Today in the United States, more than 6,000 people a year receive a liver transplant, and since liver transplants have begun, over 200,000 patients have received this therapy. They survive today due to the efforts of a legendary scientist and surgeon: Thomas Starzl (Figure 1) of the University of Pittsburgh Medical Center. He performed the first successful liver transplant in 1967 and refined the use of immunosuppressive drugs such that patients could tolerate their grafts — some for decades. With Starzl’s efforts over the last 50 years, thousands of patients with end-stage liver disease have been able to live long and active lives. The full interview can be seen on the JCI website, http://www.jci.org/kiosk/cgm.

JCI: What was your path to medical school?

Starzl: I got to medical school via the GI Bill, I was launched in what was a direc-
tive, which resulted in a PhD. After drop-
ning out again a year later, I finally went
to Northwestern in order to feed a visiting
professor. How did you weather that period
of uncertainty?

JCI: It was there that you started testing a
cocktail of immunosuppressive drugs and
steroids together on your kidney trans-
plant patients?

Starzl: Almost. The first thing that was
done within the first few months of 1962
was to obtain a supply of the drug from
Upjohn. I obtained a supply of azathioprine
(Imuran) probably a year after Roy Calne
in England had tested it. I then made some
observations that were completely missed
by the people that had the first crack of the
drug, including Calne. What they had done
was to use the Imuran from the time of
operation and then they put it together with
the variety of other drugs, including other
cytotoxic drugs; but also they had tested it
in working out the heart block problem.
And here I was wandering around not pur-
suing either field. I just didn’t know what
To do with myself. I was also getting pres-
sure from my father who was getting sick of
sending me money. I was getting pressure
from my first wife’s family, who had means,
but they didn’t like the idea of providing a
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in accepting that kind of help.

So the problem was really what field I
should be working in. I had skills in cardio-
vascular surgery, in general surgery, and
other surgical skills that I acquired over
an educational period that lasted from
the time that I got out of the Navy. I had
perpetual student syndrome or a dilettante
syndrome. I like to think of myself as a gift-
ed dilettante, but being a dilettante in and
of itself is not a good idea.

I found a trajectory at Northwestern
with the transplant studies because I spent
about two years of full-time duty, working
all day every day, on that project. I settled
the financial problem by developing a
practice of tertiary surgery at a neighbor-
hood hospital called Lutheran Deaconess
Hospital. I had a special relationship with
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five in the morning doing the cases so I
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JCI: It was there that you started testing a
cocktail of immunosuppressive drugs and
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Starzl: Those are true stories. I don’t
know that I gave it the kind of deep thought
that you’re implying I should have, but
somehow I thought that everything was
going to turn out all right. I was a missile
searching for a trajectory; I was bursting
with energy. I really wanted to do some-
thing that wasn’t conventional, wasn’t
going to be bread and butter surgery as a
means of making money, but I wanted to
do something important that would
have a life of its own, that would endure.
But what to do? I had come to be regarded
as a dilettante, having gone through a PhD
in neuroscience, and then a PhD equivalent
of the rejection patterns of liver allografts.
One of the interesting observations that
was made in those untreated animals
was an occasional recipient who rejected,
became jaundiced, and then spontaneously
recovered. In those animals, the pathology
was remarkably changed after the chemical
reversal of rejection, in that the invading
cells that were characteristic of rejection
just disappeared. Everything that we could
see from that point on looked like remodel-
ing, regeneration, and repair. So even
before the availability of immunosuppres-
sion, I had a very clear idea that rejection
was potentially spontaneously reversible.
By 1959, I also developed a model of multi-
visceral transplantation in which the liver
was transplanted with the intestine, pan-
creas, and the rest of the abdominal vis-
cera. In those experiments the rejection of
these extra organs was much less than if the
organs had been transplanted alone.
This background of behavior of grafts, and
specifically liver grafts or those organs that
were transplanted with the liver, provided
a platform upon which all of the later
observations with immunosuppression
could be built on.

JCI: In one of the interviews you have
given in the past, you mentioned that
there was a moment when you were facing
so much uncertainty about the nature of
your research that it was hard to get fund-
ing. At the time you were finishing your
clinical training, during a trip you had to
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conversations with giants in medicine

Starzl: I remember all of my patients as if they were family members. The proof of principle cases over the period between 1967 and 1980 were very precious people. I could never get them off my mind.

JCI: Given that your father was a writer and the newspaperman, it is not shocking that you also are a very prolific writer with several books, important textbooks, and over 1,800 scientific articles. Do you have a special affinity for the written word?

Starzl: It has always been easiest for me to transform thoughts on to paper. Some people have a great and wonderful fluency in speaking, and I always feel clumsy about that. When I talk to you, I am automatically envisioning written sentences and so it slows up my talk. So the written word was an escape from that. Also it was a filter, because if you write things down before you expose them, you have chance to do all kinds of corrections before they ever become visible to anyone else; and I like that. I like the care that you put in the written word. I don’t like a situation where you write something down and immediately transmit it — like with e-mail.

JCI: In September 2012, together with Sir Roy Calne, you were awarded the Lasker–DeBakey Clinical Medical Research Award recognizing the great strides that both of you took towards successful liver transplantation.

Starzl: It was tremendously gratifying. It came really unusually late in life for us. Roy is 84, and I am coming up on 87. So there is some advantage to having this occur so late because it always kept the fire burning hotter than it would have if something like this had happened 20 years ago.

JCI: Did you ever consider a different career other than being a doctor and surgeon?

Starzl: No, I don’t think I ever did. By the time I was 10 or 12 years old I was going to the hospital, the only one in Le Mars, Iowa, and watching a surgeon named Downing. He was a general practitioner who was also a quite skillful surgeon doing major operations, radical mastectomies, and other procedures. He was quite surprised when I went to his office and asked him if I could come up and watch his operations and he allowed me to do that, taking pains to be able to cart a fainted body out of the room, which happily didn’t occur. So I don’t believe I ever considered any other pathway from the time I was a sub-teenager onward.

Ushma S. Neill

Figure 1
Ushma Neill interviews Thomas Starzl in New York City on September 21, 2012, after he received his Lasker–DeBakey Clinical Medical Research Award. Image credit: Semyon Maltsev.

with prednisone. They began these secondary drugs at the same time as they started Imuran in their dogs. The prednisone actually degraded the results, made them worse. This led to an anti-steroid point of view by most scientists, but I had always treated with Imuran alone and then only when rejection developed in the dogs did I add the steroids. I found out that rejection was always reversible or essentially 95% of the time was reversible, and that sometimes, you could then stop the steroids. In our experiments, because we had limited kennels, we always stopped our drugs completely at 100 days and, to our amazement, most of the liver recipients did not reject.

The other thing that we showed is that if you pretreated the animals with Imuran for a couple of weeks before, and then continued afterwards, the results were about double in survival of what they were if you just started on the day of operation. The conditions with which we tested Imuran were quite different than the other centers, and it was that set of observations that prompted going forward with the kidney program. Why kidney when my first interest was the liver? I realized that if we proceeded with the liver without making the kidney work, that it would be considered borderline criminal.

The first objective then was to make kidneys work and use that as a porthole through which you could mount a liver program, which succeeded at least at a proof of critical principle level in 1967. So, between 1967 and the time I moved to Pittsburgh, or until the time that cyclosporine became available (1967–1979), there was a long period of time in which there were multiple successes — but the survival rate was only 50%.

Losing half the liver recipients during the first year was a very tough pill to keep swallowing. Never during those dozen years could I see any way that I could improve things. When Roy came up with cyclosporine in a report in 1979, I was all over the company to get a supply of the drug to try it. I did the first 12 successful liver cases with cyclosporine while I was still in Colorado, and about 60 kidney cases.

JCI: Do you have any memories of particular patients during that period that shaped the way that you approached your research and surgical techniques?