THE EFFECTS OF CADMIUM AND ADRIAMYCIN ON THE ISOLATED PERFUSED GLOMERULUS
OF MYXINE GLUTINOSA (CYCLOSTOMATA)

L.M. Fels\textsuperscript{1,3}, M.-M. Barbey\textsuperscript{1,3}, B. Elger\textsuperscript{1,3}, J. Abel\textsuperscript{2}, and H. Stolte\textsuperscript{1,3}

Division of Nephrology, Hannover Medical School, 3000 Hannover 61 FRG\textsuperscript{1}, Medical Institute for Environment Hygiene, 4000 Dusseldorf, FRG\textsuperscript{2} and Mount Desert Island Biological Laboratory, Salsbury Cove, Maine 04672, USA\textsuperscript{3}

INTRODUCTION

The severity and mechanisms of action of environmental and drug nephrotoxicity needs to be evaluated. While impaired renal function has often been based on chronic exposure studies, little attention has been paid to acute effects, especially renal dysfunction that occurs shortly after exposure to heavy metals or drugs. It may be difficult to define such changes in the whole animal, but in vitro techniques offer a simpler solution to assessing such changes.

Hagfish (Myxine glutinosa, Cyclostomata), are vertebrates with a kidney that consists of about 70 segmentally arranged glomeruli which are drained over a short neck segment directly into two parallel collecting ducts archinephric ducts. Because of this arrangement plus a morphology and fine structure that is similar to those of higher vertebrates (6,7), the animal lends itself to studies of glomerular processes.

The model of the isolated perfused single glomerulus (IPSG) of Myxine glutinosa has already been applied to study the effects of vasoactive substances (catecholamines) on single glomeruli (1). The technique can also be applied to study the acute effects of toxic substances on the glomerular apparatus. The IPSG allows the study of a variety of renal parameters, among which are changes of permeability for serum proteins, of charge of filtration barrier, and of the filtration coefficient.

The distribution of cadmium in the body, the uptake into the tissue, and the effects of a single injection of CdCl\textsubscript{2} on glomerular protein permeability were investigated to study the acute effect of cadmium. An increased excretion of proteins after cadmium treatment is usually attributed to tubular dysfunction (tubular-interstitial nephrosis). Low level cadmium exposure in rats causes profound histopathological changes not only at the tubular, but also at the glomerular level (2). The glomeruli showed fusion and withdrawal of epithelial foot processes and a thickening of the capillary endothelium. An increased cellular appearance and swelling of some glomeruli was caused by glomerular fibrosis and cell hypertrophy. In combination with these morphological changes, an increased urinary excretion of high molecular weight proteins (HMW) has been observed.
The effects of adriamycin (ADR) has also been assessed on the IPSG based on the fact that this anti tumour drug cause glomerular damages (increased protein permeability and reduced glomerular filtration rate) 5 days after 7.5 mg/kg in rats (3,4). Preliminary experiments have shown that the sieving coefficient for albumin in the model of the ISPG is unaltered 10 days after the injection of ADR. The involvement of reactive oxygen radicals, generated by ADR semiquinone radicals, is suggested to damage the cells (5). It was therefore investigated whether ADR alters protein permeability and whether it affects filtration rate (SNGFR) under conditions with a high oxygen pressure.

METHODS

A double barrelled perfusion cannula was inserted into the dorsal aorta and catheters in the archinephric duct using a pressure controlled microperfusion of single isolated glomeruli based on the method described (1) and shown below (Fig. 1). Perfusate was a hagfish Ringer's solution (8) containing 0.75% bovine serum albumin (BSA, MW 69,000). Perfusion pressure was held within a physiological range of 6 to 12 mm Hg.

Fig. 1 Arrangements of glomerulus, perfusion cannula and catheters for in vitro perfusion of single isolated glomeruli of Myxine glutinosa.

Cadmium. The animals were given a single injection of Cd at concentrations of 1 mg/kg (group 1) or 10 mg/kg (group 2) into the caudal blood sinus seven days prior to the experiments. A third group served as control. Cd concentrations in plasma and tissue were determined with an atomic absorption spectrophotometer.

Adriamycin. After the injection of ADR (5 mg/kg into the caudal blood sinus) the experimental animals were exposed to an artificial atmosphere of 80% O₂/20% N₂ for 48 hr and kept under normal O₂ conditions for further 8 days. Controls received O₂ in a corresponding manner. Single nephron glomerular filtration rate was calculated from the advance of fluid in the catheter and gravimetric measurement of the volume of the catheter. Analysis of albumin in perfusate and filtrate was undertaken using immunoelectrophoresis at pH 8.6 on 1% agarose gels (Gelbond Film, LKB, containing antibody from the rabbit, Dakopatts Hamburg) according to Laurell (9). Values are given as mean±S.D.