Effect of Hypophysectomy and Adrenalectomy in Nucleoside-Induced Nephrosis in the Rat. (25097)

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The effectiveness of aminonucleoside of puromycin* in production of a nephrotic-like syndrome in rats, has been reported and details(1,2,3) and timing of the syndrome have been well described. Experiments reported here were undertaken less from the point of view of the clinical syndrome than the effects observable in renal tissues. The criteria adopted, therefore, were those conventionally employed in examination of stained sections. Our purpose was to compare tolerance of rat kidney to nucleoside-induced nephrosis under 3 conditions: 1) in intact animal, 2) in hypophysectomized and 3) in adrenalectomized animal. Immature rats of Sprague-Dawley strain were used. Group I consisted of rats purchased hypophysectomized; Group II were left intact and Group III were adrenalectomized in our laboratory. Each of the latter group received Meticortelone,* 5 mg subcutaneously, at time of surgery. No further hormone replacement was given in any group. All animals were given complete rations, ground. Groups I and II were given tap water; Group III was given 0.9% saline. Aminonucleoside was administered in doses of .01 mg/g body weight by subcutaneous route, for 10 days. All were sacrificed 48 hours after end of the course. Kidney slices were made immediately; all autopsy material was fixed in usual manner, in 10% formalin.

Observations. All animals had clinically detectable ascites by the 8th day. All had massive proteinuria. Group III showed far more interstitial edema than did Group I and Group II, and the large amounts of fluid contained in the peritoneal and pleural cavities had a fibrinous appearance in Group III which was not noted in the other groups. Ascitic fluid was taken wherever feasible, upon which determinations of sodium and of creatinine were made. These data were noncontributory.

Observations made on stained sections were in general agreement with those already published, in the case of Group II. Here, architecture of the kidney was disrupted by patchy areas of recent interstitial fibrosis and edema, and by many dilated distal tubules filled with hyaline casts, such casts being particularly prominent in the collecting ducts. Few changes were noted in the glomeruli. A large amount of amorphous material, presumably protein precipitate, was visible in tubules at all levels. Fragmentation of cytoplasm and sloughing of tubular epithelium were notable, particularly around the casts.

In adrenalectomized animals (Group III), these changes were considerably less marked.

In hypophysectomized animals (Group I), renal elements were normal.

Variations in concentrations of sodium and creatinine could hardly be considered significant, in the limited number of specimens comprising this pilot study.

Conclusions. Experimental nephrosis induced in hypophysectomized immature rat is clinically similar to the syndrome seen in the

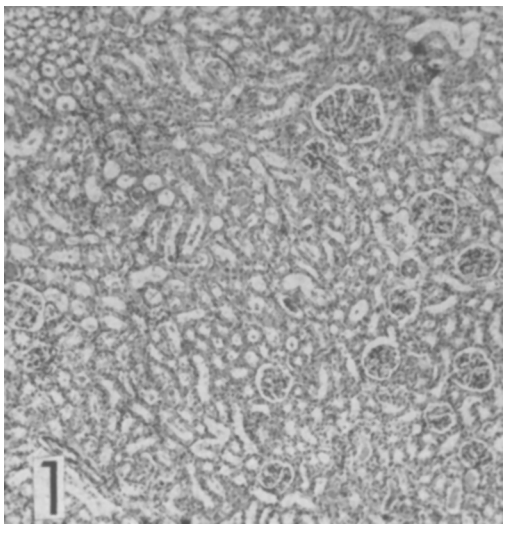

FIG. 1. Kidney from hypophysectomized rat. H & E × 73.

* Kindly supplied by Lederle Labs.

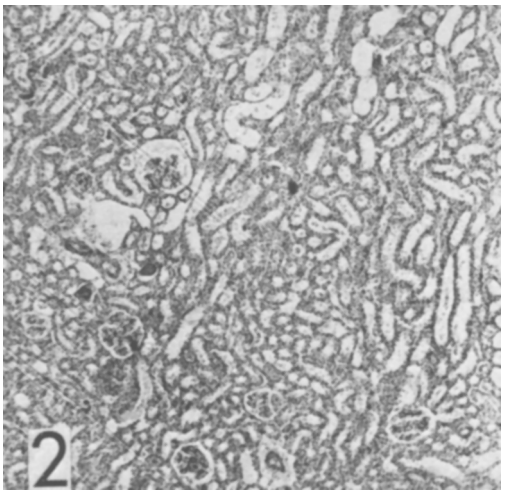

FIG. 2. Kidney from intact rat. H & E × 55.

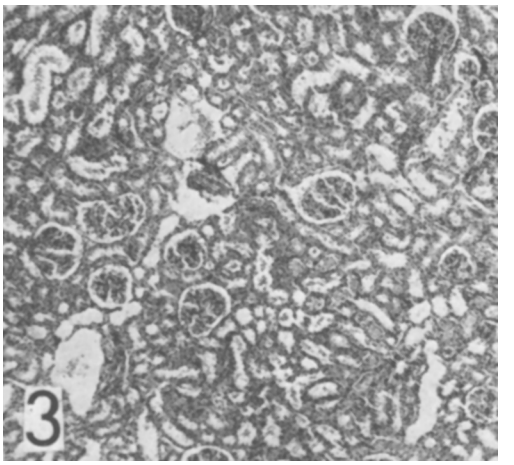

FIG. 3. Kidney from adrenalectomized rat. H & E × 55.

intact animal. Evidences of renal damage in intact animals, however, were not present in these which had previously undergone hypophysectomy. Pathological changes which occurred in kidneys of the adrenalectomized group were similar to those described in normal rats, but less severe. Whether for direct or indirect reasons absence of functioning hypophysis was associated with tolerance of renal tissue toward aminonucleoside even though the nephrotic syndrome was clinically similar.

Summary. Nephrosis was induced in immature rats by subcutaneous administration of aminonucleoside. Subjects were divided in 3 groups: I, hypophysectomized, II, intact and III, adrenalectomized. All 3 groups developed proteinuria and ascites. Examination of stained sections, however, showed that kidneys of intact rats had undergone marked deterioration. Pathological changes were less marked in the adrenalectomized group, and absent in the hypophysectomized group.

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Significance of Nystatin Uptake for Its Antifungal Action. (25098)

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Nystatin, a polyene antifungal agent produced by *Streptomyces noursei*(1), inhibits growth and utilization of various substrates by fungi, especially yeasts(2). It was previously observed(3) that nystatin is removed from solution by organisms whose growth is sensitive to its action, but not by insensitive organisms. The properties of this uptake appeared to correlate with available information both on specificity of nystatin and on its fungicidal and metabolism-inhibiting actions. It was suggested, therefore, that this uptake is essential for nystatin action and is a critical factor in determining sensitivity. To evalu-