Animal models help elucidate genetics and mechanisms of human kidney stone disease

Animal models are important in studying kidney stone disease because they help scientists understand the genetic underpinnings and basic mechanisms of human stone disease, and allow testing of drugs and dietary interventions than can be used in humans.

Three investigators discussed their latest stone disease research and the value of animal models, including rodent models, Drosophila fruit fly models and swine models, in a panel discussion during Monday’s Plenary I session.

“Single gene deletions in mice, polygenic traits in rats, as well dietary models have all provided some insights into the basic science of how stones form in humans,” said Benjamin K. Canales, MD, MPH, assistant professor of Urology at the University of Florida College of Medicine.

Dr. Canales described his studies of gastric bypass surgery in an obese rat model with a high incidence of stone disease that had an increase in urinary oxalate excretion after bypass surgery. “Probably the most effective therapy we’ve seen in the laboratory setting was that colonizing these animals with Oxalobacter formigenes completely normalized their urinary oxalate excretion,” he said.

In his studies of Drosophila fruit flies, Thomas Chi, MD, assistant professor of Urology at the University of California at San Francisco School of Medicine, discovered that the fruit fly is a new, emerging model for nephrolithiasis that can help “change the game” in understanding how stones are formed.

“It’s a translational research tool that we can use to make our vertebrate and clinical trials more effective,” Dr. Chi said. “These flies take only two or three days to form stones as opposed to 20 or 30 weeks in mice, and you can do stone research for a lower expense.”

While fruit fly models may be new in the study of kidney stones, they have been used for many years by researchers investigating such diverse diseases as Alzheimer’s, obsessive-compulsive disorder, obesity and cardiac disease. They are useful in stone disease research because they have malpighian tubules that form stones like human kidneys and cause obstruction.

Kristina L. Penniston, PhD, associate scientist in the Department of Urology at the University of Wisconsin School of Medicine and Public Health, described her stone research using swine models that have a similar anatomy and taxonomy to humans and form kidney stones with true calculi.

“We’ve shown that the renal and urologic function in adult swine is similar to humans, the gastrointestinal process is similar and the disease pathology is the same,” Dr. Penniston explained. “We’ve also shown that the swine diet can be easily manipulated to emulate that of humans. Their environment can be regulated, and biological samples can be easily collected to measure what we want.”

Dr. Penniston’s current research is looking at whether a high oxalate diet yields similar results in swine as in humans. Her research group has found that when dietary oxalate is high, urinary oxalate excretion increases significantly. When the calcium content of the swine’s diet is low and the oxalate content is high, urinary oxalate increases even more.

In a summary of the panel discussion, moderator James E. Lingeman, MD, professor of Urology at Indiana University School of Medicine, said, “Clearly we have made significant progress in the last few years. The bariatric model looks very interesting. Many of these models apply to primary hyperoxaluria and other genetic conditions. But we still have to achieve the Holy Grail, and that is for someone to find an animal model where we can grow a calcium oxalate stone over an interstitial deposit of calcium phosphate.”

Panel Discussion

Animal Models in Stone Disease

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