

Interview

Diabetes and renal and cardiovascular outcomes



Carl Erik Mogensen is Professor of Medicine (diabetes and endocrinology) at Aarhus University Hospital, Denmark. He has dedicated his long career to prevention of renal disease, specifically the diabetic kidney and the relationship between blood pressure and kidney disease, and has played a major part in the improved understanding and treatment of diabetic kidney disease over the last 30 years. Professor Mogensen has published around 410 articles and several books, as well as organized a number of international meetings in the field. He has acted as an advisor to the Juvenile Diabetes Foundation International, the American Diabetes Association and the Danish government. Professor Mogensen has received numerous awards for his groundbreaking work in elucidating the mechanisms of diabetic kidney disease and preventing renal failure, most recently the 2009 International Society of Nephrology Amgen International Prize. This important award recognizes Professor Mogensen's huge contribution to the field.



Carl Erik Mogensen

Aarhus University, Medical Department M,
Aarhus Kommunehospital,
Aarhus University Hospital,
Aarhus, DK 8000, Denmark
Tel.: +45 8949 2011; +45 8617 6433
Fax: +45 8949 2010
carl.erik.mogensen@ki.au.dk

■ You have been selected to receive the International Society of Nephrology Amgen International Prize for your work on the diabetic kidney at this year's World Congress of Nephrology: how do you feel about receiving this award?

It is a great honor. I believe it is the most prestigious award from the International Society of Nephrology and has only been awarded on a few occasions to date, so I am very happy to receive the award in Milan, Italy.

■ What has been your greatest career achievement?

There are several concepts within diabetic renal disease that I have been proud to play a part in developing. In particular, my work led to a better understanding of the background for the rapid degeneration of renal function in Type 1 diabetes. Studies conducted by my group led to the conclusion that blood pressure is a very important factor, with high blood pressure leading to a rapid deterioration in renal function. This was a new observation, and the next step in my studies was to see if antihypertensive treatment would improve the renal status in these patients. Studies on patients with proteinuria revealed that there were major beneficial effects: the rate of decline in renal function was reduced considerably. This was an original finding that was later confirmed by many others in the field, and has had a considerable impact on the clinical management of diabetic patients.

Moving on from this discovery, the problem is that proteinuria or albuminuria is quite a late phase in the disease. So the next point of interest is how you can predict or identify the patients who will develop proteinuria. It was clear that microalbuminuria (between normal excretion and proteinuria) was a very important marker. We could easily identify these patients because we had developed laboratory procedures that could measure albumin in small concentrations. We found again that high blood pressure was important: those with high blood pressure had a more rapid increase in microalbuminuria. Therefore, the next step, just as in the hypertensive patients with proteinuria, was to treat these patients with blood-pressure-lowering medication and see if we could halt the progression of microalbuminuria. This was an important step, as these microalbuminuria patients were identified before renal function had begun to seriously deteriorate, so by treating them early we could prevent loss of renal function. Current clinical practice is now to screen before starting treatment with antihypertensives in all diabetic patients with microalbuminuria, irrespective of blood pressure.

■ What has your recent research focused on, in terms of clinical trials?

In Type 2 diabetes, I have been involved in a number of studies, most recently the Action in Diabetes and Vascular Disease (ADVANCE) study and the United

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.



“The background for developing renal disease in diabetics is first high glucose, followed later by blood pressure. Therefore, it is important to treat these patients early on to normalize the blood glucose.”

Kingdom Prospective Diabetes Studies (UKPDS), which looked at whether blood glucose control was beneficial in preventing cardiovascular complications. A modest benefit was found, and antihypertensive treatment for Type 2 diabetes was also found to be important, especially angiotensin-converting inhibitors or angiotensin receptor blockers.

■ **What is the role of blood glucose control in preventing renal complications in the diabetic patient?**

If we go further back in the natural course of the disease it is clear that patients with hyperfiltration (higher than normal renal function) have a greater risk of progression of renal disease. This may seem counter-intuitive, but is caused by the effect of poor glycemic control in these patients. The background for developing renal disease in diabetics is first high glucose, followed later by blood pressure. Therefore, it is important to treat these patients early on to normalize the blood glucose. This is quite difficult: you can certainly reduce the blood glucose but it is very hard to normalize it completely. It must be taken into account that there is a risk related to very low blood glucose; for example, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, the blood glucose appeared to be too aggressively controlled, leading to increased adverse outcomes. Also, some of the newer glucose-lowering agents used in that trial have adverse effects in weight gain and fluid retention/edema.

■ **What could clinicians do better to improve the renal & vascular outcomes of their diabetic patients?**

An issue that is quite important and needs to be further developed is the co-called multifactorial intervention. This has been mostly documented for Type 2 diabetes and means that in patients with microalbuminuria, at high risk of renal deterioration, we should treat the blood pressure, the blood lipids and the blood glucose. It is difficult to control the blood glucose, but it is much easier to relatively normalize blood lipids and blood pressure, so these are the most important treatment strategies. Ideally, we

would need to identify patients before they develop microalbuminuria and apply intensive treatment. This is already happening in some clinical centers, but it has yet to be proven in clinical trials. However, there are studies ongoing using this multifactorial intervention strategy, and increasing numbers of studies suggest that when you treat early you are much more efficient. When the patient already has complications, it is more difficult. Therefore, early treatment is an important avenue.

■ **Where will you be focusing your work over the next 5 years?**

Multifactorial intervention is my primary focus, and we are looking into how low you can go with lipids and blood pressure.

Another issue that is being explored is gastric banding surgery. This appears to have a positive effect on diabetes that may not be completely explained by the subsequent weight loss. Some studies suggest that diabetes improves even if weight is not normalized. This is something that must be explored further, as this may be a new way to treat diabetes. Our current treatment strategies are good, but they certainly cannot normalize blood glucose, so we need new strategies. It is possible that we should consider diabetes as an important indication for this surgery, independent of weight. Much more research is needed.

■ **Are you optimistic about the future of diabetes care, given the epidemic of obesity and Type 2 diabetes worldwide?**

This is the key problem: when I started working in this area in the late 1960s, the problem was Type 1 diabetes: there were very few patients with Type 2 diabetes. But Type 2 diabetes has increased steadily since after the Second World War, and is now an epidemic. There is some information suggesting that an obesity epidemic, at least in some countries, may have peaked. However, this is still a huge problem, especially in the USA and certain other countries, owing to unhealthy lifestyle habits. We can advise people not to eat too much and to exercise, but this is not an easy problem to solve. Unfortunately, diabetologists are not likely to be out of work for many years to come.

“[M]ultifactorial intervention ... has been mostly documented for Type 2 diabetes and means that in patients with microalbuminuria, at high risk of renal deterioration, we should treat the blood pressure, the blood lipids and the blood glucose.”