The present paper concerns the mechanism responsible for the proteinuria in rats with renovascular hypertension and was undertaken after the observation made by some surgeons (K. Owen, London and P. Fiorani, Rome) of a further transient increase in urinary protein excretion in some hypertensive patients with renal artery stenosis following an operation for renal revascularization.

On the basis of these observations and of our previous experiments on the mechanism of proteinuria induced in the rat by the infusion of renin, we thought it interesting to verify:

1. whether proteinuria could also be produced by an increase in endogenous renin induced in the rat by the application of a clip to a renal artery;

2. whether the removal of the clip was followed by a further increase in proteinuria.

MATERIALS AND METHODS

Preparation of animals

Male Wistar rats, weighing between 200 and 300 g, were used exclusively in all experiments because of the different rate of spontaneous protein excretion in males and females.

Three different types of operation were performed in three different groups of rats under ether anaesthesia:
group 1 (7 rats): application of a silver clip (inside diameter 0.20 mm) to the left renal artery with the contralateral kidney intact (two-kidney hypertensive rats);
group 2 (5 rats): application of a clip (inside diameter 0.25 mm) to the aorta above the origin of the renal arteries;
group 3 (5 rats): application of a clip to the left renal artery and contralateral nephrectomy (one-kidney hypertensive rats).

In a 4th group of sham-operated control animals (5 rats) the renal arteries and aorta were manipulated without application of a clip.

The reason for the different operations is that although all three cause hypertension, they have a different effect on plasma renin activity (PRA): a significant increase is observed with the first type, a variable and moderate increase with the second, and no increase with the third. Before and after the operation the rats were fed a standard diet and allowed free access to water until the day of experiment.

Two weeks after the operation the rats were anaesthetized with 100 mg/kg thiopentone sodium intraperitoneally, followed by smaller doses (5 mg) intravenously to maintain anaesthesia. The trachea was cannulated. Intravenous infusions were given, using a constant flow rotary pump, via a polythene catheter in the right jugular vein. Arterial pressure was measured continuously from a carotid artery catheter by a Sanborn pressure transducer coupled to a device recorder (type 267 B). Urine was collected in plastic tubes by a polythene catheter inserted directly into the bladder through a suprapubic incision, and in three rats of the first group by two catheters inserted directly into the two ureters.

Experimental protocol

All animals were infused with saline solution (0.9%) at the rate of 0.1 ml/min starting 15 min after completion of the preparation. Following an equilibration period of 30 min, three urine collections were made, each for a 1-h period: one before and two after removal of the clip. At the mid-point of each period approximately 0.2 ml of arterial blood was obtained from the catheter in the carotid artery for PRA measurements made by the method of Boyd et al. At the end of the experiment the rats were killed with an overdose of anaesthetic.

In a few animals the stenosed kidney was removed by cutting across the pedicle; it was fixed in normal saline, and sections were examined under the microscope.

The protein content of the urine was estimated by the Lowry method. The final results were expressed as µg of protein excreted/min. In a few cases agarose gel (0.5%) electrophoresis of both serum and urine was performed using Veronal buffer (pH 8.6, 0.05 M). After the electrophoresis the agarose strips were fixed with methanol, water and glacial acetic acid (vol. 5:5:1), stained with 2% Coomassie blue and scanned with a Kipp-Zonen densitometer.

RESULTS

Blood pressure and PRA

Two weeks after the application of the clip the blood pressure of all animals was significantly higher than that measured in the controls, with little difference between the three groups (tab. 1). A constant and significant fall in arterial pressure