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The influence of experimental ascites on the diuretic action of drugs.

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In a brief series of experiments[1] it was found that experimental ascites in dogs diminished or suppressed urine flow, apparently because of a simultaneous rise in pressure within the renal vein. The influence of similar procedures on the action of diuretic drugs has been investigated in 15 anesthetized dogs, with the uniform result that small doses of saline or xanthine diuretics were unable to cause diuresis until abdominal pressure was lowered. Larger doses of salines were usually effective against a suppressing abdominal pressure, while the xanthines were ineffective in any dose. Sodium sulfate was more effective than sodium chloride or bicarbonate.

The method seemed to be applicable to estimating the relative efficiency of diuretic drugs in the presence of a controllable degree of venous engorgement in the kidney, provided that the effects of experimental ascites on urine flow are due only to high pressure in the renal vein. By a perfusion experiment, using citrated blood, in which the kidney, its vessels, and the ureters were subjected to external hydrostatic pressure, it was found that an external pressure of 27.7 mm. of mercury caused suppression of urine when the renal vein was exposed to the pressure, but when the renal vein was protected from collapse by a glass catheter an external pressure of even 69 mm. had only slight effect on urine flow. It was clear that the phenomenon under observation was due largely, if not wholly, to the rise in venous pressure.

To estimate the relative efficiency of the drugs, the salines were injected in M/7 solution with an abdominal pressure just sufficient to suppress urine, the criteria being the extent of diuresis and the additional abdominal pressure required to suppress urine after the drug. Sodium phosphate, sulfate, nitrate, bicarbonate, chloride, and acetate, as well as urea and glucose, were compared,

[1] Thorington, J. M., and Schmidt, C. F., *Am. J. Med. Sci.*, 1923, clxv, 880.

and caffeine, theobromine, and theophylline were also tried. Pituitary extract and digitalis failed to cause diuresis.

The results indicated that phosphate, sulfate and urea were by far the most effective; nitrate was intermediate; glucose and bicarbonate were weaker, but stronger than chloride; acetate was the weakest saline.

Any saline could bring out urine against a suppressing abdominal pressure, while equal or larger volumes of distilled water could not. The xanthines were all ineffective in any dose against high abdominal pressure, though definitely diuretic with lower pressure. Large doses of theocine usually caused permanent suppression of urine, caffeine was less harmful, and theobromine usually harmless, though none was effective until abdominal pressure was reduced.

These differences in degree of effectiveness seem to depend on the fact that the most effective drugs—phosphate, sulfate, urea—are non-threshold salines, and would therefore raise pressure in the tubules more than the other salines which are more readily reabsorbed. Any saline decreases the osmotic resistance to filtration or secretion, as pointed out by Cushny[2] and can therefore raise tubular pressure if enough is given to compensate for rapidity of reabsorption. Richards and Schmidt[3] found that any diuretic brought into play more functional units in the frog's kidney. It seems probable that this is the only effect of the xanthines; salines have a similar effect and in addition decrease osmotic resistance to secretion; the non-threshold salines also decrease reabsorption from the tubules and are therefore most effective in the presence of venous engorgement.

The lack of diuresis and the possibility of suppression of urine by large doses of xanthines when abdominal pressure is high indicates that these drugs should not be given in ascites until pressure has been reduced by paracentesis.

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[2] Cushny, A. R., *The Secretion of the Urine*, London, 1917, p. 121.

[3] Richards, A. N., and Schmidt, C. F., *Am. J. Physiol.*, 1922, lix, 489.