

### **Brief Communication**

#### **SALICYLATES AND CREATININE CLEARANCE RE-EVALUATED**

Salicylates have been shown to increase the serum creatinine and decrease the creatinine clearance in normal volunteers and patients with rheumatoid arthritis and systemic lupus erythematosus.<sup>1,2</sup> However, Macklon *et al.* have failed<sup>3</sup> to demonstrate any significant increase in plasma creatinine or reduction in creatinine clearance over a two-year period in rheumatoid arthritic patients undergoing constant salicylate therapy. Our clinical impression is also that patients on long term salicylate therapy do not have creatinine clearances or

serum creatinines which differ from the norm and we therefore decided to study the effect of a five-week period of salicylate therapy on the creatinine clearance and serum creatinine of normal volunteers.

#### **Patients, Methods and Results**

Nine healthy volunteers were given salicylate for a five-week period. Salicylate was administered as a sustained release preparation (SRA Boots) in a dose of 3.9 g per day taken in divided doses to sustain adequate salicylate levels throughout a 24-hour period. Twenty-four hour urine collections were made prior to salicylate therapy and at weekly intervals of five weeks and in six volunteers two weeks after cessation of therapy. Blood was collected

TABLE 1  
Creatinine clearance and serum electrolytes in normal volunteers treated with salicylates  
(mean  $\pm$  standard deviation and significance (*t*-test))

	Pre-aspirin (N = 9)	Day 8 (N = 9)	Day 15 (N = 9)	Day 22 (N = 9)	Day 29 (N = 9)	Day 36 (N = 9)	Two weeks after treatment (N = 6)
Creatinine clearance (ml/min)	117 $\pm$ 18 NS	103 $\pm$ 25 NS	140 $\pm$ 26 NS	140 $\pm$ 35 NS	128 $\pm$ 27 NS	119 $\pm$ 26 NS	114 $\pm$ 30 NS
Serum creatinine (mmol/l)	0.09 $\pm$ 0.008 <i>P</i> < 0.001	0.11 $\pm$ 0.006 <i>P</i> < 0.001	0.086 $\pm$ 0.006 NS	0.09 $\pm$ 0.003 <i>P</i> < 0.01	0.10 $\pm$ 0.007 NS	0.09 $\pm$ 0.009 NS	0.10 $\pm$ 0.006 NS
Serum potassium (mmol/l)	3.7 $\pm$ 0.09 <i>P</i> < 0.0005	4.2 $\pm$ 0.07 NS	4.25 $\pm$ 0.07 NS	4.3 $\pm$ 0.03 NS	4.4 $\pm$ 0.08 NS	4.4 $\pm$ 0.05 <i>P</i> < 0.0005	3.6 $\pm$ 0.08 NS
Serum sodium (mmol/l)	143 $\pm$ 1.7 NS	147 $\pm$ 1.4 NS	140 $\pm$ 1 NS	147 $\pm$ 0.5 NS	144 $\pm$ 1.2 NS	143 $\pm$ 1.4 NS	141 $\pm$ 2 NS
24-hour urine creatinine (mg)	1618 $\pm$ 285 NS	1915 $\pm$ 495 NS	1772 $\pm$ 293 NS	1720 $\pm$ 267 NS	1757 $\pm$ 227 NS	1826 $\pm$ 326 NS	1742 $\pm$ 219 NS

at the same time of day during each 24-hour urine collection and estimations of plasma and urine electrolytes and creatinine concentrations were performed by a Technicon Auto-analyser. The results are seen in Table 1.

Creatinine clearance fell during the first week of therapy, although this did not reach statistical significance, but then returned to a level higher than pre-treatment levels before settling over the five-week period. Serum creatinine rose significantly during the first week of treatment, but then fell and remained not significantly different from pre-treatment levels for the duration of aspirin therapy. The serum sodium level did not vary with salicylate therapy, but the serum potassium rose significantly and remained elevated until salicylate therapy was stopped. There was no significant alteration in the urinary electrolytes during these studies. Salicylate concentrations of 10, 20 and 30 mg/100 ml of serum, salicylate concentrations of 10, 20 and 30 mg/100 ml of urine and salicylurate concentrations of 100 and 200 mg/100 ml of urine did not interfere with the measurement of serum or urine creatinine and electrolytes.

#### Comment

This study suggests that changes in serum creatinine and creatinine clearance are transient when salicylate therapy is commenced in normal volunteers and that these parameters return to normal with continuation of therapy.

The studies previously cited showing reduction in creatinine clearance and elevation in serum creatinine were both short term studies, the period of therapy being between seven and ten days. The transience of these effects is in keeping with the work of Scott *et al.* showing that urine cell count is increased for a period of two to three days on the commencement of salicylate therapy before returning to normal. We feel that the creatinine clearance and serum creatinine are still reasonable screening tests for assessing renal function in patients receiving salicylate therapy as long as salicylate therapy has been continued for at least two weeks. We would suggest that some compensatory mechanism occurs in renal function and physiology when patients are first put on salicylate therapy reflected by the transient change in the measured parameters and further work is in progress to study these mechanisms.

P. M. BROOKS\*

and

P. COSSUM

Department of Medicine,  
University of Tasmania,  
Hobart, Tasmania 7000

\*Present address: Flinders Medical Centre,  
Bedford Park, SA

#### References

- BERRY, H. C. and DIEPPE, P. A. (1976): Apparent reduction of endogenous creatinine clearance by salicylate treatment. *Brit. med. J.* **2**, 16.
- KIMBERLY, R. P. and PLOTZ, P. H. (1977): Aspirin-induced depression of renal function. *New Engl. J. Med.* **296**, 418.
- MACKLON, A. F., CRAFT, A. W., THOMPSON, M. and KERR, D. N. S. (1974): Aspirin and analgesic nephropathy. *Brit. med. J.* **1**, 597.
- SCOTT, J. T., DENMAN, A. M. and DORLING, J. (1963): Renal irritation caused by salicylates. *Lancet* **1**, 344.