S-2) Sodium Intake, Sodium Handling and Body Sodium in Rats with Spontaneous Genetic Hypertension. F.O. Simpson, Wellcome Medical Research Institute, Department of Experimental Medicine, University of Otago Medical School, Dunedin, New Zealand.

The importance of salt intake in human hypertension continues to be a controversial subject. However, salt undoubtedly is a factor in the hypertension of some people and it is possible that there would be much less hypertension in the second half of life if the average intake of salt was reduced. There are many links between hypertension and the hormones related to sodium excretion, and there is evidence also that hypertensives handle salt loads differently from normotensives.

Clearly, then, there is ample scope in this field for studies in rats with spontaneous genetic hypertension, in order to investigate pathogenesis and try out theories. There are many relevant questions, some of which can be answered and some not.

How 'salt-sensitive' is the hypertension in the various rat strains? The Dahl-S strain is salt-sensitive. SHR-SP and SB rats are partly salt-sensitive (a high salt intake having played a part in their selection). SHR are only very slightly salt-sensitive, and the GH rats are not salt-sensitive.

Is there any evidence that the hypertensive is due to an 'unwillingness' of the kidney to excrete sodium? Yes. For a given perfusion pressure, Dahl-S kidneys excrete less Na than Dahl-R kidneys. A similar difference is seen between SHR and WKY kidneys; however, this may be a secondary adaptation. In balance studies (intake and urinary excretion), young SHR show apparent increased Na retention but they have an increased fecal excretion of Na.

Do any of the strains show the phenomenon of 'exaggerated natriuresis of hypertension'? The evidence is conflicting. Our studies have not show it in either SHR or GH rats.

Do any of the rat strains have an increased body sodium? Yes, the SHR do (but note that the increased body Na is reported not to segregate with the hypertension in F2 backcrosses). GH rats do not. Other strains: no data. (Note that in DOCA-salt hypertension, body Na is greatly increased.)
What abnormalities are there in the hormones related to sodium excretion? The data are somewhat variable. Recent genetic work on rats has indicated that SHR-SP (but not SHR) have a gene in the vicinity of the ACE gene that carries with it a degree of salt-sensitivity of the blood pressure.

Are there abnormalities of salt preference? Yes. When offered the choice of water and 0.5% NaCl solution to drink, the SHR show a greater preference for saline than CH, WKY or N rats.

Are the abnormalities that have been found primary or are they secondary to the hypertension? This is always a problem and there is no easy answer. Equally, the absence of an abnormality of a given parameter does not necessarily mean that there is not some primary problem related to it; secondary adjustments could have brought the value back to the normal range.

Conclusions: 1) Strains of rats with spontaneous genetic hypertension are not identical in all respects in relation to salt handling and to the salt-sensitivity of their blood pressure. In this they can be said to resemble man. 2) Breeding on the basis of selection for high blood pressure tends not to produce a salt-sensitive hypertension; breeding on the basis of selection for the effect of salt on blood pressure does produce a degree of salt-sensitivity. 3) The high body Na in SHR is intriguing but its relation to the hypertension is uncertain. 4) No consistent primary abnormality of the Na-volume control mechanism has yet been identified in the hypertensive rat strains, but many data items are still not available. 5) Research in this field has been hampered by uncertainty about the validity of the control strains. The new gene manipulation techniques should greatly improve the rate of solution of the problems; the results already suggest that the genes related to hormonal control of salt balance are important.