Scientific **A**dvisory **C**ommittee on **N**utrition

3rd MEETING OF SALT SUBGROUP
21 May 02, Food Standards Agency, Aviation House, 125 Kingsway, LONDON

Chairman	Professor Alan Jackson
Members	Professor Peter Aggett
	Professor Sheila Bingham
	Miss Gill Fine
Secretariat	Dr Lisa Jackson (FSA)
	Dr Alison Tedstone (FSA)
	Dr Sheela Reddy (DH)
	Dr Adrienne Cullum (DH)
	Ms Mamta Singh (FSA)

Chair's Introduction

1. The Chair welcomed Members to the meeting and asked them to inform him of any modifications they wished to make to the agenda. Members agreed to take item 7, *Proposed Structure of Report,* as the second item for discussion.

2. Matters arising from the previous meeting had been put on the agenda as items for discussion.

AGENDA ITEM 1 – Minutes of last meeting SACN/SaltSub/02/min02

3. Members were invited to comment on the minutes of the previous meeting. No comments were made and the minutes were agreed. It was noted that the minutes had been published on the website within a month of the meeting.

AGENDA ITEM 7 - Proposed structure of report

4. A proposed structure for the report of the Salt Subgroup's findings had been prepared by the secretariat and was divided into the following eight sections: introduction, public health issues, overview of sodium, dietary exposure, basis of the 1994 COMA recommendations, review of the evidence since 1994, conclusions, recommendations.

5. Members agreed that the section on *Public Health Issues* should not be too detailed and that the 1991/1994 COMA recommendations should be mentioned in the *Introduction*.

6. The Secretariat reported that it may not be possible to include the cluster analysis, which it had been asked to commission at the previous meeting, in the section on *Dietary Exposure* as it may take longer than the time scale envisaged for completion of the report. However, this work would still provide useful back-up information once available.

7. The Subgroup discussed whether the report should make reference to sodium or to salt. It was agreed that the report should identify the differences between sodium and salt in the *Introduction* and explain that the terms were sometimes used synonymously. As the recommendations related to salt, it was agreed that it would be more appropriate to use this term but equivalent amounts of sodium should also be included. It was also noted that the FDF report, which was submitted to the Subgroup, highlighted that less than 5% of sodium in foods is present in forms other than as sodium chloride.

8. The Subgroup approved the proposed structure as a useful basis for the preparation of the report. The Subgroup also agreed to check the structure of the report against the *Risk Assessment Framework* being developed by SACN. **Action: Secretariat**

9. The Subgroup agreed that the report should be in the form of a paper to SACN and should be finalised by the end of 2002.

AGENDA ITEM 2 – Physiological requirements

10. The Chair reminded members that previous discussions had established that:
    - Estimates of the range of sodium consumed on a daily basis to maintain health varied between 20–100mmol (0.5-2.4g) sodium (1.2-6g salt) per day;

- in response to an increased consumption of salt there was a response to increase sodium excretion which could take up to two days to be fully effective;
- sodium homeostasis represents an integrated response involving central, vascular and renal levels of control;
- following habitual consumption of higher levels of salt, vascular sensitivity becomes less responsive, sodium excretion in response to a load becomes less efficient and blood pressure tends to rise, the so-called pressure/natriuresis response;
- the pressure/natriuresis response is also modulated by other physiological changes associated with obesity, and insulin resistance;
- the nature of these interactions can be influenced by an individual's genotype, phenotype, level of activity, alcohol intake, and other factors.

11. The Subgroup noted that the Intersalt data were compatible with a homeostatic threshold of 20–50mmol (0.5-1.2g) sodium (1.2-3g salt) per day.

12. The Subgroup agreed that, on the basis of the evidence assessed to date, the 1994 COMA recommendation for a reduction in population average intake, to 100mmol (2.4g) of sodium (6g salt) per day, represented a pragmatic target, which was greater than the minimal requirement but represented an achievable objective for the population. The Subgroup needed to consider whether this target was associated with any adverse effects for certain sections of the population.

13. In a study by Miller et al (1983), *Blood pressure response to dietary sodium restriction in normotensive adults*, sodium was restricted from 150mmol per day (3.6g sodium/9g salt) to a goal of 60mmol per day or less (1.4g sodium/3.6g salt) in healthy normotensive husband-wife pairs for a 3-month period. They achieved a sodium intake of 70mmol (1.6g sodium/4.2g salt) per day. There was variability in the blood pressure response, but there were significant decreases in systolic and diastolic blood pressure which were associated with the magnitude of the reduction. No adverse effects were observed at these low levels of intake.

14. The Subgroup noted that the paper by Dahl (1958), *Salt intake and salt need,* examined the issue of very low levels of salt intake and found no adverse effects. However the acuteness of the change and the time taken to accommodate to the lower levels had not

been addressed. The question of whether there were increased losses in the form of sweating, particularly for individuals who were not habituated to low levels of intake was also not addressed. The study also illustrated the variability of responsiveness.

15. In terms of early exposure it was observed that studies dealing with infants appeared to have been chiefly designed to provide guidance for the sodium levels required for low and very low birthweight infants. The Subgroup noted that while there are follow up studies on sodium intake and later blood pressure in children, there is a lack of evidence in children who were not pre-term and/or low birthweight.

16. Members noted that:
    - The adult requirement is less than 100 mmol (2.4g) sodium (6g salt) per day;
    - infant recommendations should be for levels similar to that contained in breast milk;
    - for children, no data were available on the physiological ranges required for sodium homeostasis; it may therefore be necessary to estimate the requirements for children using physiological principles, based upon the requirements for adults.

17. The Secretariat agreed to circulate the following papers to members:
    - Lurbe E, Alvarez V, Liao Y, Torro I et al. Obesity modifies the relationship between ambulatory blood pressure and natriuresis in children. Blood Press Monit 2000;5(5-6):275-80.
    - Heino T, Kallio K, Jokinen et al. Sodium intake of 1 to 5-year old children: the STRIP project. Acta Paediatr 2000; 89:406-410.

Action: Secretariat

AGENDA ITEM 3 - Relative importance of chloride ion

18. The Subgroup had concluded at the previous meeting that chloride did not exert an independent effect on blood pressure. Further references cited in papers which had been requested by the Subgroup at the previous meeting were considered by Members.

19. In terms of dose-responsiveness to sodium, a study by Denton et al (1995), *The effect of increased salt intake on blood pressure of chimpanzees,* showed that a progressive addition of salt to the diet over 20 months had caused an increase in blood pressure, which was completely reversed within six months of salt cessation.

20. A study in humans by Luft et al (1979), *Cardiovascular and humoral responses to extremes of sodium intake in normal and black men,* observed an increase in blood pressure in response to intakes of 10-1500mmol (0.25-12g) of sodium (0.6-30g salt), as well as differences in black and white subjects. It was also observed that increased sodium intake had induced potassium loss.

21. The Subgroup requested the following reference cited in the paper by Luft:
    - Lowder SC, Brown RD. *Hypertension corrected by discontinuing chronic sodium bicarbonate ingestion.* Am J Med (1975); 58:272.

Action: Secretariat

22. The paper by Miller et al (1983), *Blood pressure response to dietary sodium restriction in normotensive adults*, found a decrease in blood pressure was associated with the magnitude of reduction. A variability in the blood pressure response was also observed.

23. The Subgroup noted that these two physiological studies demonstrated the variable response to sodium reduction and the dose-responsiveness.

24. The Subgroup had also requested a paper by Grim and Wilson (1993), *Salt, slavery and survival,* which proposed that descendants of slaves in America had high blood pressure because of problems associated with increased sodium loss such as sweating, diarrhoea and vomiting; those better at retaining sodium were much more likely to survive. Members noted the information presented in the paper was circumstantial and that there was no evidence for this theory.

AGENDA ITEM 4 - Salt sensitivity (SS)

25. The Subgroup noted the widely different uses of the term *salt sensitivity* for which there was no agreed definition. In general, the term had been used to characterise a change in blood pressure in response to an oral load of sodium chloride. There has been no consistency in the sodium load administered, or in the nature of the response elicited. Based upon the evidence available, it is likely that if the sodium chloride load is

sufficiently large it will exceed the capacity for all individuals to respond, resulting in adverse effects such as a rise in blood pressure.

Genotype

26. Members felt that it would be important to determine whether salt sensitivity varied with genotype and whether it was possible to identify specific genotypes which characterise salt sensitive individuals.

27. The Subgroup noted that studies had shown that polymorphisms in certain genes, such as the angiotensinogen gene, might be implicated in the blood pressure response to a high salt intake. However, the number of factors involved in the regulation of blood pressure, such as the heart, vasculature, and renal volume, indicates that polymorphisms in several genes may be involved. At present, many of the existing studies have limited statistical power to examine interactions and have not measured dietary factors. The extent to which genetic factors are causally related to hypertension and interact with diet remains under investigation.

28. The Secretariat reported that the authors of the DASH Sodium trial had been contacted to enquire if the genotype of the subjects had been examined. However, research on genetics in the DASH-sodium trial is still in progress and the researchers are not expecting to publish any results for at least a year. The ongoing *MRC British Genetics of Hypertension Study,* attempting to identify the major genes for high blood pressure, is expected to have only limited data on environmental exposures.

Prevalence of salt sensitivity and variation with age

29. The Chair thanked the Secretariat for the paper tabled at the meeting summarising the available information on the prevalence of SS. The key points were:
    - the lack of uniformity in study criteria and techniques could account for differences in estimated prevalences;
    - because most studies have involved small numbers of subjects, precise estimates are difficult to make;

- the variability in the populations studied, particularly the age of subjects, ethnic origin, obesity, level of intake of other dietary minerals, are also likely to have had an impact on the variation in prevalence estimates.

30. Taking all these factors into account, a higher frequency of SS has been observed in adults with hypertension. Estimates of prevalence have varied between 29-60% in hypertensive populations and 15-46% in normotensive populations, although the larger studies have indicated that over 50% of a hypertensive population and approximately 25% of a normotensive population are SS. Salt sensitivity has also been more frequently observed among black rather than white subjects in both normotensive and hypertensive populations.

31. Although SS has been more frequently observed in older rather than younger subjects, it was noted that change in prevalence with age had received limited investigation and that SS was observed in some populations during teenage years. Wilson et al (1999) had shown 22% prevalence in a study of 140 healthy African-American adolescents.

32. The Subgroup considered whether salt sensitivity may exert effects independently of blood pressure. A study by Weinberger et al (2001), *Salt sensitivity, pulse pressure and death in normal and hypertensive humans*, circulated to members at the previous meeting, showed that subjects who had been identified as salt sensitive normotensives 27 years previously were found to have a cumulative mortality similar to that of hypertensive subjects. It was noted, however, that the authors had not controlled for the effect of smoking.

33. A possible mechanism suggested for the relationship between salt sensitivity and mortality was an inability of salt sensitive individuals to regulate nitric oxide production which is related to vascular tone and therefore to blood pressure.

34. The Subgroup requested the following reference cited in the paper by Weinberger et al:
    - Morimoto A, Uzu T, Fujii T, Nishimura M, Kuroda S, Nakamura S, Isenaga , Kimura G. Sodium sensitivity and cardiovascular events in patients with essential hypertension. Lancet (1997);350:1734-1737. **Action: Secretariat**

35. The Subgroup recognised that salt sensitivity appeared to be sufficiently common in certain groups to cause some concern. Members agreed that it was worth considering whether the advice for the management of individuals in which increased salt consumption posed greater risk for health, due to limited capacity to handle salt at levels normally consumed, should be on an individual rather than on a population-wide basis.

AGENDA ITEM 5 - Morbidity and Mortality outcomes

Cardiovascular disease

36. The Subgroup felt it would be useful to collate meta-analyses carried out since 1994 to enable a comparison of the regression coefficients. **Action: Secretariat**

37. The Subgroup recognised that other environmental characteristics may also be of importance with regard to blood pressure. The example was given of the situation in Greece where high sodium consumption is not associated with high blood pressure; other factors such as diet, ambient temperature, or lifestyle may be important. The Secretariat agreed to circulate the following paper to members:
    - Powles JW, Hopper JL, Macaskill GT, Ktenas D. Blood pressure in subjects from rural Greece, comparing individuals migrating to Melbourne, Australia with non-migrant relatives. Journal of Human Hypertension 1993; 7:419-428.

Action: Secretariat

38. In order to consider whether salt intake is associated with cardiovascular incidents, the Subgroup requested the following studies:
    - Tunstall-Pedoe H, Woodward M, Tavendale R, Brook RA, McCluskey MK. Comparison of the prediction by 27 different factors of coronary heart disease and death in men and women of the Scottish heart health study. BMJ (1997); 315:722-729.
    - Valkonen VP, Voutilainen S, Myyssonen et al. Sodium and potassium excretion and the risk of acute myocardial infarction. Circulation 1998; 98 (Suppl 1):I-374(no.1962)
    - Kant AK, Schatzkin A. Graubard BI, Schairer C. A prospective study of diet quality and mortality in women. JAMA 2000; 283:2109-2115.
    - Yamori Y, Nara Y, Mizushima S, Sawamura M, Horie R. Nutritional factors for stroke and major cardiovascular diseases: international epidemiological comparison of dietary prevention. Health reports (1994); 6:22-27.

- Alderman MH, Cohen H, Madhavan S. Dietary sodium intake and mortality: the National Health and Nutrition Examination Survey. Lancet 1998; 351:781-785.
- Alderman MH, Madhavan S, Cohen H, Sealey JE, Laragh JH. Low urinary sodium is associated with greater risk of myocardial infarction among treated hypertensive men. Hypertension 1995; 25:1144-52.
- Perry IJ, Beevers DG. Salt intake and stroke: a possible direct effect. J Hum Hypertens 1992; 6 (1):23-5.
- Tobian L, Hanlon S. High sodium chloride diets injure arteries and raise mortality without changing blood pressure. Hypertension 1990; 15:9003.
- Chobanian AV, Hill M. National Heart, Lung, and Blood Institute Workshop on Sodium and Blood Pressure: A critical review of current scientific evidence. Hypertension 2000; 35:858-863.

Action: Secretariat

39. It was noted that two studies based on the same data (NHANES), had found different results. In the study by Alderman et al (1998), *Dietary sodium intake and mortality: the National Health and Nutrition Survey (NHANES I)*, had found an inverse relationship between sodium intake and mortality. In contrast, the study by He et al (1999), *Dietary sodium intake and subsequent risk of cardiovascular disease in overweight adults*, found a positive association between increased sodium intake and CVD in overweight people.

40. Information on sodium intake for NHANES was based on a single 24-hour dietary recall. Members noted that whilst both studies were based on poor intake data, the study by He et al had controlled for smoking whilst Alderman et al had not.

41. The study by Tuomilehto et al (2001), *Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study*, collected 24-hour urinary sodium of 2500 people over 10 years. A positive association was found between high sodium intake and risk of coronary heart disease independent of other risk factors, including high blood pressure.

41. The Subgroup requested a copy of the meta-analysis by Midgley et al (1996):

- Midgley JP, Matthew AG, Greenwood CMT, Logan AG. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. JAMA 1996; 275: 1590-97.

Action: Secretariat

Osteoporosis

42. It has been suggested that a high salt diet leaches calcium out of bones leading to reduced bone mineral density. The Secretariat agreed to seek further information on the relationship between 24-hour urinary calcium and bone density and any recent evidence on the impact of sodium intake on bone health. **Action: Secretariat**

Gastric cancer

43. The Subgroup noted that a previous COMA report *Nutritional Aspects of the Development of Cancer* (1998) had concluded that a high salt consumption appeared to be associated with increased risk of stomach cancer, but that these levels of consumption were not characteristic of the UK population.

44. The Secretariat agreed to circulate a recent paper by de Wardener and MacGregor:

- De Wardener HE, MacGregor GA. Harmful effects of dietary salt in addition to hypertension. Journal of Human Hypertension 2002; 16:213-223.

Action: Secretariat

Dietary exposure and variation with age

45. The Subgroup considered the Verner Wheelock report which had assessed the salt content of certain categories of products from different retail outlets in 1998 & 1999. The same products had not always been listed for the different years, but the report provided a useful indication of the ranges and wide variation within the product categories. The Subgroup were informed that some manufacturers and retailers have reduced the sodium content of some food products, however the amount per serving may have increased as some portion sizes have become larger.

46. As requested, Heinz had provided information outlining their approach to salt reduction, which they had carried out gradually over a lengthy time-period. Kellog's had also been approached for information.

47. The Subgroup discussed possible reasons why some companies might have difficulty in reducing the salt content of foods. These might include:
    - initial low levels in some foods means there is less room to manoeuvre;
    - salt levels are influenced by many factors including the preferences of the food selectors; however, new product development practices meant that more products are tested before launch with consumer and trained panellists so that a wider range of salt preferences are likely to be identified;
    - companies may or may not have formalised a nutrition strategy that identifies salt reduction as part of their product development practice;
    - labelling difficulties regarding legislative issues on salt/sodium declarations, the current guidance on the levels required for making a claim and consumer understanding of the difference between salt and sodium information on the label.

48. The Subgroup noted that although there had been a reduction in the sodium content of a range of products, the pace of change was unknown. Members recognised that the rate at which change occurred was dependent, to some extent, on customer preferences. The Subgroup considered that it would be to useful to learn if individuals were adding salt, at the table or during cooking, to products in which sodium levels had been reduced.

AGENDA ITEM 6 - Other factors

Genetic factors

49. The Subgroup noted that this topic had previously been discussed in relation to salt sensitivity and acknowledged that there were different groups within the population that carry different risks.

Alcohol and smoking

50. The secretariat reported that a literature search had yielded very little information regarding sodium homeostasis in relation to these factors; most studies had looked at their

effects in relation to renal function generally. A study by Vamvakas et al (1998), *Alcohol abuse: potential role in electrolyte disturbances and kidney diseases*, had looked at the effect of alcohol on sodium homeostasis, but subjects for the study had been long-term alcoholics.

51. Cigarette smoking might exert a direct vascular effect. A possible reason for the association between smoking and high blood pressure could also be due to the adverse dietary patterns often observed in smokers.

Other nutrients

52. The Subgroup were informed that Margetts et al (1986) had found that switching to a vegetarian diet reduced systolic blood pressure by 5mm Hg over a 6 week period. However when the different components of such a diet were examined, they were unable to establish which factor was responsible for the reduction. In contrast, the DASH Sodium trial had illustrated that when the level of a single component (sodium) in the diet was altered, an effect on blood pressure was observed regardless of alterations in the intake of fat and fruit and vegetables.

53. The Secretariat agreed to circulate the following studies by Margetts et al which had examined the effect of vegetarian diets on blood pressure:
    - Margetts BM, Beilin LJ, Vandongen R, Armstrong BK. Vegetarian diet in mild hypertension: a randomised controlled trial. BMJ 1986; 293:1468-1471
    - Prescott SL, Jenner DA, Beilin LJ, Margetts BM, Vandongen R. A randomized controlled trial of the effect on blood pressure of dietary non-meat protein versus meat protein in normotensive omnivores. Clinical Science 1988; 74:665-672.
    - Margetts BM, Beilin LJ, Vandongen R, Armstrong BK. A randomized controlled trial of the effect of dietary fibre on blood pressure. Clinical Science 1987; 72:343-350.
    - Margetts BM, Beilin LJ, Armstrong BK, Rouse IL, Vandongen R, Croft KD, McMurchie EJ. Blood pressure and dietary polyunsaturated and saturated fats: a controlled trial. Clinical Science 1985; 69:165-175.

- Barden AE, Vandongen R, Beilin LJ, Margetts B, Rogers P. Potassium supplementation does not lower blood pressure in normotensive women. Journal of Hypertension 1986; 4:339-343.

Action: Secretariat

54. Fruit and vegetables are associated with protection from CVD although the evidence is not consistent. It was noted that the EPIC study had shown higher plasma vitamin C levels to be associated with lower CVD and IHD mortality.

55. With regard to the argument that potassium, rather than sodium, was the key factor affecting blood pressure regulation, the Subgroup recognised that potassium, magnesium, calcium and sodium were all important in the regulation of blood pressure. Other micronutrients may also be involved.

56. In terms of energy intake, members noted that energy balance was an important issue as it was related to obesity.

57. With relation to macronutrients, members recognised that there were issues related to essential fatty acids and prostaglandins, carbohydrate, fibre, glucose, and protein.

58. The Subgroup noted that greater sodium consumption increased the need to consume more water. In this regard, another benefit conferred by fruit and vegetables was their high water content.

59. In terms of other routes of sodium loss, activity and environment were important in relation to heat and sweating.

Association with metabolic syndrome

60. The factors which comprise metabolic syndrome - glucose intolerance, dyslipidemia, obesity, hypertension, and lack of activity cluster and mutually reinforce each other. An improvement in any of these factors would be likely to have an impact on the others.

61. The Subgroup noted that activity was very important in relation to blood pressure regulation, but the basis of the beneficial effects needed to be clarified.

Action: Secretariat.

62. The secretariat was also asked to seek information on whether activity exerted an influence on salt sensitivity. **Action: Secretariat**

AGENDA ITEM 8 - Conclusion and consideration of further work

63. The Subgroup agreed that it was important to include a definition for hypertension in the report and to emphasise that although blood pressure was a continuous variable, cut-off points had been defined above which there was an increased risk of morbidity and mortality. The cut-off point for high blood pressure is currently 140/90 mmHg.

64. The Subgroup agreed that some additional work was required before final conclusions could be reached but evidence so far suggests there is no substantial basis for alteration to previous advice.

65. In discussing the timescale for the production of the report, members agreed that it should be completed before the SACN meeting, due to be held in October 2002. It was agreed that the Secretariat would prepare a preliminary draft by early July and this would be circulated to the Subgroup for their consideration and comment. **Action: Secretariat**

66. It was agreed that the Subgroup would finalise the report at the next meeting in September. The Secretariat would liaise with members regarding a suitable date. **Action: Secretariat**

67. Members were informed that a paper on the work of the Subgroup would be presented to SACN at the open meeting on 20 June.

68. The Chair thanked members of the Subgroup for their attendance.