To the Editor:

Recently, Griffin et al. (1) analyzed the development of hypertension in the remnant kidney model after either pole resection or partial infarction of the kidney by ligation of branches of the renal artery. We feel that the term *remnant kidney model* is not clearly defined in the literature. This term describes an animal model of uremia based on the reduction of functional renal tissue. This reduction can be achieved by at least three different methods (for a review, see Ref. 2): resection of two-thirds of one kidney, infarction of two-thirds of one kidney by ligation of branches of the renal artery, and ligation off both poles of one kidney. Any of these procedures is performed in combination with a unilateral nephrectomy. As we pointed out recently (3), the development of hypertension in these different approaches varies considerably with an immediate rise in blood pressure in the branch ligation and pole ligation model, whereas this immediate rise in blood pressure does not occur in the pole resection model. In the later approach, however, blood pressure also rises over time, reaching, after about 15 wk, the same level as in the other two models. Thus, the data of Griffin *et al.* (1) support our previously published results. It is of note that plasma renin activity is highest in the pole ligation model, lower in the branch ligation approach, and virtually neglectible in the pole resection model. In contrast to Griffin *et al.*, we could not detect a difference in the development of proteinuria.

Overall, Griffin *et al.* (1) analyzed a very difficult period of the model during which some of the animals are recovering from acute renal failure, while at the same time hypertrophy of the remnant glomeruli occurs. Thus, they are more or less describing the adaptation period (3).

Blood pressure in the pole resection model is highly dependent on sodium balance. Ylitalo *et al.* (4) noted, after 30 days, a high blood pressure only in rats on a high-sodium diet, but not in those on a low-sodium intake. In contrast, the sodium balance in the branch ligation model is only slightly positive during the first 12 wk and is subsequently negative (3). This might be caused by renin secretion from hypoperfused glomeruli adjacent to the infarcted areas. The subsequent aldosterone secretion could lead to sodium retention, which is then excreted by normally perfused glomeruli. Thus, a situation comparable to the two-kidney, one-clip model (2K1C) seems to occur in the remnant kidney. In the 2K1C model, the clipped kidney secretes renin and induces sodium retention while the retained sodium is excreted via the unclipped kidney. Also supporting this notion is the finding that the rise in blood pressure in the 2K1C kidney model is comparable to that of the branch ligation model. The hypoperfusion around infarcted areas has been described by Meyer and Rennke (5), who noted in the infarction model collapsed capillary loops with thickening and wrinkling of the basement membrane, which is regarded as an indicator of glomerular hypoperfusion. Those authors suggest that such a population of hypoperfused nephrons could theoretically promote hypertension by the same mechanisms that increase blood pressure in the 2K1C model.

Thus, our previous data provide insight into the pathophysiology of hypertension observed in the different variants of the so-called remnant kidney model.

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REFERENCES

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Response:

Although we share Dr. Gretz' concerns regarding the somewhat generic use of the term "remnant kidney model," our reasons are rather different. Dr. Gretz considers these to be animal models of "uremia," with the principal difference between them being the slower development of hypertension in the pole resection model as compared with the infarction or the pole ligation model. In fact, because of compensatory hyperfiltration, the reduction in renal function achieved is relatively modest after approximately five-sixths renal mass reduction by any of these methods, with the GFR averaging 40 to 50% of normal at 2 to 6 wk. We find these models of renal mass reduction primarily of interest because they allow an investigation of the pathogenetic mechanisms that result in progressive injury to remnant nephrons and eventually culminate in uremia.

Hypertension, proteinuria, and glomerulosclerosis develop fairly rapidly in the infarction and the pole ligation models and have generally been interpreted as representing the direct adverse consequences of a severe reduction in functional renal mass. Although the earlier studies of Dr. Gretz and others had indicated that the blood pressure response in the pole resection model was different, as acknowledged in our article, the implications of this difference in terms of the pathogenesis of proteinuria and glomerulosclerosis had not been defined. Therefore, our studies were