A Reversal of the Anuria Occurring During Diffusion Respiration. (21307)

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Although the term, "neurogenic anuria" is frequently used in clinical literature to describe the onset of acute renal dysfunction, it is generally difficult to produce experimentally such anurias in normotensive, non-traumatized, well hydrated animals. Draper and Whitehead have described a rapidly developing anuria, the onset of which roughly parallels the onset of respiratory arrest resulting from overdoses of injection anesthetics(1-3). This anuria could be largely reversed by the "pharmacological" denervation of the kidney, and hence appears to be neurogenic in nature. Although the mechanisms of such anuria may well lend insight into the general nature of acute renal dysfunction (of neurogenic and other origins) little is as yet known as to why it occurs. This lack of knowledge is largely due to the difficulty of studying renal function when urine formation is markedly suppressed. Work done by the authors has demonstrated that the anuria occurring during diffusion respiration can be reversed by the use of an osmotic diuretic. This work is presented in the succeeding paragraphs.

Methods and materials. Thirty adult mongrel dogs of both sexes and varying weights were anesthetized with 20 mg/kg of body weight of thiopental sodium. Oxygen was administered endotracheally throughout the experiment, and all animals were denitrogenated one hour prior to the onset of diffusion respiration. Respiratory excursions were recorded by means of a tambour-lever system. Carotid blood pressures were recorded kymographically by means of a mercury manometer. Two drop counting devices consisting of a secondary relay circuit activating a signal magnet when a drop of urine formed across a break in the primary circuit were employed for counting urine drops. Each ureter was cannulated individually. The animals were divided into 3 groups of 10 each. The first group of 10 animals received approximately 15 ml/kg of body weight of isotonic saline intravenously throughout the experiment. Isotonic saline was administered in a similar fashion to a second group, but was replaced with isotonic mannitol following 20 minutes of diffusion respiration. The third group of animals received isotonic mannitol throughout the experiment. Following a control period during which blood pressure, urine formation and respiratory activity were recorded, diffusion respiration was initiated by slowly administering a quantity of thiopental sodium just adequate to suspend respiration. Small doses of thiopental sodium were administered periodically to maintain the respiratory arrest.

Results. Following the onset of diffusion respiration, a profound oliguria or total anuria resulted in all animals receiving normal saline. A similar trend toward anuria resulted during diffusion respiration in the second group of

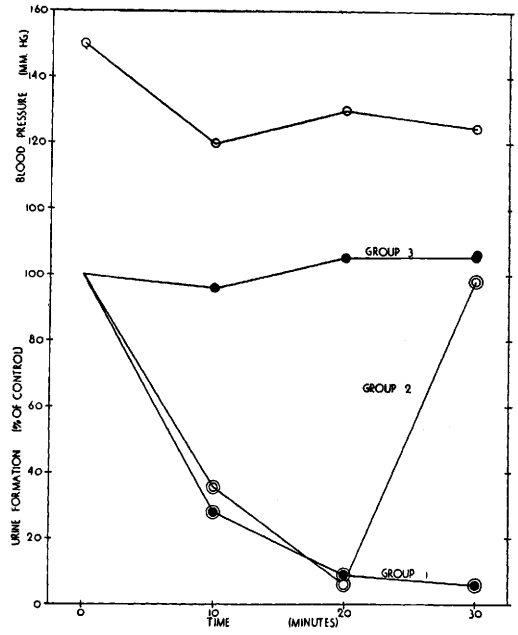

FIG. 1. Average response of urine formation to respiratory depression. Zero time represents onset of diffusion respiration. Group 1 received saline throughout experiment; group 2 received saline replaced by mannitol following 20 min. of respiratory arrest. Group 3 received mannitol throughout.

animals. This trend could be completely reversed in some animals and partially reversed in the remainder of the group by administration of mannitol. The group, receiving mannitol throughout the experiment (Group 3), maintained urine volumes, which in most instances closely approximated the control urine volumes throughout the period of diffusion respiration. Results of these experiments are shown in Fig. 1.

Discussion. One of the more recent and more promising methods for producing acute renal dysfunction in experimental animals is the technic described by Draper and Whitehead(1-3). However, little study has been given to the mechanisms involved in its development. The present work lends some insight into the development of this type of anuria, since the production of urine, even with a diuretic, would have been impossible if some glomerular filtration had not occurred. However, more important than this small insight into the mechanisms of this type of renal dysfunction is the fact that this anuria may prove a valuable tool for probing the role of neurogenic as well as other factors in acute renal dysfunction, and that the ability to reverse it with an osmotic diuretic may prove equally valuable as a means of facilitating such investigations.

Summary. Dogs, well hydrated with saline became anuric or oliguric when their respiration was suspended with overdoses of thiopental sodium. This anuria could either be reversed by administration of an isotonic mannitol solution, or did not occur when mannitol was administered throughout the experiment. The ability to reverse an experimental anuria with an osmotic diuretic presents a potentially valuable tool for the study of this type of renal dysfunction.

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"Collagenase" Activity of Cathepsins.* (21308)

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Collagen is a rather unique protein since it is not digested at neutral pH by any of the common proteinases. Its turnover rate in the normal adult mammalian organism is exceedingly slow(1) and little is known about the enzymes or mechanisms concerned with its synthesis or degradation. The only conclusively demonstrated collagenases have been described in culture filtrates of *Clostridium perfringens* and *C. histolyticum*(2). In the course of studies on collagenase activity, it was observed that the plant cathepsins, papain and ficin, and animal cathepsins were able to digest collagen by a mechanism differing from that of the bacterial collagenases, and involving a preliminary reversible alteration in the state of the substrate. It is the purpose of this report to describe these studies.

Methods. Collagenase activity was measured by the soluble nitrogen or soluble hydroxyproline peptides released from a weighed portion of purified Achilles tendon and is expressed in terms of percent digestion. Fifty mg of dried tendon was suspended in 4 ml of a buffer-enzyme mixture (3:1) and incubated for 3 hours at 37° C. After incubation, 5 ml of 10% NaCl was added and the mixture filtered. Kjeldahl analyses for nitrogen were performed on 1 ml aliquots of the filtrate. The percent digestion was calculated from the

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