Psoriasis: More Than Cosmetic

It's not easy living in Leah Bird's skin. "The worst thing is when people just stare," says Bird. "I almost like it better if someone comes up to me and asks me what it is."

Then she'll tell them, "I have psoriasis. It's not contagious."

Bird, 51, of suburban Boston, has had flare-ups of this chronic skin disease since she was a teen-ager. The dry, red, scaly patches of skin that characterize psoriasis have covered as much as 85 percent of her body, she says. "It alarms people. It looks very scary to people who don't know what it is."

But psoriasis is more than cosmetic. "This disease is common, chronic, and costly, both in monetary terms and in quality of life," says Jonathan Wilkin, M.D., director of the Food and Drug Administration's Division of Dermatologic and Dental Drug Products.

More than 5 million Americans have psoriasis, and they spend between $1.6 billion and $3.2 billion each year to treat the disease, according to the National Psoriasis Foundation (NPF). Between 150,000 and 260,000 new cases are diagnosed each year, including 20,000 in children younger than 10.

"Psoriasis can be painful and can be profoundly disruptive to a person's life," says Jill Lindstrom, M.D., an FDA dermatologist. "People who don't have it don't understand how burdensome the disease can be. There is constant shedding of scales. There can be functional impairment, itching, and pain." And health complications, such as arthritis, accompany some cases.

There is no cure for psoriasis, but a broad range of treatments is available to reduce the symptoms, clear up the skin, and send the disease into remission. FDA-approved treatments range from creams rubbed into the skin, to lasers that aim ultraviolet rays at the skin, to the newest treatments--injectable drugs made from living cells.

What is Psoriasis?

Psoriasis is an inflammatory skin disease in which skin cells replicate at an extremely rapid rate. New skin cells are produced about eight times faster than normal--over several days instead of a month--but the rate at which old cells slough off is unchanged. This causes cells to build up on the skin's surface,
forming thick patches, or plaques, of red sores (lesions) covered with flaky, silvery-white dead skin cells (scales).

In psoriasis, an activated immune system triggers the skin to reproduce every three to four days, building up on the outer layers (epidermis and keratin). The epidermis thickens, blood flow increases and reddens the skin, and silver-gray scales cover it.

Rarely life-threatening, at its mildest, psoriasis can be itchy and sore. At its worst, it's painful, disfiguring, and debilitating. About two-thirds of the people with psoriasis have a mild form of the disease, says the NPF. About one-third have moderate or severe psoriasis. Psoriasis can affect people at any age, but it most often strikes those between the ages of 15 and 35.

There are five forms of psoriasis. Plaque psoriasis is the most common--affecting 4 out of 5 people who have psoriasis, says the NPF. Plaque psoriasis may start with small red bumps and progress to larger lesions.

The plaques of psoriasis occur most frequently on the elbows, knees, other parts of the legs, scalp, back, face, palms, and soles of the feet. Psoriasis can also affect the fingernails and toenails, causing pitting, discoloration, or tissue buildup around the nails. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases, about 15 percent of people with psoriasis also get psoriatic arthritis, which can be progressively disabling if untreated.

Wayward White Blood Cells

Scientists believe that certain white blood cells called T lymphocytes (T cells) play an important role in psoriasis. "And the disease has a genetic component," says Lindstrom. In about one-third of psoriasis cases, there is a family history of the disease.
T cells circulate throughout the body, orchestrating the immune system's response to foreign invaders like bacteria or viruses. In people with psoriasis, the defective T cells are overactive and migrate to the skin as if to heal a wound or ward off an infection. This process leads to the rapid growth of skin cells, triggering inflammation and the development of lesions.

Both the environment and genetics may play a role in the development of psoriasis. "In genetically predisposed children, psoriasis can be triggered by a strep or other infection," says Lindstrom. That's what happened to author John Updike. After an attack of measles at the age of 6, Updike developed psoriasis "in all its flaming scabbiness from head to toe," as he later described it in his memoir, Self-Consciousness.

**Remission and Reactivation**

While the disease never goes away, the symptoms of psoriasis subside for a while (remission) and then return (flare-up, or reactivation). Remission can last for years in some people; in others, flare-ups occur every few weeks. Certain triggers, such as stress and seasonal changes, can reactivate psoriasis. "Certain drugs may also exacerbate it," says Lindstrom, including lithium, prescribed for bipolar disorder (also called manic-depressive illness), beta-blockers used to treat high blood pressure, and antimalarial drugs.

**Diagnosis and Treatment**

No single test exists to diagnose psoriasis, but a dermatologist can usually determine it by the appearance of the skin and by looking at an individual's personal and family medical history. In some cases, a specialist will confirm the diagnosis by examining a small piece of skin (biopsy) under a microscope.

Psoriasis treatments fall into three categories: medications externally applied to the skin (topical), ultraviolet light applied to the skin (phototherapy), and medications taken by mouth or injected (systemic).

**Topical Treatments**

Topical lotions, ointments, creams, gels, and shampoos for the skin and scalp are prescribed for mild-to-moderate cases of psoriasis or in combination with other treatments for more severe cases. FDA-approved prescription topicals to treat psoriasis include corticosteroids, retinoids, calcipotriene, and coal tar products. These drugs slow down skin cell production and reduce inflammation.

Corticosteroids are synthetic drugs that resemble naturally occurring hormones. Side effects may include thinning of the skin and stretch marks at the area where the topical is applied. Corticosteroids may also suppress the adrenal glands' production of natural steroids, which could leave the body susceptible to disease.

Retinoids are derivatives of vitamin A and calcipotriene is a synthetic form of vitamin D. Retinoids and calcipotriene are not the same as over-the-counter vitamin A and D supplements, which have no value for treating psoriasis, says Wilkin. "These topical creams on the skin deliver the vitamin-like chemicals
right to where you want them," he says. Skin irritation where the topical is applied may be a side effect. Retinoids are also available by prescription as oral systemic drugs.

Coal tar products can help with scaling, itching, and inflammation but are not used as commonly as some other topicals, says Lindstrom. They are messy, can stain, and have a strong odor.

Carol Bentson of Washington, D.C., has had plaque psoriasis for more than 30 years, causing "major itching" all over and pain along the scalp line. She has treated it with topical corticosteroids, ultraviolet light, and cortisone injected into her scalp, elbows, toes, and legs. At times, "ointment wouldn't penetrate the areas of heavy plaque buildup, no matter how much I put on," she says.

Bentson has accumulated "sacks of lotions" to treat psoriasis. She would find a topical treatment that worked for a while but then quit working, forcing her to switch to another one.

"With a potent topical steroid, there is a phenomenon called tachyphylaxis," says Craig Leonardi, M.D., associate clinical professor of dermatology at the Saint Louis University Medical School. "Prolonged use can cause down-regulation [decrease] of steroid receptors in cells. The net effect is that the skin becomes less responsive to steroids over time."

Wilkin adds that this unresponsiveness may be a temporary effect. "A patient may need to be off the steroid for a few days or a week and when put back on it, the responsiveness could come back."

**Light Therapy**

Exposing the skin to ultraviolet (UV) light--either from the sun or an artificial source--sets off a biological process that kills T cells, which slows the buildup of skin cells and reduces inflammation.

Light boxes that emit UV light to treat moderate-to-severe psoriasis and other skin diseases are medical devices that require licensing by the FDA. A person steps into the light box, which is about the size of a telephone booth, while lamps direct the light onto the body.

"Treatment with these devices is complex," says Richard Felten, an FDA chemist and senior medical device reviewer. The physician must determine an individual's sensitivity to UV and adjust the light emissions for the most effective treatment with the least risk of side effects, he says. Side effects may include burning, darkened skin, premature aging, and skin cancer. Three to five treatments per week for several weeks or months may be needed to get the psoriasis under control, followed by weekly maintenance treatments.

Light therapy, or phototherapy, is usually done in the physician's office or a medical facility that has the devices, says Felten. "The FDA has cleared some devices for home use under certain conditions and with a doctor's prescription," he says. Home devices include handheld devices for scalp psoriasis and stand-alone light boxes for other areas of the body.
Light therapy usually involves a short wavelength of ultraviolet light, called UVB. For people with resistant moderate-to-severe psoriasis, a combination of an oral or topical drug called psoralen and a longer wavelength ultraviolet A (UVA) light is used. This treatment is called "psoralen plus UVA" (PUVA).

"Psoralen makes the patient more sensitive to the UVA," says Lindstrom, "so once they've taken a dose of psoralen, a smaller dose of UVA is needed to treat them." Patients must be very careful to protect both skin and eyes for 24 hours after psoralen use to prevent damage, she says.

The FDA has also approved a special type of laser, an excimer laser, as a phototherapy device to treat mild-to-moderate psoriasis. "These lasers can deliver a much more controlled beam of light to small areas of the affected skin," says Felten.

**Systemic Treatments**

The FDA has approved oral and injected drugs that circulate throughout the body to treat psoriasis that is moderate, severe, or disabling. These systemic drugs are very powerful, and while some may be used continuously, others can only be used for a limited time because of their severe side effects. Once a drug is discontinued, the psoriasis may reactivate. The risk of birth defects prevents many systemics from being taken by pregnant women or women planning to become pregnant.

Systemic drugs that may be prescribed for psoriasis include acitretin, methotrexate, cyclosporine, and biologics, which are drugs made from proteins of living cells. Methotrexate, cyclosporine, and the biologic drugs are immunosuppressants, meaning they lower the body's normal immune response. "These drugs suppress the immune cells that cause psoriasis, but they don't distinguish these cells from the immune cells that protect our body from infections," says Elektra Papadopoulos, M.D., an FDA dermatologist.

Acitretin, a retinoid that is given orally for severe psoriasis, helps normalize the growth of skin cells. One of the side effects is raised fat (lipid) levels in the blood, and people taking this drug must get regular blood tests to monitor their cholesterol and triglyceride levels.

Methotrexate and cyclosporine slow the growth of skin cells. Methotrexate, taken orally or by injection, is also a chemotherapy drug for cancer patients. Cyclosporine, taken orally, was first approved to prevent organ rejection in transplant recipients. People using either of these drugs must be closely monitored and should use them only for short periods of time because of serious, potentially fatal, side effects.

Biologics are the newest systemic psoriasis treatments. Since 2003, the FDA has licensed three biologics to treat moderate-to-severe plaque psoriasis: Amevive (alefacept), manufactured by Biogen Inc.; Raptiva (efalizumab), made by Genentech Inc.; and Enbrel (etanercept), marketed by Amgen Inc. and Wyeth Pharmaceuticals. Enbrel was first licensed in 2002 to treat the arthritis associated with psoriasis, and in 2004 to treat psoriasis itself.

"All are immunosuppressive and have different proposed mechanisms," says Papadopoulos. Amevive simultaneously reduces the number of immune cells, including T cells, and inhibits T-cell activation.
Raptiva inhibits the activation of T cells and the migration of those cells across blood vessels and into tissues, including the skin.

Enbrel inhibits the action of an inflammatory chemical messenger in the immune system called tumor necrosis factor-alpha (TNF-alpha), which is believed to play a role in both the skin and the joint symptoms of psoriasis.

All three biologics are injected. The FDA has licensed Amevive to be given in a physician's office, either injected into the muscle or into a vein (intravenously). It's a once-a-week treatment for 12 weeks; further treatments may be given after a waiting period.

The FDA has licensed Raptiva and Enbrel for home treatment. People can inject themselves with Raptiva under the skin once a week or with Enbrel once or twice a week. Both drugs are recommended for continuous use to maintain results.

Since biologic drugs are immunosuppressants, they may carry an increased risk of infection and cancer. Rare but serious effects have also included blood abnormalities and autoimmune diseases such as lupus. Other side effects are flu-like symptoms and pain and inflammation at the injection site.

Some dermatologists prescribe biologics alone for psoriasis or in combination with topical treatments. Leonardi says when he prescribes biologics, "I don't have to resort to adding other systemic therapies such as methotrexate, cyclosporine, acitretin, or phototherapy."

"Biologics are an alternative treatment to some of the traditional therapies," says Papadopoulos.

"Now we need to get the expense down," says Leonardi, who has patients who pay $30,000 per year on drugs to treat psoriasis.

Bird feels fortunate that her insurance company covers most of the expense of Enbrel, which is prescribed for both her psoriasis and psoriatic arthritis. Because of the arthritis pain, she has used a cane to help her walk and has had surgery on her wrist to correct some of the arthritis damage. Although Enbrel has been less effective over time for the psoriasis, she says, it's reduced her arthritic pain by about 95 percent. "I can jog down to the corner to chase after the dog," she says. "And last summer, I went hiking with my children in Colorado."

**Reducing Treatment Risks**

Biologics, other systemic drugs, and phototherapy are powerful treatments with increased risks, says Lindstrom.

Biologics may raise the risk for developing cancer and serious bacterial or fungal infections that spread throughout the body (sepsis).

Cyclosporine can damage the kidneys, methotrexate puts the liver and lungs at risk, and phototherapy can cause skin cancer. To reduce these risks, doctors often put patients on "rotational therapy."
thought is by moving from one therapy to another therapy over time, the risk to any individual organ is reduced," says Lindstrom.

"We also try to choose a drug with an appropriate benefit-risk ratio," she says. For mild psoriasis, a topical steroid may be appropriate. For more severe disease, where it becomes impractical to apply topicals over a large surface area several times a day, a patient may need a systemic treatment.

Most of the highly effective treatments for psoriasis affect the immune system in some way. For steroid drugs, which have been around for more than 50 years, the risks are well known. But less is known about the long-term side effects of newer drugs, such as the biologics. The safety and side effects of biologics and other immune-suppressing drugs to treat psoriasis continue to be monitored by drug manufacturers and the FDA.

**Emotional Impact**

For many people, dealing with the emotional impact of psoriasis can be as challenging as treating the disease.

Bird says that mothers have pulled their children away from her on the subway, and some people, horrified by her skin lesions, have asked her if she has AIDS. As her disease has evolved over 30 years, so has Bird's way of dealing with these reactions. In her teens, she'd tell people she had leprosy just for the shock value, she says. Today, Bird is open about the disease but still relies on her defiant attitude to "steel myself for the experience" of going to the beach. "I love to swim," she says. But Bird knows that without covering herself up in a public place, she "runs the risk of people just rubbernecking."

"When I'm feeling forgiving, I try to ignore them," she says, "but when I'm angry, I think 'didn't your mother teach you not to stare?'"

Bird advises others with psoriasis to find out what works best for them to cope with the emotional effects of the disease. Going to therapy has helped her, she says. So has leading a support group for psoriasis sufferers. "It's important for people to work on their emotional well-being," says Bird, "however they choose--whether it's meditation, yoga, or putting on long pants and going out dancing."

**The Future of Psoriasis Treatment**

Researchers continue to look for reasons why immune cells overreact and what genes may be responsible for psoriasis, hoping to find better treatments, and eventually a cure. Psoriasis research is aided by the visibility of the symptoms on the skin.

"You can see the disease," says Leonardi. "You don't have to do invasive testing to see the effects of therapy." Psoriasis research has a "tremendous spillover into other fields besides dermatology," he adds. "There is a huge need for drugs to suppress the immune system without the side effects."

Multiple sclerosis, Crohn's disease, rheumatoid arthritis, and type 1 diabetes are just a few of the diseases that may also benefit from psoriasis research.
Sea, Salt, and Sun

Some psoriasis sufferers have tried salt water to relieve their itchy or painful skin. Some have even made pilgrimages to the world's saltiest lake, the Dead Sea.

"The Dead Sea is excellent for psoriatic treatment," says Lawrence C. Parish, M.D., clinical professor of dermatology and cutaneous biology at Jefferson Medical College of Thomas Jefferson University in Philadelphia. "But no one knows if the water itself has merit or whether the sun is the important part." As the lowest point on the planet, the Dead Sea region has unique weather and receives a distinctive spectrum of ultraviolet light from the sun.

Soaking in bath water containing Dead Sea salts or Epsom salts may have limited value. "It can help remove the scales of psoriasis and make people feel better," says Parish, "but no one has shown these salts to have a therapeutic effect."

Whether at the Dead Sea or anywhere else, sunlight can have a positive effect on psoriasis. "But be reasonable about it," Parish says. "A little bit of sun is fine." He advises wearing a wide-brimmed hat and applying sunscreen several times a day. "Anyone who wears makeup knows if you put it on at 8 o'clock in the morning, it doesn't last until 8 at night," he says, and neither does sunscreen.