The Wayward Angel

Investigating Autoimmune Disease
Picture the immune system as a guardian angel. We are normally unaware of its relentless vigilance in identifying and attacking the bacteria, viruses and parasites that threaten our health. And as women, our immune systems face an additional challenge in pregnancy — not to reject that very different bit of DNA growing in the womb. It’s a darn smart angel, but given its daunting tasks, it’s not surprising that it sometimes gets confused.

**What is Autoimmune Disease?**

In a normal immune response, the immune system identifies a toxin and produces antibodies to destroy it. Several types of specialized white blood cells called lymphocytes are involved in this process. Among these lymphocytes, T-cells identify the antigens and instruct B-cells to produce antibodies. Autoimmunity occurs when our immune system mistakes “self” tissue for “non-self” tissue and begins producing autoantibodies, that is, antibodies against “self.” Researchers have found autoantibodies in many healthy people, and it is believed that autoimmunity is benignly present in everyone to some extent. But sometimes autoimmunity becomes pathogenic, resulting in an autoimmune disease.

Autoimmune diseases can attack the joints (rheumatoid arthritis), the skin (scleroderma), the thyroid gland (Graves’ disease and Hashimoto’s thyroiditis) and the nervous system (multiple sclerosis). They can be life threatening if not treated, as in type I diabetes and systemic lupus, but many of them are under- or misdiagnosed, dismissed as mere complaints of tiredness or soreness. Because of this variability, the medical profession only began to consider them as a group in the past fifty years, and there is still some debate as to whether diseases such as chronic fatigue syndrome fall into the autoimmune disease category. Most sources estimate that there are over 80 autoimmune diseases. The most common are the thyroid disorders, Hashimoto’s thyroiditis and Graves’ disease, which affect 3 percent of all adult women. Overall, about 75 percent of patients with autoimmune disease are women and, for some diseases such as Hashimoto’s thyroiditis, the ratio of women to men is as high as 10 to 1. And studies indicate that women in the Pacific Northwest are at an even higher risk, particularly for multiple sclerosis.

**Genetic factors in autoimmune disease**

No one knows why autoimmunity becomes pathogenic in some people, but the consensus is that both genetics and environmental triggers play a part. Autoimmune diseases are not directly inherited but they do run in families, and the faulty genes don’t always produce the same problem. One family member may have a thyroid disease, and another rheumatoid arthritis, while other family members are healthy. Human leukocyte antigens, also called HLAs, are key to the immune and autoimmune responses, and HLAs are governed by genes.

In the late 1990s Dr. J. Lee Nelson, a researcher at the Fred Hutchinson Cancer Research Center, noticed the similarities between graft-vs.-host disease in bone marrow transplants and certain autoimmune diseases. This led her to look closely at HLAs and their role in the immune response. She began investigating microchimerism, which refers to the persistence of fetal cells in the mother’s body long after the birth of the child. In Greek myth, a chimera is a she-monster with a lion’s body, a goat’s head and a serpent’s tail.

"In medicine it just means having cells and DNA that’s different from the majority of your cells," explains Dr. Nelson. She speculates that it could be the similarity between the fetal and maternal HLA that confuses the immune system. “What happens with women that’s unique is that they have some cells persisting from their mother, and then they also get the ones from their child. We think that part of the problem with autoimmune disease like scleroderma may arise because of things across generations.” (We knew we were stuck in the middle, didn’t we?) “When something’s easily visible as foreign it’s not a problem.” Dr. Nelson continues. “It’s when it’s extremely similar but actually not identical that it can be a problem because then it’s almost like a computer virus or a Trojan horse.”

**All this and hormones, too!**

Many women who suffer from autoimmune diseases, notably rheumatoid arthritis and multiple sclerosis, actually get better during pregnancy, and then relapse several months after giving birth. Combined with the much higher incidence of autoimmune disease in women, this has led researchers to study the role of hormones in autoimmune disease. In lab experiments with animals, estrogen can induce autoimmunity. But researchers think that hormones like estrogen may act more like an on/off switch than a cause of autoimmune diseases. Cortisol, a natural steroid, is a stress hormone that is elevated during pregnancy. It modulates immune activity like inflammation, and synthetic corticosteroids such as prednisone are used to successfully treat lupus.

**Pulling the trigger**

Research indicates that there’s more to autoimmune disease than genetic susceptibility. “I’m interested in the genes that lead to autoimmunity, but we know there are multiple genes and we know that that’s not enough,” says Dr. Jane Buckner, a researcher at the Benaroya Research Institute at Virginia Mason. She directs the translational research program there, which is designed to collect and analyze all kinds of information from both healthy volunteers and people with autoimmune disease, an approach she calls “bench to bedside.” “Then we can study what’s the difference between an MS patient who has rapidly progressive disease versus the one who has mild disease or relapsing/remitting disease,” she says. In addition to blood samples, researchers collect information about where people have lived, their family members’ health, and what environmental exposures they have had. Collaborating with similar researchers all over the country, they hope to unlock the mysteries of why certain people get the diseases and others with similar genes don’t. “We’ve tried to take a more comprehensive approach to asking questions about autoimmunity so that we can address the many issues that are probably additively leading to these diseases,”
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immune diseases are multi-factorial. He
specifies five components to autoimmune
disease: says Dr. Hibbs. “I think
disease: genetic susceptibility, nutritional
deficiency, xenobiotic factors (chemicals
acquired and stored in the body), stress,
and viruses or some other microbial influ-
ce, Not all factors must be present, but
two or three can result in disease. “Vitamin
D is the most obvious thing that comes to
mind for the latitude relationship with auto-
mune disease,” says Dr. Hibbs. “I think
that the more that’s studied, the tighter
that argument gets.” Like everything else
about autoimmune disease, the reasons for
higher incidence among us mossbacks are
complex, and much remains to be learned.

Is the incidence of autoimmune dis-
ease increasing? The CDC estimates that
the number of Americans suffering from
lupus has skyrocketed from 239,000 to
upwards of 1.4 million in the last four years.
Dr. Buckner says the change could be the
result of changes in the demographics of
the population, a true increase in disease,
or an increase in the identification of cases.
But Dr. Hibbs feels certain there is an actual
increase in disease. “I think it has everything
to do with endemic and epidemic nutrient
deficiency and environmentally acquired
chemical toxicity,” he says.

Coping with autoimmune disease
“The thing I tell my patients is they’re going
to get to know me, because I can’t cure
them,” says Dr. Buckner, who carves out
one day a week from her research respon-
sibilities to see patients. While autoimmune
diseases are rarely fatal if treated, patients
require regular monitoring once they obtain
a diagnosis, which is not always easy. “For
about two years I went from doctor to
doctor trying to find out what was wrong.
One said it was maybe allergies and one
thought it was in my head,” says Joyce
LaPlant, a West Seattle woman who has
lived with lupus for 33 years. “The hard part
is you look fine, but you feel awful.”
Joyce takes prednisone, a corticoste-
roid, which controls the flares, but comes
with some unpleasant side effects, like
fluid retention and a hump on the back of
her neck. Like many autoimmune disease
suffers, Joyce has more than one. “I
have Sjögren’s too, which is the dry eye,
dry mouth,” she says. All told, she takes
eleven prescriptions every day. Still, she is
grateful for the support of her family, and
even for the gray skies of Seattle. “Here
the weather is perfect for somebody who
can’t go out in the sun a lot,” she says. “I
tell myself I’m not sick, I just have a prob-
to work around.”

Positive thinking is equally evident when
speaking with Kristen Nelson, a Poulisbo
woman with rheumatoid arthritis. “The
whole process kind of slows you down
and makes you take perspective on what’s
important—it’s good from that standpoint,” she says. Kristen was only 25 in 1983 when she was hit “pretty hard and
pretty suddenly.” She went from playing
basketball regularly to taking up to 22
aspirin a day. “It made my ears ring and it
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