

# PLATINUM ANNIVERSARY

*Four decades after curing testicular cancer, Dr. Lawrence Einhorn talks about the prospects of defeating — or learning to live with — other forms of the dreaded disease.*

Back in 1974, when Indiana University Distinguished Professor Dr. Lawrence Einhorn was a young, unknown oncologist at the Indiana University School of Medicine, getting testicular cancer was considered a death sentence. The thousands of males who contracted it annually — men typically in their 20s and 30s — usually succumbed within a year.

But 40 years ago, Einhorn helped change all that by adding a new, experimental drug called Cisplatin to the chemotherapy regimen for testicular cancer patients. To put it very, very simply, the drug uses trace amounts of platinum to disrupt cancer cells' DNA. Administered in concert with other drugs, it created something that's vanishingly rare in the world of medicine — a definitive cure for one type of cancer. Today testicular cancer is the farthest thing from a death sentence, with a roughly 95 percent cure rate.

But Einhorn hasn't rested on his laurels. Though 72 years old, he still zips around the Indiana University Melvin and Bren Simon Cancer Center at a pace younger men struggle to match. We managed to keep up with him long enough to ask some questions about his professional life, the future of cancer research, and his current project — finding effective treatments for lung cancer, which kills roughly 160,000 Americans each year.

## LET'S START WITH THE BASICS. WHAT IS CANCER?

"Cancer cells start out as normal body cells. They have certain growth advantages. Normal cells will grow, mature and die. But cancer doesn't undergo what we call programmed cell death. The cells don't get older and die of their own volition. Also they're capable of developing small blood vessels around the cancer cells, allowing it to proliferate and grow to other parts of the body. So it has growth advantages over normal cells, plus the capability of spreading and metastasizing. The word 'cancer' applies to over a hundred different diseases, none of them the same. What causes it, drives its spread, and what can be used to battle it can be very different from breast cancer to lung cancer to leukemia to lymphomas."

## WHAT DOES IT FEEL LIKE TO DEVELOP A CURE FOR CANCER?

"It's a great luxury to be able to treat a disease with curative intent rather than treat a disease in the hope that the patient will live a couple of months longer. But no one does anything by themselves. I was very fortunate to be here at Indiana University with a world-class urologist, (the late) Dr. John P. Donohue, which gave me access to patients. And the university has always been very supportive of our research. That means financially supporting it before anyone knew that it would be successful."

## HOW MANY PEOPLE HAS THE TESTICULAR CANCER CURE SAVED?

"In the United States it's a rare disease, amounting to only one percent of all cancer. So we see about 8,000 cases of testicular cancer a year, and of those maybe 2,000 or 3,000 could be cured with surgery alone. So there are probably about 5,000 patients a year in the United States, and obviously many more around the world, who have metastatic testicular cancer that for the most part are able to be cured because of the advent of platinum combination chemotherapy. Before this treatment, 95 percent of patients were dead within one year of diagnosis. And these were primarily people in their 20s."

## WHAT ARE YOUR DAYS LIKE?

"Wednesday is my lung clinic day. Basically Monday and Tuesday I see patients with testicular cancer and lung cancer and a variety of other unusual tumors. I teach students and medical residents. We have people who shadow us from other cities, states and countries, trying to learn some of the techniques we do here. I travel, give lectures, write papers, and do research on Thursdays and Fridays. Everyone in medicine has long days, and I love the job that I do. This is the best oncology job in the world because we're treating curable disease. Or at least we are during my Monday and Tuesday clinics."

## WHY ARE YOU PURSUING LUNG CANCER?

"Lung cancer is overwhelmingly the number one cause of cancer death in this country and in most parts of the world. In fact, over one fourth of all cancer deaths in the United States are due to lung cancer. I've always been interested in lung cancer, and the advances in molecular biology and in looking for genomic differences between cancer cells and normal cells has really exploded in the last five years. We have a lot of new targets to go after and a lot of new drugs that we can employ that didn't exist 20 years ago. These days there's not quite the pervasive feeling of pessimism in people who have the disease."

## ARE THERE ANY NEAR-TERM PROSPECTS FOR NEW LUNG CANCER TREATMENTS?

"Actually the most important thing isn't necessarily treating lung cancer but preventing it. That's why smoking cessation programs are so important, and why they need to start at the grade school level. The fewer cigarettes that patients smoke, the fewer lung cancer patients we're going to see. Because the connection between smoking and lung cancer and many



↑ Hundreds gathered at the Indianapolis Museum of Art to celebrate Dr. Einhorn. The audience included several testicular cancer survivors.

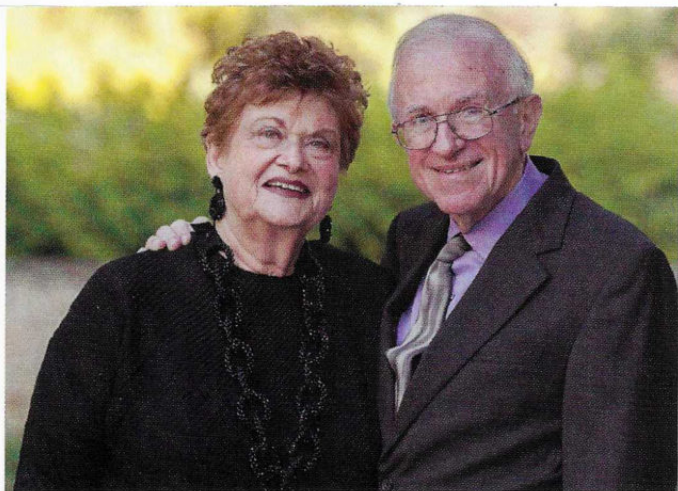
other types of cancers is no secret. It's still a challenge to eliminate the specter of smoking from our society, but that's the low-hanging fruit that would produce major benefit. We see about a quarter of a million deaths from cancer in the United States each year. We could cut that by about 35 percent if no one smoked at all. And remember that cigarettes also contribute to head and neck cancer, bladder cancer, cancer of the esophagus and many other forms of the disease. It's the number one cause of cancer."

## WOULD YOU HAVE BELIEVED, BACK IN THE 1970S, THAT 40 YEARS DOWN THE ROAD TESTICULAR CANCER WOULD BE ONLY ONE OF A HANDFUL OF CANCERS TO ACTUALLY HAVE A CURE?

"When you're younger you have a lot of youthful enthusiasm. It seemed that if you could cure one cancer with one type of treatment, then you could find a unique and specific treatment for other forms and cure them as well. But the results in solid tumors, including of course lung cancer, have lagged way behind. There are no tumors for which we don't provide supportive care, relief of symptoms and prolongation of survival. But for the most part we're extending life rather than curing disease."

## WHY IS TESTICULAR CANCER DIFFERENT? WHY DID IT LEND ITSELF TO A CURE?

"There are probably several reasons, along with some other reasons that nobody really knows. Testicular cancer patients are generally young and healthy and can tolerate aggressive chemotherapies. However there are many other, less-treatable types of cancers that strike young or middle-aged people that could also tolerate aggressive therapy. In the case of testicular cancer we have a very accurate blood test that allows us to make informed decisions about when to stop and start



↑ Dr. Einhorn and his wife Claudette at his 40 year celebration.

therapy. And when we're looking at chemotherapy with drugs like platinum, it's not difficult to get remissions with most common solid tumors. In fact it's used against 12 different types of solid tumors. But what's unique about testicular cancer is that remissions are durable, complete and sustained, whereas in most disease remissions, several months later the patient develops resistance to that drug. Testicular cancer is less prone to develop mutations that become resistant to chemotherapy than, say, lung cancer, bowel cancer, breast cancer, what have you."

#### **WHAT'S THE MOST COMMON MISCONCEPTION ABOUT CANCER?**

"There are two: That it's a death sentence, and that we're going to somehow eliminate it. Well it's not going to be eliminated, any more than we're going to eliminate heart disease. Because it's a disease of aging. But while we can't eliminate it, we can eliminate the fear of it. We can have open dialogues when people have cancer and let them know what their disease is and that their prognosis is, and try to have a world free from the fear of cancer. But we're never going to have a world free of cancer itself."

#### **WHAT'S NEW IN CANCER TREATMENT?**

"The revolution is with personalized therapy. Doing precision genomics and finding out what drives an individual cancer cell to become a cancer cell. In many chronic diseases – and cancer is a chronic disease, like heart disease or diabetes – we don't cure. We manage. The idea is to prevent cancer from growing and spreading, even if it's not surgically operable. Over the last decade major medical centers, including the IU Simon Cancer Center, have been involved in what's called personalized genomics, where we look at tissue and try to find the specific mutation that is actually driving the spread

of the cancer. And if we're lucky enough to find a specific mutation, then we and others can develop a drug to block that mutation and make a major difference. So we've moved away from chemotherapy, which was the only treatment for metastatic disease in the '70s and '80s and early 1990s, toward looking at personalized therapy. We want to find, say, the specific mutation that's driving a particular type of lung cancer, then see if we can develop a drug to block it. We could develop drugs and turn lung cancer into more of a chronic disease rather than a disease that patients usually succumb to within 12 months of diagnosis."

#### **WHERE WILL WE STAND IN ANOTHER DECADE?**

"I think if you asked that question in the '70s and '80s it would have been more chemotherapy. And if you asked that question from 2000 to 2010 it would have been looking at these molecular target agents and looking at genomic abnormalities. But I think in the next 10 years we're learning more and more about immunotherapy which had been kind of eschewed in the '70s and '80s as being a less effective type of treatment. But we learned that cancer is a foreign invader, just like bacteria or infections are a foreign invader. Usually our immune system is strong enough to recognize a foreign invader, so we don't die when we get the flu, for example. But the cancer cells are able to overcome what we call the immune surveillance. Drugs have been developed called immune checkpoint inhibitors. It prevents the cancer cell from blocking the normal activity of what are called T lymphocytes (a type of white blood cell) that use the immune reaction to fight cancer cells. These immune checkpoint inhibitors allow the host, namely the patient, to regain immunological control over the tumors.

They've had spectacular results in melanoma and kidney cancer, two diseases where the immune system is of pivotal importance. But they've also been very valuable in bladder cancer and lung cancer. These drugs are still experimental in lung cancer and bladder cancer, and were approved in melanoma and kidney cancer just last month. We're learning the dose, the schedule, what other drugs to combine them with. It's just like chemotherapy in its infancy, when we didn't know what drug to use with what disease and what dose and what schedule and what to combine it with. So I think the immune checkpoint inhibitors with the new forms of immunotherapy are probably what I would look into my crystal ball as being the big difference in the next 10 years. But as Yogi Berra said, 'It's tough to make predictions, especially about the future.' ■