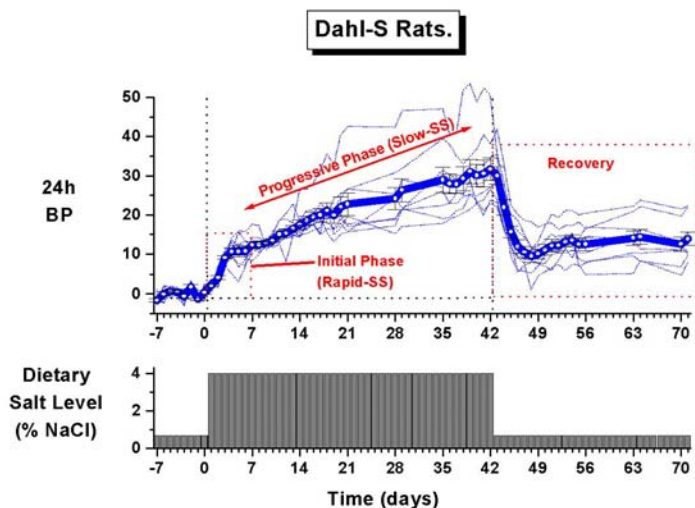


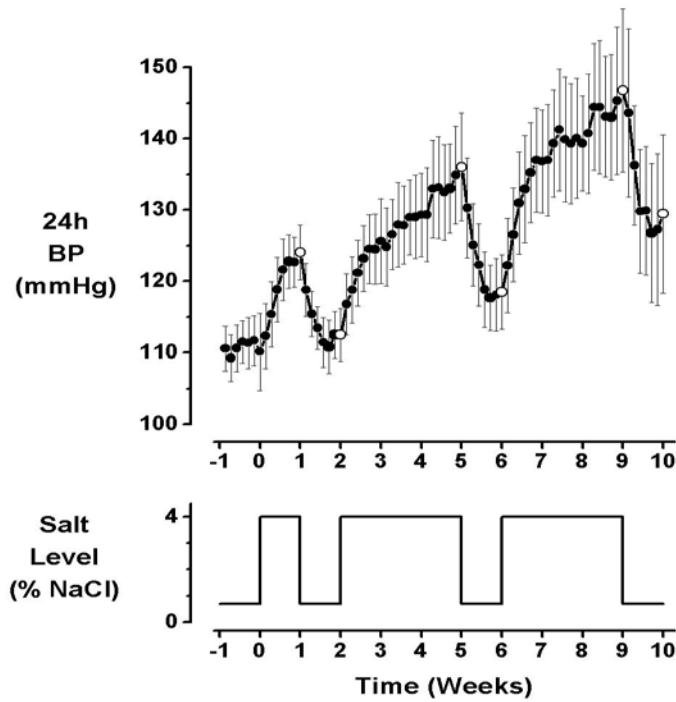
## Salt and Blood Pressure

Cardiovascular disease is the number one cause of death in Canada. A high level of dietary sodium (salt) may provide an important contribution to cardiovascular disease. From canned vegetables to pizza, our diet is rich in sodium, most of it being added during the industrial preparation and processing of foods. In susceptible individuals, consumption of a diet rich in salt can raise blood pressure, putting the individual at increased risk of cardiovascular disease. Indeed, it has recently been estimated that among Canadians, limiting salt intake to a moderate level would lead to a 30% reduction in the rate of high blood pressure (Joffres et al, 2007). Dr. Van Vliet is working to understand precisely how a lifetime exposure to salty foods affects our blood pressure, and the underlying mechanisms.

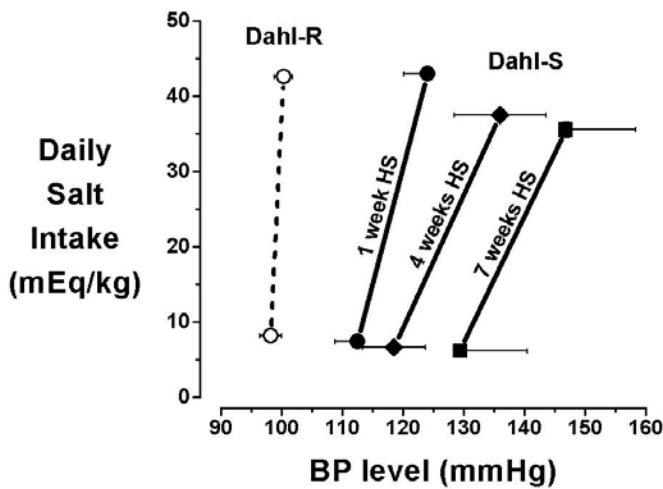
- Dr. Van Vliet's recent research has emphasized that the effect of salt on blood pressure is not quite as simple as it is often assumed to be. Rather, salt-induced hypertension has multiple phases and components, each likely having a unique explanation (Van Vliet et al, 2006). In the Dahl strain of genetically salt-sensitive rats, the blood pressure response to a high salt diet was shown to exhibit two distinct phases (Figure 1): one rapid (within ~ 5 days), the other much slower and progressive (over many weeks). While the initial effect of salt on blood pressure was reversible, the effect of continued salt exposure to raise blood pressure became progressively irreversible (Figures 2 and 3). Overall, these results suggest that salt-induced hypertension is complex, with distinct mechanisms underlying the initial and subsequent phases and the reversible and irreversible components.



**Fig 1:** Time course of the blood pressure (“24h BP”) response to a high salt diet in Dahl salt sensitive rats. A step up to a 4% salt diet led to an initial phase of blood pressure increase within the first week that was then followed by a slower and progressive elevation of blood pressure in subsequent weeks. The dark blue line with open symbols represents the average response of 9 rats. Data from individual animals is shown in the

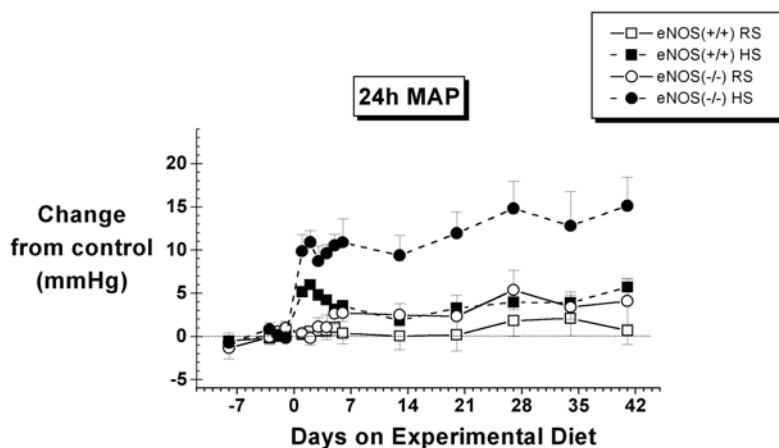


**Fig 2:** Continued exposure to a 4% salt diet leads to a progressively irreversible component of salt-induced hypertension in Dahl rats. The irreversible component is revealed by briefly reducing the salt level back to control levels. Each point represents the mean of 5 rats.



**Fig 3:** Components of salt-induced hypertension represented within the steady state relationship between salt intake and blood pressure. Data were taken from the experiment shown in Figure 2. In the Dahl-R rat strain, the relationship is almost vertical, consistent with the lack of affect of salt intake on blood pressure in this strain. In contrast, the Dahl-S rat strain exhibits a shallow slope following 1 week of high salt (HS), indicative of their acute salt sensitivity. With continued exposure to high salt, there is a further reduction in slope and the relationship is progressively shifted rightward to higher blood pressure levels. This shift represent the irreversible (or at least, not rapidly reversible) components of salt-

- In a recent review (Van Vliet et al, 2008), Dr. Van Vliet linked the phases of salt-induced hypertension observed in the Dahl rat strain (see above) with reports of similar phenomena in regular rats, chimpanzees, and humans. **Acute salt sensitivity** generally refers to the widely studied effect of salt loading or restriction to affect blood pressure within a short period of time (typically a few days to weeks) in susceptible (salt-sensitive) individuals. In contrast, a **slow and progressive phase of salt-induced hypertension** usually requires very longer periods of salt exposure that approach a sizable fraction of the lifespan of the species being studied, and only a small number of such studies have been undertaken. For example, a slow and progressive salt-induced hypertension has been observed among regular Sprague Dawley rats studied for more than one year (Meneely et al, 1953), and a similar effect was observed by Denton and coworkers in chimpanzees over a period of 22 months of a high salt diet (Denton et al, 1995). In humans, a corresponding effect is apparent in analyses of large cross sectional data sets. In this case, the slow and progressive elevation of blood pressure occurs at a rate that is proportional to the level of salt intake, and is slow very slow (occur over years or decades) that it may easily be mistaken for simply an effect of aging. Because the progressive and irreversible components are slow to arise, many of Dr. Van Vliet's studies make use of the Dahl rat strain in which the ordinarily slow blood pressure response to salt that was greatly accelerated through selective breeding. However, because the progressive response to a high salt intake could be altered in such specialized strains, he is also investigating how regular rats and mice are affected by long-term exposure to salty foods.
- “Nitric oxide” is one of many mechanisms that helps our kidneys cope with a high salt load. Impaired production of nitric oxide is associated with an increased salt sensitivity of blood pressure in both animals and humans. Dr. Van Vliet has conducted studies demonstrating an increased salt sensitivity of blood pressure in mice lacking one particular source of nitric oxide (“eNOS” or “NOS3”) (Van Vliet et al, 2006). In contrast, salt sensitivity of blood pressure was not increased in mice lacking another source of nitric oxide (“iNOS” or “NOS2”).



**Fig 4:** Increased salt-sensitivity of blood pressure in eNOS knockout mice (eNOS<sup>-/-</sup>). The graphs show the change in blood pressure induced by a switch to a high salt diet in mice lacking the gene for endothelial nitric oxide synthase (eNOS<sup>-/-</sup>, filled circles) and in regular mice (filled squares). eNOS<sup>-/-</sup> mice exhibited 2.5 fold increase in salt sensitivity, which appeared within the first few days and remained relatively stable during the subsequent 5 weeks. Blood pressure was largely unaffected in mice left on their regular diet (open symbols). Blood pressure was assessed as the 24 h mean blood pressure

- The sympathetic system has been implicated as an important contributor to salt sensitive hypertension. Dr. Van Vliet has established a method for recording renal sympathetic nerve activity by telemetry (see [Telemetry Section](#)) which he will use to further investigate the role of increased sympathetic nervous system activity.
- Dr. Van Vliet is working with other scientists and clinicians to provide information and educational materials to promote the reduction of salt intake to healthier levels.

## **Some Useful Salt (Sodium) Links:**

[Why Salt Matters \(Australia\)](#)

[Information on reducing salt intake.](#)

[Advice from the Heart and Stroke Foundation \(HSF\).](#)

[Some general information on salt and BP from the HSF.](#)

[HSF description of the DASH diet.](#)

[Brief summary of the salt issue by Health Canada.](#)

[Slide presentation on Sodium from Hypertension Canada.](#)

[HSF, on the need to reduce sodium in food.](#)

[Recommended lifestyle modifications to reduce blood pressure \(CHEP\).](#)

[Consensus Action on Salt \(CASH\)](#)

[World action on salt \(WASH\)](#)

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