otherwise, things are routine. You will be advised to feed the baby in a chair and to wear a gown. The baby should not be in your bed while sores are active. You need not wear a mask unless you have a sore on your mouth. You need not wear gloves unless you have a sore on your hands. You can breast-feed without problems unless you have a herpes sore on your breast. Just remember the mode of transmission. As opposed to that daring young man on the flying trapeze, herpes does not fly through the air with the greatest of ease. You should not find yourself in strict isolation in the hospital because of herpes. You might find an isolation sign on your door saying "contact isolation" or "wound and skin isolation." That means your sore, if active, should be isolated while you are in hospital. Nothing else need be isolated. Most precautions in hospital make sense. Someone should be able to explain why, or why not, you and your baby are isolated. Neither too little isolation, nor too much isolation, should occur. If your questions are not properly answered, you might ask to speak with the infection control officer (usually a nurse or physician) for an explanation.

If I get primary herpes during early pregnancy should I have an abortion?

We have discussed the problems of primary herpes several times in this book. Because it is more severe, it *seems* more likely that if herpes were to get into the bloodstream or spread into the uterus, it would be most likely to do so during primary herpes. If a fetus *were* to become affected with herpes early in gestation, the likelihood of spontaneous miscarriage of that fetus would probably be very high. This sequence of events is thought to be very, very rare, however. In fact, there is *no* evidence whatsoever that primary herpes poses any specific risk for this occurrence. In those rare events where it has occurred, mothers have given a wide range of medical histories, including recurrent herpes, primary herpes and *no*

awareness of herpes. On the other hand, a few well respected herpes experts feel that abortion may be a good idea if primary herpes (and only primary) occurs in early pregnancy. I, personally, do not agree. But then, I do not know the answer any better than these others. A lot will depend on the individual's attitude toward abortion and toward the pregnancy. Even if a mother is in her eighth week and having full-bloom primary herpes, her baby's risk of getting infected in the womb is very low indeed. *You* must decide what to do. By no stretch of the imagination is early primary herpes an "accepted indication" for abortion. It is a personal opinion and a personal decision.

In order to make the decision you must first be sure that what you had was *primary herpes* not just initial herpes. The diagnosis must be unequivocal. This means determining that the following were true:

1) It was your first vaginal sore like this
2) A herpes *culture* test was positive
3) A herpes antibody test was negative at the outset of the infection and later turned positive ("seroconversion"), AND/OR
4) Your physician feels that your symptoms were typical for *primary* herpes.

There is no further information you can know which will help you make the decision. Generally, you should *not* have an amniocentesis test to find out anything about herpes. This can be a misleading test for herpes. You may have a positive test but a normal baby, or a negative test but an affected baby. If your physician recommends amniocentesis for herpes, it will generally be done after the primary herpes is over to see if infection is present and persistent in the womb.

What, then, do I do to prevent the baby I'm carrying from contracting my herpes?

Discuss herpes with your doctor early in your pregnancy.

If it is early in your pregnancy, an **ultrasound study** which might be useful later for deciding dates may be selected for you.

Learn to monitor yourself for herpes. Learn the active phases of infection. Report recurrences to your doctor.

Some centers make available **special herpes examinations** for pregnant women. The American Academy of Pediatrics recommends examination and culture at 32, 34, 36, 37, 38, 39 and 40 weeks. Cultures are taken for possible herpes from the lips of the vagina and the cervix. This is not the only way to follow herpes in pregnancy, but this system allows for careful monitoring and it serves to develop special diagnostic skills in that center which may be useful in a pinch. Most of these "blind" cultures taken when sores are not present are, of course, negative. Thus, the system may not be "cost-effective." In other words, the expense of doing negative cultures is very high and the likelihood of a positive test is low when these cultures are done in the absence of sores. On the other hand, these examinations may point out small sores that are not noticed by the mother, and may increase her awareness of her herpes. Too, they are especially useful when sores heal, so that the end of an active outbreak can be clearly marked by a change from a positive to a negative culture. This change can then be used as a good reason to clear the path for normal vaginal delivery. A culture test should not be used to say that a visible sore in an active phase is not infectious. The "clinical" appearance should take precedence over the lab test in that instance.

The most important examination of all during pregnancy occurs during labor. Make sure you are examined externally with care. The trained eye of a physician should be used to inspect the external genitals, including the lips (labia majora and labia minora, both sides), the vaginal entrance (introitus), the area around the clitoris, the pubic region, the thighs, the perineum and the area around the anus (perianal). A speculum is used to examine the cervix for sores.

Unless a very important reason exists for needing one, **a fetal scalp monitor should probably be avoided** if you have a history of herpes.

Obtain a cesarean section if and only if you have

active herpes, or if you have just had active herpes which your doctor thinks might not be healed when you go into labor. A decision about healing can be a tough one. Essentially, we are considering the active phases (Chapter 3) as active and the inactive as inactive. Because of the high stakes involved in pregnancy, something a bit more than usual is tacked on at the end for safety. You will find numbers like four days, one week and even two weeks after the end of an active phase used as the safety ground between the end of an active recurrence and the "clearance for normal vaginal delivery." This is where the culture comes in as especially useful in keeping the time to a minimum. If the episode near the end of term is a **primary herpes**, it will be wise to extend the safety period even further.

Once membranes rupture, **an urgent cesarean section is indicated if your herpes is active**. This operation can be more leisurely arranged during labor if membranes are intact. If the herpes is not active a cesarean is not necessary because of herpes.

Does a cesarean delivery always prevent transmission?

Because herpes is generally transmitted by direct contact, when a physical barrier remains between a herpes sore and a baby's skin (the barrier is the sac of waters), the risk of neonatal infection is extremely small. Thus, bypassing an active sore by delivering the baby through the abdomen (cesarean section) will not allow the direct spread of the infection. This is an extremely effective method of prevention. Whether you will need a cesarean section or not will depend upon whether you happen to be in the midst of a herpes recurrence (active phase of infection) when labor begins. The statistical likelihood of needing a cesarean section will depend upon how often you get recurrences. As far as we know, your recurrence frequency rate will not affect the risk to your baby. It will only affect your chances of needing a cesarean section.

Once the sac of waters barrier is broken, the possibility of direct transmission to the baby becomes more likely. If this

occurs without your knowing it (remember the small holes that may heal up without symptoms), then a cesarean section might not prevent infection. The practical risk of this causing problems in your baby is very small indeed.

Confusion might arise when the bag of waters breaks (leaky fluid is usually obvious, but sudden clear fluid discharges in late pregnancy need checking out at a hospital). Once the membranes rupture, and this may be the first symptom of labor, it is only a matter of time until an active herpes on the outside gets to the inside.This is because the barrier is broken and a **wet path** has developed. In other words, there is a fluid connection from outside to inside held nicely at body temperature, allowing the virus to find its way inside. If herpes is active on the skin when the membranes rupture, it is only a matter of time before the virus gets to the baby. Therefore, cesarean section has to be done immediately. Some confusion has arisen recently, suggesting that it is all right to wait for as long as four hours from the time membranes rupture until the cesarean section is performed. This is not true. A cesarean section should be performed the minute that preparations can be made, if herpes is considered to be active at the time the membranes rupture.

In summary, cesarean section does prevent herpes transmission to the newborn when herpes is active and membranes have not been ruptured for a prolonged period of time. This holds for almost all situations that might arise if everyone involved, from mother to physician, is thinking of herpes and ready to handle each situation thoughtfully.

Why don't all pregnant women with genital herpes have a cesarean section?

There is often a feeling among some mothers with herpes that cesarean is the way to go regardless of the situation. Often this stems from the burden of potential guilt which the mother feels would arise from an infection in the baby. This is a very noble thought indeed. Unfortunately, it is often based upon a lack of understanding of the facts.

Fact 1: Genital herpes is a common problem, while neo-

natal herpes is an uncommon problem.

Fact 2: When necessary, a cesarean section may need to be performed for active herpes during labor. When herpes is inactive, however, cesarean section offers no advantages over normal vaginal delivery.

Fact 3: The risk of cesarean section to the mother is much higher than that of vaginal delivery. After all, cesarean section is surgery. It means a longer hospital stay, a higher risk of postpartum (after birth) complications such as fever and infection. The risk of cesarean section is still low, yet the risk of surgery clearly outweighs any potential benefits when herpes is not active at the time of labor.

Fact 4: Even cesarean section won't necessarily prevent neonatal herpes which may come from other sources than the mother's genital herpes. It is much better to think out the problem and use care in avoiding transmission. A panacea prevention may just confuse the issues.

Is there treatment for an affected baby?

Yes. Antiviral treatment in general will be discussed in Chapter 11. You may find more specific information there. Newer antiviral chemicals have made drug treatment for active herpes a reality. We now have very effective means of killing the virus while it is active. Our problems, in general, in devising new ways to kill herpes are twofold. First, therapy cannot undo damage already done to vital structures, although it can probably stop progression of damage from the infection. Second, it does not alter latent infection (see Chapter 1), and therefore virus infection may recur. In this situation, one is concerned about recurrences, but since they are not life-threatening, they can be dealt with later on much as the adult deals with recurrences. At the time of neonatal infection, however, one is very concerned about damage already done. This is why suspected neonatal herpes should be quickly and aggressively diagnosed. If a newborn baby becomes ill and the mother has a history of herpes, she should make sure that

the pediatrician knows of her history. If the father or any other sexual partner has herpes, that also may be important since the mother could then have herpes without knowing it. Make sure it is explained to you how the possibilities of herpes (and other problems) are being investigated. If herpes is not a consideration to the physician, is that because there is a good reason not to consider it? It is certainly possible to have good medical reasons to be not considering the diagnosis of herpes in a newborn. You can make sure that your doctor's reasons do not include not thinking of the possibility, by suggesting the possibility. If herpes is not a possibility, your physician will explain why it is not.

Adenine arabinoside (ara-A, Vira-A®) is presently the most widely used therapy for newborn herpes. In the laboratory, it is not as potent a herpes killer as another agent, acyclovir (Zovirax®) which has not yet been shown in the setting of neonatal herpes to be a superior drug. At this time the two drugs are being compared in many different centers around the U.S., Canada, Great Britain and Europe. As soon as one drug is shown to be superior to the other, these studies will be stopped and the inferior drug will be dropped from use.

What are my baby's chances of getting herpes?

No matter what you do, your newborn is not likely to get herpes from you. The actual risk is just not known. In some centers in the U.S. neonatal herpes occurs as often as one in every 7,500 live births. In Canada, the general chances are a bit lower. Remember that most of these babies come from parents with no history of herpes. The lower incidence in Canada may be the result of overall better nourishment of mothers and more likely prenatal care. A mother with genital herpes who seeks prenatal care, discusses herpes with her doctor, eats a well-balanced diet and has a cesarean section if and only if necessary for active genital herpes at the time of labor, is extremely unlikely to have a baby who suffers from neonatal herpes.

CHAPTER SEVEN

Who cares about your questions, you still won't be going back home. You may as well give back your glasses. And your pajamas.

ALEXANDER SOLZHENITSYN, *Cancer Ward*

HERPES AND CANCER

What evidence seems to show that herpes causes cancer?

Because there is no *proof* that herpes simplex is a cause of cancer, we can only examine the weighty circumstantial evidence which suggests that cancer and herpes might be related. After all the evidence is in, we find that it is a suggestive, but muddy argument. The association between herpes and cancer is not nearly as certain, for example, as the relationship between smoking and cancer.

Firstly, we know that sexual activity is almost certainly related to **cervical cancer**. Cancer of the cervix is common in prostitutes; rare in Catholic nuns. It seems to occur more often in women who experience their first sexual contact early, and who have a fair number of sexual partners in their lifetime. It should be logical to find a sexually-transmitted virus such as herpes simplex more common in women with cervical cancer than in those without. About fifteen years ago studies began to show, over and over again, a **sero-epidemiologic** association between the two diseases. In other words, a blood or serum ("sero-") test for herpes antibodies—specifically antibodies to herpes simplex Type 2, or genital

herpes—would show up more often in groups of women ("-epidemiologic") *with* cancer than in groups without. By themselves, however, these studies tell us little. We already know that sex is associated with cervical cancer. We are also virtually certain that sexual activity predisposes an individual to genital herpes. So why the surprise when both herpes and cancer of the cervix were found to be more common in women with a higher sex-related-risk factor? It would have been more surprising *not* to find this—and we *still don't know* if the real cause of cervical cancer is herpes or some other factor or factors. Among the other suspect causes being actively investigated:

Chlamydia trachomatis—a cause of **urethritis** (NGU or NSU) in men and **pelvic inflammatory disease** (PID) in women. It may also cause **cervicitis** (inflammation of the cervix) and abdominal discomfort in women. It has also been linked to **acute urethral syndrome**.

Sperm—if a sex factor is the cause, why not one that is nearly universal? It has been suggested that the DNA (hereditary material) in sperm may somehow associate itself with cells from the cervix, causing a change to a common cell. Another conjecture is that proteins on the surface of a sperm head may lead to cancerous mutations.

Wart virus—the **human papilloma virus** (HPV), which causes venereal warts, is also thought of as an **oncogenic** (cancer-causing) virus. It may be related to cervical cancer, and is considered by some scientists to be a prime candidate.

Smegma—the name for the slightly sticky collection of secretion fluids and sloughed skin cells, sometimes with a characteristic odor, which may be found under the foreskin of the penis.The association of smegma with cancer stems almost entirely from the low statistical evidence of cervical cancer in women of the traditional Jewish faith whose partners are likely to be circumcized.

A host of other agents of cervical cancer are suspected, including such viruses as **Trichomonas vaginalis** and **cytomegalovirus**. Continued research may provide some answers.

Aside from the seroepidemiologic association, however, other characteristics of the herpes virus suggest it as a possible cause of cancer. Herpes simplex can, under special lab-

oratory conditions, cause a cell to change in nature. That is, a normal cell taken from a hamster and treated with herpes in a special way has been known to form a cancerous tumor when reintroduced to the hamster's body. Certain parts of herpes viruses can be detected in some human cervical tumors using specialized tests called *nucleic acid probes*. And some investigators claim that herpes antibodies, also specially detected, can be used to determine how well a cervical growth is responding to anticancer therapy. When the herpes antibody test is high, the tumor is active; when it is low, the tumor is less active.

We may never find out the truth about herpes and cancer. Meanwhile, as we get better and better at medical detecting, it is clear that invasive cancer of the cervix is becoming less and less common. Early Pap smear changes may be getting more common, but are often treated so quickly that cancer is never allowed to develop. When all is said and done, if you have genital herpes your risk for cervical cancer is two to eight times the risk of those women without the infection. That is still a very low risk. You should realize that a cervical cancer is unlikely to develop, and an abnormality is very easy to detect before it becomes cancerous. At a more serious stage, it develops very slowly, giving you lots of time to take curative action that has proven completely successful in the early stages. The Pap smear is a detective—employ it regularly and properly.

One other cancer is associated with herpes: cancer of the **vulva**, the external genitals. This is also a slow-growth cancer, and much less common than cancer of the cervix. Its association with herpes is also confusing. The symptoms are commonly external itching or pain, or the observance of a growth, and its most common locations are those of genital herpes. Although itching of the vaginal area is very seldom related to cancer, persistent vaginal itching should be explored for possible causes. See your physician if you are concerned.

If I have herpes, is it on the cervix? Inside the vagina?

During primary genital herpes, nine out of ten women with herpes on the labia also have herpes on the cervix. Sometimes this may cause **cervicitis**, or true inflammation of the cervix with discharge and so on. Sores can develop on the cervix as well. For the most part, however, the cervix seems to contract the virus without changing much to the naked eye. Cells from the cervix taken in a Pap smear *will* show changes during the course of primary genital herpes infection quite commonly.

Herpes is probably a cause of nonspecific cervicitis more often than is realized. Cervicitis and discharge are common from primary herpes and may occur in the absence of external sores—sometimes because external sores develop a bit later in the course of infection, and sometimes because external sores never develop during primary herpes.

Involvement of the internal genitals, particularly the cervix, in recurrent herpes is quite another matter. A carefully performed study has shown that herpes might be recovered from the cervix in only 4 to 15 per cent of recurrent cases. In fact, it may be that three out of four cases are not really infection of the cervix, but simply virus cultures found positive there because of the "wet path" which exists between cervix and sore, making it possible to find herpes there on a swab—*not necessarily* because of an active internal infection. If a sore is near the entrance to the vagina, then one must come so close to it on the way in to examine the cervix that a positive culture might even result from the virus innocently passing by. Internal infection with herpes is by no means the rule—genital herpes is an external infection for the most part. It occurs mainly on the vaginal lips, the perianal area, the perineum (between anus and vagina) and the pubic region in women. The cervix may be a site of infection in unusual circumstances during recurrences, but a rare one.

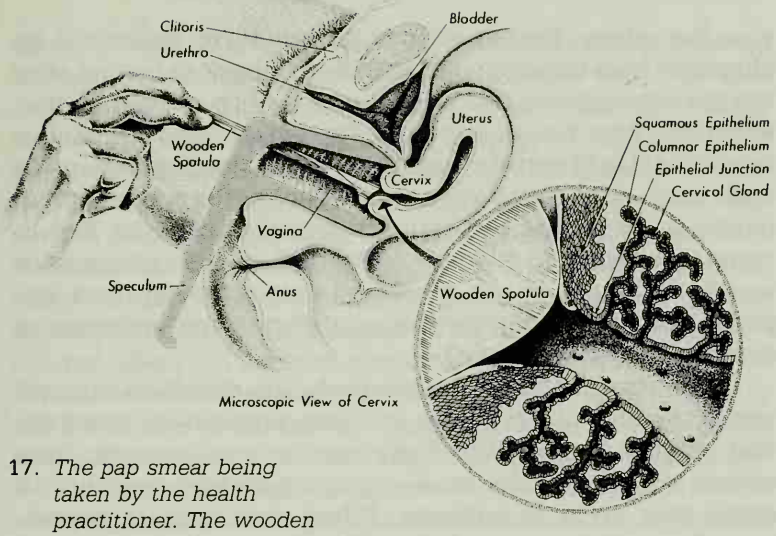
What are my chances, then, of getting cervical cancer?

There are different types of cervical cancer according to both epidemiologists, who look at the problem, and to women, for whom the seriousness of cervical cancer can vary. Cancer detected in a Pap smear before any damage whatsoever is done to the person generally occurs in about one in one thousand women over the age of 20. Depending upon the study you believe, the risk increases to 2 to 8 per 1,000 women with genital herpes. Clinically significant cervical cancer (one that has gone far enough that it might do harm to the owner if not dealt with immediately) occurs with much less frequency (closer to 7 or 8 of 100,000 women over the age of 20). The risk of this type of cancer occurring after genital herpes is diagnosed increases to approximately 15 to 100 cases per 100,000 women over the age of 20. The average age of occurrence is in a woman's late 40s, although it can be seen as early as the teens or as late as the 80s.

What should I do to prevent cervical cancer from becoming a problem?

A **Pap smear** is a simple procedure and can become a part of your annual gynecological examination. It is quick and simple to do correctly. The best time to have it done is just before or at ovulation, when estrogen (hormone) levels are high. This means the cells are flatter and easier to interpret under the microscope. The test can also be done at any other time, if ovulation is an inconvenient time to make the visit to the physician. Any vaginal discharge and cervical mucous coating the cervix are swabbed away using a cotton swab. Then a wooden scraper, shaped something like a popsicle stick and made for the purpose, is used to painlessly scrape a sample of cells from the surface of the cervix onto a slide which is sent to the laboratory.

The Pap smear will detect any unusual cells from the cervix. If cells are cancerous, it will detect them. If cells are just upset from infection, it will detect them also. All of these



17. *The pap smear being taken by the health practitioner. The wooden stick swabs the cells of the cervix (insert) which are placed onto a glass microscope slide. A person called a cytologist then examines the cells under the microscope to see if they look the way they are supposed to look.*

cells will be termed *abnormal*. Since cancer of the cervix is very slow to grow, a regular (yearly) Pap smear will be an adequate test. Some physicians feel that even fewer Pap smears are needed. As long as they stay normal—Class 1—one per year is plenty. If your Pap smear is abnormal in any way, more frequent smears may be appropriate. Discuss this with your doctor.

Whether you have herpes or not, the yearly Pap smear is a good idea. Rest assured that if you follow this regimen, you will detect any cancer of the cervix while it is 100% curable. I recommend putting this cancer out of your mind except for one big red mark on each new calendar—the day for your yearly Pap test.

My Pap smear is abnormal. What does that mean?

The Pap smear is a method of examining the cells that line your cervix. Anything that changes those cells will change

your Pap smear. During primary herpes, a Pap smear will be abnormal from infection, but will change back to normal after the primary episode has cleared and is of no concern. Other infections may also change the Pap smear, such as **trichomoniasis**, **Gardnerella vaginitis**, **gonorrhea**, and so on. In each case, if the Pap has become abnormal as a symptom of infection, treatment of the infection will cause the Pap to revert eventually to normal. A Pap will also be abnormal if cancer of the cervix has developed. It is obviously quite important to find out if your abnormal Pap is from infection or cancer. How is this done?

Pap abnormalities are classified. The classifications will vary from city to city, state to state, province to province, and country to country. There are "scores" ranging from normal to distinctly abnormal, signifying obvious cancer, with many gray areas in between. When your score is normal, regardless of where you live, a little celebration is in order along with a mental note to repeat the process in a year. When the score is abnormal, there are several things to do. If the most severely abnormal condition is detected, indicating invasive cancer, a **colposcopy** is generally performed (see below). If you have a mildly abnormal Pap test, your best bet is first to make sure that all possible infections have been ruled out. Your doctor will do (or may already have done) a culture test for **Chlamydia**, **gonorrhea**, **Candida** and **Gardnerella**. A wet mount examination or another test for **Trichomoniasis** is also performed. If your abnormal Pap was taken during or shortly after your primary herpes, you may also simply want to repeat the test to see if the situation has improved. If an infection is present, get your Pap repeated two or three months later to see if it has returned to normal. Your doctor will help you sort that out.

Now, let's say that you still have an abnormal test. You've had your infection treated, if one was present. You've waited several months. If the score shows only a mild abnormality, you will likely be advised to wait and see and to have another test in a few months. Probably this abnormal score will eventually vanish. If your test shows consistently abnormal cells, you may be sent for a **colposcopy test**. This is an examination of the cervix much like the Pap smear. A speculum

exam is used, and a microscope-like instrument is inserted through the speculum, giving the physician a very close look at the surface of the cervix. Biopsies are taken for further laboratory examination. A cervix biopsy, in which a small amount of tissue is removed, may feel like a pinch or may feel like nothing at all. The procedure is very, very safe, and a small amount of bleeding is to be expected. The laboratory will examine these biopsies and offer a fresh opinion. If invasive or microinvasive cancer is present on the biopsy, the therapy is removal of the cancer. This may require surgery—but not always. The most common surgical course taken is called a **cone biopsy** which removes, through the vagina, only the inner core of the cervix. Generally, a cone biopsy allows you to experience a normal pregnancy in the years to come.

If your initial biopsy puts your problem into a less severe category, you enter a gray zone where medical arguments are ongoing about what therapy you should have. The many different possible kinds of therapy to be chosen from at this point are beyond the scope of this book. You might be advised at one institution to have a cone biopsy for "severe dysplasia" and at another to wait, see and repeat a test biopsy. Why all the confusion? Most women whose infection falls into a gray area will tend *not* to progress to invasive cancer if untreated. Many patients will revert to a normal condition with no intervention—however, many physicians will argue that "most is not good enough."

The safest (and most serious) thing to do with cervical tissue diagnosed in a gray area is to treat and remove it from the cervix. Have you ever been asked if you see the proverbial glass of water as "half full or half empty"? The right course of action is not cast in stone—everyone is looking for answers, and if you are faced with the possibility of cervical cancer, discuss it at length with your doctor and read a lot more on the topic. Remember this, however: if you have been told that you have an abnormal result from a routine Pap smear, you have found the problem early, and can get treatment that is one hundred per cent effective and safe!

CHAPTER EIGHT

Yet it is hardly possible to take up one's residence in the kingdom of the ill unprejudiced by the lurid metaphors with which it has been landscaped.

SUSAN SONTAG, *Illness as a Metaphor*

THE PSYCHOLOGY OF HERPES

What emotional impact does herpes have on people?

Remember that a herpes infection may cause a spectrum of physical distress ranging from **asymptomatic** (no symptoms—the individual may not know they have herpes) to very severe. Just as the physical symptoms of herpes are not the same for everyone, so the emotional impact of herpes is also variable. It cannot be typified, categorized or compartmentalized. If you have herpes, the emotional effect on you will obviously depend to some extent on how severely it affects you physically. A painful and prolonged primary infection might result in a severe reaction of shock and anger. Any emotional reaction will also depend on how you were informed of the diagnosis. Was the person knowledgeable? Judgemental? Informative? What were your preconceived notions about the virus? Had you learned about herpes before it happened and prepared yourself for the possibility, or had you thought, "It could never happen to me?" Is your background a religious one? Had you believed that herpes was a punishment visited on those who have it? Have you known others with herpes? What were their reactions, emotional and physical? What have been their experiences with the infection?

Can you accept the inevitable about herpes? Do you feel guilt or shame about the circumstances under which you received the infection? Do you feel hurt by the person who transmitted herpes to you? Do you know how you got it? Has herpes interrupted your lifestyle? By how much? Are you afraid of getting involved because you will have to tell your partner? All the possible scenarios would more than fill this chapter. Some of the more common reactions to herpes are listed below. Some may be only temporary, others may have lasting impact for the individual. You should not necessarily expect to feel *any* of these things. You *should* realize that you are not alone with your feelings, whatever they may be.

On first learning about herpes, you may have a feeling of **shock**. There might be a sudden change in the image you have of your own body, or a sense of loss. Some people react with panic upon hearing the word "herpes," which they associate with other words such as "contagious" and "incurable." You might feel this, for example, during a severe primary infection, when you're ill and terribly uncomfortable, and not sure how long it's going to last. You might be told that you have herpes, but told little else. You may have heard that herpes is painful or incurable, and might imagine (incorrectly) that either this primary herpes will recur with the same intensity, or that it will go on forever.

Shock may also be the response if the diagnosis has been unexpected. You may have gone to the doctor because of something like a recurring yeast infection, hemorrhoids, or a spider bite, only to be told you have genital herpes. You may feel trapped inside a defective body over which you've "lost control." Regaining emotional and physical control of the situation requires regrouping your thoughts. Adjustment to herpes cannot be instantaneous. It comes through experience, study and observation. After all, any major change in life requires a period of adjustment. I would stress the idea of normalization. People with herpes should be striving toward that goal. The normalization process requires the passage of time—time to gain perspective. Normalization comes through an active process of learning the facts about herpes and, just as importantly, passing *through* the stage of self-pity to an ability to work with those facts.

At first, the diagnosis of herpes may be frightening be-

cause of the possibility of cancer, problems with future pregnancies, or the effect herpes may have on future romances. Think back: we were the vaccinated generation, the children of the penicillin era. Marcus Welby, M.D. never failed to cure our diseases, no matter how serious. Everyone knows that "you could be hit by a bus while crossing the street," but nobody thinks it will happen, not really. Everyone knows that herpes is the "disease of the 80's," but nobody expects to get it—much in the way that VD has been something that *other* people get. You may have feared getting herpes and now you may fear having it. Yet, upon having it and understanding it, we can see that the physical symptoms are not life-threatening or sanity-threatening. Nor does the physical distress of herpes have to be health-threatening. You can certainly be sexually healthy, physically healthy, mentally healthy and spiritually healthy *and have herpes*.

Until these facts are clear, your own fear might well be the dominant emotional reaction to your herpes. It may be more difficult to relate to others while you are afraid. There may be a desire to seek out unrealistic cures rather than face the issues directly. This may arise in part from the difficulty of finding material to read which does not scare you even more. Alternatively, you may have come across literature on herpes which reassures you beyond expectations—so much the better. You may not yet have located a health practitioner who explained the details of herpes to you, however. Herpes is a well-characterized, recurrent viral infection which you can fully understand. Being in possession of all the facts will help put things into perspective.

A person with herpes may feel **shame** about having a "social disease." For most people, this has always been amplified by the jokes of friends, as well as by our social climate. If and when you get herpes, a feeling may predominate that there is something shameful to hide. In fact, you may not wish to discuss herpes with some people. Because its origin and domain is the sexual act, you may feel strongly about keeping herpes a secret; private; discreet. This might reflect how you feel about the sexual encounter which you think, or know, resulted in herpes. However, anxieties which may arise because you're keeping the secret should be distinguished

in your mind from any feeling of shame *for having herpes*. Whom you tell is up to you. Some people feel that by telling friends, the situation can become more "acceptable." But don't rely on other people to give you your peace of mind. And remember that confession cannot solve the problem. Occasionally, if circumstances dictate, confession of some kind may be appropriate, even necessary. You may need to clear the air and confess the details of a love affair because having herpes has made it difficult *not* to discuss. A religious person may feel the need for absolution. Any "confession" will be based on individual needs and individual circumstances. But you'll be confessing a feeling or a deed—*not the virus*.

It is critical that we separate the deed from the virus. Good deeds or bad; right deeds or wrong; happy deeds or sad; these definitions are left to the philosopher, if anyone, and moral choices are left to the individual. Viruses are another matter. Viruses are in the realm of the virologist, the physician, and the epidemiologist. They do not make moral choices. Like their brethren bacteria, viruses need treatment. We accept them as *bad* because they can cause sores and are parasitic—but viruses do *not* choose their victims on the basis of moral principles. A virus called polio can paralyze children. Before the advent of polio vaccine 25 years ago, countless thousands of children were paralyzed each year. There was nothing moral or immoral about this phenomenon, however; it was simply a result of the nature of the virus combined with the susceptibility of children. Even herpes may be passed by contact from the mouth of a mother to the eye of her child because of the most innocent and morally correct act which the mind could imagine—a loving kiss. How can we see herpes sores on the genitals of an adult, then, as a moral comment? Shame may be appropriate to one person's circumstances, and inappropriate to another's. But it should have nothing to do with the biological fact that you have contracted a virus.

If you're feeling **guilt**, it could be because of the nature of the sexual involvement linked to the virus. You may also feel guilty because of your potential to transmit herpes—a problem minimized by education and awareness, and by open

and frank discussion with any new sexual partner. Ironically, people with herpes occasionally find themselves in the position of soothing the guilt of the partner who transmitted the infection.

Anger is a common reaction to herpes. Initial feelings of shock may give way to anger. Herpes has invaded your domain. Even though you know that active herpes phases follow a cycle, you are faced with accepting the fact that the virus itself is impossible to eradicate.

Anger may also be directed at the person who imposed the infection on you; you may feel "tainted" or "betrayed" or "compromised"; perhaps you feel they have abandoned you. The fact is that while the rare person with serious underlying emotional disturbances might purposefully transmit their herpes to others, the overwhelming majority of people who transmit herpes will fall into one of these categories:

He/she *did not know* what their sores (or "cuts," or "slits," or "pimples," or whatever) were.

He/she *never had any symptoms* suggestive of herpes.

He/she *knew about the presence of herpes*, but was mistaken about the active phases of their infection.

He/she *showed* the sores to a health practitioner and was told it was "nothing to worry about."

He/she was tested for herpes, but *the virus culture was negative* and he/she did not understand what this meant.

He/she *understood* the active phase of infection, was careful, and *still unwittingly transmitted the virus*.

Most situations are like one of the first five, and none of the six categories describe evil people, or "malice aforethought." Though conscientious, a person with herpes may have been told that herpes was "just a virus infection" or "just a cold sore of the genitals." They may not have realized the need to avoid transmission.

In fact, most partners of persons who have contracted primary genital herpes deny any history of herpes. This is not because they are liars. They are often misinformed. Even the person who knew about his or her herpes infection, but failed to tell, may not have had the courage or known enough medical information to properly explain the problem. Perhaps he or she felt inarticulate or shy, or was afraid to tamper with

the relationship. Possibly, the first time they told a partner, it resulted in a traumatic breakup. He or she is in a confusing position, with a tough responsibility.

Later you might find yourself turning your anger inward for being "foolish" enough to catch herpes. This feeling may become more intense if your initial anger at your partner was very deep. This can be the more destructive form of anger. If you are angry at a friend, the friend can walk away. You cannot walk away from yourself. In order to best cope with anger, you can do two things: first, try and find healthy ways of venting it. For example, physical exercise, relaxation methods, etc. may work for you. Secondly, try to understand the source of the anger. In other words, remember that distinction between *virus* and *deed*. Be aware that herpes is a reality among people in the '80s who make love, a reality that encompasses those who are rich or poor, clean or unkempt, "cool" or not.

You may feel anger and resentment toward the person who informs you of the diagnosis—the health professional. He or she is also the one who dares to fail to offer you a "cure," and this may be seen as the worst "sin" of all. Every physician or health care professional must be prepared for this. If the physician's answers to patients' questions are thoughtful and informed, their anger and frustration will be minimized. When the physician makes the mistake of sitting in judgement, however, or of offering inadequate information, physician-directed anger can be expected.

Depression is a common emotional reaction to herpes. Many people are understandably "depressed" by having the infection. Anyone would rather not have herpes if that were possible. Depression may result from the frustration of having an "incurable" disease. A sense of hopelessness will arise in some people with each active recurrence. Please note that it is "normal" to feel depressed over having herpes. It would be a sign of not caring for yourself and others, or of just plain stupidity, not to feel sad over the change of life which herpes may impose on you. There is now an obligation to discuss herpes with future sexual partners, to become aware of your recurrence patterns and avoid sore contact during active phases, and to monitor childbirth. This means some loss of

spontaneity and total freedom. Depression may also result from a loss of self-esteem—a feeling that you'll never be perfect, that you haven't lived up to your expectations. And whether it's fear of transmission or concern over the temporary discoloration of skin, the self-esteem we have tied up in our sexuality is very real. Sexual acts leave the participants vulnerable. When herpes complicates this vulnerability, there may be a strong tendency to feel wronged. A tendency to isolate yourself may follow. Isolation, after all, can protect you from further losses. Isolation carried to its extreme, however, can result in a self-imposed "sexual leper" effect: in other words, the feeling that one is alone and *should* be alone—for protection as well as for self-punishment.

There is a point, for some people, when depression becomes overwhelming, when a healthy degree of sadness changes to an overbearing feeling of hopelessness. At this point, depression becomes a problem quite separate from herpes. It may be difficult to tell where predictable feelings about an upsetting thing like herpes end, and where **clinical depression** begins. This is an unusual type of reaction to herpes, however. If it does occur, clinical depression may make you feel as if life's efforts are futile. Most (but not all) people who are clinically depressed will feel "blue" or low, so low that it becomes increasingly difficult to enjoy life—to have "good times." The appetite may decrease (or occasionally increase) with weight loss (or gain). Commonly, people who are depressed will feel a loss of their normal body energy and vitality. Sleep patterns may be interrupted by difficulty falling asleep (tossing and turning) or by awakening in the middle of the night and not being able to get back to sleep. Depression may also lead to loss of the usual "drive" at work. Sexual desire may disappear. It may become difficult to concentrate. There may be thoughts of suicide—there may even be a plan for suicide. Other manifestations of clinical depression might be aches and pains which turn out to have no physical cause, or phobia e.g. fear of heights or fear of closed spaces. If symptoms of depression take on an importance of their own in your life, apart from herpes—especially if several of these symptoms occur together—then you owe it to yourself to treat the depression seriously. Clinical depression can

happen to anyone, with herpes or not, and should not go unchecked. If you think you might be clinically depressed, it's treatable—seek help.

Can my emotions trigger a recurrence?

The acknowledged "triggers" of an active herpes recurrence are all termed **stressors** (anything that causes stress, whether good or bad). Triggers can include such things as menstrual periods or surgery or excessive sunlight. Most people feel that one stressor or another is responsible for triggering *some* recurrences. However, the overwhelming majority of herpes recurrences in any one individual happen *for no apparent reason*. They occur in no relation to stressors and without changes in immunity. Recurrences just *happen*. Under careful analysis, there is a suggestion that people who are undergoing a high degree of emotional stress *may* have more recurrences than those who are not. However, there are numerous factors which may interact at all times to affect a recurrence, and they are difficult to categorize and control. There has never been any proof to suggest that learning to diminish emotional stressors will diminish herpes recurrences—or alter your chances of having a heart attack, or of getting an ulcer. Every effort should be made, however, to take control of the stressors in your changing life; not because you can count on a reduction in herpes recurrences, but because life is, by its nature, a series of stressful events of which a herpes infection is one. There is a great tendency in the lay press, in newspapers and in magazines to make stress control and coping with herpes seem synonymous. This is not based in fact, but rather in the hope that new stress control methods may help to diminish recurrences of herpes. Unfortunately, this may bring on a boomerang effect, whereby you feel stressful and inadequate when herpes recurs by whatever mysterious mechanisms it uses. A feeling of recurring failure can develop: "Why couldn't I prevent this one?"; "What have I done wrong?" A straight cause—effect relation between emotional stress and herpes is not realistic. Furthermore, herpes is a very strong stressor in its own right. Stress control and coping

methods are useful means of living with herpes. If you find that certain types of stress controls also become useful for you in keeping your recurrence rate low, then you are among the lucky.

What can I do to cope?

Follow these steps, or replace them with reasonable alternatives of your own:

Go to a clinic or your own doctor for a diagnosis (see Chapter 4). Believe it or not, you will have your distress partially relieved by *knowing*. If you know for sure that you have herpes, you can deal with it in a logical and straightforward fashion.

You are not alone with herpes, and you are not alone with your feelings. Realize that your emotional response, whether it be shock or anger, is something others have also experienced.

Face yours fears directly. Expect certain aspects of herpes to bother you more than others and learn more about those aspects.

Be realistic. Researching herpes for the sake of knowledge and in order to regain control over your own life is a goal to be applauded. You will *not*, however, find a "cure" by frantically reading all the latest literature. Hoping for a cure is fine. It is critical that a cure be sought; that adequate treatment be found. It will not come, however, from panic or fear. A cure for herpes may become a reality, eventually. For now, establish an easy, reliable method for keeping up with the latest in herpes research so that good treatments come to your attention.

Avoid discussions about herpes with casual friends and acquaintances. The truth about your herpes *needs* to be shared if the following is true:

if sharing the information will help *you* in some important way. For example, *tell* your doctor in order to find out if you have herpes, *tell* members of a self-help group with whom you might share similar personal experiences, or tell your obstetrician. You may also choose to share the information

with a close friend. This is a personal decision. Some choose never to tell friends. They lose in some ways, but they diminish the risks of misunderstanding inherent in "going public";

if your sharing of the information will help someone else in some important way. For example, tell your present and future sexual partners, a friend who has just discovered they have herpes, etc.

Try to avoid making your herpes the subject of others' gossip. Gossip is painful and useless, but it's a social fact. It stems from ignorance. Herpes is a "juicy story," and you are best off not becoming the subject. You may not wish to mention your herpes casually or socially. It's simply nobody else's business, unless you plan to have sexual contact with that someone. If you have also chosen to tell a friend with whom you have no sexual intimacy or plans for sexual intimacy, remember the following:

- Avoid telling casual acquaintances.
- Think about who might be the right person in advance.
- Ask for confidentiality.
- Explain up front to this friend that you want to avoid pity. The last thing you need is someone to feel sorry for you. If you feel that you would benefit from having someone close to talk to about herpes, search out an equal who will not use the information for a "superiority trip," but who will be expected to offer personal advice and criticism. The right friend will not pity you, but rather will help you to avoid self-pity.

Sort out your thoughts concerning the telling of sexual partners. (More on this a little later.)

If your anger is a problem for you, make sure that you seek and find logical and acceptable answers to your questions. Participate actively in finding those answers and get herpes in perspective. *Herpes is not you.* It is, however, a reality in your life. In other words, if you are pregnant, make sure that the person scheduled to follow your pregnancy and help you deliver your baby knows what to do when the time comes. If you are frightened of cancer, arrange for yearly Pap tests and try to understand the fact that the risk is low. If

your concern is spreading herpes to others, you must realize that the caring and educated person with herpes who is trying to avoid transmitting herpes generally does so with a great deal of success. Find your appropriate person to talk to about herpes, whether that be a health practitioner, another person with herpes you find at a self-help group, and/or some other knowledgeable and trusted friend.

If you believe that your feelings or symptoms fit the category of clinical depression, you should seek assistance. You should call either your own doctor or a crisis hotline in your community, or go to an emergency room of a hospital. Tell the person there you are feeling depressed and would like to get some help.

Avoid unproven promises of cure. Even if you choose "alternative" methods of therapy, be careful to obtain standard therapy for your medical complaints. Be selective in choosing either a standard or an alternative therapy.

Should I tell my new sexual partner that I have herpes?

This is a very delicate question, and one that no third person outside a relationship can answer. Through my clinic experience I have heard both sides defended. Rather than offer you yet another set of prejudices, and in order to avoid the natural tendency to moralize, I will draw some analogies and ask some questions based upon the concerns of patients as they have expressed them to me. I can present some of the pros and cons for you to consider, but when addressing such questions as honesty and integrity, please don't look for those answers in a book. For a person making his or her own decision about whether to discuss herpes, past experience, advice from others, and intuition may all be helpful.

We live in an age of informed consent. Recently, the courts have decided that the physician must inform the patient about inherent risks from drugs or from surgery. Even if I, as a physician, believe the chances of side-effects occurring from a certain drug in any one individual to be very small, I remain duty-bound to discuss them, in order to allow

the individual the opportunity to decide. Sharing the information relieves me of the responsibility I would have held had I not explained the side-effects. I am still held responsible to uphold my duty to prevent those side-effects, if possible. My responsibilities fit the situation in that I am responsible for my actions but not responsible for withholding the truth.

Telling a sexual partner about herpes presents a similar situation. As a physician trained to know, or at least expected to know, about side-effects I can easily appreciate that the chances of bad things happening to a particular person are very low. I may choose to skip telling, thinking I can avoid creating a needless concern in a patient unlikely to be troubled. I will be right ninety-nine times out of a hundred. I will have saved those patients some anxiety and I will have saved myself having to face an awkward situation which takes time and may be difficult to explain. Indeed, for practical reasons, many physicians do this daily. The physician chooses which side-effects to discuss on the basis of their severity and their likelihood to occur, as well as on the basis of the individual physician's ease with the patient and how well he or she understands the side-effects. Many other issues play a role: for example, how busy is the office? How many times has the same thing been said? How well will the patient understand the information? Will the patient be frightened?

Prior to discussing your herpes with your partner, you have a relationship which closely parallels that of the doctor and the patient. Indeed, there may be legal parallels as well. You are holding information in your head about you which may influence how your partner feels or how your partner may act. You have a kind of power over your partner, in the sense that knowledge is power. If you avoid sharing the information, you tip the balance in your partnership. Any secret between lovers will change that delicate balance.

On the other hand, your relationship with this person may not be at the stage where you wish to establish that balance or equality. For example, if you are involved in a casual relationship, you may feel that this person is not close enough to share such information with. The risk of transmitting herpes during one encounter in an inactive phase is certainly quite low. Furthermore, any two people in a one-

encounter situation take certain risks, in terms of transmitting and receiving infections. If you have a short-term encounter, you generally know what you might be getting into.

Your decision about whether to tell is an individual one. Another person in the same situation might decide differently. It's a decision that will be based partly on personal experience. For example, were you told about the risk when you contracted herpes? Could you conceivably have been? Have you previously passed herpes on to anyone? You may decide to withold the information because it is difficult to tell, or because you are a shy or a private person. You may decide to tell because of your conscience or your moral convictions. It may be easier for you to tell than not to tell. If may be a matter of personal integrity. Your conscience must compare your right to privacy with your partner's right to informed consent. Choosing to tell is, in some circumstances, the more difficult path to choose. Sometimes it seems unnecessary. Discussing herpes before having sex may give herpes unwarranted status, especially if you feel in physical control of your infection. Some people note that even though most people have oral herpes, the average person with cold sores does not talk about cold sores before kissing or having oral-genital contact. If a person knows that there is a risk, albeit small, what should be told and what should not be told? Should the person who had one episode of genital herpes five years ago discuss the herpes before each new sexual encounter? If not, where is the line of severity drawn? Should the same individual not discuss oral sores which have recurred monthly since he or she was kissed as a child—because they came from mother, not lover?

Utilizing the notion of informed consent implies that the person doing the telling has information to convey. On the other hand, anything you know about people you are going to make love to may be potentially useful. This is the whole point. If you wish to tell your partner everything, say the following: "By the way, I get recurrences of herpes on my mouth, so when I have a sore we will have to avoid kissing and oral sex," or "By the way, I get recurrences of herpes on my genitals, so when I have a sore we will have to avoid genital sex," or "By the way, I have trouble with my back,

so when we sleep together I will need to use a board in the bed," or "By the way, I got sick with Salmonella food poisoning back in December and I am now a carrier, so you will have to do the cooking until that is better."

How should I tell my sexual partner?

There is a lot of advice around, published and unpublished, about herpes discussions. Generally, it is agreed that herpes should be made into no more and no less than it is. Remember that your own overall feeling about this infection will come through in spades when you tell your lover. If you think of yourself in a positive way, that will come through. Avoid preparing for the discussion by painting a picture of impending doom. In other words, avoid a tone or words that suggest, "Sit down, I have something horrible to tell you" or "Prepare yourself." Your role is simply to inform. In other words, tell your partner everything you know about herpes—what it is, how you know you have it, how you avoid transmitting it, how you have handled telling people before, etc. Tell your partner early, but not too early. Once you've established mutual trust, (and thus *know* you want that kind of a relationship from this person), then talk about herpes *before* you are physically involved. The subject of herpes has a powerful way of curbing spontaneity or spoiling the moment. Thought and sexual arousal are not well-suited partners. *You* must be comfortable with the knowledge you possess, since you must serve as an initial resource of information. Despite your other emotions, you must be able to teach with confidence. Avoid using your knowledge to "one-up" or "one-down" the person you're talking with. Instead, educate your partner on an equal basis—make it a *shared experience*. Expect some expression of fears from your partner. Acceptance without fear could mean your partner knows about herpes already. Alternatively, he or she may not be dealing with the subject. Expressed fears can be dealt with, and placed into perspective. It's a rare person who will get up and run from a relationship solely because of herpes. The majority will not. Remember that herpes is not you, any more than the acne on your back is

you or the bump on your nose is you. You need not apologize for having herpes—not to yourself *or* to your partner. You need not apologize for talking about it. If you find it especially difficult to talk about herpes in the situation of the casual encounter, you might opt for avoiding casual relationships, or telling anyway, or going ahead with the relationship and avoiding the subject. It all depends upon what is important to you.

What is a self-help group?

Since the dawn of history, people with similar problems and related goals have shared them for mutual benefit. This special kind of community has proven useful for anything from coping with recurring genital sores to fighting world wars. People with herpes may wish to come together for a number of different reasons:

Emotional support
- participating in group discussions
- sharing similar experiences
- relying on group support
- venting anger in a sympathetic forum
- allaying your own fears by relating them to others.

Information transfer
- making accurate information available to everyone
- keeping abreast with changes in the field

Political forum
- working with government in deciding key political issues related to herpes, such as education in prevention and treatment, and spending of health-care dollars

Charitable support
- fund raising
- organizing direct monetary support of clinical facilities and herpes hotlines
- supporting clinical, field, and laboratory research
- training personnel to meet future needs

In deciding how to organize a self-help group it is important to set goals. Which of the reasons listed above (or not listed above) have brought you together? If emotional support is the only goal, then a local support group is the only necessity. First, check to see if a group already exists in your community. You may call local health resource centers, women's health centers, sexually-transmitted disease clinics, public health authorities or a local herpes clinic, if one exists in your area. Call the national organizations below. They may be able to refer you to a local chapter. It remains critical, in any group, that some or all members be well-informed. It would serve no useful purpose if a self-help group were to perpetuate myths and fallacies. If any others on the list of reasons seem worthwhile, it becomes helpful to join a national organization—if your nation has one. In the United States:

Herpes Resource Center
P.O. Box 100
Palo Alto, California 94302
Tel (415) 328-7710

In Canada:

REACH
Box 70
Station G
Toronto, Ontario
M4M 3E8
Tel (416) 862-0803

The key to a successful herpes self-help group is letting people know about it (where it is, how to access it, etc.). If moneys exist, this is best accomplished with a telephone, an answering machine and a trained person to answer the phone. You may want to use trained volunteers and/or paid personnel if possible, and toll-free numbers may be available. The organizations listed above have tested methods for establishing new self-help groups. They have newsletters, medical advisers and organizational know how. Use them if you wish—and good luck.

What's good about herpes?

The diagnosis of herpes is a crisis. It is an unexpected, uninvited and unwanted intruder into life. It comes suddenly and strikes in subtle ways. Yet there is always potential in crisis. If nothing else, herpes is a learning experience. Most people who get herpes learn more about biology, medicine, pharmacology, nutrition and personal communication in the few months following diagnosis than was previously acquired in a lifetime. A herpes crisis is an opportunity to get to know yourself.

Sexual freedom without a care is over. The disadvantages to this are clear—or are they? Herpes adds a new dimension to sex. This has obvious negative potential, but also promotes honest and open discussion early in relationships. In some cases, this may serve to upgrade the quality of those relationships. Establishing communication over herpes may make it easier for your partner to discuss serious personal concerns as well. Because of the stress introduced into a personal relationship by herpes, other problems may be brought forward. Often, these would have been worked through sooner or later. If your partner picks your herpes as a reason to leave—as long as it was not based on medical misunderstanding, which can be corrected—*it may for the best*. Possibly, you've found the worm in your apple before you bit too early.

Herpes forces people to learn about themselves and about herpes. It forces them to talk about themselves with others. For those who have never been able to talk about intimate feelings and personal matters, herpes can be a springboard. There is a distinct advantage in knowing definitely that you *have* herpes: unlike the person who has it and doesn't know (a great number, remember!), you are relieved of worry and are able to distinguish the active herpes phases from the inactive. In fact, the person who knows he or she has herpes and takes care to avoid active phases of infection may be better equipped *not* to transmit the infection than those who feel they do not have herpes. After all, if you think you don't have herpes, you might be right and you might be wrong.

Herpes is a change. It is a big change for some and a small change for others. The change has some obvious bad

points which must be confronted and dealt with. Changes for the good are also a reality with this infection. Get over the tough parts by facing them directly: learn the coping methods; be aware of new developments and, for now, accept the change and the challenge to *normalize* your life in the face of adversity. This virus will probably affect you only once in a while—you have a *virus* for life, you do not have a *disease* for life. Recurrences may come and go, but herpes will not cause you to lose your job or die a premature or painful death. Herpes need not threaten your personal relationships. It may, however, teach you enough in terms of coping that you continue to grow.

CHAPTER NINE

Homosexuals are really (physiologically) like heterosexuals! (Catholics are, physiologically, like Protestants; Jews are, physiologically, like Moslems.) Indeed they are. But the plea for accepting a minority because it resembles the majority is, in effect, a denial of the minority's right to be different.

THOMAS SZASZ, *Sex by Prescription*

SOME SPECIAL PROBLEMS

Herpes and the homosexual male

Because of several factors, homosexual men have a much higher risk of contracting sexually-transmitted infections than heterosexual men. As we discussed in detail earlier, the herpes simplex virus tends to cause infection where it is inoculated. As far as we know, penile sores in the homosexual are no different from penile sores in the heterosexual man. However, because anal intercourse may result in inoculation of virus to the anus, herpes may commonly affect the anus of the homosexual male.

Inflammation of the anus is called **proctitis**. Many different infectious agents can cause proctitis, including gonorrhea, Chlamydia, syphilis and a host of others. In addition, there are noninfectious causes, such as tearing or abrasion from sexual intercourse, ulcerative colitis, etc. Recent reports have now documented herpes simplex as a cause for proctitis. Generally speaking (but not always) proctitis results from a primary herpes infection of the rectum. Whereas recurrent herpes in this area tends to be mild and external—in other

words, similar to recurrent herpes anywhere else—primary herpes proctitis may result in multiple discomforts during this initial episode. Rectal pain is very common. An urgent feeling of needing to pass stool, whether stool is present or not, is universal. A discharge from the rectum is also common. This discharge may be bloody. Most people with proctitis become somewhat constipated and itching may be disturbing. Pains of the low back, buttocks and thigh are often present. These are also noticed less frequently with genital herpes and are called **sacral paresthesias**. Nearly half of affected men will have difficulty passing urine during this primary episode. Other problems which result from inflammation of nerves may occur less often, such as temporary impotence. Lesions may be seen externally around the anus or may be present only internally. Fever and swollen glands in the groin are also common. The overwhelming majority of men with herpes proctitis will have a positive virus culture from the rectum. After one to six weeks the symptoms clear. This infection parallels cervical infection of women in that the primary infection is both internal and external, while recurrent herpes is almost exclusively an external disease.

If I am female and homosexual, can I get herpes?

Yes. There is no reason for you *not* to get genital herpes if you are a lesbian. The risk of acquiring genital herpes may be slightly decreased because of diminished genital-to-genital contact. On the other hand, it will be slightly increased because of increased oral-to-genital contact. Because the main methods of transmission will be oral-to-oral and oral-to-genital, there will be a greater theoretical chance of acquiring herpes simplex virus Type 1. Otherwise, the risks and outcome of a herpes infection are identical in the female homosexual and heterosexual.

Are herpes and A.I.D.S. related?

It is not possible to leave the subject of herpes and the homo-

sexual without a comment about **A.I.D.S.** or **Acquired Immuno-Deficiency Syndrome**. This disease is not limited to homosexuals, but has appeared most visibly in this community. For reasons that are not clear, persons with A.I.D.S. lose certain parts of their immune defense system—specifically the part known as the cellular immune system. These are the **lymphocytes** and so forth spoken about earlier in the book. As a result, persons who develop A.I.D.S. may fall victim to any infection or tumor which is generally kept away from our system by these cells. Specifically, tumors such as **Kaposi's sarcoma** or **lymphoma** are found.

Very unusual infections that are not seen in non-immunodeficient people are also encountered, specifically PCP or **Pneumocystis carinii pneumonia** and a host of other infections, including herpes simplex. When herpes affects someone with inadequate immunity many complications can occur. The sores do not heal spontaneously as they normally would; instead they might develop into larger and more extensive ulcers. Parallels exist with the newborn herpes syndrome where, because of loss of immunity, the virus may spread to internal organs. Herpes is highly treatable under these conditions, and intravenous acyclovir (Zovirax®) will generally stop the progression while it is being given. Unfortunately, the immune suppression continues. If given early, the treatment for herpes in the immunosuppressed relieves the problem while the drug is being administered. If the immune suppression continues (as it does in A.I.D.S.), this virus infection, or another infection, may recur and progress again.

Herpes has not been, in any way, related to A.I.D.S. as a possible cause, although it is a well-known and common complication. The cause of A.I.D.S. is unknown as this book goes to press. It is likely to be an infectious cause. People at highest risk of acquiring A.I.D.S. at this time are homosexual men, especially those with higher numbers of sexual partners; hemophiliac patients receiving blood products; intravenous drug abusers; and Haitian immigrants to the U.S.A. and Canada. The mode of transmission is poorly understood, however. In fact, cases with no ethnic, sexual or habit-related risk factors are also reported. Once again, this has no relationship to herpes, except that people who get A.I.D.S. may have

difficulty recovering from herpes as well as a host of other infectious agents.

Can herpes kill?

Yes herpes can kill. It does so rarely. In general, herpes does not cause serious physical illness in anyone who starts out having regular skin-type herpes which suddenly, say, goes wild. It can kill only under very specific circumstances: the newborn baby whose immune system has not matured; the adult who for reasons we do not understand develops encephalitis, a brain infection; or the person whose immune system fails, resulting in rampant and widespread herpes. In fact, it can generally be said that if you have herpes somewhere on your skin—whether on your lip or your genitals or your toe—herpes is no more likely to kill *you* in the future than someone else who doesn't have the infection now.

Will I have herpes for as long as I live?

Yes—and no. As far as we know, once a latent herpes infection has been established in the ganglion (which usually occurs before you even realize that you have it the first time), this latent state persists for life. Active infection is not persistent or lifelong, however. As you already know, active recurrences may occur depending on whether the herpes reactivates. Recurrences tend to be much more frequent and severe early in the course of herpes. Many people with a recurrent herpes infection are bothered less frequently after the first couple of years. Occasionally, however, an individual's recurrence pattern will just keep going with no change. If a high frequency pattern persists this may be quite distressing. This is the person who might look forward to possible benefit from drug suppression of outbreaks if and when that becomes possible in the future. Why this persistence of high frequency of outbreaks happens to some, but not to most, is unknown.

For many people with herpes, there comes a time when

recurrences cease to be a problem. This "burnout" of herpes is a pleasant thing if and when it occurs. There are no good explanations as to why this happens. Burnout is poorly understood. Possibly, the body's immune system has figured out new tricks to kill the virus. If this is the case, scientists have so far been unable to detect any new tricks. Another possibility would be that many of the ganglionic nerve cells affected by latent herpes have reactivated, leaving the person with fewer total affected cells and thus without recurrences. Nobody knows the answers. If this burnout phenomenon could be bottled, it would be an excellent patent to hold. It is possible for herpes to seem to slow down for a while and then suddenly become more frequent. In fact, herpes can slow down, speed up and slow down again. There is no predicting how herpes will behave. If your recurrence pattern becomes more frequent, realize that this will change. It may slow down again, just as it speeded up.

Herpes And Eczema

Skin diseases such as eczema, which cause multiple breaks in the integrity of the skin barrier, may predispose persons with these afflictions to severe herpes simplex infections. Then, in the unfortunate victim, during an otherwise uncomfortable, but routine primary herpes—oral or genital, the virus can work its way into every available skin tear causing skin dissemination. The names for this syndrome are Eczema Herpeticum or Kaposi's varicelliform eruption. Generally, after about six weeks all lesions heal. Recurrences are not as threatening, since the general immunity of the person is not a problem—the immune problem here seems to be only in the mechanical skin barrier. Recurrent herpes may wind up in unusual places because of all the sites involved with the primary infection (for example, the scalp area is common).

Persons with significant eczema who develop primary herpes should take extreme care in avoiding self-inoculation. They should also be considered prime candidates for specific antiviral therapy, if available.

Occupational herpes hazards: can I get herpes at work?

The answer is yes or no, depending on the type of work you do. If your contact with people on the job is a potential handshake only, you have a very low risk of contracting herpes at work. If you sell kisses at carnivals your chances would likely be increased quite a bit. If you sell kisses on the street your chances become close to 100%. Many types of other less obvious occupations result in close person to person contact. One example occurs at the office of the dentist. The dentist sees many people every day, and has his or her hands in thousands of mouths. The hands are washed very often to prevent the spread of infection. The skin cracks. A patient who has active herpes might donate the virus to a dentist's fingers. The herpetic whitlow or finger infection is a well-established occupational hazard for the dentist. The dentist unlucky enough to get a herpes infection on the finger can, in turn, give it to patients by continuing to work without gloves. Dentists with skin rashes or sores on the hands (and dental hygienists and dental assistants) should wear gloves. In fact, I advise new dental students to learn to work with gloves all the time. It is very difficult to relearn the art of dentistry using gloves, but new students who choose to wear gloves with all patients make a wise decision.

Who else can get a herpetic whitlow? Anyone whose ungloved hands regularly touch the face or mouth or genitals of another person. Thus, the list includes doctors, nurses, respiratory therapists, wrestlers, rugby players, and more. In fact, herpes may become a problem in any contact sport. It has been known to occur on many players on an affected team. What happens to the players on that team just before a big challenging event? If you believe in emotional stress as a trigger for herpes, you will then expect that the event will trigger recurrences of sores which peak with virus during the match. These special circumstances have resulted in special names: **herpes gladiatorum** (wrestling), **herpes rugbeiforum** (rugby), etc.

If your occupation has you seated at a desk, standing at a teller's window, or working in the fields, herpes is not an

occupational hazard. If you sit in the diagnostic virus lab as a technologist, or work as a dental hygienist, the situation is quite different. Remember the cardinal rule. Herpes does not fly through the air with the greatest of ease. It will not jump out at you from the plant in the corner, or from the people sitting to your left, right and behind who have genital herpes and share your toilet seat. However, if you commonly make direct skin to skin contact with others, and if the contact might include an area of active herpes on the body, then the possibility of transmission is a real one. Add a little heat, broken skin, and moisture as you would find in a wrestling match, or if a dentist, filling a tooth, and you've got a good transmission situation.

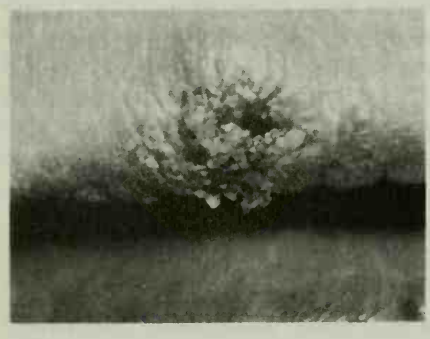
CHAPTER TEN

So Satan went forth from the presence of the Lord, and smote Job with sore boils from the sole of his foot even unto his crown.
Job

NONGENITAL HERPES INFECTIONS

Herpes of the face, mouth and lips

The lip is the most common location for a herpes simplex infection of any kind. There are probably three to five times as many people with cold sores of the lip, than there are people with genital herpes. It is a very common thing to see a facial herpes outbreak. Look at the people on a beach on the first day of bright sunshine. Look at the skiers on the slopes on the first bright day of snow. The sun triggers the recurrence of a fever blister. Its most common location is the "vermilion border"—the border between the skin of the face and the thinner mucous membrane of the lips and mouth.



18. *A recurrence of oral herpes simplex. Instead of recurring by reactivation of herpes simplex from the sacral ganglion, facial herpes recurs from reactivation of virus latent in the trigeminal ganglion.*

The fever blister is the recurrent form of herpes of the face. It may erupt repeatedly. Facial sores behave in a similar way to genital sores. They have the same pattern of recurrences which may be frequent or nonexistent and which are likely to decrease in frequency with time. Facial sores have active phases of infection with similar warnings (prodrome) followed by sores. Because the skin around the lip is a bit drier than the skin of the genitals, the vesicle (blister) stage is more common.

Like primary herpes infection anywhere, primary facial herpes is usually more severe than recurrent facial herpes. The classic tale of transmission of oral-facial herpes is as follows: Father, mother, grandmother, aunt, uncle, etc. might transmit herpes to child as the result of a kiss. However, facial infection can really come from any oral to oral contact whether during childhood or adulthood. Herpes simplex virus does not care where it is inoculated, just as long as it gets inoculated. Thus, oral herpes resulting from genital to oral contact is becoming more common. The primary event causes a bigger and more painful collection of skin sores. It also can create a sore throat from sores at the back of the throat. Severe first time mouth infection in a child commonly results in something called "gingivostomatitis". In this situation almost everything inside the mouth becomes a target for the virus. Ulcers burst out everywhere. It may make swallowing food very difficult. Lymph nodes (glands) in the neck may also be swollen and tender. The victim is miserable for the usual primary period of two to three weeks. It may be necessary to use topical anesthetics like lidocaine (Xylocaine®) to help swallowing. Children who suck their thumbs need to stop this habit immediately when they have this infection, in order to avoid painful autoinoculation to the fingers (herpetic whitlow).

Just as with herpes in other parts, the primary or first infection may pass unnoticed. If the child has gingivostomatitis, generally it will be easily diagnosed. If the child has only a sore throat or only a little fever, the whole event may pass unnoticed until the first recurrence. Then the cold sore or fever blister raises its little vesicles on the face. It usually reactivates near the lip, but the nose, the cheeks and even

the earlobe are fair game. There are rules for oral herpes like those for genital herpes:

1. Oral herpes is active during active phases. During those phases avoid kissing, especially newborn babies. Also avoid oral sex, thumb sucking, nose picking and eye rubbing.
2. Keep contact lenses out of your mouth at all times, especially when cold sores are active.
3. Stay away from your dentist when you have a cold sore. It would not be nice for the dentist.
4. What about treatment? Many of the same rules apply here as for genital herpes, so they will not be repeated. Treatment is coming, but is not here yet. Avoid using things that are now available—specifically, acyclovir ointment, idoxuridine drops, and ara-A ointment. You should also avoid a host of other drugs being sold outside of the drugstore. They are listed in the treatment section for reference.
5. A wet, moistened warm face cloth is used to soak the affected area. Then, blow dry with a hair dryer set on low. Ice, ether, alcohol, BHT, soap, and vaseline are best avoided.

Herpes of the eye

Herpes of the eye is very much like herpes elsewhere. That is, there is often a primary first episode with pain and swelling. Primary infections may be followed by recurrences. As for all herpes infections, recurrences cause less systemic (total body) involvement and less tissue is upset, etc. However, because of their location (in this instance, the eye) recurrences may lead to local complications which interfere with vision. If these progress, and/or if the complications become quite severe, decreased vision in the infected eye can result.

Generally, herpes of the eye is caused by herpes simplex Type 1. The time of infection and source of virus are identical to oral herpes. In other words, a baby or young child, more often than a young adult, may become infected with herpes

simplex, generally resulting from mouth contact with someone close, for example, a kiss from Mom or Dad. The person doing the kissing may have a recognizable fever blister (but he or she might also not have a recognizable sore). Possibly, the most ironic situation arises when a small child falls (for example, off of a bicycle) and scrapes the face or forehead near the eye. Mom, wishing to soothe the pain, kisses it to make it better. The result? Herpes has ready-made access to epithelial cells from the cut. The inoculation comes from the kiss. As far as the virus is concerned, this is as easy as using a needle for access. There are no barriers to jump across. Direct inoculation to the eye, specifically, is also made easy because the barrier is generally so thin. The protective layer of the eye is not tough and thick like skin, but rather thin and fragile. Transmission from genital sores on one person to the eye of another through direct contact of genitals to eye is possible. It is not commonly seen.

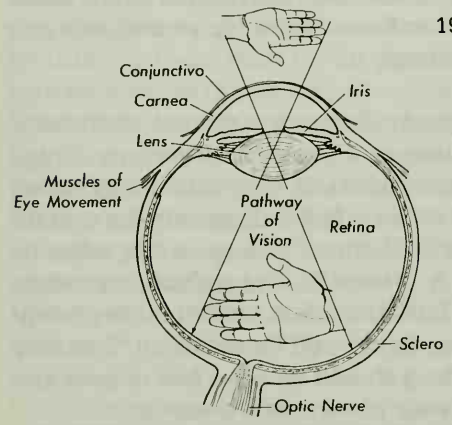
Primary herpes of the eye

Once inoculated, some 2 to 21 days later, an infection may occur. The primary or first event with ocular (eye) herpes is characteristic, yet sometimes difficult to diagnose. Generally (not always), only one eye is affected. Redness and discomfort of the eye develops. This is the appearance of "pink-eye" or **conjunctivitis**. The sac protecting the eye is inflamed. When you pull down the bag under your eye and stare into the mirror you are looking at the conjunctiva. Conjunctivitis is an extremely common infection in children. Most times the virus causing this is not herpes simplex. A very common cause of conjunctivitis in children, for instance, is *adenovirus* which commonly occurs in small epidemics or outbreaks from swimming pools, schools and so forth. Unlike herpes simplex, this virus is a very hearty one capable of withstanding drying and so forth. It does "fly through the air with the greatest of ease". Adenovirus usually involves both eyes. Other viruses, bacteria and Chlamydia can also cause conjunctivitis. Along with the red, uncomfortable eye comes a watery, tearing discharge. Often the neck "glands are swollen". In this case, a lymph node (gland) just to the front of the ear on the same

side as the eye infection is inflamed and tender. The eyelid may be swollen on the involved side. Often (but not always), a careful search for typical herpes lesions (see pictures in Chapter 3) will yield a positive result. They may be on the eyelid, under the eyelashes, or even on the forehead, in the hair, or near the nose or the mouth.

At this point, all is well in terms of vision. The child may feel sick, but vision is normal. The whole process of conjunctivitis lasts about two or three weeks. The physician may elect to send you to an eye specialist (ophthalmologist) at this point who may elect to start using antiviral (antiherpes) eye drops. There is no information which proves that treatment at this point is effective or even helpful in preventing more severe eye involvement. Despite that, if it were my eye, I'd put in the drops.

Usually, herpes conjunctivitis just heals at that stage and that's it. Herpes may occasionally affect the cornea on the first go around, however. If this occurs, the person will notice that the symptoms described for conjunctivitis are just beginning to clear, when new symptoms begin which are quite different. During herpes conjunctivitis there may have been swelling and inflammation, but vision was not affected. As keratitis begins, however, vision may begin to blur. Blurred vision which occurs because of herpes means the cornea is inflamed. The cornea covers the front of the eye where light



19. *The anatomy of the eye. The conjunctiva which forms a protective outer sac around the front of the eye (sort of like "eye skin") is the first place for herpes of the eye to affect. Recurrences can be a problem because of involvement of the cornea, since the cornea is part of the visual pathway. If the cornea is blurred, it may have the effect of blurring the vision. If only the conjunctiva is affected, vision is not blurred.*

first enters. It is a protective outer coat of transparent material. Keratitis is a name for inflammation of the cornea. Keratitis is a much more serious problem than conjunctivitis, since the conjunctiva is a protective membrane which we don't actually look through. We look through the cornea, however. It is the part just under a contact lens. Inflammation of the cornea leads to blurred vision. If a deep opaque scar of the cornea were to develop, decreased vision in the involved eye might result. Universally with keratitis, the eye feels gritty to its owner, as if it has a sandpaper surface, and it responds to bright light with a spasm of pain called "photophobia". If this occurs, the following things should be done:

Go to an eye specialist or "ophthalmologist". The tests to make the diagnosis of keratitis can only be done properly by someone with the right equipment and experience in eye diseases.

In order to see the lesion properly, the specialist will need a slit lamp, which is a sort of rotating microscope that allows the doctor to see an enlarged view of your eye as you hold your head still on a resting post. A dye called rose bengal or fluorescein will be used which makes a herpes sore stand out clearly.

The diagnosis of herpes depends mostly on the specialist's opinion, although he or she may also wish to do a virus test at the same time, like those described earlier in the book.

If herpes simplex is confirmed, you (or your child) may be treated with several things:

(A) **An antiviral agent.** There are several good anti-herpes drugs which can be used in the eye. Drugs help a lot in the eye which is a very different situation from herpes elsewhere. Useful drugs for the eye include idoxuridine (IDU, Stoxil®, Herplex D®), adenine arabinoside (ara-A, Vira-A®), and trifluorothymidine (TFT, Viroptic®, Trifluridine). A host of other chemicals are also being developed for use here. It is very arguable which drug should be used first or next and why. Stick with your physician's decision.

(B) A **cycloplegic**. This is a drug which relaxes a muscle

in the eye called the ciliary muscle. It will cause your eye to dilate and relax just as it does when you get drops at the eye doctor's office. This reduces the pain of **photophobia**, or eye pain due to light.

(C) **Pain relievers** are generally useful here, and these will vary depending on the need and the individuals involved.

(D) **Sunglasses** or very dark glasses may also help.

(E) Early keratitis is often treated with **debridement**. This is a minor surgical cleaning procedure and is quite helpful for early keratitis. It is not used in later stages of keratitis.

Recurrent herpes of the eye

We have seen that primary herpes of the eye generally causes only a self-limited two or three week period of conjunctivitis which does not affect vision. Furthermore, we have reviewed what happens to a few people as the conjunctivitis improves, that is, they get keratitis which can cause further problems. When ocular herpes recurs, it does so by causing recurrent keratitis. Eventually, the feeling of grittiness and pain may decrease because herpes of the eye causes a loss of feeling on the eye surface (cornea) called "hypoesthesia". Instead, there may be a recurrence of a feeling that something is in the eye, like sand or dust—a feeling of irritation. With each recurrence there may be an increase in tearing. There may be a recurrence of eye pain on exposure to light (photophobia). There may also be a simultaneous occurrence of sores on the lips, face, mouth or nose. The eye specialist will assess you each time this occurs to make sure it is herpes once again. You may be treated with the same drugs listed above. Drops of cortisone or any of its derivatives (an incomplete list of examples includes: Betnesol®, Cortisporin®, Decadron®, Metimyd®, Metreton®*, Neo-Cortef®*, Neo-Medrol®*, Optimyd®*, Sofracort®*) which are *absolutely contraindi-*

* These drops contain mixtures of antibiotics and cortisone derivatives. Mixtures are generally not useful for herpes at any stage. Any from this list are avoided during the early stages of herpes.

cated during conjunctivitis and early keratitis *may* become useful when carefully administered during some deeper forms of keratitis called **disciform keratitis** or **stromal keratitis**. Generally, cortisone drops are combined with a specific antiviral drug so that the virus growth is held back. The eye specialist may wish to repeatedly perform the minor surgical scraping procedure called **debridement**.

Herpes Encephalitis

Encephalitis means inflammation of the brain tissue. It is different from **meningitis** which means inflammation of the sac around the brain—the protective sac called the **meninges**. In some clinical situations both brain tissue and meninges become infected at the same time with the same agent and this would be called **meningoencephalitis**. Herpes simplex can cause either encephalitis or meningitis. The outcome is very different.

Herpes encephalitis in an adult is a very serious disease. Without treatment, encephalitis is often deadly. With treatment it may be deadly also, or it may cause significant brain damage. It does not have any correlation, whatsoever, to herpes of the mucous membrane, skin, or eyes. It is a disease of its own, which happens for reasons we do not understand. A person with genital herpes, or eye herpes, or herpes of the toe, is no more (or less) likely to get this horrible disease than someone else who has never had herpes.

Herpes meningitis, on the other hand, is a direct complication of genital or anal herpes. Meningitis should not be confused with encephalitis. It commonly occurs as a part of the primary herpes syndrome of symptoms. It may cause a severe headache. It may cause eye pain when looking at light (photophobia). It does not cause permanent damage to the nervous system. Left alone, meningitis gets better and almost never recurs. Treated, it also gets better and almost never recurs.

Herpes encephalitis may also occur during neonatal herpes. The neonatal herpes symptoms and its prevention are discussed in Chapter 6. Remember that neonatal herpes en-

cephalitis usually, but not always, follows genital herpes in the mother. Most mothers giving birth to babies with this problem have never thought they had herpes. We need to find these people because studies are showing that we can prevent neonatal herpes quite effectively by doing a cesarean section for active herpes. The diagnosis must be known, however, in order to take preventative action.

Herpes encephalitis of the adult occurs by an altogether different mechanism. For some reason, which we do not understand, herpes simplex makes its way to the brain. It may get there by any number of ways. It most likely gets to the brain by travelling up a nerve called the **trigeminal nerve**. Normally, the virus stops at the trigeminal ganglion where it stays as a latent infection (see Chapter 2). In the rare case of encephalitis, however, the virus does not stop for a latency rest at the ganglion. Instead, it keeps travelling right to the brain tissue. Once inside the brain it picks a spot for infection. That spot can be, literally, anywhere. However, it is most commonly in an area of the brain, more or less underneath the temple or the ear, called the temporal lobe of the brain. Oddly enough, the virus stays right there and just damages the area of the lobe it is in. In doing so, however, it causes swelling and inflammation. This can result in more widespread damage, because the brain is encased in a cranial vault of bone, leaving no place for it to swell into.

Herpes encephalitis can occur at any age from infancy to old age. During the first few weeks of life, encephalitis is more often diffuse and is associated with the neonatal herpes syndrome. Fewer than 10% of patients with "adult-type" encephalitis are under 10 years of age. Common symptom complaints include fever, which is present in 90% of cases, and a change in consciousness (something ranging from sleepy or disoriented to deep coma) is nearly universal. The patient may complain of headaches early in the course of the infection. Often there is a sudden personality change or a tendency to bizarre behavior. A seizure (fit, convulsion) may occur. Speech may be abnormal. Paralysis or weakness on one side of the body may sometimes occur. In most cases paralysis like this results not from herpes, but from stroke. It is difficult to diagnose herpes encephalitis. Several tests may be per-

formed in the search for the answer, among them **computerized tomography** (CT scan), **electroencephalography** (EEG), and a **brain scan**. None of these tests, unfortunately, are specific. As with all herpes infections, the diagnosis depends upon finding the virus. In the case of herpes simplex encephalitis, the virus is in brain tissue and only brain tissue. Thus, the diagnosis is made by brain biopsy. This is an operative procedure requiring a neurosurgeon who drills a small hole in the skull and removes a small piece of brain tissue for examination. The biopsy, itself, carries minimal danger when compared to leaving infection of this severity untreated or wrongly treated. Experts agree that if this diagnosis is considered a brain biopsy should be performed.

Treatment for encephalitis is intravenous adenine arabinoside (ara-A, Vira-A®). Therapy is quite helpful in decreasing an otherwise seventy-five percent death rate. It is not a miraculous therapy for everyone because damage may have been done to vital brain tissue before therapy has had the chance to work. Other drugs, including intravenous acyclovir (Zovirax®), are now being compared to adenine arabinoside. Therapy is likely to be refined and improved in the future. Unfortunately, until we can make this diagnosis earlier*, we will be stuck with a frightening and serious disease which is, happily, very uncommon, and which has no connection whatsoever to genital herpes.

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* Making an early diagnosis of encephalitis is an important and exciting challenge for the future. Scientists have tried blood tests, spinal fluid tests and scans. In order to make the diagnosis earlier, we are going to have to devise a "noninvasive test"—one which does not "invade" the body like a brain biopsy. Recently, it has been suggested that one of the thymidine analog drugs or other drugs which are specifically included by virus-infected cells and excluded by healthy cells might be labelled with a radioactive label. Then, if herpes encephalitis is suspected, the drug would be given by vein. A special camera which detects the radioactive label might take a picture of the herpes from outside the body! This trick may work, but it has only been tried in animals who get very different kinds of encephalitis. It will be vital and very important to watch this very carefully in the future. It may be that herpes encephalitis is not rare at all, but that it is only rarely so severe that it gets to brain biopsy and then diagnosed. After all, not too many physicians do a brain biopsy on every person with a headache or a personality change! Imagine if herpes were the cause of schizophrenia and it became treatable with an antiviral drug!

CHAPTER ELEVEN

Finding a solution to a problem is helped enormously by the certain knowledge that a solution exists.

CARL SAGAN, *The Dragons of Eden: Speculations on the Evolution of Human Intelligence*

THERAPY NOW AND TOMORROW

Accepted therapy today: what can I do right now?

If you have **primary genital herpes** or think you might have it:

Go to your doctor or clinic. Have a trained professional diagnose the problem and confirm its presence by a virus test (culture test, fluorescence test or electron microscope test).

A blood test for syphilis should be done, and should be repeated in a couple of weeks.

If the pain is severe, you may wish to discuss obtaining a **pain reliever** by prescription to help you "make it through the nights."

Soak in the tub or take a very warm shower in order to **run water over the area** three to four times per day. In the tub, you may put the water up just a few inches (sitz bath). Occasionally, individuals find water on these sores to be absolutely intolerable. If that happens to you stop using water. Most people find water to be very helpful, however.

When you get out of the shower or bath, **blow the genital area dry** with a hair dryer which has adjustable temperatures. Set it on low or "cool," being careful not to burn yourself.

Make sure you are passing urine without difficulty. If you try to go and it won't come, try again. Try urinating in the shower or tub to decrease the sting. Turn on the sink tap for background noise. Outside of the bath, you might try to direct the urine stream away from your sores with a bit of rolled up toilet tissue. Pouring warm water over the area using a glass of water may also be helpful. Some have found that drinking a lot of water (eight glasses per day) dilutes the urine enough that it hurts less. Others point out that this increases the number of times you have to urinate. Whether you would rather it hurt more intensely on fewer occasions, or less intensely on more occasions, is up to you.

If you cannot pass urine and you've tried several times, wait a couple of hours—even three or four. If still no result, you must have medical attention. Not passing urine can lead to serious problems which are totally preventable. If you can find your own doctor, call or visit him or her. If the physician is difficult to locate, go to the emergency room of a local hospital.

Avoid tight undergarments. If possible, avoid undergarments altogether. Try loose fitting things, labelled pure cotton. If you are able to go to work, upon returning home take off your clothes and soak yourself in the tub. Leave your clothes off if you can.

You may be treated with a drug called acyclovir (Zovirax®). This is available as an ointment in a tube. (See the specific drug section for more information.) It may also be given by the intravenous route in the hospital and will probably be available within the next few months in an oral form. Not all forms of this drug will be available in every country. You must discuss availability and advisability of prescription drugs with your doctor. This drug may help sores to heal more quickly. The treatment of a primary outbreak, however, has not proven to have much effect on future recurrences of herpes. Drugs other than acyclovir are being tested. For now, all others are in the experimental stages, or are unproven. You may wish to be hospitalized for intravenous treatment. If your outbreak is quite severe and giving you trouble walking, or if your head feels like the top is going to come off, or if you are having trouble urinating, then intravenous acyclovir

will help you feel better sooner and should be considered.

Avoid, because they may be worse than doing nothing:

- Cortisone cream or ointment
- Antibiotic cream or ointment
- Any cream or ointment unless it contains a useful, specific antiherpes drug
- Vaseline
- Antibiotics (unless you have a clear-cut secondary infection)
- Alcohol
- Ether
- DMSO (dimethyl sulfoxide)

If you are pregnant during primary herpes let your physician know, and read Chapter 6. Care for yourself at this point by giving yourself time to heal, treating other infections if they are present, and treating your herpes.

Remember that it is hard to learn and understand everything all at once. The answers will come. The ability to cope will also come. There is no truth to the rumors that stress will make your primary herpes worse. It is very distressing to have primary herpes. Accept the stress for now. Follow the suggestions above to take care of the immediate problem.

After my primary herpes is over

At this point, it is usually not clear whether you will have recurrences. The precise percentage of people who will get recurrences after their first infection is unknown. In general, the medical profession only gets to know those people who do get recurrences; the others are not going to the doctor. It is guessed that slightly more than 50% of people who get one herpes outbreak will get at least one more recurrence. If you don't get recurrences, you do not need treatment. Treatment would be truly unwise unless there is something to treat. Latent infection inside the ganglion does not hurt you. By itself, latent infection is untreatable by anything available in

the drug department. Leave latent infection alone. Some will have you believe that you can intervene and affect this latent infection with a drug. For now, you cannot.

What if I am having recurrent herpes, or think I might have it?

You may decide to try **therapy**, or you may decide not to. The discussions of various kinds of therapy which follow apply *generally*—but not always to the individual. Any decision concerning your own therapy, therefore, should be made after consultation with your physician. For most people, recurrences are more of a problem in the first year, or two, than in subsequent years. Generally, the frequency decreases by itself. This is, of course, not always the case. If your recurrences are mild and only come every four or five months, or less often, you would probably be best advised to leave well enough alone.

You should learn about active phases of infection so you can avoid sore-to-skin contact when necessary.

You may wish to use the hot soaks and hair dryer routine described for primary herpes, depending upon the amount of discomfort your sores cause when they are active.

You may choose to do nothing specific in the way of therapy.

The average recurrence of herpes lasts about six to ten days from start to finish. Because it is over so fast, it is difficult for any drug to show an effect. Thus, I find that topical acyclovir (Zovirax®) ointment while beneficial sometimes is in my opinion often not helpful enough in recurrent herpes to be considered worthwhile. However, in some studies it killed the herpes virus slightly faster during recurrences than if it had not been used. Concerning topical acyclovir, Dr. Richard Reichman and his co-workers recently reported the following results of a carefully conducted trial in the *Journal of Infectious Diseases*. "There were no significant differences between the acyclovir- and placebo-treated groups of either sex in time to crusting of lesions, time required for lesions to heal, time to cessation of pain, or in frequency with which new lesions developed during the course of therapy. Mild, transient burn-

ing or pain associated with application of the study medication was a common complaint." In fact, recent data shows that using topical ointment acyclovir (Zovirax®) for recurrent herpes by starting it very early, at home with the first sign of recurrence (prodrome), has no useful clinical effect. It should be avoided for recurrent herpes, altogether, in my opinion.

The oral form of acyclovir may soon be released in the drugstores. Acyclovir by mouth has been shown to speed the time of healing by approximately one day. In studies on people with recurrent herpes who went to the clinic because of the recurrence, the placebo recipients healed in 6.9 days, whereas lesions healed in 5.9 days in the group receiving acyclovir. Follow-up studies of this trial showed that people who took the drug at home at the first indication of recurrence (prodromal phase) improved this result by another one half day (5.7 days vs. 7.2 days). Now that it has been "proven" that oral acyclovir "works" (by decreasing time to healing), the question is, "Is it worth it?". It is certainly not a panacea taken as a drug to treat recurrent herpes, but it does have a positive effect of one to one and one-half days' difference. Clearance in the United States is pending at the time of writing, and the price has not been announced. The price in England where acyclovir is sold in an oral preparation is about £5 per day of treatment. So far trials with this drug suggest it to be very safe as an oral agent. Acyclovir will be further discussed in the next section.

Several other forms of newer treatments are being developed and are in various stages of testing (see the next section).

The following compounds have been rigorously tested in scientific studies and have been shown to be **ineffective**. The ones which are marked (*) are also considered worse than using nothing, either because they may prolong lesions or complications, or because of real or potential harmful effects:

- Alcohol applied to the sores
- Bacille Calmette-Guerin (BCG) vaccine*
- Chloroform* applied to the sores
- DMSO* (Rimso-50®, dimethyl sulfoxide) applied to the sores
- Ether* applied to the sores

- idoxuridine (IDU, Stoxil®, Herplex-D®) applied to the sores
- Levamisole*
- nonoxynol-9* applied to the sores
- Ointments or creams not containing a specific anti-herpes drug (including cortisone, antibiotics, etc.)*
- Oral polio vaccine
- Photodynamic inactivation (light and red dye treatments)*
- Smallpox vaccine*

What does the future hold?

The field of drug therapy against herpes has rapidly progressed over the last few years. During 1982, we saw the first proven effective therapy for genital herpes achieve government approval and appear in the drug stores. The numbers of herpes researchers has increased dramatically, possibly with more rapidity than the incidence of the infection itself. Pharmaceutical firms have joined up for the herpes battle, each one hoping for a chance to have the best therapy for herpes.

Many objective targets for therapy are used to assess the usefulness of a drug. The herpes researcher uses his or her own buzz words such as , "double-blind", "randomized", "controlled", "time to total healing", "virus titer", "time of virus shedding", "pain scores", "itching scores", "patient-initiated therapy", and "clinic-initiated therapy". This list is nearly endless. These words are descriptions for different points used to measure drug effects, or for different methods of conducting a human drug test—often called a "clinical trial". Today, in studying genital herpes, a new drug will be considered to be effective only if it can satisfy some basic tests:

It must be safe and effective at killing virus **in vitro**—in the test tube. Some drugs are not intended to kill the herpes virus, per se, but rather to boost the body's natural immunity. These drugs would be ineffective in the test tube, but would have to show an effect in the animal model.

It must be safe and effective in **helping animals** experimentally infected with herpes.

It must be studied for use in herpes in a **double-blind, placebo-controlled, randomized trial**. The trial is called double-blind because both the patient and the investigator are blind to which patient is getting which therapy i.e. neither knows which volunteer is getting the real drug and which volunteer is getting a placebo (fake drug) until the end of the trial. The placebo control drug is one which looks like, tastes like, smells like, and for all intents and practical purposes is indistinguishable from the real drug (except it does not contain the real drug). The study is randomized by a statistician, so that there is no possible way to predict which volunteer might receive the real drug.

In conducting the clinical trial a person with herpes uses the new test drug. Factors that might reveal if the drug is useful are monitored very closely; for example, the appearance of sores, the duration of sores, the pain and itching of sores, or the virus quantity in sores.

Certain things that are "known" to affect the course of the illness are grouped together for study. For example, since recurrent herpes lasts about one week and primary herpes about three, it is clear that the experiences of primary and recurrent herpes should not be compared to each other. Rather, they must be separately studied. Many other factors also affect a study.

Results of the drug testing are tabulated and then locked into a computer. Once the results are locked in an unchangeable fashion, the code is broken. Then the statisticians and scientists and physicians can analyze whether the people who got the drug responded in a way that is different from the group who got the look-alike, smell-alike, taste-alike placebo. Then, and only then, if the drug works better than the placebo, one can draw conclusions about whether the drug will be useful or not. If the good effect is clear, in mathematical terms, this is termed "statistically significant". This means the effect of the drug is unlikely to have occurred as a result of chance alone. Many drugs, chemicals, natural substances, food additives, solvents, methods of biofeedback, hypnosis, acupuncture, and so forth have been purported to work for herpes. Of the ones which have been tested in a carefully designed double-blind, placebo-controlled, randomized clinical trial, however, only a handful show any positive effects.

These drugs and some others will be discussed further. Indeed, as far as anti-herpes drug therapy goes, the present and the future are beginning to overlap. We are actively discovering new chemicals to kill the virus, and also new ways in which to use those chemicals.

Any infection results from an imbalance between the number of infecting particles (the invasion size) and the immune defense network. Drugs for herpes are being developed to affect both sides of the network. We might try to boost the body's natural defenses, in other words, boost immunity. Then the body might kill the virus faster or keep it latent more effectively. Alternatively, we can develop drugs to actively kill the virus, like penicillin kills gonorrhea.

Drugs to kill the virus (antiviral agents):
Acyclovir (Zovirax®)

Acyclovir (ay-sigh-klō-veer) is known as a **nucleoside analogue**. Nucleosides are the natural chemicals which are used to build DNA. DNA, the hereditary material used in cells and viruses for transmitting information from one generation to the next, is made up of four chemicals put into place in different sequences—thymidine, adenosine, cytosine, and guanosine. These chemicals make up a sort of chemical computer code. Acyclovir is a chemical which looks like one of these code chemicals. It looks so much like thymidine that enzymes often get confused by it and think that it is thymidine. Luckily, herpes simplex viruses make an enzyme called thymidine kinase (TK). This TK from herpes is fooled every time it sees acyclovir. The TK adds phosphorus to the drug and thereby activates it making acyclovir triphosphate. When TK from a cell with no herpes sees acyclovir the TK does not activate the drug. Acyclovir is only activated by TK from herpes-infected cells. It gets into those cells best and kills the virus. Once acyclovir triphosphate, "the activated form," is made inside the cell, the DNA synthesizing enzyme called DNA polymerase can be inhibited, altering the DNA, resulting in death to the virus and to the infected cell. A report published in **The Journal of Biological Chemistry** in 1981 by Dr. Y.—C. Cheng and co-workers at the University of North Carolina in conjunction with scientists from Burroughs Well-

come showed that acyclovir triphosphate inhibited herpes DNA polymerase better than it inhibited cellular DNA polymerase, although the human cell DNA polymerase called "alpha" was clearly affected by this activated drug. Despite this, however, this drug is relatively safe and specific since without herpes around it is an inactive drug. Acyclovir also has some disadvantages:

1. Because it depends on the TK it can only attack herpes that is actively growing—not latent.
2. It is absorbed poorly (but partially) from the intestine, so when given orally, the amount which gets to the action is not as high as when the drug is given by injection.
3. It is poorly soluble. In other words, when in a liquid (like urine), it can crystallize or precipitate (like making rock candy). Under some circumstances, it has done this in the kidneys and caused damage there. This problem is now avoided by diluting the drug and giving it slowly. This should not be a problem, however, when the drug is given orally or applied topically.
4. Because it depends on TK the virus can experimentally become resistant to acyclovir by getting rid of its own TK and using the cell's TK. This may or may not turn out to be important in the future. We do not know yet.
5. It is inactivated or neutralized by thymidine. Remember, thymidine is a naturally occurring substance everywhere in the body. In other words, acyclovir's natural antidote is everywhere. This may make a significant difference when it comes to using the drug as an ointment. Thymidine may be neutralizing the ointment before it can treat the infection. Thymidine seems to matter little if the drug is given by the intravenous or oral route.
6. By itself this drug has great difficulty getting through the skin. Probably only very small amounts of acyclovir get to the infected cell when it is painted on as an ointment.

In the June 3, 1982 issue of the *New England Journal of Medicine*, Dr. Lawrence Corey and his collaborators reported that acyclovir applied as an ointment can decrease the time to total healing of genital sores during primary herpes on average from 12.3 to 10.6 days. When genital herpes occurs for the first time in a person with previous herpes immunity (non-primary, initial herpes), it is much less effective. In the same report, it was suggested that this drug applied in recurrent herpes could improve the healing time in men* (8.4 days vs. 6.9 days), but not at all in women (7.6 vs. 7.4 days).

Another report appeared in the *New England Journal of Medicine* of April 21, 1983. In this issue Dr. Yvonne Bryson of the U.C.L.A. School of Medicine reported that given by the oral route, acyclovir induced primary herpes sores in women to heal in 10 days instead of 16.2 days. In men, primary sores healed in 12 days in drug recipients versus 21 days in placebo recipients. Dr. Bryson and her co-workers also showed that oral acyclovir decreases some complications of primary herpes, such as urinary tract complaints and lymph node swellings. Another recent report on this drug came from Dr. Richard Reichman at the University of Vermont who headed a collaborative study involving centers around the United States and Canada. These workers showed that recurrent herpes healed in 5.9 days instead of 6.9 days, and 5.7 days instead of 7.2 days when applied very early. Following intravenous treatment, a study performed in England by Dr. A. Mindel and co-workers and published in *The Lancet*, showed that primary sores healed in 7.0 days instead of 14.0 days.

Acyclovir has not been shown to have any effect on latent herpes. It cannot change the course of future recurrences. Rather it affects the course of one outbreak. Investigators are now looking at the possibility of giving this drug as a suppressive agent. In other words a person with recurrent herpes might take this drug every day. Theoretically, the drug should not affect the latent infection, but each time the virus reactivates it *might* be killed before (or as soon as) it gets to the skin. In that way there might be fewer or less severe recur-

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* This difference does not achieve mathematical (statistical) significance. In other words, this effect could have been seen because of the drug or by "luck of the draw".

rences if it turns out to be effective. Dr. Straus at the National Institute of Health in Bethesda, Maryland has recently reported that oral acyclovir may be a useful form of "prevention" in some people. In this study, people with herpes received acyclovir or placebo orally at a dose of three capsules per day for four months after receiving a five day "loading dose" of five capsules per day. Four of sixteen people on acyclovir had recurrences during the study, while fifteen of sixteen people receiving a placebo had recurrences. This was effective, in both sexes, at reducing the frequency of outbreaks while taking the drug. Because of the nature of the study design it will not be known whether interrupting the cycle of recurrences in such a manner will have a positive effect on future recurrences after the drug is stopped. Will this become a therapy for only a few months? Will it be necessary to take this for a year? For two years? For life? The details are unknown, but this concept of preventative therapy may radically change the therapeutic future for people with herpes. It may be possible to effectively, and possibly safely, suppress recurrences while taking an anti-herpes drug. This is not yet the radical cure; it is not yet 100% effective. There is a lot to be discovered in the future in terms of prevention. In my opinion it would make little sense to take expensive drugs three to five times per day for months to suppress a few outbreaks each year. For the person with very frequent recurrent herpes, however, this may be the first important and realistic therapeutic solution.

Other Nucleoside Analogues

Bromovinyldeoxyuridine (BVDU) is undergoing active testing. It is extremely potent (ten times as much as acyclovir) in the test tube against herpes simplex Type 1, but it not so good when it comes to Type 2. This will make it less useful for genital herpes, but possibly important in other herpes infections.

Several derivatives of acyclovir are being examined as to their effects in animals. This might ultimately improve on acyclovir's absorption characteristics or potency. DHPG (1,3-dihydroxy-2-propoxymethyl guanine) is one such example. It goes by other names also, including BIOLF-62,2′-NDG. The people responsible for synthesizing this agent report that it

is sixty-eight times as effective as acyclovir given orally to mice. This means nothing now to those of us without tails but a few years from now that may turn out to be a very important number.

Another interesting group of chemicals which were developed at the Sloan-Kettering Cancer Institute are showing some promise. FIAC (fluoro-iodoaracytosine) is the name for the extremely potent parent drug. When administered it "explodes" into several other drugs, but unlike other antiviral drugs, the results of the explosion, namely two new drugs called FIAU (Fluoro-iodo-ara-uracil) and FMAU (fluoro-methyl-ara-uracil), are also potent anti-herpes drugs. These drugs may turn out to be useful in herpes simplex, herpes zoster and cytomegalovirus infections. It is too early to know how these tests will turn out but preliminary reports are encouraging.

Ethyldeoxyuridine (EDU, Aedurid®) is also undergoing active testing. This drug is now sold in Germany and has been reported there to be effective. However these studies were small. Now this drug is being actively studied in North America as a topical agent (cream) in large, double-blind, controlled trials. It is the only nucleoside analogue which inhibits herpes Type 2 in preference to Type 1. Acyclovir, for example, does the opposite. It is not known whether this matters clinically. It may have potential as a future oral drug as well. No data are in, as yet, to give a realistic clinical report.

Ribavirin (Virasole®) was synthesized in 1970. Recently, it was shown to have some benefit in certain viral infections of infants called respiratory syncytial virus. One report of possible benefit in genital herpes appeared in *Chemotherapy* in 1981. Dr. S.M. Bierman and his associates from Los Angeles, California, performed a double-blind placebo-controlled study using Ribavirin orally. Unfortunately, a positive virus culture was not a requirement for all entrants to the study. The authors suggested that drug recipients had reduced disease severity as compared to the placebo recipients. Studies are now being planned to examine the effects of this drug in carefully controlled, randomized clinical trials.

Phosphonoformic acid (foscarnet; Foscavir®)

Foscarnet is a small chemical which works by very different mechanisms than the nucleoside analogues. It does not depend on TK at all. Rather, because of its small size, it gets into all kinds of cells whether infected or not. It also penetrates skin without much difficulty. As well Foscarnet is an enzyme inhibitor. The enzyme it has chosen to inhibit is called DNA polymerase. We discussed DNA before—the hereditary material made up of code sequences of four chemicals. It is DNA polymerase that tells these four chemicals to start building the DNA chain. In a way it is the "start and keep going" button. Herpes has its own DNA polymerase and cells have their own. Foscarnet is a much more potent inhibitor of viral DNA polymerase than of cellular DNA polymerase. This drug has recently been tested in Sweden where it was shown to decrease the time to healing for recurrent herpes from 5.0 days to 4.3 days. When people in this study were "crossed over" the effects were also interesting. People with herpes were followed for two recurrences and given either drug or placebo at each recurrence. Those who got placebo for the first recurrence and drug for the second healed in 3.3 days on the drug instead of 4.6 days on placebo. Those who got the drug first healed in 3.5 days on real therapy, versus 4.1 days on placebo. This study is now being repeated. It may be a few years before this drug is fully tested, but it holds significant promise as a topical agent—a cream or ointment. Oral and intravenous use of foscarnet has not yet been widely tested. Therefore, it is impossible to comment on its potential usefulness given by these methods.

Miscellaneous compounds

Arildone is a relatively potent inhibitor of herpes simplex virus in the test tube. For reasons that are not clear, the drug interacts with proteins in the nucleocapsid of the virus (see Chapter 2). It seems to be relatively effective as a topical agent (8% cream) in treating genital herpes in guinea pigs. Clinical trials are ongoing.

Another interesting agent is modified snake venom. In 1962 Drs. W.B. Clark and J.A. Baldone from New Orleans, in collaboration with Dr. C.I. Thomas from Cleveland, reported

in *The Southern Medical Journal* on the use of modified snake venom in the treatment of recurrent herpes of the eye. Unfortunately this trial was uncontrolled. In addition Dr. J.E. Yourist and co-workers from the University of Miami have reported that this cobra detoxified ("unpoisoned") snake venom is useful in diminishing disease at certain doses of virus in a suckling mice animal model.

Only a few humans with herpes have been treated with this agent to date so it is not possible to make conclusions concerning its usefulness for humans. It is my understanding that double-blind, placebo-controlled, randomized trials are just beginning. In a few years we will be able to assess this agent and comment further.

Immunity Boosters

Interferon and related drugs

You may remember interferon as the miracle cure for cancer that still has a long way to go. Interferon originally got its name back in 1957 because it "interfered" with viruses. Now it has become reasonably cheap to make this drug in bacteria using recombinant DNA tricks. Active testing against herpes is underway in clinical trials. This might take the form of active treatment for new sores, or daily or weekly prevention shots. The data are not in for genital herpes, but we already know that one type of interferon can suppress oral herpes outbreaks if taken just before the outbreak. The trick is to know when the outbreak is coming. Is this going to work as a treatment? Nobody knows. Unfortunately, interferon also has had a number of uncomfortable side-effects, which might be intolerable to a person with herpes. These have included fevers, muscle aches, weight loss and hair falling out. In addition, it must be administered by injection. It is possible that the side-effects can be controlled, the good effects maximized, and the injection problem solved. We will know those answers soon.

Inosiplex

Inosiplex (Isoprinosine®) has a direct antiherpes effect in the

test tube. Furthermore, it has been shown to increase lymphocyte transformation against herpes simplex virus. In other words, one can measure a laboratory effect on people receiving this drug which shows that human lymphocytes (see Chapter 2) get more excited and more active around herpes than they do in people not receiving inosiplex. This is a very interesting phenomenon.

In 1972 Drs. Steinberg and Ruiz reported the results of a double-blind controlled study in a Mexican medical journal. This showed that patients receiving inosiplex healed their herpes in 5.2 days as opposed to 9.0 days for placebo recipients. Both oral and genital herpes were studied, but not separately. Primary and recurrent herpes were not kept separate in their analysis. Furthermore, virus cultures were not routinely performed to document herpes infection.

The next year a report by Drs. Chang, Fuimara and Weinstein at the Interscience Conference on Antimicrobial Agents and Chemotherapy, suggested that this drug could be useful in primary herpes. Their double-blind, placebo-controlled trial did not suggest any effect on recurrent herpes, nor any effect on the rate of recurrences. In 1975, Drs. Wickett and Bradshaw presented results of a study of 53 patients. They concluded from this double-blind, placebo controlled trial that this drug shortens the course of a herpes outbreak. Once again, the most critical error of study design possible was present in this study, in that persons with both primary and recurrent herpes were analyzed together. As we already know, primary herpes may last for up to three weeks as opposed to a period of seven to ten days for recurrent herpes. In fact, in assessing their results one notes that twice as many primary patients are included in their placebo group. In other words, the people one expects to be having longer outbreaks are having their outbreaks averaged in with the placebo results. Then one compares placebo and drug and the drug looks great. Is this because the drug is effective or because one has compared apples to oranges?

Another study from Paris, France has suggested in a double-blind placebo controlled trial that inosiplex may be effective in recurrent herpes. In this study where virus cultures were not obtained, lesions dried up by day three in over

50% of the drug recipients and only 25% of placebo recipients. In a letter to the editor of *The Lancet*, Dr. M. Galli and his co-workers from Milan, Italy have reported the results of giving inosiplex to 31 people with genital herpes. These people were treated for one week at a time on four separate occasions. Herpes recurrences declined from the year before treatment to the year after, but this effect could not be attributed to the influence of the drug.

This agent has so far been associated with one side-effect, the elevation of uric acid levels in the blood. Uric acid is a metabolite of the drug (a breakdown product) and this elevation is not surprising, nor especially worrisome.

Inosiplex is an interesting drug worthy of further study. All too often, it has been the unfortunate victim of less than optimal study design. Some of these trials have left more questions than answers. At this time a long-term trial of suppression of recurrences is ongoing in California. This is double-blind, placebo-controlled and randomized. It will be interesting to see the results.

Other immunity boosters

There is one more important class of future drugs to be discussed called pyrimidinones. These drugs do nothing harmful to herpes in the test tube. When painted on the skin of a guinea pig they somehow resist herpes infection. There is more to find out since nobody really knows why it works. On the other hand, the effects in animals have been interesting. Clinical trials with these agents may soon be in the offing.

Vaccines

Herpes vaccines have actually been around for a while. In some European countries, vaccines are generally available (Lupidon-G®). There has always been some concern about their safety because herpes in a killed form, such as is present in the vaccine, still has its DNA. This might be a concern in terms of inducing cancer. Despite these reservations, many people are attracted to these "whole virus vaccines" because they have a reported capability to induce a 70-80% "improvement rate" in the frequency and severity of recurrences. These studies were not controlled and are not generally accepted.

There are no good data on risks with this vaccine. Because there is no *proven* positive effect and no proven safety record, the vaccine has not yet been approved in the United States or Canada.

Recently, however, some progress has been made in finding which part of the virus is instrumental in giving immunity. These parts that induce immunity, also known as "subunits", can be purified and given as a vaccine, thus theoretically circumventing the problem with possible safety risks. Subunit vaccines are now being produced for clinical trials. It may also become possible to effectively change the living virus enough to create a live vaccine. This might be more effective at inducing good immunity because it is living. Using special DNA techniques the virus genes could be changed so that it loses its ability to cause cancer or its ability to form latent infection, etc. Then this altered strain could be safely administered to people. The work is still theoretical.

Vaccines effectively protect mice *before* infection. They also effectively result in antibody production in humans. But why should any vaccine be useful to *treat* recurrent herpes? People with herpes already have antibody and other types of immunity to herpes. As far as we can tell, people with herpes have normal amounts of antibody and normal lymphocyte responses to herpes. So what will vaccine-induced increases in immunity accomplish? Will this alter the course of recurrences? There is no good clinical reason to think that vaccines will do anything for the person who already has established infection. On the other hand, vaccines may turn out to be very useful for the general population. In other words, if we could give everyone an effective vaccine in early childhood, then there may be enough immune protection to make it more difficult for an unaffected person to get herpes. If this occurs, the risks would decrease. This is more likely to be helpful for our children and their children than for us.

Regardless, trying vaccines, once made safe or more effective, will be worth it in recurrent herpes. These clinical trials are underway. Their results will require very careful interpretation. There are no good ways at this time to predict the outcome and we cannot say that we have discovered a "cure" for herpes in the form of a vaccine, no matter what the popular press now says.

What are the alternative treatments?

Alternatives to standard medical therapy have been present ever since there were accepted standards. These alternatives are most popular when standard therapies are inadequate. Until recently, with the advent of new and effective specific anti-herpes drug therapy, alternatives were all that was available for someone who wanted to do something specifically therapeutic for herpes.

Some of the alternative chemicals listed here are not drugs in the legal sense. A drug in the legal sense has to undergo rigorous testing before it is allowed to be licensed and sold for physicians to prescribe. In order to gain the license,the drug must be shown to be effective in the treatment of the disease for which it is being recommended. Next, it must be safe enough that the treatment effect is considered better than its side-effects. Alternative drugs and chemicals do not necessarily fit these criteria, however, making some of them possible to obtain without fulfilling these criteria. Some reasons that alternative chemicals may remain available are as follows:

1. The chemical was given drug status before the laws giving government control came into effect, i.e., these drugs comply with the "grandfather clause".
2. The chemical is considered safe without testing because it is a food by-product. An example is L-lysine.
3. The chemical is considered safe because it is an "accepted" food additive. BHT is an example here.
4. The chemical is licenced by another government, for example in a European country and imported for personal use.

It is important to realize that just because you are able to buy a chemical which someone says you can take as medicine does not necessarily mean that anyone knows it is safe or effective. It is only tested for safety and efficacy if it is called a drug and taken through drug clearance channels*. BHT and L-lysine, among others, have never been shown to be safe or effective in humans in the doses being recommended by

some people for herpes. Nevertheless, just like drugs in the pharmacy, these chemicals go into the body, circulate in the blood, deposit in body tissue, and so on. The only difference is that we do not always know if these chemicals are safe at the doses used, and their usefulness in terms of positive effects is unknown.

When it comes to specific antiherpes treatments the list of potential alternative approaches is very long. We often seek easy answers which mainly address our hopes of cure, rather than those which require painfully long adherence to difficult rules. This is fraught with potential dangers. For example, if alternatives are sought in lieu of standard treatments for a life-threatening, but potentially curable disease, needless deaths may result.

Happily this is not the case with herpes because it is not normally life-threatening. Yet, simplistic answers to difficult problems can harm the person victimized. It can rob the person of money, time and even hope. Be selective and careful when choosing alternative therapies or standard therapies. The alternatives arousing the greatest interest are listed below. This is not intended to be a complete list.

Butylated Hydroxy Toluene (BHT)

BHT is a food additive. The chemical is synthesized from two organic compounds called p-cresol and isobutylene. It cannot be dissolved in water, but is easily dissolved in organic solvents such as alcohol, gasoline, etc. BHT is literally everywhere. In 1976, Americans consumed, by mouth, nearly 9 million pounds of the stuff. BHT hides in margarine, instant potatoes and chewing gum, to mention only a few. It is fed to chickens and other animals and lives with us daily. We consume 1 to 2 mg. each per day. Each American has on the average 1.3 ± 0.82 parts per million in body fat.

BHT kills herpes simplex virus in the laboratory. When dissolved in mineral oil at a concentration of 5% and 15% and

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* Even then, some of the older drugs and drug combinations commonly used and prescribed are not considered effective. There has been a book written on this subject which I would encourage anyone to read if interested, called, "Pills That Don't Work" by S.M. Wolfe, M.D., and C.M. Coley, Farrar Strauss Giroux, New York.

applied to the skin of hairless mice infected with herpes simplex virus Type 1, or guinea pigs infected with herpes simplex virus Type 2, BHT was better than mineral oil alone at reducing the number of herpes lesions. BHT is probably a virus envelope interrupter. In other words, it can kill viruses which depend on having an envelope because it may dissolve the envelope. Certainly other mechanisms are also possible. Two important criteria in drug testing have been satisfied in the testing of BHT as an antiherpes treatment:

1. It kills herpes simplex virus in the test tube.
2. It is effective at speeding the healing of sores in an animal model (mouse) when applied to the skin in mineral oil.

As a topically applied mixture in mineral oil, BHT therapy also resulted in skin reddening and some skin sloughing. This agent has never been reported to have been given by mouth to animals for treatment of herpes. Despite this it is being discussed in a recent popular book* at doses ranging from 250 mg. per day to as much as 2000 mg. per day in the treatment of herpes. There are no published data anywhere in the scientific literature on the safety of this type of agent being administered in these doses to humans. Because we take BHT every day as a diet additive, this compound is "presumed safe". However, these doses are as much as 1000 times the usual daily intake. At doses, even higher, the following things happen to animals in experiments (not a complete list):

- LAF1 mice given an otherwise improper and incomplete synthetic diet live longer if the diet is supplemented with BHT.
- BHT did not affect the life span of C57BL/6J mice who were given proper nutrition, although it did seem to partially reverse the hazardous effects of inadequate nutrition.

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* *Life Extension.* A Practical Scientific Approach, by Durk Pearson and Sandy Shaw. Warner Books, New York, 1982.

- BHT prolonged the life span of BALB/c mice who began supplementing their diet with BHT at 11 weeks of age. It was of less benefit if started earlier in life.
- At higher doses, it can cause animals to bleed into the brain or even bleed to death.
- It can damage heart cells.
- It can retard weight gain.
- It can decrease the metabolism of the adrenal glands.
- It can cause disorganization and destructive changes of lung cells and can lead to serious lung damage.
- The liver becomes enlarged, a phenomenon which disappears when the agent is stopped. A system of liver enzymes called the P-450 system is induced. (If this system stays induced for prolonged periods it will change the way other drugs and natural products are metabolized. For example, if vitamin D is metabolized more quickly by induced enzymes, over a period of time, a vitamin deficiency might develop which can lead to a bone disease called osteomalacia.)

Most of the effects of BHT, both "good" and "bad", occur at high doses, much higher than the amounts we ingest incidentally every day. However, the long-term effects of small doses normally used are poorly understood. Indeed, the wisdom of ingesting even these small amounts might well be questioned. There have been no human studies at these doses with BHT for herpes treatment or for safety. On the other hand, this chemical has passed the preliminaries in terms of developing a new antiherpes drug—it works in the test tube and on the skin of animals. It should next be tried *on the skin* of humans, or tested against herpes as an oral treatment in animals. In fact, I am told that clinical trials using BHT in mineral oil are beginning in the United States. These studies are going to be conducted at a major herpes research clinic in a double-blind, placebo-controlled trial. We will look forward to the results. At this point there is no precedent for humans to ingest BHT orally in these doses. Orally, in my opinion, it should be best avoided until more information becomes available. Topically, trials are underway.

L-Lysine

L-lysine is a naturally occurring substance called an amino acid. Amino acids are the building blocks for all proteins. Proteins in the body are used to make the structure that holds us up and the molecular array that runs our metabolic processes. Our bodies have immense control over amino acids because we depend on them so much. We are constantly making and destroying amino acids and interconnecting them one to the other in order to maintain the exquisite balance—just so.

Nearly twenty years ago, an effect of L-lysine against herpes simplex virus was noted in the test tube. It seems that changing the nutritional environment of herpes alters its capability to make its essential proteins. This amino acid balance can be critical, especially between two amino acids, lysine and arginine. These work in a somewhat opposing manner, in that the lysine in excessive amounts damages the virus, while the arginine, if deprived from the culture media, has a similar effect. People talk about the lysine/arginine ratio as the important factor. There is little doubt that a high ratio will have a negative influence on herpes simplex virus in culture. It is a giant leap to say that altering these chemicals in the diet will change your ability to combat clinical infection. There has never been a test of changing lysine/arginine ratio in the diet to see if it is effective in herpes. In fact, it is not known whether this ratio can be changed in the body. To my knowledge there has never been a published test of changing the lysine/arginine ratio in the diet to see if it is safe. There have been clinical trials with L-lysine, though they have never involved total dietary management as is being suggested by a number of the L-lysine advocates. The lysine work to date in humans can be summarized:

Dr. R.S. Griffith and his co-workers published an article in 1978 describing a multicenter trial of L-lysine for herpes infections. Doses of 300 mg to 1000 mg per day were used. A long-term "beneficial effect" was observed. However, this study had no control group. Yet, many herpes owners swear by L-lysine. Recently, popular trade magazines have attested to this fact. It has also been clearly and scientifically established that without proper controls, however, placebo effects

are quite profound. In one study, 77% of 26 patients reported their oral herpes lesions to be markedly reduced in severity and duration by treatment with water! Ether, which was the test substance in that clinical trial, was shown to be no more effective than the water placebo. Back to lysine. If water works for 77% of people who think they are using a drug, then in my opinion it would be wise to be very critical of studies which have no control group.

Two controlled trials of L-lysine have been performed in Denmark by Dr. N. Milman and his co-workers. First, L-lysine was used as treatment for oral herpes recurrent attacks. Treatment took place immediately upon sensing a coming recurrence. This was tested on 251 recurrences. There was clearly no beneficial effect when used in this fashion. Next, patients with recurrent oral herpes were given 1000 mg. daily for 12 weeks. The control group received starch powder tablets. After 12 weeks, the groups switched places. One can argue strongly about the statistical validity of such a switch. Regardless, the patients in each group had herpes recurrences. There was no effect of the drug on the number of recurrences, the rate of recurrences, the rate of healing of recurrences, or the symptoms of recurrences. Fourteen patients had no recurrences at all during lysine treatment, whereas four patients had no recurrences during starch treatment. This was considered to be of "borderline significance".

In conclusion, we do not know whether the lysine/arginine ratio matters for herpes in the human. We have never seen dietary controls as part of the experimental design. We do not know if altering the amino acid intake actually changes the nutrients available to the virus inside the cell. Knowing the safeguards in the system against tampering with such important building blocks, it seems doubtful to me. We are also in the dark concerning the safety of this regimen. Because amino acids are "natural" nutrients they can be put into tablets and sold for consumption at any dosage. However, alterations of amino acids have undetermined effects on the body. Unfortunately, because these are not called "drugs", they are not controlled as drugs. We may never know.

2-Deoxy-D-Glucose (2-DG)

Glucose is simple sugar. Cells and viruses use simple sugar for a number of different processes. 2-DG is an analogue of glucose. It is a look-alike as far as a metabolic system is concerned, so that a cell needing a glucose molecule might grab and try to use a 2-DG molecule instead if one were around to grab. When viruses grab 2-DG they seem to put the molecule into the virus envelope. This effectively antagonizes herpes simplex growth by creating a useless envelope. A lot of excitement was stirred up by a report in a June, 1979 issue of the *Journal of the American Medical Association* stating that human genital herpes infections could be effectively treated with this agent applied in a topical cream. This aroused a great deal of interest, for the investigators claimed that using this cream decreased the severity of the disease while it was being used, and furthermore, that it decreased the rate of subsequent recurrences.

This study has come under intense criticism. In the study the number of placebo patients was very small. In recurrent herpes episodes, the *average* number of days to healing of lesions was 12.0 after the patients started using the cream which occurred on average four days after the onset of symptoms. In other words, the healing time of the placebo group for a recurrence of herpes was more than two weeks. This is indeed an extraordinary period. When compared to the treatment group who had healing times of 6.8 days (plus the four days before enrollment) there was a great statistical difference. This means that drug recipients healed in 6.8 to 10.8 days, a standard and expected duration for an untreated recurrence. The reasons for the very long placebo group healing time are unknown. Subsequent studies in humans with this drug are not published. However, animals were tested for effect. 2-DG has been extensively tested against genital herpes in a guinea pig and in a mouse animal model. No positive effects were seen. The drug did not inhibit the development of sores, nor did it inhibit the quantity of virus present. 2-DG has been reported to be useful in rabbit eye infections with herpes simplex, although these effects are not impressive when compared to other antiviral agents.

For now, 2-DG is on the back burner, pending further

studies. Four years have passed since the initial publication. This compound is not available for purchase or other use in the treatment of genital herpes.

Contraceptive Foam

Nonoxynol-9 is a "surfactant". It acts very similarly to soap. In the test tube, this agent, like soap, effectively inactivates herpes simplex virus. It was reported in early observations (uncontrolled) to be effective in the therapy of genital herpes infection. When tested in a placebo controlled trial, nonoxynol-9 was not beneficial. In fact, herpes lesions in recipients of this drug healed more slowly than those in the placebo group.

The direct antiviral activity of this birth control agent, however, makes it a good candidate for methods of "possibly effective" prevention against transmitting herpes.

Lithium

Lithium satisfies the requirement of being effective against herpes in the test tube. It inactivates herpes simplex at a concentration of 30 to 60 milliequivalents. This is 20 to 60 times the levels considered appropriate for treating humans for manic depressive illness (the only clinical setting where lithium should be used).

Very few people with herpes have been reportedly helped (for herpes) by lithium. Furthermore, there are very important and potentially dangerous side-effects to lithium. Regardless of what alternative you wish to use, lithium is dangerous unless under the rigid control of experts administering this agent. It should not be used for herpes unless as part of a carefully controlled clinical trial.

Zinc

Zinc is also capable of inhibiting herpes simplex virus in the test tube. It is a common component of various skin creams. Zinc has been tried as a cream combined with ultrasound treatment, and has also been given by mouth. Neither of these settings, although reported in the literature, was set up as a trial with placebo controls, randomization, etc. Therefore, conclusions cannot be drawn.

Dimethyl Sulfoxide (DMSO)

This organic solvent rapidly penetrates skin. It is highly effective at penetrating skin. Some recipients have been able to taste it seconds after applying it to the skin surface. DMSO is also very effective at carrying with it, antiviral agents. Thus, it has been thought that mixing a good drug in DMSO, may make it penetrate better and work better. Indeed, in the case of acyclovir and BVDU, DMSO does markedly enhance drug penetration through the skin of guinea pigs. DMSO has been tried clinically in the case of idoxuridine. Early reports suggested that a combination of idoxuridine with DMSO might be an effective herpes treatment. Drs. Silvesri, Corey and Holmes, however, published an exhaustive study in the *Journal of the American Medical Association* in August, 1982. Idoxuridine in DMSO was found to have no clinical effect on primary or recurrent herpes. People receiving the treatment complained of burning and allergy. One patient developed local cancer at the site of drug application.

Adenosine Monophosphate (AMP)

In 1979, Drs. S.H. Sklar and E. Buimovici-Klein reported that adenosine-5'-monophosphate was "effective" in the treatment of patients with recurrent oral herpes. The drug was given by intramuscular injection in 9-12 alternate day injections. The authors claimed from this uncontrolled study that pain and discomfort were ameliorated quickly. Adenosine-5'-monophosphate is a natural cellular compound. Side-effects (which have not been extensively looked for) are not seen. It has been suggested that this agent might stabilize membranes in the nervous system preventing reactivation. Indeed, in a mouse model of recurring herpes simplex infection, it was suggested that this agent might be able to prevent recurrences under certain experimental conditions. Although the animal results were interesting, studies were also not placebo-controlled, making the results difficult to interpret.

Unfortunately, unverified reports of this agent's usefulness have repeatedly appeared in the newspapers, but not in the scientific literature. We await the results of double-blind, placebo-controlled, properly randomized clinical trials. Until these become available, we have another agent on the list of who knows.

Other treatments

The following agents have not yet been discussed. Space does not permit a full analysis of each. None have been reported in the scientific world as proven effective with herpes in a clinical trial using placebos and controls. Their real usefulness, then, is as yet unknown. Some have received "anecdotal" treatment in medical literature. In other words, they may have been suggested as possibly effective, but the numbers or the design of the experiment were not possible to evaluate. Some may be more carefully studied in the future. Others may not.

Such agents include: **Acidophilus**, **acupuncture**, **Aloe Vera**, **antibiotics***, application of **heat**, application of **ice**, **aspirin**, **Ginseng**, **Herbal** mixtures, hypnosis, **Laser therapy***, **Providone-Iodine** (Betadine®), **red algae** extract, **transcendental meditation**, and **Vitamin B complexes**, **B 12**, **C**, and **E**.

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* Potential or established side-effects of these agents mean that they should not be used for herpes unless the human experiment is part of a carefully designed, properly supervised clinical trial, including informed consent.

ADDITIONAL SUGGESTED READING

The following list of books and articles on the subject of herpes is recommended for those who wish to read more. This list is not intended to be a complete bibliography or reference section for this book. You will need to visit a medical library for access to all of these articles except those with an asterisk (*). They are selected for inclusions in this section because they are, more or less, readable by a nonprofessional and accurate.

To find a medical library, you may call your local medical society and ask. Often the society or local hospital will have their own. A trip to a university with a medical school is occasionally necessary. Call locally first, because often a local small library will be able to obtain a copy of an article on a specific subject by interlibrary loan.

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THE TRUTH ABOUT HERPES

Having herpes doesn't mean you will lose your job, your friends, contract cancer, or miss out on future relationships. It *does* mean adjustments and knowing yourself a lot better. This book enables you to understand herpes and provides answers to many of the questions surrounding this most misunderstood disease:
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