High blood pressure takes big toll on small filtering units of the kidney

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Dr. Edward W. Inscho, physiologist in the Medical College of Georgia Schools of Medicine and Graduate Studies. Credit: Medical Colllege of Georgia

Take a kidney out of the body and it still knows how to filter toxins from the blood. But all bets are off in the face of high blood pressure.

"How does the kidney know how to do it and why does it break in hypertension?" says Dr. Edward W. Inscho, physiologist in the Medical College of Georgia Schools of Medicine and Graduate Studies.

The kidneys filter about 200 quarts of plasma daily, eliminating about two quarts of waste product and extra water as urine, according to the National Institute of Diabetes and Digestive and Kidney Diseases. But

the complete physiology remains a mystery.

He challenged colleagues to fill in important blanks in how this process works normally and how to make it work better in disease during the Sept. 19 Lewis K. Dahl Memorial Lecture at the 62nd High Blood Pressure Research Conference and Workshop in Atlanta.

One thing is clear: Hypertension takes a serious toll on the kidneys and damaged kidneys worsen hypertension. Dr. Inscho believes the kidneys' million hard-working filters, or glomeruli, are direct victims of high pressure. His research focuses on the minute arteries, or arterioles, that feed blood into each of them. These afferent arterioles are responsible for keeping blood pressure at a comfortable 60 mmHg inside glomeruli. At a healthy blood pressure of 120/80 mmHg, blood enters the artery at a mean pressure of 100 mmHg, but higher pressures mean the arterioles must work even harder to reach the 60 mmHg target. They seem up to the task at least initially, contracting to make it harder for blood to pass and reducing pressure in the process. "We want to know how it does that," Dr. Inscho says as he watches the near instantaneous contraction.

He thinks he may at least know the messenger. The first reaction to high pressure actually is for the small vessel to stretch. That stretch prompts smooth muscle cells on the vessel wall to release ATP, a common molecule known as an energy source but also gaining acceptance as an extracellular messenger, he theorizes. "It's an action-reaction kind of event."

When he puts ATP on the vessel it rapidly constricts; when he blocks the ATP receptor it won't. Unfortunately ATP works best in the face of normal pressures: constricting pressure about 25 percent as opposed to 2-3 percent when it's high. Still there are plenty of questions. Whether ATP is really released by the initial stretching is a critical one, he says. Whether ATP really comes from smooth muscle cells is another.

University of Southern California researcher Dr. Janos Peti-Peterdi thinks high pressures tugging the tethers connecting smooth muscle cells to others in the blood vessel wall may really be what releases ATP, a theory Dr. Inscho presented during the Sept. 19 meeting. It may be that hypertension changes the attachment of those tethers so they don't respond and the blood vessel can't either.

"We are trying to figure out how all this fits together," says Dr. Inscho. Figuring out the critical steps of this "amazingly elegant, amazingly precise and very complicated" process will lead to better understanding of what gets corrupted by diseases such as hypertension and diabetes and maybe how to stop kidney destruction.

As scientists are finding with many diseases, Dr. Inscho says inflammation likely plays a big role. "We know we can make these animals hypertensive, treat them with anti-inflammatories and prevent this whole process from occurring," he says of glomeruli destruction. "I think that's pretty exciting, but we don't know exactly how we are doing that." Blood pressure is not affected, just the negative impact on the kidneys. Inflammation, he notes, is likely well-intended but ultimately ends up thickening blood vessel walls and hampering flexibility.

Source: Medical College of Georgia