specific. The *nature of the soluble material* extracted from group A streptococcal skin lesions which is responsible for preparing animals for the generalized Shwartzman reaction is being investigated. The precise relationship of this product and the provoking factor in the reduced culture filtrate to the generalized Shwartzman reaction is under study.

Summary. A soluble factor from group A streptococcal skin lesions prepared American Dutch rabbits for the generalized Shwartzman reaction. The reaction can be provoked in rabbits prepared with this material not only with toxins from Gram-negative organisms but also by reduced filtrates of streptococcal cultures with a high streptolysin O content. The tissue changes associated with the reaction brought about with these materials include myocardial necrosis and cortical necrosis of the kidney. Although these reactions simulate those observed in the classical generalized Shwartzman reaction, points at difference are discussed. It was possible to immunize rabbits against the preparative activity of the soluble factor by repeated injections of the streptococcal skin lesion extract.

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Renal Function During Viomycin* Administration to Dogs. (20238)

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An intermittent dosage schedule for administering Viomycin (2 g twice a week) to patients with pulmonary tuberculosis, proved to be free of nephrotoxicity(1). It is not apparent whether this absence of toxicity is due to administering the antibiotic intermittently or due to smaller doses than those employed in the original studies when nephrotoxicity(2,3) was observed. Therefore, before giving larger doses of Viomycin to patients, a preliminary study of nephrotoxicity and electrolyte disturbances using larger daily doses (15 to 60 mg/kg/day) in dogs seemed indicated. The purpose of the present communication is to report these observations.

Methods. Six female dogs were studied. The dogs were observed for a control period of two weeks during which time renal function (clearance) and electrolyte (plasma) studies were completed. Then they were placed on a Viomycin regimen receiving one-half the daily dose intramuscularly in the morning and one-half in the evening. Three of the dogs received a dose of 15 mg/kg for 3 months which was then increased to 30 mg/kg for an additional 3 months. Three of the dogs were started on 30 mg/kg. After 3 months this was increased to 60 mg/kg which they received for an additional 3 months. After the drug was started, renal function studies were repeated once a month as long as Viomycin was being administered. The dogs were weighed daily throughout the study. Creatinine was used to measure glomerular filtration rate, p-aminohippurate (PAH) for renal

* Supplied through the courtesy of Parke-Davis and Co.

TABLE I. Effect of Viomycin on Renal Function in 6 Dogs.

	Dose, mg/kg		Wt, kg			GFR			RPF			TmG		GFR/TmG		RBF		
	D_1	D_2	C	D_1	D_2	C	D_1	D_2	C	D_1	D_2	C	D_2	C	D_2	C	D_1	D_2
	15	30	11.9	13.5	14.9	29	30	33	113	104	91	110	116	.26	.28	177	186	175
	15	30	9.9	10.5	11.3	25	31	30	100	102	84	81	80	.31	.38	167	179	156
	15	30	9.5	9.2	9.1	25	24	23	65	60	62	64	70	.39	.33	81	71	72
	30	60	10.6	11.9	12.5	26	29	30	94	113	68	81	76	.32	.39	159	182	97
	30	60	10.0	10.7	10.0	28	27	32	74	67	69	82	91	.34	.35	119	120	105
	30	60	11.4	11.1	11.6	28	33	40	84	122	115	106	105	.26	.38	153	298	205
Mean	23	45	10.6	11.2	11.6	27	29	31	88	95	82	87	90	.31	.35	143	173	135

C, control; D_1, after receiving Viomycin for 3 mo; D_2, after receiving Viomycin for 6 mo; GFR, glomerular filtration rate in ml/min.; RPF, renal plasma flow in ml/min.; TmG, maximum tubular reabsorption of glucose in mg/min.; RBF, renal blood flow, $\frac{\text{RPF}}{\text{1-Hct.}}$

TABLE II. Effect of Viomycin on Electrolytes and Hematocrit, in 6 Dogs.

	Serum Na*			Serum K*			Na exc.†			K exc.†			Hematocrit		
	C	D_1	D_2	C	D_1	D_2	C	D_1	D_2	C	D_1	D_2	C	D_1	D_2
	135	138	131	3.5	3.3	3.6	.06	.22	.09	.10	.03	.08	36	44	48
	133	139	141	2.7	3.4	3.8	.24	.34	.40	.09	.02	.03	40	43	46
	133	138	135	2.7	3.5	3.1	.09	.21	.05	.07	.04	.07	20	16	14
	136	142	140	3.5	3.4	4.1	.13	.44	.16	.17	.19	.16	41	38	30
	137	144	137	3.0	3.3	3.9	.13	.20	.36	.04	.02	.06	38	44	34
	133	143	141	3.1	2.7	3.4	.07	.65	.76	.02	.17	.23	45	59	44
Mean	135	141	138	3.1	3.3	3.7	.12	.34	.30	.08	.08	.11	37	41	36

C, control; D_1, after receiving Viomycin for 3 mo (see Table I); D_2, after receiving Viomycin for 6 mo.

* mEq/liter. † mEq excreted in urine/min.

plasma flow and dextrose for the maximum reabsorptive capacity of the renal tubules (TmG). The latter determination allowed an evaluation of renal tubular damage. Mean blood pressure was measured by a manometer connected to an indwelling arterial needle. Arterial blood was used for chemical analysis. Serum sodium and potassium concentrations were determined once a month throughout the study. A Beckman flame photometer was used for these analyses. Except for minor modifications, the techniques used have previously been described (4).

Results. The observations on renal function are presented in Table I. There was some variation in glomerular filtration rate and renal blood flow from month to month but this was inconstant and represents normal variation, even while receiving doses as large as 60 mg/kg for 3 months. Three of the dogs actually gained weight during the study.

Viomycin seemed to have very little effect on serum electrolytes. There appeared to be a slight increase in sodium excretion. However, this may have been due to altered sodium intake since it was not increased significantly after the first 3 months of treatment despite the increase in the amount of Viomycin being administered.

Discussion. The freedom from nephrotoxicity in this group of dogs who were being given large daily doses of Viomycin suggests that Viomycin in current use may not be as toxic to the kidney as the earlier studies would indicate provided, of course, that patients are not more sensitive to the antibiotic than are dogs. Although 60 mg/kg may not be a large dose for a dog, this amount of drug given to a 70 kg man would amount to 4.2 g per day. The relatively normal plasma electrolytes during the study while the animals were receiving Viomycin further suggests that the drug does not affect the kidney adversely, particularly the tubular reabsorptive mechanism.

Summary. Daily doses of 15-60 mg/kg of Viomycin administered for a period of 6 months did not appear to produce any evidence of renal toxicity as estimated by renal

function studies (clearances). There were no serious alterations of the concentrations of serum sodium and potassium. These data suggest that the renal toxicity and altered electrolyte metabolism associated with Viomycin therapy may not be as serious as the earlier observations indicated. Therefore, we believe that further use of Viomycin with careful observations for signs of renal toxicity is indicated, particularly in patients unresponsive to the other more effective therapeutic approaches.

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Regeneration of Lens and Retina in Thyroidectomized and Hypophysectomized Adult Newt (*Triturus v. viridescens*).* (20239)

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The senior author(1-4) has been making an experimental study of factors affecting the release and inhibition of lens regeneration from the dorsal iris in adult eyes of the newt, *Triturus v. viridescens*. It has recently been reported by Hall and Schotté(5) that hypophysectomy, and by Richardson(6,7) that thyroidectomy and hypophysectomy markedly affect regeneration of the limb of the newt. In view of this it became essential to know what effect, if any, the removal of these endocrine glands might have on the regeneration of the lens from the dorsal iris as well as the neural retina pigment cells(8) in the newt. Already Nikitenko(9) has claimed that hypophysectomy in adult newts (species?) had no direct effect upon lens regeneration, and Lenhard(10) reported that the lens could regenerate normally in thyroidectomized adult *Triturus cristatus*, although the results were not consistent.

In the present experiments one group of adult newts was hypophysectomized, another was thyroidectomized, and in another both the hypophysis and the thyroids were excised. Four to 8 days later the lens was removed from the right eyes and both the lens and the neural retina were removed from the left eyes. Many animals did not survive the duration of the experiments. Therefore the results here are based on a study of a total of 173 eyes (81 in the first group, 48 in the second and 44 in the third) in animals sacrificed at frequent intervals from 2-43 days after the eye operations. In many specimens in each group the right eyes were later excised in alcohol and cut along the equator to separate the anterior half for gross examination of the relations of the regenerating lens to the iris. These were later prepared in serial sections as were all other eyes. Also serial sections of all heads and jaws were studied to detect whether or not all the thyroid and pituitary tissue had been removed. Similar gross and histological preparations, fixed at frequent intervals from 2-60 days after operation, were examined as normal controls in 178 eyes from which only the lens was removed in order to determine in eyes with intact retina the average, as well as the individual variations, in the rate of lens regeneration and

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