American Healthcare Professionals and Friends for Medicine in Israel
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Dr. Liran Levy hopes to breathe new life into lung transplantation.

The 2016-2017 APF Research Fellow at Toronto General Hospital is studying aspects of the "acute" phase of organ rejection heretofore uninvestigated, he says.

Lung transplantation, despite being a life-saving procedure for patients with end-stage lung disease, still posts grim statistics compared to those of other solid organs such as the heart, kidney, liver and even pancreas. "At least 50 percent of lung transplant patients die within five years," says the 40-year-old moshav Gealya (near Rehovot, outside of Jerusalem) native.

"The main hurdle to long-term survival is c*hronic rejection*. This condition shows up as an airway disease very similar to asthma. But unlike asthma it is progressive and irreversible. The patient subsequently becomes short of breath, requires oxygen and ultimately dies from respiratory failure. The only treatment for chronic rejection (aside from easing breathlessness) is re-transplant.

"One of the main risk factors for chronic rejection and subsequent graft failure is episodes of a*cute rejection* – when the recipient's immune system battles the donor lung," he says. "It is very common among lung transplant recipients, especially during the first year post-transplant. And it can occur more than once to any transplant patient.

"But a patient can return to baseline after being treated for acute rejection and, in mild cases, even without treatment. The main concern with episodes of acute rejection is their association with long-term complications and failure of the transplanted organ."

Levy, a non-surgical lung transplant specialist, is analyzing the subset of patients with acute rejection who experience only minimal problems and hence do not get treated at his hospital. (Severe acute rejection is always treated aggressively, but treatment for limited acute rejection is debatable and depends on a hospital's policy.) "This enables us to follow the natural development of the disease and to try and figure out why some patients in this group will subsequently develop chronic rejection and others in the same group will not. This could be a great opportunity to learn about mechanisms that affect the occurrence of late complication and chronic rejection."

The Levy family of six includes wife Mirit Shoshani-Levy, 40, who is a fellow in pediatric emergency medicine at Toronto's Hospital for Sick Children (also known as "SickKids"). Sons Ori and Ron, 9; Noam, 6 and Eitan 4 complete the group. They all came to Canada from Rehovot in 2015 when Dad accepted a clinical fellowship in lung transplantation at Toronto General. They are hoping to stay in Toronto for at least two more years.

The senior physician in pulmonology and internal medicine at Hadassah Hebrew University Medical Center grew up around healthcare and decided to become a doctor while in high school. "My grandfather and mother were nurses. Early on I was exposed, more than others, to medicine and the concept of treating people. I think this was a major factor in my choosing to pursue medicine."

But Levy stressed that "the connections you make with people, the impact you have on their lives and the lives of their families" was what truly drew him to this profession. "As a doctor, you are granted a great privilege to really touch people's lives and to share their most intimate thoughts. This is also a

tremendous responsibility, one that you can never take lightly.

“Medicine is also “the most gratifying and vast opportunity” to help people both through clinical work and research. It is amazing that you can actually lead teams that dedicate their careers to finding ways to help people by prolonging and improving the quality of their lives.”

After his IDF intelligence service, Levy attended Hadassah Hebrew University Medical School. He then completed his internship at Kaplan Medical Center (Rehovot) followed by residencies in internal medicine and pulmonology at Hadassah’s Medical Center.

As an attending physician he teaches internal medicine and pulmonology on hospital wards and in the classroom.

“Hadassah is one of the leading teaching hospitals in Israel where you see a lot of students on wards. Teaching is a major aspect of our everyday work which we take very seriously. We have learned to appreciate the way it makes you a better physician by regularly challenging you and making you find better ways to handle cases.”

Levy hopes to contribute to further development of Hadassah’s teaching system based on what he’s learned in Toronto. “North America has a different approach with emphasis on different aspects of education. I think we could implement some of these techniques in order to create a more inclusive and comprehensive approach. There is a lot that I am planning to try back in Israel.”

How did he come to pulmonology and to transplant medicine in particular?

“I have come to believe that people’s decisions are rarely based on facts and research. Often it is your heart or your gut pushing you in a certain direction as well as mentors who light a fire in you.

“Going with internal medicine was an easy decision. It is a ‘classic’ all-inclusive area -- quite diverse -- allowing you to solve multiple medical issues. You are able to maintain your clinical skills in many different areas.

“And I like the holistic approach; internists tend to be better at that.”

For his sub-specialty in pulmonology, it came down to someone he really admired.

“Dr. Neville Berkman, Director of the Institute of Pulmonology and Head of the Adult and Invasive Pulmonology Unit at Hadassah, truly inspired me and had a great influence on me when I was a student. He was my mentor and set the bar very high as an outstanding physician and an amazing person.

“When you are inspired by someone and look up to them, you become more interested in what they do and get more and more involved in their field and the focus of their work.”

Why did he choose to specialize in lung transplantation, where doctors see only “end-stage” patients, people for whom a successful transplant may buy only few extra years?

“As a lung transplant specialist, you are exposed to severely ill people and I have made a commitment to work with this group of individuals. These cases are often far from straightforward but I embrace the challenge of very sick and complicated patients. Even if I give someone only two extra years, I will do my best to make sure they are high-quality years. I want years that will allow patients to maintain their everyday activities, do some of the things they enjoy and to spend more precious time with their loved ones. This can be a great gift and being part of it is truly satisfying.

“Also, a hospital setting is the environment in which I feel most comfortable. I love the dynamics of a large multi-disciplinary team and a fast-paced busy practice.

“When you meet patients in the ER or ICU, they are in great distress and you become closely involved in their worlds; they often stay your patients for life. I

enjoy building long-term relationships with people and guiding them through their journeys.

“Israel is a small country with a shortage of transplant physicians. Working in a large hospital like Hadassah, to which very ill patients are referred, puts you in the center of a field where you can really make a difference and apply all your knowledge and expertise. I feel like I’m doing something unique.”

Levy’s research area has come full-circle from his very first project in residency – genetically personalized medicine. “In our research we tried to look for genetic differences that affect the response to Coumadin, a common blood-thinner. We compared the degree of blood-thinning to the doses patients received and tried to explain it using their genetic profiles.

“We did this because we know that different people need different doses of this drug to get the same results. And we know that if you give the wrong person a higher dose he/she can bleed to death and a dose that is too low may not be effective.”

Tentative results show his research hypothesis may be correct. Levy may have found that genetic factors can be responsible for the way patients respond to treatment and for the levels of required dosage adjustment.

He participated in several research projects at Hadassah, one after winning entrance to the prestigious “Marom” excellence fellowship program, in Hadassah’s Laboratory of Pulmonology Research. Levy chose to study whether splenectomy can inhibit lung cancer growth in mice. “It was one really intensive year of laboratory training.” And he proved his hypothesis correct. This research was partly funded by an APF Edward H. Kass Medical Research Award.

Levy also worked on a multi-specialty task force inventing and pre-marketing a gun-like device that helps insert chest tubes under combat conditions, when conventional resources are unavailable. The device, ThoraXs™, is currently in pre-clinical testing and a scholarly paper about it has been accepted for publication.

Chronic rejection is a popular focus of research studies, but Levy wants to take it in a different direction. He wants to study chronic rejection through the lenses of acute rejection and personized medicine, the latter concept being similar to what he investigated in the Coumadin study.

“Here in Toronto we have banked nearly 10 years of lung transplant tissue and fluid samples. And a large percent is from patients with acute rejection who were not treated, so it is ‘clean’ material. The plan is to examine the samples and look for biomarkers for acute rejection.

“An attempt to look for biomarkers for acute rejection in this specific population is something that is unique to this hospital. Biomarkers for acute rejection might tell you whether there is a higher risk for chronic rejection and when the best time is for a specialized, appropriate intervention.

“The problem is that if you just keep giving anti-rejection drugs to everyone, regardless, you may potentially subject them to infections and malignancy (risks of both increase as a consequence of anti-rejection medication).”

Why Toronto General? And was it necessary for Levy to leave Israel to accomplish his goals?

“I want to be a physician/scientist and this is one of the world’s leading places for this particular ambition. The departure was definitely justified because the volume and diversity of patients here is huge and the volume of ongoing research is very high.

“In Israel they do about 35 to 45 lung transplants a year and most are single lung. Here the numbers are about 130 to 140 a year and most are double lung transplants. In addition, Toronto General Hospital is following about 800 patients who have had lung transplants here in the past.

"The physicians, the researchers, the staff and the equipment are all the 'gold-standard.' Toronto General is one of five leading lung transplant hospitals around the world. It is undoubtedly the place to be in order to gain expertise in this area.

"Besides, when you come from a small country you can't compare to a place of this magnitude no matter how good you are."

What are his goals upon returning from Canada?

"My hope is to set up a research lab that will continue with lung transplant work. And I dream about contributing as much as I possibly can to making Hadassah one of the main transplant centers in Israel," Levy says. "I think that the structure and function of Toronto General's Multi-Organ Transplant Program is an amazing example. I would like to promote this model back home.

"Also, the role of a physician/scientist, so common in Toronto, is something we should strive for and incorporate all over Israel. Here physicians get compensated for dedicated research time which unfortunately is not the case back home. Hadassah is the one place where this is becoming possible."

What about family life?

Levy's family has traveled some around Canada and hopes to travel more.

"We've indulged in traditional Canadian activities such as skiing and skating classes and, of course, the kids have made a lot more progress than the parents. It's nice to experience 'real' winter for a change, something that we never get in Israel."

The family is enjoying Toronto's "big city" offerings, including its ethnic diversity.

"I think this has been a great gift for me and my family because we have been exposed to so many different cultures, religions and traditions.

"It has also allowed us to look at our culture with the eyes of an outsider. We Israelis are very open, straightforward and direct, which often comes across to Canadians as disrespectful and aggressive. We have learned to watch our manners, to be more polite and considerate and to keep our thoughts to ourselves once in a while."