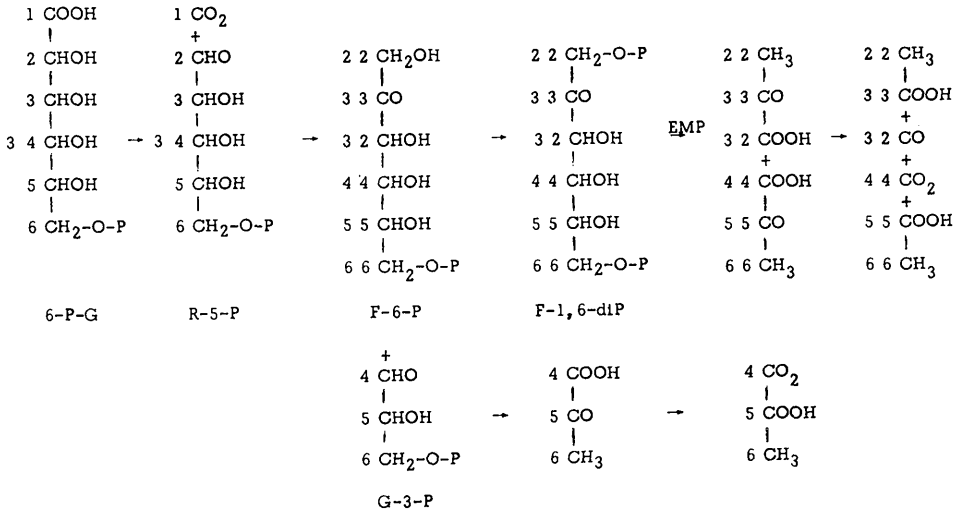

FIG. 4. Catabolic mechanism for utilization of gluconate by rat. 6-P-G = 6-phosphogluconate, R-5-P = ribose-5-phosphate, F-6-P = fructose-6-phosphate, F-1, 6-diP = fructose-1, 6-diphosphate, G-3-P = glyceraldehyde-3-phosphate.

carboxylation, therefore, appear to be minor pathways which may account for utilization of less than half of the administered glucose.

Summary. When glucose is administered to intact rats *per os*, it is catabolized mainly by way of the EMP pathway. Some of the administered glucose was also routed into the phosphogluconate decarboxylation and glucuronate decarboxylation pathways. Gluconate can be readily utilized by intact rats *via* the phosphogluconate decarboxylation pathway. The pentose phosphate so formed is believed to be converted to F-6-P which in turn is further catabolized primarily by way of the EMP route.

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Effect of Pyrogens on Urine Tonicity and Renal Papillary Sodium Concentration in the Rat.* (27714)

I. J. VOUDOUKIS AND J. L. BRANDT
Renal Laboratory, Department of Medicine, Jewish General Hospital, Montreal, Canada

Large intravenous doses of a pyrogen to the dog results in a diuresis which is associated with an increased solute excretion, a fall in urine osmolality, and is uniformly associated with a rise in total renal blood flow(1,2). In the dog, the fall in urine osmolality (and refractoriness to ADH) has been related to a

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decreased concentration of medullary tissue sodium incident upon a presumed increased medullary blood flow during the renal hyperemia induced by pyrogens. In the framework of a counter-current system, decreased urine concentration of a pyrogen diuresis would reasonably relate the rise in total renal blood flow to a decreased efficiency of the counter current diffusion exchanger.

The renal effects of large doses of pyrogen noted above have never been studied in the rat. The present experiments were undertaken to determine whether large doses of a pyrogen cause a consistent fall in urine osmolality and whether this is associated with a fall in renal papillary sodium concentration.

Materials and methods. Seven groups of 12 rats each, weighing 200-300 g, were studied under *ad lib.* hydration and feeding conditions. Six rats were given 0.5 cc saline and the other six 0.5 cc saline containing 5γ pyrogen.† All material was given *via* the tail vein. The rats were placed in metabolic cages and urines collected over the next 5 hours. One week later (day 8) an identical procedure was carried out except that this time the 6 rats which had received pyrogen now received the saline injection and the 6 which had received saline received the pyrogen. Two weeks later (3 weeks from the start of experiment) 3 rats were randomly selected from each of the 2 original groups of 6 and given 0.5 cc saline I.V. The remaining 6 rats were given 0.5 cc saline containing 5γ of pyrogen. One hour later the rats were rapidly sacrificed, the kidneys quickly removed, and the papilla excised. The papillae from the rats which finally received saline were kept in one tared beaker and those which finally received pyrogen in another. For the 7 groups of rats there were thus 84 urine collections for Uosm after pyrogen and 84 following saline. Finally, there were 84 renal papillae each from rats which either received saline or pyrogen one hour prior to sacrifice.

Following harvesting of all papillae (control and pyrogen) the contents of each beaker was brought to constant dry weight and digested overnight in equal parts of concentrated nitric and sulfuric acid. The sodium content of the digest was determined by flame photometer and the data expressed as sodium concentration per gram wet weight of papilla using the data of Manitius, *et al.*(3) for the water content of rat papillae. Urine osmolalities were determined cryoscopically with the Fiske Osmometer.

† Piromen—An extract of *Pseudomonas aeruginosa* kindly supplied by Baxter Laboratories, Morton Grove, Ill.

TABLE I

	Urine osmolality—Mosm/kg H_2O	
Group*	Saline control	Saline + pyrogen
1	1744†	1313†
	1644	1123
2	2310	1198
	997	826
3	2635	1417
	1636	1235
4	2322	1809
	1477	1149
5	1392	1041
	1346	785
6	1004	876
	1456	1338
7	2243	1438
	1573	1206
Mean	1698	1196
P value	>.001	

* Each group consists of 12 rats (see *Methods*).
† Each figure represents avg Uosm for 6 rats; figures for each line, data obtained on the same day and under identical levels of hydration.

Results. Table I shows the data for the 7 groups of rats. The mean Uosm for the 7 groups which received saline was 1698 Mosm/kg H_2O and for those which received saline plus pyrogen 1196 Mosm/kg H_2O. The p value for the difference between the means was highly significant at less than 0.001.

Analysis of the 84 pooled papillae of the rats which received saline just prior to sacrifice showed the sodium content to be 248 meq sodium per gram wet weight and those which received pyrogen prior to sacrifice 187 meq sodium per gram wet weight. It is of interest that the mean Uosm of the rats which received pyrogen was 29.5% lower than the control and the papillary sodium content of the rats which received pyrogen 24.6% lower than the correspondingly harvested control papillae.

Discussion. According to the counter current hypothesis final concentration of urine for a normal kidney is determined by a counter current multiplier mechanism operative in the loops of Henle, a counter current diffusion exchanger which is dependent upon blood flow in the vascular loops of the vasa recta and the level of ADH. With minor modification ample confirmation of the validity of the counter current mechanism has been forthcoming from direct micropuncture studies(4-8).

It has been shown previously in dogs(1,2) that 60-90 minutes following intravenous administration of pyrogen an increased total renal blood flow develops. In a counter current system the efficiency of the exchanger is inversely related to the rate and volume of renal medullary blood flow. Increased medullary flow through the vasa recta would "rinse away" interstitial sodium deposited by the counter current multiplier. A reduced osmotic gradient between the interstitium and collecting ducts would make for less efficient movement of water toward interstitium even in the presence of increased epithelial permeability in the collecting ducts induced by ADH. Such a reduction would result in a low $Tc H_2O$ and diuresis(1).

Our present study in rats is similar to those in the dog as regards the effect of a pyrogen on urine tonicity and medullary tissue sodium concentration(9). The findings reported herein are also best explained on the basis of a reduced medullary interstitial to tubule osmotic gradient making movement of solute free water out of the tubule less efficient. No good method is available for measuring medullary blood flow. It is presumed that the increased total renal blood flow induced by pyrogen is probably significantly medullary and thus causes a disruption of the efficiency of the counter current diffusion exchanger with resultant decreased urine tonicity and medullary tissue sodium concentration.

Summary. 1. A series of 7 groups of rats (12 per group) were studied using alternating subgroups of 6 each. Urine osmolality and papillary sodium concentration was determined after intravenous injection of saline and after saline plus pyrogen. 2. There was a highly significant fall in urine osmolality in rats which received saline plus pyrogen as compared to their saline controls. Similarly, renal papillae from rats which received pyrogen had a lower sodium concentration than the corresponding saline controls. 3. The data are best explained in terms of a counter current system relating the renal hyperemia of pyrogen administration to disruption of a counter-current diffusion exchanger.

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