


Hie-Won Hann, MD

Breaking the Chain of Hepatitis B Infection

BY KAREN L. BROOKS





After a healthy childhood in Korea, a young man moved to the United States, built a career, got married and raised two children. Suddenly, at age 52, he developed excruciating back pain. An ultrasound revealed a large tumor. Although he'd had no prior symptoms, liver cancer had been progressing in his body for years.

Hie-Won Hann, MD, begins many of her presentations with stories like this. A revered leader in liver disease management, Hann champions awareness surrounding hepatitis B, the virus that causes approximately 80 percent of all liver cancers. For unknown reasons, three-quarters of the 400 million people infected worldwide are from Asian nations—so Hann has focused her work on these populations.

“The virus ruminates for decades without symptoms, because the liver has no nerves. If a patient has symptoms, the cancer has spread,” says Hann, director of the Liver Disease Prevention Center at Jefferson. “People listen better to stories than statistics, so I tell them about my cases ... then they agree to get screened.”

Most people with hepatitis B were infected during childbirth; an infant born to a carrier has more than a 90 percent chance of acquiring the virus. A simple blood test can detect surface antigens (a marker for infection) long before liver cirrhosis or cancer develops, and early intervention saves lives. But early intervention is only possible if people at risk know why and how to get tested. That's where Hann comes in.

By pioneering extensive educational, screening and treatment programs, Hann has helped change the course of hepatitis B around the world. She has played a key role in identifying carriers, testing antiviral agents aimed at curing them and promoting vaccination for uninfected individuals. The two ambitious goals that have consumed her for nearly 40 years—preventing death from liver cancer through early detection of the hepatitis B virus and preventing infection from occurring in the first place—have resulted in unprecedented success in overcoming a stealth menace to public health.

SETTING RESEARCH ROOTS

Hann is best known for her work on hepatitis B, but her initial interest was cancer biology. One of only two women in her class at the elite Seoul National University Medical School, she fulfilled a dream to train at Harvard, where she completed a residency and fellowship at Dana Farber Cancer Institute. She moved to Philadelphia when her husband, Richard Suhung Hann, MD—an immunologist and classmate from medical school—got a fellowship at St. Christopher's Hospital for Children.

Unable to find an oncology position in the area, Hann explored research opportunities and in 1971 joined the lab of Baruch Blumberg, MD, PhD, at the Institute for Cancer Research, one of two institutions that ultimately merged to create Fox Chase Cancer Center. Blumberg was renowned for discovering the hepatitis B virus and subsequently devising the first vaccine (he would go on to win a Nobel Prize).

Hann's early studies involved the correlation between iron and cancer. One of her most significant discoveries involved the childhood cancer neuroblastoma; she showed that serum ferritin levels (which correlate to the amount of iron stored in someone's body) were increased in these patients and were also their prognostic indicator. She also produced the first clear animal documentation of the relationship between excessive iron and cancer growth. Published in *Cancer Research*, this work was featured in the National Institutes of Health Research Resources Reporter as one of the most significant papers of 1989.

When the hepatitis B vaccine Blumberg developed was introduced to the market in the early 1980s, the manufacturer donated an abundance to Fox Chase. Hann and her colleague W. Thomas London, MD, devised a campaign to visit local Asian immigrants to identify carriers and uninfected people who would benefit from vaccination.

FACULTY PROFILE

“Since I am from Korea, it was easy to approach Koreans, so I started with my church,” Hann says. “There was resistance—hepatitis has a stigma—and it took time to persuade them.”

But their program proved a success. Word spread, and invitations to other churches—Korean as well as Japanese, Chinese and Taiwanese—poured in. Supported by a National Institutes of Health grant, Hann and London screened and vaccinated thousands of immigrants across the Philadelphia region. Hann’s husband, whom she calls her “most important coworker,” drove her from church to church and helped to educate participants and obtain blood specimens.

“Many Koreans were clustered in other areas: New Jersey, New York, Washington, Virginia, Maryland,” Hann says. “But our grant limited us to the Delaware Valley, so we couldn’t go any farther.”

Until she got a call from Jefferson.

NO MORE BOUNDARIES

In 1988, Dean Joseph Gonnella, MD, and Department of Medicine Chairman Willis Maddrey, MD, recruited Hann as founding leader of Jefferson’s Liver Disease Prevention Center. With geographic restrictions lifted—and her husband at the wheel—she expanded her reach along the East Coast and traveled as far as California to speak to church congregations. Over two decades, they screened more than 30,000 Asian Americans for hepatitis B. Many of those identified as carriers became Hann’s patients, whom she continually monitored for tumors.

“People come to see me from far away, because I treat patients like family,” she says. “Unfortunately, for many years, if someone had even the smallest tumor resected, cancer would come back since the virus lived on in the remaining liver.”

Until the early 1990s, aside from surgery, Hann had little to offer patients in terms of treatment. Her team tried to suppress the virus with injectable interferons, but they brought severe side effects and inconsistent results. “I was desperate to stop disease progression and became an ambassador for antiviral therapy,” she says.





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The first antiviral drug for hepatitis B, lamivudine, was launched in 1998—starting what Hann calls “a new era.” She worked on the initial lamivudine trial, the results of which were published in a landmark study in the *New England Journal of Medicine*. Since then, she has conducted more than two dozen clinical trials evaluating all five currently available antiviral agents.

“Oral antiviral therapies have few adverse effects, and with them we can suppress replication of the virus in the liver, normalize liver function and even reverse cirrhosis or prevent or delay the development of cancer,” she says.

By showing that antiviral drugs can deter tumors, Hann and her peers have offered an essential alternative to liver transplantation for patients who develop liver cancer. A shortage of available donor livers often means a waiting list of three years or longer for a transplant; many patients die in the meantime.


The next step for researchers, Hann says, is to find ways to tackle the latent virus that remains in the livers of all chronic hepatitis B patients. “We have learned to get rid of the replicating virus, but the non-replicating virus is still in the body. It’s like a template, a grandmother or grandfather virus, sitting inside the liver cell nucleus. That one we haven’t been able to touch yet, but there is a lot of work going on in this area,” she says.

PRIDE AND HOPE

As fulfilled as she is by her professional accomplishments, Hann is equally proud of her family, which includes two daughters, Christine and Carolyn. Christine, MD, PhD ’00, is a medical oncologist specializing in small-cell lung cancer at Johns Hopkins (her husband, neurosurgeon Gary Gallia, MD, PhD ’00, was a Jefferson classmate and also works at Johns Hopkins). Carolyn, a University of Chicago Law graduate, is a consumer protection attorney at the Federal Trade Commission.

Hann has received many awards, including the Distinguished Leadership Award from the Hepatitis B Foundation; the Women in Leadership Award from Women’s Way; the Korean American Pioneer Award; and one that perhaps brings her the most pride, the 2003 Distinguished Daughter of Pennsylvania Award, with which she joined the likes of notable women including Pearl Buck, Grace Kelly, Marian Anderson, Mamie Eisenhower, Julie Nixon Eisenhower and Dorrance Hamilton.

Hann’s impact on controlling the global spread of hepatitis B is undeniable; as a key opinion leader, she has spoken across the United States and in Korea, China, Taiwan, Vietnam, Malaysia, Australia, Panama and more. Since she began campaigning to raise awareness, distribute vaccines and introduce antiviral therapies, the infection rate in Asian and Asian-American populations has decreased significantly. Many nations now have formal vaccination programs in place and have seen carrier rates in children drop below 2 percent.

“I am so glad to have seen these results during my lifetime. They give me hope that hepatitis B could be eradicated,” Hann says. “I tell all my patients to keep going, keep taking their medicine—because in five or 10 years, there will likely be a cure.” 

To learn more about Dr. Hann or to support her work at Jefferson, contact Margaret Fala, Assistant Vice President, Department of Medicine, at 215-955-7556 or margaret.fala@jefferson.edu.