Subtotal nephrectomy and increased dietary sodium were combined to produce hypertension in the dog. A transient increase in cardiac output at the onset of hypertension preceded an increase in vascular resistance. This temporal relationship suggested that autoregulatory vasoconstriction might be responsible for the hypertension. The gist of the theory is that disruptions in one system of the body might be responsible for the hypertension. I originally thought that the renin-angiotensin system was suppressed; this avoids the ambiguities of Goldblatt's model wherein both elevated renin levels and sodium retention are implicated. I was a graduate student in the mid-1960s, and Arthur Guyton was my mentor. We built a mathematical model based on the theory outlined above, and it predicted that a transient increase in cardiac output would occur over about a week at the onset of nephrectomy-salt hypertension. Thus, a natural experiment was to look for the transient in the experimental model. We looked and we found it. This was not a definitive test of the theory, but the temporal relationship between cardiac output and total peripheral resistance suggested that a generalized autoregulatory response might be occurring. We missed the mark in one respect. Liard subsequently showed that it is only skeletal muscle (and not all of the tissues of the body) that participates in the observed hemodynamic response.

The sodium retention-autoregulation theory, like many competing theories, is stuck somewhere between general acceptance and outright rejection. The genesis of hypertension—both experimental and clinical—is complex and often insidious. Definitive experiments are needed but are generally not possible.