Roundtable Discussion: Hypertension, Renal Disease, and Diabetes

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Following a symposium on Hypertension in Atlanta, Georgia on April 25, 2001, which was sponsored by the National Heart, Lung, and Blood Institute, a panel was convened to discuss the problems of renal disease and hypertension. Moderating the panel was Dr. Marvin Moser, Clinical Professor of Medicine at Yale University School of Medicine. Other panelists included Dr. Jan Basile, Associate Professor of Medicine at the Ralph J. Johnson VA Medical Center and the Medical University of South Carolina in Charleston, SC, Dr. Edgar Miller, Assistant Professor in the Department of Medicine at Johns Hopkins University, and Dr. Keith C. Ferdinand, Professor of Clinical Pharmacology at Xavier University College of Pharmacy in New Orleans, LA.

DR. MOSER: We all know that hypertension and renal disease are inexorably bound together. In recent years, a great deal of attention has been paid to the effects of hypertension treatment on the prevention or slowing of progression of renal disease. More attention may have actually been paid to the renal consequences of hypertension than to cardiovascular complications, especially in diabetics. What we would like to discuss today are the connections of elevated blood pressure to renal disease and how much difference the lowering of blood pressure makes in terms of outcome. First, is renal disease a cause of hypertension, as Dr. Arthur Fishberg wrote in his major textbook in the 1940s, or is it a consequence of hypertension? Or is it both a cause and a consequence? Some people with renal disease develop hypertension, and some people with hypertension develop renal disease.

DR. FERDINAND: Clearly, it is both. There are rat models that have suggested that with the destruction of a certain amount of kidney mass, hypertension results. Moreover, there are some epidemiologic data that black babies with low birth weight and less renal mass may be at higher risk for hypertension later in life. That being said, the overwhelming proportion of patients we see on dialysis with end-stage renal disease (ESRD) are there simply as a result of poorly controlled glucose, or poorly controlled blood pressure, or both. Diabetes is the number one cause of ESRD, but 80% of diabetics have hypertension; therefore, it is very difficult to separate these factors as causes. In the African American community, hypertension is as common a cause of ESRD as diabetes.

DR. MOSER: What about such diseases as glomerular nephritis or pyelonephritis? Those used to be major causes of trouble. Are these diseases of the past?

DR. FERDINAND: They certainly are less common now. The wider use of antibiotics and early treatment for infective conditions have lessened the occurrence of infections, but glomerular nephritis still does occur. However, when all is said and done, uncontrolled high blood pressure and poorly controlled diabetes are the overwhelming causes of progressive renal disease.

DR. MOSER: So the old idea that renal disease causes hypertension may be obsolete?

DR. FERDINAND: Well, not completely. It is partly true. If you buy into the concept that hypertension represents a derangement of the renin-angiotensin system and that the kidney is the site of that derangement, there is a theoretical basis to suggest that kidney disease itself may lead to hypertension.

DR. MOSER: Dr. Basile, do you agree with what has been said?

DR. BASILE: I would agree. If you walked into any renal dialysis clinic, you would find that more than 75% of patients are there because of either hypertension or diabetes, or both. Within the African American community, hypertension is a more common etiology of ESRD than is diabetes, although the prevalence of chronic renal disease is more than three times higher among blacks with diabetes than among whites. Although hypertension increases the risk for progressive renal dis-

ease, there are patients with parenchymal renal disease who develop salt and water retention and become hypertensive. Often forgotten is that the most common non-tumor-related cause of secondary hypertension is underlying renal parenchymal disease. One often leads to the other, but we see much more essential hypertension as a cause of renal disease than the other way around.

DR. MOSER: Renal parenchymal disease is not nearly as common as it used to be, but it still accounts for probably about 5% of cases of hypertension. Dr. Miller or Dr. Ferdinand, how long does it usually take from the time someone develops hypertension to the time they develop evidence of renal insufficiency—not just proteinuria, but increases in creatinine and blood urea nitrogen levels?

DR. FERDINAND: The epidemiologic data come from a 16-year follow-up of the Multiple Risk Factor Intervention Trial (MRFIT), which screened and followed a large number of middle-aged men and did a subgroup analysis. Increasing levels of blood pressure above 120/80 mm Hg were related to progression to dialysis and ESRD. The data are clear: an elevation of blood pressure above about 120–125/75–80 mm Hg begins to have some effect on renal function. When pressures rise >140/90 mm Hg and remain there, the chances for renal insufficiency have already increased. The reason that the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) defined optimal blood pressures as lower than 120/80 mm Hg was not just related to coronary events and strokes, but also to note that pressures at these levels are optimal for preventing progression of renal disease.

DR. MOSER: We use 140/90 mm Hg as a cut-point to define hypertension because there has to be a reference point to signify a need for intervention. Although there is some increase in risk at levels of 120–140 mm Hg, this does not really increase rapidly (on an individual basis) until pressures are above levels of about 140/90 mm Hg.

DR. FERDINAND: I disagree. There is a statistical step up in the rate of ESRD in the MRFIT cohort before 140/90 mm Hg.

DR. MILLER: I believe that there was a direct linear increase in the incidence of ESRD in the MRFIT screeners over time, with increasing blood pressures. Optimal blood pressure—about 120/80 mm Hg—was the most desirable place to be.

DR. MOSER: This is something that we could debate for hours. Optimal pressures are obviously most desirable, but should a range not be established to equate benefit to risk of treatment? Do we know how long it takes someone with elevated blood pressure to develop evidence of renal disease with proteinuria or a decrease in creatinine clearance?

DR. MILLER: The evidence we have is from epidemiologic studies, and in these, proteinuria is a major predictor of progression of disease.

DR. MOSER: But take a guess: in stage 1 hypertension (140–160/90–100 mm Hg), is it 5, 10, or more years before these signs appear?

DR. MILLER: I would guess that the risk for developing proteinuria with stage 1 hypertension is double that of someone with optimal blood pressure at 10–20 years.

DR. MOSER: So you believe that it might take 10–20 years for a stage 1 hypertensive to develop evidence of decreased creatinine clearance, even accounting for age-related changes?

DR. MILLER: I believe that.

DR. MOSER: Well, what about diabetes? Do type 1 diabetics usually develop kidney failure?

DR. BASILE: This is a difficult question to accurately answer. As more type 1 diabetics are living longer, the number of individuals with chronic renal disease related to diabetic nephropathy continues to increase, with renal failure eventually developing in about 30%–50% of patients with insulin-dependent diabetes mellitus. The key determinate for progressive renal disease is the initial development of microalbuminuria (30–300 mg/day). This defines diabetic nephropathy. It has been estimated that up to 50% of type 1 diabetics will never develop nephropathy (microalbuminuria) and accordingly are not at risk for the development of progressive renal disease. Once a type 1 diabetic develops microalbuminuria (i.e., >300 mg/day of protein in the urine) and is untreated, the stage is set to develop progressive ESRD. Clearly, the amount of protein excreted by a type 1 diabetic patient is predictive of the risk for developing ESRD. Once persistent proteinuria occurs, diabetic nephropathy is usually rapidly progressive, advancing to ESRD over the next 10 years.

DR. MOSER: But given 1000 type 1 diabetics, how many do you believe will go on to ESRD?

DR. BASILE: Without therapy, probably 300–500. With our current therapy, my guess would probably be no more than 5%–10%. We have been able to significantly change the natural history of diabetic nephropathy with excellent glucose and blood pressure control, as well as through monitoring for proteinuria. However, my estimate is not based on any long-term intervention trials.

DR. MOSER: How many of them develop hypertension?

DR. BASILE: About 40% of those with type 1 diabetes.

DR. MOSER: There are about 15,000,000 type 2 diabetics; how many end up with hypertension?

DR. FERDINAND: About 80%.

DR. MOSER: So type 2 diabetics have a greater chance of developing hypertension than type 1 diabetics. Is that because they die earlier with type 1?

DR. FERDINAND: No, type 2 diabetes has different pathophysiology related to comorbid conditions, which are also associated with hypertension—obesity, sodium retention, high plasma volume, and perhaps endothelial dysfunction. That is a term that is poorly defined, but it may be related to the inability of the endothelium to respond and vasodilate under appropriate stimuli. This seems to be more common in type 2 diabetics. There are a lot of markers for type 2 diabetes that are also markers for primary hypertension.

DR. MOSER: So they are at greater risk of hypertension than type 1 diabetes?

DR. FERDINAND: Correct.

DR. MOSER: We have mentioned microproteinuria. Define it more specifically, Dr. Miller.

DR. MILLER: Well, clinically, microproteinuria is defined as ≥30 mg/24 hours….

DR. MOSER: Is there a fixed number, or is it a range of 30–300 mg/day?

DR. MILLER: Yes, 30–300 mg/day is correct, but proteinuria can also be defined by a spot urine dipstick or a spot protein-to-creatinine ratio.

DR. MOSER: Is it easily detectable? Can I detect it as part of a routine office visit?

DR. MILLER: You may not pick it up on a dipstick unless you are screening with a dipstick specific for albuminuria or proteinuria.

DR. MOSER: The routine dipstick will not pick up anything below about 300 mg/day, will it?

DR. MILLER: I think some can pick up under 150 mg.

DR. FERDINAND: There are dipsticks that detect microalbuminuria. Although the National Kidney Foundation says that every diabetic should be checked for microalbuminuria, I do not know how accurate the dipstick is, or whether the test is reimbursed. Realistically, although this is a recommendation from a national association whose job it is to protect diabetics, I think the way you protect diabetics is by controlling blood pressure and lipids along with glucose. The presence or absence of microalbuminuria, although a marker for cardiovascular disease, may not change therapy. I realize that this may sound anti-academic, but clinicians should lower blood pressure as much as possible, using intensive approaches.

DR. MOSER: What you are saying is that if the blood pressure is elevated, you are going to treat it vigorously, whether or not someone has proteinuria.

DR. FERDINAND: Right.

DR. MOSER: I agree, but the presence of proteinuria might affect the choice of medication.

DR. BASILE: May I go back for a minute? Most physicians who order a urinalysis are not detecting microalbuminuria. Once the patient has 1+ or greater protein in the urine on a routine urinalysis, there is at least 500 mg/day of protein in the urine. Accordingly, there is no further need to use special tests to detect microproteinuria (microalbuminuria).

DR. MOSER: To go further, a dipstick will not pick up minimal amounts of proteinuria unless you use a micro dipstick. There are two brands on the market; one is about $4, and one is about $7 (Micral 2), but very few physicians are using them. However, as Dr. Ferdinand pointed out, it might not make any difference. You are going to treat vigorously, anyway. Dr. Miller, will you choose different therapy with different levels of proteinuria?

DR. MILLER: Yes, I believe so. In the African American Study of Kidney Disease (AASK) study, patients with non-diabetic renal disease and protein excretion—up to 2500 mg/day—were randomized to the calcium channel blocker (CCB) amlodipine or an angiotensin-converting enzyme (ACE) inhibitor, ramipril. Across all levels of baseline proteinuria, the ACE inhibitor treatment group had a decrease in proteinuria by about 40%, including patients with proteinuria of less than 300 mg/day of protein at baseline. The amlodipine-treated patients experienced an increase in proteinuria by about 40% across all levels of proteinuria. The glomerular filtration rate (GFR) actually increased in the amlodipine group and decreased in subjects on an ACE inhibitor. The study was stopped because progression to a GFR event, ESRD, or death was lower in the ramipril group.

DR. MOSER: So the amlodipine group had worsening proteinuria than the ACE group, and although the GFR increased with amlodipine, there was more progression to ESRD in the group that had an "improvement" in GFR?

DR. MILLER: There was an acute rise in the GFR in the amlodipine group at 6 months, compared with the ramipril group.

DR. MOSER: Dr. Ferdinand, can you explain that?

DR. FERDINAND: Vasodilatation of the renal arteries results with a dihydropyridine CCB, with an early rise in the GFR. Later on, there is a decrease in GFR, so at 12–15 months, for example, there is not going to be a difference; there may actually be some loss in renal function. In one study, which was an extension of the original Appropriate Blood Pressure Control in Diabetes (ABCD) trial, there did not appear to be any worsening of renal failure at 5 years with a combination of amlodipine and enalapril.

DR. MOSER: And when lisinopril and amlodipine were combined in another trial (the Fosinopril vs. Amlodipine Cardiovascular Events Trial, or FACET), there also seemed to be a beneficial effect with an ACE inhibitor and a CCB that was greater than when the ACE was used alone. Here, too, the use of an ACE inhibitor alone appeared to reduce cardiovascular events more than a CCB alone. In FACET, there was an added benefit.

DR. MILLER: In the AASK trial of African American hypertensive patients with evidence of renal disease, the amlodipine arm of the trial was stopped because of a better outcome in the ACE inhibitor group compared to the CCB group.

DR. MOSER: There was a third group of patients. What about the β blocker arm of the study? What happened?

DR. MILLER: The β blocker arm remained blinded, so we do not have any comparative data with this group yet. The AASK trial finished on October 1, 2001. Results were presented at the American Heart Association (AHA) scientific sessions in November, 2001.

DR. MOSER: However, at the date of the first report, the β blocker group was not worse than the ACE inhibitor group.

DR. MILLER: No, it was comparable to the ACE group.

DR. FERDINAND: A question: if a person has microalbuminuria and the blood pressure is 150/100 mm Hg on monotherapy with an ACE inhibitor, is that better for the patient's outcome in terms of renal failure than being on a dihydropyridine CCB and having a blood pressure of 120/80 mm Hg?

DR. MOSER: Obviously, an important question. Probably, the blood pressure lowering is more important than anything else, regardless of the drug used. But if I had a patient on an ACE inhibitor whose pressure was not controlled, I would add a small dose of a diuretic. Most of these patients end up on an ACE inhibitor or an angiotensin receptor blocker (ARB) plus a diuretic, and that is really what happened in the clinical trials; a majority of patients were also on a diuretic.

DR. FERDINAND: I think your answer is that the ACE inhibitor and probably an ARB, based on some newer data, plus a diuretic represent preferred treatment.

The protective effect of the renin-angiotensin-aldosterone blockers has to be combined with blood pressure lowering. You use a low-dose diuretic to get additional blood pressure lowering. Primary care physicians and other clinicians should not be smug or content with simply putting a person on an ACE inhibitor or an ARB and think they are protecting the kidneys.

DR. MOSER: Well said. You raise a point that has bothered me since the publication of the diabetic nephropathy study in type 1 diabetics. This was advertised as the "captopril" or ACE inhibitor trial. It was not just a captopril or an ACE inhibitor trial; it was captopril plus a β blocker and a diuretic in more than 75% of cases, which was necessary to lower blood pressure. Many physicians were led to believe that an ACE inhibitor alone produced the benefit. Not so—and we should emphasize that an ACE or an ARB plus any other medication necessary to lower blood pressure is the message of all of these trials.

To extend Dr. Ferdinand's question, given a choice of two equal blood pressure responses, i.e., to 120/80 mm Hg on a CCB alone or on an ACE inhibitor, an ARB, or a β blocker plus a diuretic, is there some advantage to having an agent that blocks the renin-angiotensin-aldosterone system (RAAS) as part of the treatment regimen?

DR. FERDINAND: There is.

DR. BASILE: I would not necessarily agree with that. In special populations, such as the diabetic with microalbuminuria, patients with renal insufficiency, patients with systolic heart failure, patients post-myocardial infarction, and in other populations that may have heightened activity of the renin-angiotensin axis, it appears to be extremely important. I think it is unfair, however, to generalize to all patients the results of trials in which specific high-risk patient populations have benefited from blockade of the RAAS. The AASK trial is very specific; these patients were nondiabetics and had compromised renal function on entry (baseline creatinine of about 1.75 mg/dL in women and 2.22 mg/dL in men) and, as noted, the ACE inhibitor group appeared to do better than the CCB group on the combined secondary renal end points. In the ongoing Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), in which amlodipine is being compared to lisinopril and a diuretic, no difference in these agents has thus far emerged to stop any arm of the trial. Of importance, patients in ALLHAT have normal renal function on entry and included in the trial are over 15,000 diabetics, of whom 40% are African American. A creatinine at or above 1.8 mg/dL excludes them from the trial. It appears fair to say, therefore, that in those with both diabetic and nondiabetic renal disease, the initial agent of choice should be an agent that blocks the RAAS, but in other groups this may or may not be true, and future trials will determine the best therapy.

DR. MOSER: The bottom line is that in a hypertensive with no obvious evidence of renal disease, the choice of medication may not be restricted to one or two. The goal is to lower the blood pressure

as much as possible. If a CCB is successful, that is fine; if a diuretic works, that is okay, too. Does everyone agree with that?

DR. FERDINAND: If there is no evidence of renal failure or microalbuminuria, then I would agree. We do not have outcome data to say that all primary hypertensives need to be on an ACE inhibitor to protect against kidney disease, but in patients with evidence of renal disease, it may be different.

DR. MOSER: In the real world, where we may not detect small amounts of proteinuria, lowering the blood pressure seems to be as or more important than the drug with which you accomplish it. However, many physicians might say, "Let's protect those patients who may have proteinuria that we did not detect and use a RAAS blocker plus a diuretic."

DR. FERDINAND: That sounds fair.

DR. MOSER: What is the significance of microproteinuria? We measure it, we use the more sensitive dipsticks, we spend the $4 or $7, and we find out that the patient has microproteinuria. Does it help to define the prognosis in terms other than renal disease progression? I believe that it does. It not only correlates with progression of renal disease, but there is a close correlation with the presence of strokes and coronary heart disease events. So the detection of proteinuria is not important only as a prognostic indicator of renal disease.

DR. FERDINAND: I am still concerned. Although it is the recommendation of the National Kidney Foundation that we check microalbuminuria in all diabetic patients, in everyday clinical practice I do not spend $4–$7 dollars on a dipstick in these patients; I just treat them vigorously.

DR. MOSER: Okay, let me preface this by saying that most doctors are not checking this, and I tend to agree with you that it may make absolutely no difference in treatment outcome. A hypertensive with or without diabetes, with or without proteinuria, should be treated with a blood pressure goal of as close to 120/80 mm Hg as possible. Is the discovery of microproteinuria of academic or prognostic significance only?

DR. BASILE: Here is something to think about. In the HOPE (Heart Outcomes Prevention Evaluation) trial, more than 3500 diabetic patients were enrolled, with at least one other cardiovascular risk factor and usually some evidence of cardiovascular disease (>80% had evidence of cardiovascular disease). The mean blood pressure was <140/90 on entry. Although this was not a trial of patients with baseline hypertension, a large percentage (46%) were receiving antihypertensive medication. These patients benefited with a reduction in morbidity/mortality by being on an ACE inhibitor in addition to all the other baseline therapy. As the data do not allow a definition of specific therapy in specific patients, the study suggests that an ACE inhibitor should be included in therapy—certainly in diabetics where proteinuria is quite common.

DR. FERDINAND: But what about the nondiabetic with microalbuminuria?

DR. MOSER: Well let's be specific—which is preferred treatment in a diabetic or in a nondiabetic with micro- or macroproteinuria?

DR. FERDINAND: In a diabetic, I would use an ACE inhibitor or an ARB, based on the data. In a nondiabetic, I might be disinclined to do the same.

DR. MOSER: Okay, but we have no data as yet to prove that a CCB may not be acceptable if it lowers blood pressure to the new goals as close to 120/80 mm Hg as possible.

DR. BASILE: We have the AASK trial, but that was in a special population who had chronic renal insufficiency.

DR. MOSER: Do we agree on the goals for initiating treatment in a patient with evidence of renal disease; i.e., a slightly elevated serum creatinine level or microproteinuria? We all agree that the goal of therapy should be lower than the usual 140/90 mm Hg goal, i.e., 130–135/80–85 mm Hg. But what about the level where we start treatment? Do we withhold therapy until 140/90 mm Hg, or should a person who has proteinuria and pressures consistently ≥135/85 mm Hg, i.e., between 135 and 140/85–90 mm Hg, be treated with medication?

DR. BASILE: I am not aware of any evidence-based trial that suggests that treating microalbuminuria in the essential hypertensive reduces overall vascular or renal end points. Furthermore, JNC VI does not recommend microalbuminuria as a routine screening test. It is clear, however, that the presence of microalbuminuria is associated, in the nondiabetic hypertensive, with higher blood pressures, risk factor clustering, endothelial dysfunction, and a greater risk of ischemic cardiovascular disease. At the present time, recognizing this increased risk and having evidence to support more aggressive treatment...

DR. MOSER: ...are two different things.

DR. BASILE: Yes. Therefore, my answer to your question is that I get to the goals in the essential hypertensive that are recommended, regardless of whether or not there is evidence of proteinuria. I believe, however, that in the next JNC report, the specific recommendation to screen for microalbuminuria may be added.

DR. MOSER: But what level do you decide to treat? Forget a treatment goal—we all agree that the goal is as close to 120/80 mm Hg as possible. But what level do you start to treat?

DR. BASILE: Above 140/90 mm Hg.

DR. MOSER: So you would not treat a person with 135/85 mm Hg, for example, even with some proteinuria.

DR. BASILE: I would not. However, I await further trials to change my recommendation.

DR. MOSER: Do all of you agree with that?

DR. FERDINAND: Let's review this patient again. This is an important point.

DR. MOSER: The patient has consistent pressures of 135–140/85–90 mm Hg and 1+ proteinuria on a dipstick. There is no history of renal disease; blood urea nitrogen and creatinine are normal. If lifestyle changes do not work, would you use medication or would you wait until pressures were >140/90 mm Hg, even with proteinuria?

DR. FERDINAND: I do not think I would wait until pressures were >140/90 mm Hg. Large, well done epidemiologic trials actually predict the results of controlled clinical outcome trials using medications.

DR. MOSER: So you would go ahead even without firm outcome data in patients with these levels of blood pressure?

DR. FERDINAND: Data suggest that these patients are in the early stages of renal insufficiency. As we know, the presence of renal insufficiency is not always predicted by the level of serum creatinine or blood urea nitrogen, especially in older patients.

DR. MILLER: However, proteinuria—aside from diabetes and hypertension—is an important predictor of progression of renal disease.

DR. MOSER: And also other risk factors.

DR. MILLER: Yes, and other risk factors as well.

DR. MOSER: So you would tend to treat earlier.

DR. MILLER: More aggressively and with an ACE inhibitor or ARB, plus other medications.

The results of several recent trials in type 2 diabetics (reported after the symposium was held) have helped to clarify the role of ARBs in the treatment regimen. The Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus With an Angiotensin II Antagonist, Losartan (RENAAL), the Irbesartan Diabetic Nephropathy Trial (IDNT), and Irbesartan Microalbuminuria Type 2 Diabetes Mellitus in Hypertensive Patients Trial (IRMA-II) indicate that a regimen that includes the use of an ARB in type 2 diabetic patients with evidence of either definite or minimal renal disease will slow the progression of renal disease, reduce proteinuria to a significant degree, and decrease the evidence of ESRD, compared with regimens that do not include an ARB or an ACE inhibitor. Thus, it appears that these agents are effective and improve outcome in type 2 diabetics and should also be considered as possible initial therapy (usually with a diuretic) in these patients.

DR. MOSER: Can we agree, then, that based upon the data we have to date in diabetics, an ACE inhibitor or an ARB plus a diuretic, or in some instances a β blocker plus a diuretic, are preferred initial therapy? In the nondiabetic patient with proteinuria or minimal evidence of renal disease, the jury is still out. There are some physicians who might still use a CCB, usually with a diuretic, to bring blood pressure down to goal levels. If blood pressure is lowered, the patient will benefit regardless of the therapy used. Are there any final comments?

DR. FERDINAND: If proteinuria is present in any form, from micro to macro, regardless of the blood pressure I would put the patient on an ACE inhibitor, or based on the more recent data, an ARB. I do not have outcome data to support treating patients who are not diabetic and have proteinuria and blood pressures of less than 140/90 mm Hg, but I am going to depend on the predictive power of large epidemiologic trials that suggest that blood pressures over 120/80 mm Hg in those patients are too high, to help in my decision.

DR. MOSER: Whether they have diabetes or not, an ACE inhibitor or an ARB is going to be part of your therapy.

DR. FERDINAND: Yes.

DR. MOSER: Do we all agree?

DR. BASILE: I understand the position that Dr. Ferdinand has taken, but before I recommend this to the physician community, I would like to see appropriate trials that address this important question.

DR. MILLER: I feel more comfortable with that.

DR. MOSER: Okay, fair enough. Now let's try and summarize the data that demonstrate a hypertensive patient's slowing of renal disease progression in treatment. We have good data in the type 1 diabetic. We also have some data in type 2 diabetes from the FACET and the ABCD studies that suggest that there may be a preference in terms of the choice of therapy. As we have noted, an ACE inhibitor appears to be more effective than a CCB. These studies were small and not as well controlled as other studies. The AASK trial confirms these results in African American patients with evidence of pretreatment nephropathy. There were also several trials in the l980s that demonstrated a slowing of renal disease progression if blood pressure was lowered with triple-drug therapy—a diuretic, a β blocker, and a vasodilator. New data (reported after this symposium took place and summarized above) from three controlled trials that evaluated the use of ARBs in type 2 hypertensive diabetic patients with evidence of renal disease strongly suggest that progression of renal disease can be slowed—and to a greater degree

with an ARB than with a dihydropyridine CCB. We should emphasize again that none of these trials was a study of monotherapy.

DR. FERDINAND: A last word, to reiterate: one primary objective is to prevent ESRD, and to do that, the blood pressure must be kept as close to 120/80 mm Hg as possible.

DR. BASILE: My final words would be to remember that there are other risk factors that we should control in the patient with hypertension. Reduce the low-density lipoprotein cholesterol level to <130 mg/dL, and in a diabetic to <100 mg/dL, control glucose in the diabetic to at least a glycosylated hemoglobin as close to 7 as possible, use aspirin to prevent clotting, and make certain that patients do not smoke.

DR. MILLER: We need to pay special attention to people with renal disease and hypertension. Our management strategies would likely result in more aggressive treatment and better blood pressure control. This may require more frequent monitoring, and more careful monitoring for proteinuria.

DR. MOSER: Dr. Ferdinand?

DR. FERDINAND: We should never lose track of the fact that treating diabetes aggressively, treating blood pressure aggressively, and using ACE inhibitors or ARBs appropriately will reduce the scourge of ESRD. Progression to renal failure is not inevitable. While African Americans have considerably more ESRD than Caucasians, a great portion of this can be prevented or delayed by adequate treatment of hypertension and diabetes mellitus.

DR. MOSER: Thank you.