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HEALTH

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Why Did She Have Trouble Getting Pregnant?

It Turned Out to Be a Baffling Hormonal Imbalance That Doctors Are Only Beginning To Understand.

PLUS: MORE PATIENT INFORMATION RECOMMENDED ON MEDICAL IMPLANTS ■ DEBUNKING MYTHS ABOUT FOOD ■ GIRL FACED PARALYSIS FROM TICK BITE

Infertility. Excess Hair. Unexplained Weight Gain.

Doctors are linking these symptoms to a hormonal imbalance that has severe lifelong consequences. New treatments may provide some relief.

By Randi Hutter Epstein

AS SHE LOOKS BACK, CHRISTINE GRAY REALIZES that the signs of her illness had been obvious since puberty. She always had irregular periods, embarrassing hair growth on her arms and legs, and she tended to gain weight more easily than most of her girlfriends.

At the time, it never dawned on Gray, pictured at left, that these seemingly unrelated teenage worries were hallmarks of a potentially serious ailment, one that strikes about 5 percent of women. It's called PCOS, or polycystic ovarian syndrome, a poorly understood hormonal imbalance. Not only is the syndrome now seen as a major cause of infertility, but emerging evidence suggests that women with PCOS are at increased risk for such chronic illnesses as heart disease, high blood pressure and diabetes.

"I knew something was truly wrong when I was about 27 and I started to gain weight out of control," says Gray, 34, a Mount Prospect, Ill., product manager.

Gray gained about 70 pounds, weight that would not come off no matter how little she ate, it seemed. She was eating one nonfat granola bar for breakfast and another one for lunch. Dinner was a small serving of pasta without a drop of butter or cream. Little did she know—nor did anyone else seven years ago—her seemingly healthful low-fat diet wasn't good for her.

Then she noticed even more hair growth, particularly on her upper lip. "And my periods were so irregular, I never had a clue when they were See PCOS, Page 14

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coming. I got married at 26 and started trying to get pregnant without any success. But the doctors told me everything was fine."

Things were far from fine. Finally, after seven years and $30,000 worth of fertility treatments, Gray searched the Internet for information and support.

"I began participating in an infertility support group online," she says. "One day a woman posted something about 'polycystic ovarian syndrome' and described her symptoms. . . . I immediately identified with her."

Gray says her doctor later said he knew she had PCOS but hadn't mentioned it because "it's no big deal."

Sometimes ovarian cysts are no big deal—upwards of a quarter of premenopausal women have them. But sometimes they are a big problem. A necklace of cysts—doctors say they look like a strand of pearls hugging the ovaries—can be a clue that a woman has PCOS.

The classic signs include weight gain, menstrual irregularities, excess body hair (or thinning hair on the top of the head) and adult acne. Some women are also prone to "skin tags," teardrop-shaped pieces of skin, about the size of raisins, that hang in the armpits or other parts of the body.

For years doctors thought women with PCOS were unlucky, but not unhealthy. Now PCOS is regarded as a significant health issue for many women, affecting their lives throughout the childbearing years and well after menopause.

Scandinavian studies suggest that women with PCOS are five times as likely to get diabetes as other women. Even thin women with PCOS sometimes get diabetes, according to a 254-woman study by Richard Legro, associate professor of obstetrics and gynecology at Pennsylvania State University College of Medicine in Hershey, Pa.

PCOS is "clearly the largest cause of ovulatory dysfunction and may be the single largest cause of female infertility," Legro said. Research into PCOS is also pointing toward a fresh approach to treatment—with drugs and possibly a high-protein diet—that not only helps diminish the embarrassing symptoms but may also prevent the chronic health problems.

Many Symptoms, One Source

PCOS is a devious disorder. Few women who have it realize they are at risk. It's easy to dismiss facial hair and weight gain as cosmetic problems, not reasons to get a medical checkup. Plus, many doctors don't think of PCOS when they treat women with irregular periods who also have acne or hirsutism (excess body hair).

While medical tests can produce a definitive diagnosis for many diseases, detecting a syndrome is a different matter. It takes an astute clinician to pull all the clues together, and in the case of PCOS, the clues often seem like a hodgepodge of annoyances.

"PCOS is probably one of the most common, yet least understood, endocrine disorders affecting women in the developed world," says Legro. "Although specialists are very aware of the syndrome and its health consequences, there are many doctors who still do not realize that all the symptoms are related and emanating from a single syndrome."

Armand Newman, a dermatologist in Beverly Hills, Calif., who specializes in PCOS, said women who don't suspect PCOS often see a dermatologist, primarily to treat hirsutism or acne. Few dermatologists ask women with these symptoms about their menstrual cycles or fertility, he said.

Even the name of the illness is misleading. It harks back to the 1930s when doctors thought PCOS patients had a lot of untreatable cosmetic ailments stemming from cysts on the ovaries. Now doctors say cysts from PCOS are just one manifestation of hormones gone awry. Some doctors suspect there are even a few women who suffer from the syndrome but do not have any cysts.

As doctors unravel more clues about PCOS, they are detecting it in more women. They say women can have the syndrome and the long-term consequences without all the symptoms. Not all PCOS women, for example, are obese. Not all have facial hair. Yet they may all have the same underlying hormonal imbalance and many may face

Ending Seven Years of Frustration

During the summer of 1992 I noticed that I was not having a regular menstrual cycle. A doctor at Howard University Hospital informed me that I had a syndrome known as PCOS. Because I was about to graduate from Howard and had no real health insurance, I decided to delay seeking proper treatment until I got a job with health care coverage.

A few months later, I started to grow little hairs under my chin, just like my mom. I figured this was hereditary and just a cosmetic nuisance.

In the winter of 1992, I moved to Delaware and started my career. At 5 foot 9 and 140 pounds, I was considered shapely but not fat. Three years later I was 190 pounds and miserable. The hair on my face was now a disgrace, requiring a daily ritual of shaving. My body seemed to belong to someone else. Several doctors told me that I needed to go on a diet and that I would be fine if I lost weight.

The hair on my chin forced me to wear my hair long to cover up this cosmetic nightmare, and my self-esteem hit an all-time low. My career in investment banking was progressing rapidly yet my life was in a shambles. I had irregular menstrual cycles. Once, a cycle lasted for seven weeks, followed by four months with no cycles. I knew something was wrong, but I did not know how to combat the problem.

In 1998, my weight had climbed to 220 pounds and I was more miserable than ever. My social life had come to a complete halt and my sense of self-worth was diminishing markedly. I entered a relationship that became abusive, which reinforced my shame and feeling of hopelessness. I was anything but the fashionable young woman I thought I should be.

I began to learn about polycystic ovarian syndrome (PCOS) on the Internet and was amazed at the information I found. I joined chat sessions with other women who had excessive hair on their face, legs and stomach. Some of them had gained up to 30 pounds in six months. Others were developing male-pattern baldness. Many were young, vibrant women of all ethnic backgrounds. Our frustration was our bond.

After I relocated to the Washington area last year, my primary care physician referred me to a reproductive endocrinologist—the same doctor I had seen seven years earlier when I was a student. He quickly diagnosed my PCOS and told me that women with PCOS have a greater risk of diabetes, endometrial cancer and other problems. I sobbed in his office as I described the havoc PCOS had played on my life—the shame of hair on my chin, the scars from shaving, the weight gain and the abusive relationship.

Two weeks later I began treatment with medication. In addition, I met with a cosmetic dermatologist who helped with the scarring and the skin bumps caused by the hair growth.

Since April I have lost 20 pounds. My appetite has diminished. I exercise regularly and eat more healthful foods. The hair growth has slowed. Most important, my confidence is returning because I am taking care of myself.

I still have a long way to go to reach my goal of 150 pounds, but I am active and enjoying my life again. I am still afraid to date seriously, but that will soon pass.

I am writing this very personal piece because so many women with PCOS either don't know they have it or don't take it seriously. I hope my story will encourage them to start asking questions and seeking answers—the sooner the better.

Karen Maria Alston/Special to The Washington Post

BY NANCY ANDREWS—THE WASHINGTON POST

Diagnosed with PCOS in 1992, Karen Maria Alston only recently began treatments for the hormonal imbalance.

the later health risks.

"I thought I had four or five different things going on," said Patricia Barfield Hicks, 33, of Lexington, Ky. "The weight gain, the infertility. It was such a relief to finally find out it's all tied together. Ideally it can be taken care of with the right combination of medicine."

Hicks, like many women, was told by her physician that nothing was wrong except that she was too fat. It was not until last year, after she saw a television show about PCOS, that she found help. She switched doctors and insisted on trying one of the new treatments. Since then, many of her symptoms have faded.

Some scientists speculate that women with PCOS are born with a faulty gene or set of genes that trigger abnormally high levels of male hormones. That explains the "male" features, such as body hair and thinning hair on the scalp, and perhaps even the infertility. While all women have a bit of testosterone, too much of the hormone botches the messages between the ovary and brain.

Many PCOS women also tend to be resistant to their own insulin, the hormone that clears sugar from the blood, and this may explain the tendency for weight gain and the link to diabetes. Whether these two imbalances—testosterone and insulin—stem from one flawed gene or whether one causes the other is hotly debated among doctors studying PCOS. Tantalizing evidence suggests a link, because treatments targeted at insulin cause testosterone levels to plummet.

A study published last year in the Proceedings of the National Academy of Sciences suggests that the follistatin gene may be linked to PCOS. Interestingly, follistatin has at least two functions: It is necessary for the ovaries and for the insulin-making system.

"Follistatin is particularly intriguing because it could play a role in both the reproductive and the metabolic features of the syndrome," said Andrea Dunaif, the senior author of the paper and the chief of the Division of Women's Health at Brigham and Women's Hospital in Boston. "Follistatin could explain some cases of PCOS; however, it is likely that at least several other genes are involved."

BY ERIK S. LESSER FOR THE WASHINGTON POST

Kristin Chapman, shown here playing with her daughter, Grace, became pregnant after taking an anti-diabetes drug to treat her polycystic ovarian syndrome.

Getting a Diagnosis

Traditionally women treated symptoms of PCOS individually. They used electrolysis or tweezing to remove facial hair. With fertility drugs they increased their chances of becoming pregnant. And they confronted their weight problem with diets galore. But it's now clear that none of these measures tackled the root of the problem or addressed the serious later effects of PCOS.

"When I was a teenager I was having wacky periods—every 10 days—and I had some of the hair problem," said 30-year-old Suzanne Cerquone, of Philadelphia. "My doctor said I probably had cysts on my ovaries and here's a package of birth control pills to regulate your periods. He said I had the facial hair because my testosterone was too high.

"It wasn't until last year when I got on the Internet that I found out all the new treatments and diets. Because the majority of the symptoms are cosmetic, no one considers it a serious thing, but the underlying thing is it's not just cosmetic."

The challenge lies in distinguishing healthy women who just have a few extra pounds to lose and an occasional irregular period from those whose hirsutism and menstrual irregularities signal a disorder that may require treatment.

In a study published in 1998 in the journal Fertility and Sterility, Ricardo Azziz, a professor of obstetrics and gynecology at the University of Alabama at Birmingham, looked at 132 women with too much body hair who thought they were having regular periods. By measuring their progesterone levels, he found that 40 percent of them actually ovulating irregularly. That suggests PCOS.

A Harvard study found that 80 percent of women with fewer than six periods a year had abnormally high levels of male hormones. They, too, may be PCOS women.

"These were women not going to the doctor to complain," said Dunaif. "The most frequent thing the doctor would say was, 'You are too fat, lose weight,' or 'Take a birth control pill.' The disturbing thing is that not only

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Low Carbohydrate PCOS Diets: Hype, Hoax or Cure?

It sounds too good to be true, but many women with polycystic ovarian syndrome (PCOS) say that when they eat more vegetables and meats and less bread and fruit, they start ovulating and lose weight. As a result, a growing number of nutritionists and a few physicians are advocating so-called insulin-sensitizing diets, which are similar to the "protein power" regimes being promoted in many best-selling books.

When a healthy person eats a carbohydrate, insulin levels rise to break down the resulting sugar in the blood. But women with PCOS are insulin-resistant, meaning they have defective cells that hamper this metabolism and increase the risk of diabetes. In addition, to try to compensate for the defect, their bodies produce more and more insulin, which can damage the insulin-producing system.

To make matters worse, this excess of insulin can trigger bouts of hunger that lead to overeating and weight gains.

Proteins and fats, by contrast, do not spark the same insulin surge in women with PCOS. As a result, these nutrients are metabolized normally.

Most doctors treating PCOS do not advocate high-protein diets, and they warn their patients not to eliminate carbohydrates completely. Yet these same physicians acknowledge that many patients who change their eating habits do feel better—and some have even gotten pregnant without fertility treatments.

Brenda Fruchtl, a 26-year-old from Hershey, Pa., is a believer. Last January she tried a high-protein diet because nothing else had enabled her to shed weight and start ovulating. While giving in to a hometown Hershey's Kiss now and then, Fruchtl said, "I would eat tuna and salads, even nuts and cheese, but very little fruit and breads." (Fruits have natural sugars that boost insulin.)

Within a month, Fruchtl got a menstrual cycle without drugs for the first time in years. By mid-March, she was pregnant. "We'd been trying for two years," said Fruchtl. "I was so happy because we could no longer afford the fertility drugs and this was something with no side effects and no risk of multiples."

Her physician, Richard Legro, associate professor of obstetrics and gynecology at Pennsylvania State University College of Medicine, says the diet "definitely contributed to her pregnancy. This is not an isolated incidence."

Other specialists are cautious but optimistic. Andrea Dunaif, chief of the Division of Women's Health at Brigham and Women's Hospital in Boston, does not promote the protein diet but suggests that women with PCOS should try a diet with fewer carbohydrates than one that focuses on low fat and high carbohydrates. She and several colleagues say the protein diets make sense, but there is no scientific evidence proving that they correct the underlying abnormalities of PCOS.

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the irregular periods need to be taken care of because of the increased risk of endometrial cancer, but women need to be treated because of all of the other health consequences associated with PCOS."

There is often no simple proof that a woman has polycystic ovarian syndrome (PCOS); diagnosis is based primarily on a woman's medical history and tests for insulin resistance. But the presence of several of the symptoms—infertility, hirsutism, menstrual irregularities and insulin resistance—is strong evidence.

Doctors advise any woman with menstrual irregularities—which are signs of a metabolic problem—to consult an endocrinologist or gynecologist and insist on a thorough examination, including blood tests to measure hormone levels. Those who think they may have PCOS should also be checked for diabetes.

Kristin Chapman, 32, of Atlanta, found out about PCOS when her ovaries nearly burst after a fertility treatment. "The doctors told me they blew up to the size of cantaloupes," she says. Chapman, like many other women with PCOS, had ignored her other symptoms until she wanted to have a baby.

Chapman was hospitalized and the fluid was drained. Two subsequent attempts to get pregnant were unsuccessful—the culmination of six years of failed attempts with fertility drugs. She and her husband had had enough. Then Chapman attended a seminar by Mark Perloe, director of reproductive endocrinology and infertility at the Atlanta Medical Center. He talked about metformin, a diabetes drug, which apparently corrects the insulin defect in some women with PCOS and helps to restore ovulation.

As a last-ditch effort, Chapman went through a series of tests and learned that she was "borderline" insulin-resistant. She opted to try the drug, which is marketed as Glucophage. "It was refreshing to hear this approach," says Chapman. "It wasn't treating the symptoms but treating the PCOS."

Chapman started metformin in January 1998, got pregnant the first time she ovulated in April and gave birth to a daughter this past January.

Treatment With Drugs and Diet

No one knows why metformin or another insulin-sensitizing drug, troglitazone (Rezulin), seem to promote ovulation. But since word of these treatments hit cyberspace, women with PCOS-like symptoms are demanding prescriptions. Experts warn that many women on the drugs do not get pregnant, but they have been hyped nonetheless as a diabetes-fertility cure that also helps you lose weight. What could be better?

The drugs "offer exciting possibilities," said Brigham and Women's Dunaif. "However, I don't think we yet have enough information to recommend them for all women with the syndrome. That caution is especially appropriate for women with PCOS who want to get pregnant, because there is very little data on the safety of these drugs on the developing fetus."

In addition to the few experimental drugs under study, low-carbohydrate diets—the kind touted in the popular protein-power books—are gaining a reputation for relieving many PCOS symptoms. No formal studies support this impression, but many women who changed their eating habits say they lost weight and got pregnant. (See "Low Carbohydrate PCOS Diets: Hype, Hoax or Cure?" Page 15.)

While much research remains to be done on the causes and treatment of the syndrome, one encouraging sign for women who have it is the growing awareness that PCOS is common and can be dangerous.

Gray, the Illinois woman who went through years of unsuccessful fertility treatments, founded the Polycystic Ovarian Syndrome Association three years ago out of desperation. "There were no associations, no books, no one to talk to," she recalls. "I got the names of 30 women from the infertility support group who seemed to fit the PCOS pattern and I e-mailed them. As we started to talk, we decided to form a group."

A combination of a low-carbohydrate diet and anti-diabetes pills have helped minimize Gray's symptoms and, she hopes, are preventing the later consequences. Better yet, Gray has shed 70 pounds and is back to her slender, pre-marriage physique.

Perhaps best of all, Gray feels like her body is starting to act the way a woman's body should. She has a regular period, though she is not ovulating every month.

"I get terrible PMS," she says. "I'm nasty, bloated, and my breasts get tender.

"Thank God." ■

PCOS Signs

There is no simple test for polycystic ovarian syndrome (PCOS), but the common symptoms of the disorder include:

- Infertility.
- Excess body hair.
- Unexplained weight gain.
- Menstrual irregularities.
- Insulin resistance.

A woman who has several of these symptoms may have PCOS and should consult an endocrinologist or gynecologist for a thorough examination, including blood tests to measure hormone levels and check for diabetes.

Resource

For more information, contact the Polycystic Ovarian Syndrome Association toll-free at 1-877-775-7267 or on the Web at *www.pcosupport.org*.