The two Dahl or Brookhaven substrains of rats were developed by inbreeding at the Brookhaven National Laboratories in the 1960's. They have been named "salt-sensitive" and "salt-resistant" since one becomes hypertensive when placed on a sodium-rich diet while the other remains normotensive.

The most striking differences between these two substrains have been found in the kidneys. The evidence points to a causal role for renal dysfunction in the hypertension of the "salt-sensitive" substrain. This substrain shows some narrowing of the renal arteries and decreased medullary blood flow even before the hypertension-producing, salt-rich diet has been started. After hypertension has developed, further renal vasoconstriction has been observed and the excretory capability of the kidney is suppressed. When kidneys from hypertensive "salt-sensitive" rats are transplanted to normotensive "salt-resistant" recipients, hypertension develops. Conversely, when kidneys from normotensive "salt-resistant" rats are transplanted to hypertensive "salt-sensitive" rats, normotension results.

Non-renal factors have also been studied. Several aspects of vascular responsiveness in the "salt-sensitive" substrain are increased. Observed biochemical abnormalities involve adrenal enzymes and unusual proteins found in colloidal material in the pituitary cleft of the "salt-resistant" substrain. This last factor is probably not related to blood pressure control.

THE ORIGIN OF DAHL OR BROOKHAVEN SALT-SENSITIVE RATS

Lewis Dahl was intensely interested throughout his career in the role of salt in the genesis of hypertension and he invested considerable effort in developing and maintaining two complimentary substrains of rats (203). One of these substrains remains normotensive with normal sodium intake but becomes markedly hypertensive when given salt-rich
diet. Because of this it has been called a "salt-sensitive" substrain. The other substrain remains normotensive on normal and salt-rich diets and it has therefore been called a "salt-resistant" substrain. Diets with a very high sodium content have been used. Hypertension persists even after the salt-rich diet is discontinued (206).

HEMODYNAMICS

Ganguli and colleagues (337) observed an increase in cardiac output in the "salt-sensitive" strain when a salt-rich diet was instituted. Flow returned to normal as hypertension became fully developed. These transients could be interpreted as an autoregulatory response, except that "salt-resistant" animals showed the same response without developing hypertension. A possible explanation is that the two substrains have quite different autoregulatory responses to overperfusion.

Exchangeable sodium is normal in "salt-sensitive" rats with established hypertension (829).

HORMONES

A humoral explanation for the development of hypertension in Dahl rats has long been sought, but with little success. Plasma renin activity appears to be less than normal in "salt-sensitive" animals (478),(783). Rapp and colleagues (783) have investigated additional endocrine factors. Plasma aldosterone is low in the "salt-sensitive" animal. Corticosterone and deoxycorticosterone are normal. 18-hydroxy-deoxycorticosterone is elevated and is genetically linked to increased 18-hydroxylase activity (779). While 18-hydroxy-deoxycorticosterone could be making a large contribution to the observed hypertension, the results of cross-breeding experiments indicate that only 16% of the total blood pressure increase is directly attributable to this steroid (781).

Rapp and colleagues (778),(780) have discovered some unusual proteins in the pituitary of "salt-resistant" Dahl rats. These proteins have been genetically linked to blood pressure. However, the physiological role of these proteins remains unknown and it is likely that they are not directly involved in the etiology of the hypertension