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— DR. PATRICIA CORBY

SUPPORTING CANCER CARE, EXPANDING CLINICAL RESEARCH

RECENT RECRUIT DR. PATRICIA CORBY IS TAKING HER RESEARCH TO CANCER PATIENTS UNDERGOING RADIATION, WHILE LOOKING TO ADVANCE CLINICAL RESEARCH SCHOOL-WIDE

WHEN DR. PATRICIA CORBY, the new Associate Dean for Translational Research at Penn Dental Medicine, was leading clinical research operations at New York University (NYU)'s College of Dentistry and working with radiation oncologists at its Langone Medical Center, she started paying attention to the oral health of patients with head and neck cancer. Radiation therapy is commonly used to treat such patients, but can wreak havoc on their oral cavity. Oral mucositis, where radiation triggers painful ulcers that make it difficult or impossible for patients to eat and function normally, is a common but debilitating side effect of treatment.

OPPOSITE: Dr. Patricia Corby joined Penn Dental Medicine in April as Associate Professor of Oral Medicine, also taking on the new position of Associate Dean for Translational Research. "It can affect the whole oral mucosa, the tongue, the throat, even the intestinal tract," Corby says, who joined Penn Dental Medicine in April as Associate Professor of Oral Medicine, "and it's a disaster. Severe cases place patients at risk for secondary infections and even sepsis due to open sores in the mouth. Sometimes it interrupts cancer treatment, and in the worst cases, treatment can't continue."

Corby had a thought after seeing the poor oral health of some patients at the outset of radiation therapy: What if a thorough, professional cleaning of their mouths during cancer treatment, aimed at preventing the colonization of "bad" bacteria in the mouth, could help reduce or even prevent this side effect of cancer care?

That thought led to a small pilot study, which has grown into an \$8 million National Institutes of Health-funded project that she is embarking on at Penn this year.

"I never look at the teeth, or even the mouth, as one thing," Corby says. "I look at them in the context of the whole body, and systemic health."



Joining Penn Dental Medicine with a wealth of experience in microbial genetics, bioinformatics, and clinical research operations, Corby is bringing this holistic approach to bear in her new role heading up clinical research at the School. Working with Morton Amsterdam Dean Mark Wolff, with whom she collaborated extensively on clinical trials while both were at NYU, Corby aims to develop a robust translational medicine program for the School, expanding opportunities and support right on campus for faculty to move their findings from the lab into the clinic.

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A WAY TO HELP

Upon graduating from dental school in Brazil, Corby began her career by opening her own practice. If a patient came for treatment and was unable to pay, she would see them anyway. But soon she came to the realization that there was a way to help patients and still have a sustainable career: by moving into clinical research. The field had the added benefit of being continually engaging.

"I also saw how beneficial clinical research would be to bring novel approaches and new ideas to improve patient care and their health overall," she says.

She started her oral health research by designing studies examining the role of genetics and environmental factors in modulating the microbiome and affecting health and



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disease. The work involved 500 pairs of twins and tracked connection between heritable and environmental factors when it came to oral conditions such as caries, gingivitis, and periodontal disease. She found that, while genetics had a strong influence in healthy individuals, once oral health was compromised, the environment held much more sway.

"Even if your genes didn't predispose you to that disease," Corby says, "once environmental factors such as bad oral hygiene lead to something like periodontitis or caries, it overrides what the genes dictate. Similarly, tobacco use, heavy alcohol use, and human papillomavirus (HPV) infection increase the risk of oral and oropharyngeal cancer."

Those findings from early in her career underscored an important lesson: preventive approaches are critical.

ABOVE: Dr. Patricia Corby reviewing head and neck cancer patients with Dr. Alexander Lin of Penn Medicine, her co-principal investigator on a clinical trial to study the impact of oral care on reducing the oral mucositis side effect of radiation treatment.

"Everything I do," she says, "it's aimed not at treating disease, it's to preserve health."

Armed with expertise in implants and periodontics, in addition to her genetics and microbial research, in 1998, she took a faculty position at the University of Pittsburgh. While there, she also earned a master's degree in biomedical informatics to help understand how computer science and cutting-edge technology could inform her burgeoning studies of the microbiome, which she further explored during a few-year stint as a research associate at Harvard University and Forsyth Institute, Boston.

By 2006, she joined the faculty of NYU, an institution that, at the time, had recently finished building a new center for clinical research—the first of its kind housed within a dental school. There she began leading operations for the center, overseeing hundreds of studies, from phase 1 through 4, which ran the gamut from medical to dental applications, for pharmaceutical clients and others. After seven years within the dental school, she moved over to NYU School of

Medicine's Langone Medical Center. There as director of clinical research operations and interim director of the Office of Clinical Trials from 2015-2016, she was responsible for the oversight of roughly 3,000 active trials at any given time. At the same time, she carried out research alongside her administrative responsibilities and became skilled in managing the intricacies and details involved in applying for highly competitive, complex NIH grants. She assisted investigators in grant development, submission, and successful implementation.

THE POWER OF PREVENTION

It was also during this time at NYU that she transitioned her work from looking primarily at caries and gum disease and their relation to systemic health, toward the pilot project involving cancer patients receiving radiation.

It began by Corby simply asking the head and neck surgeons and radiation oncologists if she could do a thorough cleaning of patients' mouths before commencing their therapy. She kept tweaking the protocol, eventually building up to weekly cleanings designed to rid their mouths of as much pathogenic bacteria as possibly, setting the stage for more beneficial microbes to recolonize. The cleanings involved clearing the dead, damaged, or infected oral mucosa tissues in combination with physically removing dental plaque and tartar.

After she had treated a dozen or so patients, she got a call from the medical director of the cancer center, a radiation oncologist. "He said, 'Pat, I know you've treated a few patients but I want to know what you're doing.' I thought to myself, 'Oh am I doing something wrong?" and asked him if there was anything wrong with the patients."

As it turned out, the opposite was true. Patients who received the weekly prophylactic cleanings from Corby were doing well: they weren't losing weight like some other patients, and importantly were not experiencing the severe oral mucositis that untreated patients were. Because they had less pain and distress, they also felt much more positively about their treatment.

Corby crafted a more formalized trial, showing that this proactive approach to cleaning patients' mouths was not only safe, but beneficial. "The difference between the experimental group and the controls was amazing," Corby says. In addition to looking for signs of oral mucositis, the study also involved collecting microbiome samples from the oral mucositis lesions, taking saliva samples to test for markers of local and systemic inflammation, and conducting a number of patient surveys to assess pain and quality of life. Because experiencing oral mucositis can compromise a patient's ability to complete a round of radiation therapy, if one could reduce the incidence of this painful condition, it could increase the likelihood that a patient receives the appropriate treatment they need to tackle their cancer (see patient Erica Casucci's story, page 16).

Over the last two years, Corby used an NIH planning grant to prepare for a fullfledged clinical trial to test her protocol in a much larger population of cancer patients. And when she made the decision to come to Penn late last year, she began the process of transitioning the full study here.

RIGHT: Dr. Patricia Corby (center) with her collaborators on her clinical trial, including (left to right) Drs. Katherine France and Takako Tanaka (far right) of Penn Dental Medicine's Dept. of Oral Medicine and Drs. John Lukens, Samuel Swisher-McClure, and Alexander Lin of Penn Medicine.

A VISION FOR CLINICAL RIGOR

To do so, Corby has made the most of her short time at Penn Dental Medicine, reaching out to Dr. Alexander Lin, Chief of the Head and Neck Oncology Service and Medical Director of the Roberts Proton Therapy Center in Penn's Perelman School of Medicine, to be a co-principal investigator on the larger NIH study. The ARMOR Trial is a collaborative effort between faculty from Penn Dental Medicine's Departments of Oral Maxillofacial Surgery & Oral Medicine (including Corby and Drs. Takako Tanaka,



and Katherine France) and Penn Medicine's Department of Radiation Oncology (including Drs. Lin, Samuel Swisher-McClure, and John Lukens). Putting patient comfort and convenience at the forefront, patients will be recruited and receive their study-related oral cleanings in the same building where they receive their radiation therapy, one of the benefits of sharing a close partnership and proximity with Penn's medical school.

Yet looking ahead, as an expert in clinical trials, Corby has ambitious plans to build up the dental school's capacity for supporting faculty conducting clinical trials in its own facilities. With support from Dean Wolff, Corby is overseeing the development of a clinical research center at Penn Dental Medicine, an area that may be small at first, but private and easily accessible for participating patients. She hopes to leverage the relationships with pharmaceutical companies that she and Dean Wolff developed during their past experiences working on clinical

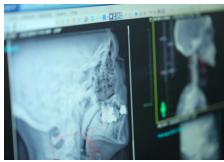
"It [oral mucositis, a debilitating side effect of radiation] can affect the whole oral mucosa, the tongue, the throat, even the intestinal tract."

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CLINICALRESEARCH





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trials to begin building a larger portfolio of clinical work to be conducted at Penn Dental Medicine.

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"We want to build up a hub for faculty conducting clinical trials, so that patients can be seen there, screened and included in studies," Corby says. "And if they may need referrals for more comprehensive dental care, they'll be right here in the clinic to receive that."

And Corby's attention will not be solely on the trials themselves, but on the work that must be done to get a discovery or product to that stage of testing.

Dr. Corby hopes to encourage more faculty at Penn Dental Medicine to push boundaries and find new and useful applications for their work.

"My primary role here as the associate dean for translational research is to build up a program to support faculty in the whole spectrum of clinical and translational research," Corby says, going from the beginning stages of developing pilot studies, designing the first-inhuman studies, and writing a grant, to implementing the projects and ensuring compliance with various regulations.

In Corby's view, with NIH supporting more translational research than in the past, there hasn't been a better time to do the types of clinical research that she has overseen in her past positions, and she hopes to encourage more faculty at Penn Dental Medicine to push boundaries and find new and useful applications for their work.

"Scientists can work for years, even decades, to find something novel in their lab, and pushing to test that for the first time in humans is really challenging," she says. "I think without the evidence that clinical research provides, health care would never progress. That's the only way to find new technologies, new drugs. How can you improve the care we offer to patients if you don't do that?" ■

- By Katie Unger Baillie

A CRUCIAL PART OF CANCER CARE

Erica Casucci, an elementary school teacher from New York City, had been experiencing mouth discomfort for a long time, but around the holiday season of 2014, she couldn't ignore it any more. "The pain was unbearable," she recalls. After a bumpy road to a diagnosis, she learned that she had oral cancer.



Radiation was going to be part of her treatment, and her surgeon at New York University brought up a study that Dr. Patricia Corby was conducting, intended to evaluate how intensive oral cleanings influenced a patient's response to radiation. Casucci became part of the treatment group, and began having weekly visits with Dr. Corby. "She would clean my mouth, she'd floss my teeth for me, and put fluoride on my teeth," says Casucci. "And she'd show me how to clean my mouth. She was amazing and so kind, always asking me generally about my oral health and how I was feeling."

Casucci had always paid attention to her oral hygiene, but she stepped up her efforts after learning about how crucial oral health was to overall health. And while her surgeon had warned her about the possible side effects of radiation, Casucci was fortunate, avoiding nearly all signs of oral mucositis. Since then she has weathered a recurrence of her oral cancer, but now, more than four years since her diagnosis, is healthy, has an energetic two-year-old, and remains appreciative of the care she received. "When you're told you have something like cancer, you kind of just stop thinking," she says. "To have people like Dr. Corby who can inform you and help you along the way so you can have a positive outcome is so important."

ABOVE: Erica Casucci, a cancer patient, who was part of Dr. Patricia Corby's clinical trial, with her daughter