action of PVP is poor, but in either albumin or PVP medium the sensitivity is good. The alternate simple technic given in Section 3 of the Table appears to give excellent results and avoids the cumbersome washing and incubation which is necessary in the indirect Coomb's test.

Although our case studies of sensitized mothers and infants carrying anti Rh antibodies is incomplete, the indication is that PVP detects these antibodies in rather high dilution even though albumin technics are negative or weakly positive. In addition, we have revealed an abnormal antibody to be present in the serum of a young woman who has been clinically diagnosed as lupus erythematosus. PVP revealed this antibody in equal titer to anti-human globulin, whereas saline and albumin titrations were completely negative. A similar case is reported by Callender(7). It appears that polyvinylpyrrilodone offers a simple, economical and sensitive method of Rh antibody detection.

Summary. (1) Using the indirect Coomb's technic we have found that 10% PVP offers results comparable to anti-human globulin when dilutions are carried out in albumin or PVP. (2) An alternate rapid PVP tube test (of equal sensitivity to antihuman globulin) is described. (3) In certain "collagen" or hypersensitivity diseases, PVP may detect an agglutinating antibody on homologous erythrocytes.

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Effects of X Irradiation on Renal Function in Newly-Hatched Chicks. (19179)

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The effects of X irradiation on young birds is dependent on dose rate as well as on total dose(1,2). Chicks and ducklings given 1000 r within a period of 30 minutes showed 75 to 80% mortality in the initial period (24 to 48 hours) after irradiation. When the same total dose was delivered over a 3-hour period, few deaths occurred until 5 to 7 days after exposure. Birds that died in the initial period showed necrosis of the renal tubules and accumulation of urate crystals in and around the tubules. A few individuals showed a urate polyserositis, in which a thin layer of urate crystals covered all serous membranes. Uric acid is the principal end product of protein metabolism in birds, and its precipitation throughout the body indicated a rapidly developing azotemia. This condition may be assumed to result either from renal failure or from an increased rate of nitrogen metabolism without a corresponding increase in excretion. The experiments reported here were concerned with the effects of X irradiation on renal function in the newly-hatched chick, as determined by estimations of blood urate levels and excretion of uric acid and phenol red.

Materials. White leghorn chicks, weighing 35 to 45 g, were treated 2 to 4 days after hatching. The irradiation dose was 1000 r, delivered at 6 r or at 43 r per minute. The conditions of irradiation were: 200 kv, 15 ma, 0.5 mm Cu and 3.0 mm Bakelite filters. Variation in dose rate was obtained by vary-

TABLE I. Effect of X Irradiation on Excretion of Uric Acid in Newly-Hatched Chicks.

	Control	1000 r X radiation		
Exposure	—	6 r/min or 43 r/min*	43 r/min	
No. animals	10	6	5	11
Survival after X ray (hr)	—	24	5–6	3–4
Time after X ray (hr)	mg uric acid			
0-1	5.88	6.74	5.34	3.79
1-2	4.46	4.31	2.91	.67
2-3	4.72	5.66	1.65	.21
3-4	4.17	4.06	.38	.08
4-5	3.88	5.76	.02	
5-6	—	—	0	
5-24	117.8	150.2		
Mean (mg/hr)	5.59	7.43		

* Excretion of 24 hr survivors not influenced by exposure rate.

ing the target field distance. Blood urate determinations were made on heart blood, using the method described by Brown(3). For estimations of rate of urate excretion, accumulated material was removed from the cloaca at intervals of 0.5 hour or more and the quantity of uric acid present was determined colorimetrically. The amount of phenol red in excreta was estimated at the same intervals for 2 hours after intraperitoneal injection of 0.2 mg of the dye. All quantitative determinations were made photoelectrically.

Results. Determinations of blood urate were made at 0.5, 1, 3, and 5 hours after irradiation. At 1 hour after irradiation, the mean blood urate in 15 animals (10.8 mg %) did not differ from the mean established in 26 control animals (8.2 mg %). A marked increase (27.1 mg %, 17 animals) occurred at 3 hours after exposure at 43 r/min and a further increase (33.0 mg %, 17 animals) at 5 hours. Values were still higher (60.0 mg %) in six animals moribund at 3 to 5 hours. After exposure at 6 r/min, only a small increase (10.2 and 18.8 mg %) occurred at 3 and 5 hours. Visible precipitated urates in the kidneys were present in all animals that had high blood urate levels.

Table I shows urate excretion in control and in irradiated chicks, grouped according to survival time after exposure. Following irradiation, urate excretion continued at a normal rate for at least 1 hour. Beginning inactivity was accompanied by a decrease in urate excretion, and an essentially complete anuria preceded death. The rate of urate excretion was normal in irradiated birds that survived more than 24 hours, whether the exposure rate was 6 r or 43 r per minute. At death, the deficit in excreted urate ranged from 20 to 60 mg per 100 g body weight. If the urate space is assumed to equal the extracellular body water (approximately 20% of body weight), then the urate deficit corresponded to blood levels of 90 to 290 mg % in excess of normal. These calculated values are much higher than observed blood values, which ranged from 30 to 60 mg % in excess of normal, and indicate that some urate was present in the solid phase. This condition had been observed in numerous individuals sacrificed in a moribund condition. Concentrations of blood urate tended to be slightly higher than normal in irradiated chicks surviving at 24 hours, and a few birds sacrificed 24 hours after exposure showed accumulated urate in the kidneys.

The effect of X-ray exposure on renal tubular function was determined by measurement of phenol red excretion. In 2- to 4-day untreated birds, one third of the injected dose was excreted in the first 30 minutes and a total of two thirds was eliminated within 2 hours. On the basis of amount of phenol red excreted, chicks irradiated at 43 r per minute fell roughly into two groups: those that died within 10 hours after exposure, which excreted only a small amount within the first two hours; and those that lived 24 hours or more after irradiation, in which the excretion rate was essentially

TABLE II. Effect of X Irradiation (1000 r, 43 r/Min) on Excretion of Phenol Red.

Hr between irrad. and inj. of .2 mg phenol red	No. of animals	Survival time after irradiation	% of inj. dose excreted in 2 hr
Not irrad.	17	—	63.5
.5	4	5.5–8.5 hr	28.2
	2	1–3 days	76.9
1	3	5.5–6 hr	28.3
	1	3 days	79.4
2	9	4.5–8 hr	9.3
	2	1–2 days	39.9

normal during the first few hours (Table II). Exposure at a dose rate of 6 r per minute had little effect on phenol red excretion, and results resembled those obtained on 24-hour survivors exposed at 43 r per minute.

Determinations of the simultaneous excretion of urate and phenol red were made following exposure at 6 r and 43 r per minute. Birds that received phenol red 1 hour after a low rate exposure excreted urate and phenol red at a normal rate. When phenol red was injected 1 hour after a high rate exposure, excretion of both substances was essentially normal in 24-hour survivors, but was low or unmeasurable in birds that died within 10 hours after exposure. In some individuals, phenol red excretion was completely inhibited during a period when minute quantities of urate were collected, but in no case was the dye excreted in the absence of urate. These data indicate a similar mechanism of excretion for the 2 substances or the simultaneous failure of 2 different mechanisms.

Discussion. The radiation-induced renal lesions, primarily necrosis of proximal convoluted tubules, as well as the effects on urate and phenol red excretion, indicate that renal failure is the immediate cause of the early deaths that follow high rate exposures. Mammals with complete renal failure may live for several days, but in birds an obstructive uremia (produced by bilateral ligation of the ureters) results in death within 12 to 24 hours(4-6). Blood urate levels, 5 hours after ureteral obstruction, averaged 50 mg % above normal, and at death the birds commonly showed a severe urate polyserositis. The rapidly developing toxemia may not be only the result of toxicity of the accumulated urate. Lithium urate solution administered intraperitoneally in quantities sufficient to raise the extracellular urate concentration 200 mg % above normal was rapidly excreted and produced no visible clinical effect nor any change in radiation sensitivity in newly-hatched chicks(6). It is probable that lithium protected these birds against death through its effect on urate solubility. In addition, other accumulated byproducts of metabolic processes may contribute to the toxemia.

Comparison of urate deficit at death with the estimated total amount present in the blood and precipitated in kidneys and on serous linings indicated that ionizing radiations did not interfere with the synthesis of urate. In chicks, the formation of urate from ammonia is probably carried out entirely by enzymes present in the liver(7). It would be of interest to study acute radiation effects in the pigeon, in which the final conversion of hypoxanthine to uric acid takes place, at least in part, in the kidney.

Shannon(8) has shown that the primary mechanism for urate excretion in the chicken is by means of the renal tubules. The necrosis of renal tubular cells following high rate exposures indicates a possible widespread inactivation of mechanisms essential for urate excretion, and it would appear that in birds the tubular epithelium has a greater radiation sensitivity than it has in mammals. Other factors can also influence renal function, *e.g.*, (1) maintenance of a minimal blood pressure necessary for glomerular filtration, (2) activity of enzyme systems in the cells of the secretory tubules, and (3) extrarenal factors, including the adrenal cortex and the pituitary-adrenal relationship. X irradiation has been shown to produce a sharp fall in blood pressure in rabbits(9) but its effect on the blood pressure of the irradiated chick remains to be investigated.

These experiments indicate that, in the bird, death in the initial period after irradiation is preceded by acute renal failure. Further investigations will be concerned with determination of the relative importance of (1) direct radiation damage to the kidney and (2)

indirect effects upon renal function produced by generalized physiological disturbances in the organism.

Summary. Young chicks were exposed to 1000 r X radiation at dose rates of 6 or 43 r per minute. Determinations of excretion rate of urate and phenol red and of blood urate levels indicated that death in the initial period (within 8 to 24 hours) following high rate exposures was preceded by renal failure and a rapidly developing azotemia. Individuals that survived 24 hours or more after exposure, whatever the dose rate, continued to excrete at a normal rate. Phenol red retention invariably accompanied failure of urate excretory function.

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Effect of Cortisone on Anaphylactic Response of Guinea Pig Ileum. (19180)

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A diminished antibody production(1), interference with antigen-antibody reaction(2), and altered reactivity of tissues(2) have been considered as possible mechanisms by which ACTH and cortisone influence certain hypersensitive states. The anaphylactic response of the isolated guinea pig ileum (Dale-Schultz Phenomenon) appeared to be a simple method of evaluating the importance of these postulated modes of action of cortisone on hypersensitivity of the Arthus type. In contrast to the intact guinea pig, the response of the isolated ileum is more easily standardized, and therefore tests of significance can be made with fewer animals. Other investigators have reported the inefficacy of cortisone treatment on guinea pig anaphylaxis(3,4). It is not known whether this is a species difference or a matter of dosage, since cortisone has been claimed to be effective against anaphylaxis in the mouse(5), rabbit(6), and the anaphylactoid reaction in the rat(7). Accordingly, experiments were performed on the isolated sensitized guinea pig ileum to study the effect of prolonged administration of cortisone acetate on (1) the level of tissue antibody, (2) the reactivity of tissue to histamine, and (3) the effect of cortisone acetate *in vitro* on the antigen-antibody reaction. The effects of sodium salicylate and of ethyl alcohol on the latter reaction were also investigated.

Method. Twelve virgin, female guinea pigs weighing between 260-350 g were divided at random into 4 groups of 3 animals each. Each group was injected intraperitoneally with 0.5 ml of undiluted horse serum, without preservative. Beginning on the day of sensitization and for a period of 20 days, one guinea pig in each group was injected subcutaneously with 5 mg/kg of a saline suspension of cortisone acetate, a second guinea pig with 1.0 ml/kg of 0.9% saline, and the third guinea pig in each group served as the untreated control. The saline suspension of cortisone acetate was prepared by dissolving the material in warm acetone, reagent grade, adding saline, and then removing most of the acetone by evacuation. The suspension was diluted so that each milliliter contained 5 mg of cortisone acetate. On the 20th day, all animals in