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Possible Role of Potassium in Pullet Disease.*

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So-called "pullet disease"[1,2] represents primarily an acute hepatonephrosis associated with degenerative changes in pancreas and voluntary muscles. It attacks chickens over 3 months of age during the summer, and occurs widely in the Northeast. Our laboratory diagnostic data on 1154 case lots for 1940-43 showed an average incidence of 22.7%, second in rank to the avian leukosis complex which was 29.9%. During 1943 the attack rate was particularly severe, 34.5% of 269 lots, causing severe drop in egg production and an average mortality of 5.2%. The entire cause is unknown since it has been impossible so far to reproduce the field syndrome with the virus isolated by Waller.[3,4] The characteristic explosiveness of outbreaks suggests a wide seeding of the etiologic agent acting synergistically with secondary factors. As empirical treatments, molasses in the feed, 1:2000 copper sulphate or 1:4000 potassium dichromate in the water[1] have been used, the first one being apparently effective, according to available field reports. Shortage of molasses for treatment during 1943 prompted studies on therapeutic substitutes.

Induced Renal Obstruction. In support of previous findings,[1] the 1943 data showed that out of 265 individual pullet disease affected birds, 37% were grossly and 67% were histologically affected with visceral gout (uric nephrosis). There are, therefore, reasons to believe that pullet disease is accompanied by renal damage. Experimental renal obstruction has been induced regularly in birds by parenteral injection of potassium dichromate[1] and recently of alloxan[5] but only irregularly by feeding of certain substances.[2] Oppenheimer[6] together with Kunkel[7] produced in chickens, fed an exclusive meat diet, articular gout which is rare under field conditions. Selye produced nephrosclerosis in chicks by repeated subcutaneous injection of desoxycorticosterone acetate,[8] watering with physiological salt solution, or both[9] and believed the experimental condition to resemble pullet disease.[10] Correll[11] in studying the relation of acid and alkaline-ash foods to vitamin D metabolism, observed sodium citrate and acetate to be toxic to chicks, causing the precipitation of an insoluble material in the body which phenomenon he termed the "salt effect." Feeding sodium citrate together with potassium citrate allowed for normal survival.

Experimental. Correll's[11] work appeared to offer an opportunity for studying protective factors against induced renal obstruction and was therefore repeated and extended. Pullorum clean day-old or 1-week-old R.I.R. or B.R. chicks were housed in sanitary batteries and fed simplified diet G7† and water *ad libitum*.

* Supported in part by grants from the E. S. Farmers' Exchange and the Big "Y" Foundation.

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3 Waller, E. F., *Science*, 1943, **95**, 560.

4 Waller, E. F., Tepper, A. E., Halpin, R. B., and Davis, H. A., *New Hampshire Agr. Exp. Sta. An. Rep.*, 1942, Bul. 345, 59.

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7 Oppenheimer, E. H., and Kunkel, H. G., *Bull. Johns Hopkins Hosp.*, 1943, **73**, 40.

8 Selye, H., *Can. Med. Assn. J.*, 1942, **47**, 515.

9 Selye, H., and Stone, H., Proc. Soc. Exp. Biol. and Med., 1943, **52**, 190.

10 Selye, H., *J. Am. Vet. Med. Assn.*, 1943, **103**, 140.

11 Correll, J. T., *J. Nutr.*, 1941, **21**, 515.

† Diet G7: Yellow corn meal 59.75, tech. casein 20, bagasse 10, brewer's yeast 5, gelatin 2, $Ca_3(PO_4)_2$ 2, NaCl 0.5, wheat germ oil 0.5, cod liver oil 0.25. Plus $MnSO_4$ 0.01%, pyridoxine 500/, calc. pantothenate 1400 γ/100 g feed.

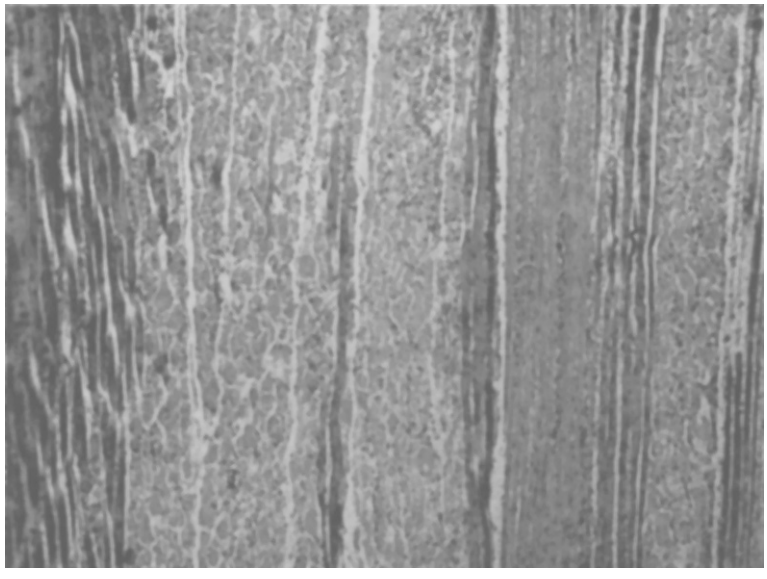

FIG. 1.
Kidney of chick fed toxic level of sodium citrate; marked tubular dilatation and cast formation. Azur II. 80×.

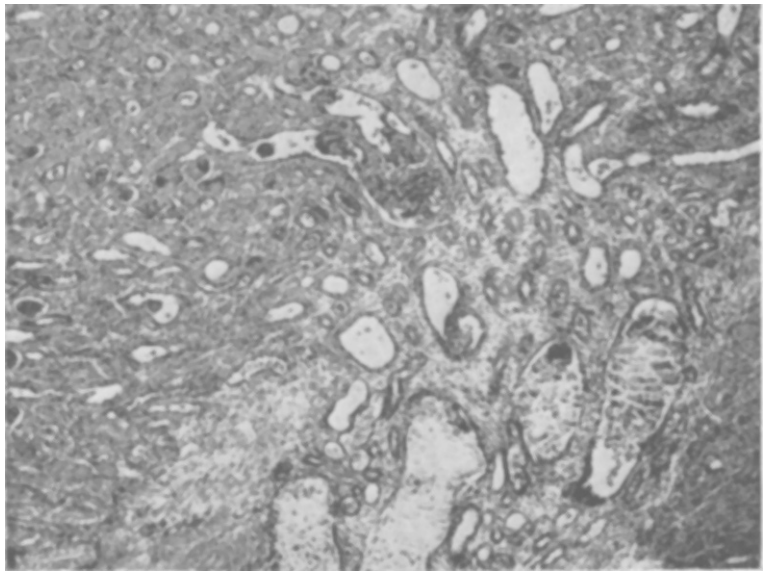

FIG. 2.
Breast muscle of clinically normal chick receiving excess of potassium chloride; the wide, lightly staining bands show Zenker's degeneration. H.E. 80×.

Various "toxic" and "protective" substances were added directly to the diet. The chicks were weighed once per week and, if surviving, sacrificed after 2 weeks of observation.

In general diet G7 was found to produce normal chicks with fair growth (average 89 g at 2 weeks). Renal obstruction induced by feeding high dosages of sodium citrate did not materially influence the growth rate of the survivors, but caused very high blood uric acid levels by the 3rd day which tended to fall off by the 8th day; these days corre-

TABLE I.
Mortality of Chicks 14 Days on Diet G7 Plus Various Supplements.

Serial item No.	Supplements: Toxic Nature	Toxic %	Protective Nature	Protective %	No. of chicks	Mortality %
1	—		—		274	3.6
2	$NaHCO_3$	1.15	—		11	0
3	Trimethyl citrate	1.5	—		11	9.1
4	$C_6H_5O_7Na_3$	1	—		69	21.7
5	”	2	—		69	47.5
6	”	4	—		355	70.4
7	”	”	$KC_2H_3O_2$	1.97	11	9.1
8	”	”	K_2CO_3	1.39	11	36.3
9	”	”	$K_3C_6H_5O_7$	2.17	11	36.3
10	”	”	KI	3.34	12	83.3
11	”	”	KNO_3	2.03	10	0
12	”	”	$KMnO_4$	3.18	11	36.3
13	”	”	KCl	0.015-0.5	210	74.8
14	”	”	”	1	35	11.4
15	”	”	”	1.5	53	16
16	”	”	”	2	116	16.4
17	”	”	Muriate of Potash	1.57	42	7.1
18	”	”	Molasses in Feed	40	42	19
19	”	”	” ” Water	10	30	33.3
20	”	”	Glucose	10	46	71.7
21	”	”	$K_2Cr_2O_7$ in Water	0.05	54	72.2
22	”	”	$CuSO_4$ in Feed	0.05	54	81.5
23	”	”	” ” Water	0.05	30	50

sponded roughly to the period of highest mortality.

The so-called "salt effect" was found to be pathologically indistinguishable from the well-known picture of visceral gout or uric nephrosis. The kidneys were enlarged and showed fine whitish striation of the lobules; the ureters were distended due to urinary retention and the serous membranes of the body cavities were often covered with whitish urates. Microscopically, renal tissues showed extensive tubular dilatation and necrosis, together with formation of hyaline or heterophile casts (Fig. 1); occasionally typical "gout rosettes" were observed. In a few experimental lots high levels of "protective" potassium salts caused the appearance of asymptomatic whitish striation of the voluntary muscles (similar to those seen by Liebow *et al.* in mice[12]) which microscopically presented alternating bands of dystrophic and healthy muscle bundles (Fig. 2).

Results. To simplify presentation, the data for lots of chicks subjected to the same dietary regime but in various experiments have been combined and listed serially in Table I. A weighted average of the percent mortality of the lots was used as the main criterion, since major intercurrent diseases could be reasonably ruled out.

In *toxicity* experiments, the mortality on diet G7 without any supplements ranged from 0 to 27.3, with an average of 3.6%, and was considered nutritionally adequate (Item No. 1). Sodium bicarbonate shown by Witter[13] to cause renal obstruction in chicks if given in water, was found innocuous in the feed (No. 2); the citrate radical alone in the form of trimethyl citrate was likewise found to be nontoxic (No. 3). Sodium citrate proved toxic at levels of 1 and 2% (Nos. 4 and 5) but gave the most consistent results at the 4% level with an average of 70.4% mortality (range 28.6 to 91.9) (No. 6).

In all *protection* experiments 4% sodium citrate was used as the toxic principle. In preliminary trials several potassium salts such

[12] Liebow, A. A., McFarland, W. J., and Tennant, R., *Yale J. Biol. and Med.*, 1941, **13**, 523.

[13] Witter, J. F., *Poultry Sci.*, 1936, **15**, 256.

as potassium acetate (No. 7), carbonate (No. 8), citrate (No. 9), nitrate (No. 11), and potassium permanganate (No. 12) were found to afford varying degrees of protection. Potassium iodide (No. 10) seemed to be protective since none of the chicks showed the "gout" effect, but was toxic otherwise as indicated by retarded growth and high mortality. Since potassium, which is known to be essential for chicks[14] and animals in general,[15] seemed to be the protective principle a simple compound, potassium chloride, was tested on a larger scale. Six graded levels of from 0.015 to 0.5% (No. 13) failed to give protection, but 1 to 2% reduced the mortality by about ¾ (Nos. 14 to 16). Whether the 1% level was actually more protective than the higher level as it would appear from the data, must be rechecked on a larger number of birds.

To study the protective value of readily available substances and of empirical treatments for pullet disease, a sample of muriate of potash (Agri. grade 95-98%, Am. Potash and Chemical Corp.) as used in commercial fertilizers, was tested at the level of 1.57% and found to be protective (No. 17). Blackstrap molasses gave a significant measure of protection, more so in the feed (No. 18) than in the water (No. 19). The protective effect was apparently due to the known high potassium, and not the carbohydrate, content of molasses, since glucose alone (No. 20) afforded no protection. Potassium dichromate in water (No. 21) or copper sulphate either in the feed (No. 22) or water (No. 23) at the highest previously determined tolerated levels failed to give protection under the prevailing experimental conditions.

Pullet disease therapeutic trials. From a commercial flock of 3,500 chickens, aged 2½ to 17 months and known to be acutely affected with pullet disease, 30 clinically affected hens were brought to the laboratory and divided into two comparable lots. They were continued on the same brand of commercial feed except that 2% KCl was added to the mash feed of the one lot. Blood samples for uric acid were taken at the beginning of the experiment and again after 3 and 6 weeks. Chemical tests failed to show any significant differences between the groups, by analysis of variance. All birds were subjected to pathologic study. Only birds surviving for the 6-week experimental period were used in the computation of the data.

In the control lot of 15 birds, 3 died within one week and 1 within 2 weeks, all with typical gout. The average number of eggs laid per bird was 2.18. The average initial and final weight was 1943 and 2077 g, respectively. Pathologic examination showed gross enlargement of kidneys in 7 and microscopic residual kidney lesions in all of the 11 survivors.

In the KCl-fed lot of 15 birds, 6 died within less than 2 weeks and 1 in 5 weeks. The average number of eggs laid during the period of observation was 4.25. Initial and final weight figures were 2050 against 2040 g or about stationary for producing birds. Of the 8 survivors none showed gross and only 2 microscopic kidney lesions.

Although the number of birds used in this phase of the work was small, it would seem that those receiving the supplement of KCl were able to regain egg production faster and to combat kidney damage better than the individuals of the non-supplemented lot.

Summary. 1. According to laboratory records so-called pullet disease ranked second in pathologic importance in Connecticut chickens during the last 4 calendar years. 2. It was characterized in over ⅔ of the cases by kidney damage similar to visceral gout. 3. The "salt effect" resulting from feeding sodium citrate to chicks according to Correll, was found to correspond to experimental visceral gout. 4. The protective action of potassium salts against the "salt effect" was confirmed and shown to hold for simple compounds like potassium chloride or a good agricultural grade of muriate of potash at levels of 1 to 2% in the feed. 5. Molasses due to its potassium content was found to be protective, which rationalizes the corresponding empirical treatment for pullet disease. 6. In a small-scale experiment on spontaneous pullet disease cases, potassium chloride seemed helpful which suggests its use during molasses shortage.

[14] Ben Dor, B., PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 341.

[15] Follis, R. H., *Arch. Path.*, 1942, **34**, 451.