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IMPACT

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OREF Clinician Scientist Seeking to Redefine Minimally Invasive

Achieving a spinal fusion or regenerating a diseased spinal disc by way of a simple injection may sound to some like science fiction, but **Francis H. Shen, M.D.** is working to make such surgery-free treatments possible, now with the help of a Clinician Scientist Award given by OREF.

Dr. Shen was named a 2007 recipient of the award, which provides an annual stipend of $100,000 for three years to compensate for the loss of income associated with devoting more time to research, and less time to clinical practice.

In return, OREF Clinician Scientists are asked to devote extensive time to research, serve as role models for orthopaedic residents, interns, and medical students, and organize and participate in conferences.

Dr. Shen's award will be funded by the **Dr. Dane and Mrs. Mary Louise Miller Endowment Fund.**

"I'm just beginning to understand what a large honor it is to receive this award," said Dr. Shen. "And I'm beginning to understand the significance it has for me as a clinician scientist, for my career, for what our lab can do and for how much we can accomplish for our patients."

Dr. Shen, an assistant professor in the department of orthopaedic surgery at the University of Virginia School of Medicine, and recipient of a 2006 OREF-Zimmer Career Development Award, will use the Clinician Scientist Award to continue his search for new sources of bone tissue and, ultimately, less invasive treatments for spinal disorders.

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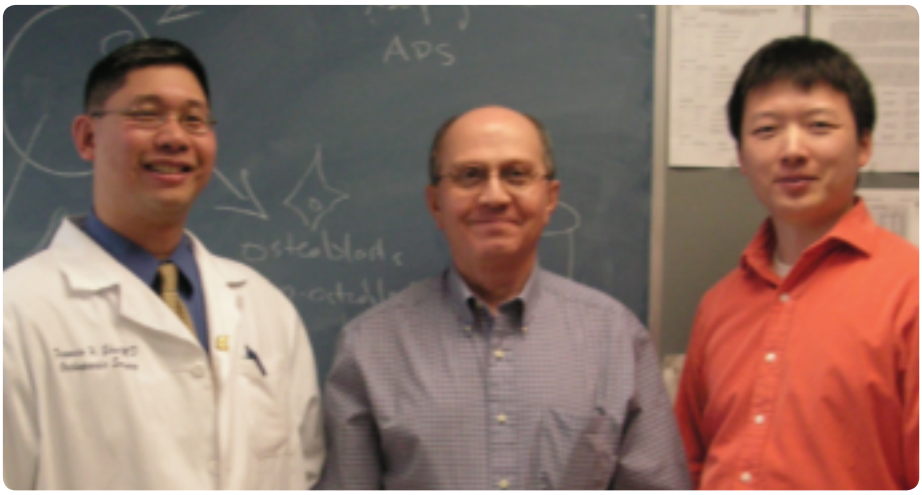

Dr. Shen is pictured with Gary Balian, Ph.D., the Mary Muilenburg Stamp professor of orthopaedic research at the University of Virginia School of Medicine. Dr. Balian is Dr. Shen's research mentor and a world-renowned specialist in stromal cell and cell tissue research. They are joined by Joshua Xudong Li, M.D., Ph.D. (Right), assistant professor of orthopaedic research and frequent collaborator.

Getting to Zero: How OREF-funded Research Fits in the Fight to Eliminate Intra-operative Infection

Preventing surgical infection is fundamental to total joint replacement procedures, so it's no wonder the topic has been the subject of numerous research studies. With an OREF Research Grant, **Harlan C. Amstutz, M.D.** was among those who sought to establish a correlation between operating room ventilation systems and reduction of intra-operative infections.

"Intra-operative infections, I would say, were the plague of the very earliest joint replacements done in this country," said Dr. Amstutz, professor emeritus and former chief of orthopaedic surgery at the University of California at Los Angeles (UCLA), who is best known for his work on total hip replacements and for founding the Joint Replacement Institute. "Unfortunately, the operative

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and immediate postoperative wound provides an excellent environment for the development of infection."

Because of the danger of wound sepsis, it is important for doctors to control the threat of possible airborne contamination. This had already been a topic of debate for about a century when Total Joint Replacement (TJR) emerged in the late 1960s. Infections can develop at the site of TJR prostheses months or even years after the operation, a complication that may lead to costly revision surgeries, which are traumatic for patients. Some surgeons thought reducing contamination during surgery should reduce the risk of immediate, or intra-operative, infections as well as the risk of periprosthetic infection.

To avoid the potential complications of intra-operative infections, orthopaedic surgeons began practicing several precautionary measures. These measures included: administering antibiotics prophylactically; requiring surgical teams to wear whole-body, exhaust-ventilated suits to control the amount of contamination they transferred to the patient during surgery; reducing operating room traffic; carefully preparing and cleaning the operating room and the wound site; covering exposed hair and skin; and using double gloves.

The Advent of Laminar Air Flow

In the 1960s, **Sir John Charnley, M.D.**, an orthopaedic surgeon at Wrightington Hospital, Lancashire, United Kingdom, who was renowned for inventing low-friction hip arthroplasty — the first truly successful total hip replacement procedure — introduced a clean air enclosure. The enclosure filtered air coming into the operating room to remove small bacteria-laden particles. Dr. Charnley's thought, according to Dr. Amstutz, was that preventing contamination in the operating room atmosphere could reduce the potential for intra-operative infection among joint replacement patients, and perhaps negate the need for prophylactic antibiotics.

Dr. Charnley's laminar air flow system recirculated a continuous flow of highly filtered, bacteria-free air under positive pressure in the operating field and removed air contaminates generated during surgery. In the 1970s, orthopaedic surgeons debated whether such an air flow system truly reduced the risk of infection. As Dr. Amstutz began his career at UCLA, he found that university operating rooms lacked laminar air flow systems, and decided it was an excellent opportunity to research the value of the technology.

"What we wanted to do was to equip the rooms with laminar air flow and measure how effective it was over the old, standard operating room, with the idea that perhaps antibiotics would not be necessary following surgery if your operating room was quite sterile," Dr. Amstutz explained.

Enlisting the expertise of **Harry Buchberg, M.S.,** an engineer in the UCLA School of Engineering, Dr. Amstutz set out to control the operating room environment and to compare the air quality in the old versus new operating rooms to learn if there was, in fact, a reduction in contaminated particles using the laminar air flow system. He would also investigate the hood system, also developed by Dr. Charnley, to see how much further it could reduce the chances of intra-operative infection.

With Mr. Buchberg's help, Dr. Amstutz designed a study using the Reyniers Slit Sampler to test the air in the operating room.

"The Reyniers Slit Sampler samples the air, counting the number of particles, which are then plated on blood agar," said Dr. Amstutz. "The bacterial colonies are counted and the type of organisms identified to determine the level of circulating contamination that could potentially cause an infection."

Dr. Amstutz collected data from the existing operating rooms before and after he had the laminar air systems installed and noted a precipitous drop in organisms.

"We were just doing joint replacements in the existing rooms, covering our patients with antibiotics and trying to do everything we could to minimize the risk of infection," Dr. Amstutz said. "Fortunately, with antibiotics the incidence, and thus the infection rate, was low: less than 2%."

A Clean Environment

The research grant Dr. Amstutz received from OREF aided this study which also gained the attention of NASA.

"Harry Buchberg was a consultant for NASA, which became involved because they needed the best clean rooms available to do studies that would dictate what the protocol should be for their space programs. So NASA was extensively involved in this clean room technology."

Eliminate Intra-operative Infection

In addition to the interest from NASA, and a discussion of results at several symposia, the findings of the OREF-funded study were published in the September 1975 issue of *Clinical Orthopaedics and Related Research*.

"We were able to reduce the infection rate to less than 1%, but decided to continue with prophylactic antibiotics," Dr. Amstutz said of the results. "It correlated with the reduction of particles. Additionally, the organisms identified were less virulent than in the old rooms. That led to further studies in terms of effectiveness of horizontal laminar flow versus vertically oriented flow, which Charnley favored, to prevent infections."

This resultant investigation showed that the horizontal system had the advantages of simplicity, lower cost, and the possibility of providing unobstructed purging of the wound for hip surgery. The vertical system, according to Dr. Amstutz, makes it virtually impossible to protect the wound from being contaminated by the surgical team unless each member of the team is isolated by an all-inclusive garment with an aspirator or body exhaust system. Yet, some later studies showed slightly lower contamination rates than those found with a horizontal system. Overall, however, Dr. Amstutz found the contamination rates of both systems to be low.

An Ounce of Prevention

The initial hypothesis of the laminar flow research was that in a sufficiently clean operating environment the use of antibiotics would be unnecessary. Today most surgeons take advantage of both measures to prevent infection.

"It turns out that there's not really a good enough reason to stop using antibiotics, although there is always a concern that if you continue their use, you will end up with resistant organisms," Dr. Amstutz explained. "But most of us really want to prevent infection, so most surgeons try to get that environment as modern as possible — with a high rate of air exchange to purge the OR of contaminants — and they also use antibiotics."

Dr. Amstutz said that he quickly understood the importance of initial research in building the case for further investigation, as occurred with his OREF grant.

"When I came to UCLA, I was still quite young. Even as chairman, when you arrive at the university, they give you a title, authority, and some salary lines for faculty. They do not provide money for research so you have to seek grant support. **The OREF grant was one of the first we received at UCLA, and it was definitely the catalyst that allowed us to activate our study to assess the reduction of organisms in the operating room following installation of a laminar flow system. I made the case that through this study we might prove that laminar flow was a step toward eliminating intra-operative infections."**

Stimulated by his research grant, Dr. Amstutz studied other causes of infections and ways to prevent them. He developed a research program that involved residents, fellows, internal medicine, infectious diseases, and engineering. This multi-disciplinary group received several NIH grants in the bioengineering field.

But the important aspect of any research, Dr. Amstutz said, is how it ultimately affects patients. His original OREF-funded laminar flow research is no exception.

"Although infections can still occur years after surgery, what we were trying to prevent was an intra-operative infection of any joint replacement. For TJR procedures done today, the risk of infection is considerably less than 1% for most operating room environments in most large centers," said Dr. Amstutz. "But ideally, of course, we would like it to be zero. The work continues."

Harlan C. Amstutz, M.D.