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TOXOPATHOLOGY OF GOUT INDUCED IN LAYING PULLETS BY SODIUM BICARBONATE

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ABSTRACT :

A total of sixty laying pullets (3 weeks old) were obtained from a local governmental farm and acclimatized for one week. At 4 weeks of age, the experimental birds were divided randomly into 5 equal groups, the first 4 groups received excess sodium bicarbonate (SB) in their drinking water at the levels of 2 g/L (0.2%), 7.5 g/L (0.75%), 20 g/L (2%) and 40 g/L (4%), successively. Birds of the fifth group was served as control. The experimental birds were subjected to pathological and toxicological examination. Birds of the 0.75% and 2% -groups developed gross picture of visceral gout, while birds of 4% -group showed acute kidney damage. Erythrocytic count (RBCs), packed cell volume (PCV), and hemoglobin (Hb) levels were increased in the exposed birds. The dose-related increments in the serum level of sodium (Na^+), chloride (Cl^-), and potassium (K^+) were decreased. Serum levels of uric acid were increased in a dose-related pattern. Blood pH of the treated birds was shifted toward the alkaline side. Microscopic examination revealed significant renal changes in birds manifesting visceral gout and these changes included urate deposits associated with tubular necrotic changes. Some birds in the third group (2%) developed urate granulomas (tophi) in their renal interstitium. It was concluded that development of gout in birds may be related to a state of metabolic alkalosis which is associated with significant changes of the electrolyte balance.

INTRODUCTION :

Sodium bicarbonate (SB) has been used for long time by poultry producers for the benefits of their flocks. SB has a laxative effect when added to drinking water and it's addition to ration increases the egg shell thickness [1-5].

Addition of SB to the feed improves body gain and decreases losses due to heat stress [6,7]. SB has been also used to correct disorders of acid-base balance in poultry production [8]. Moreover, SB is used in the treatment of a variety of medical conditions in human being [9].

The aforementioned beneficial effects of SB can be only attained when the recomended doses are administered. Toxicity due to excess SB has been reported and nephrotoxic effect of SB overdosing was documented [1,5,10,11,12]. Visceral gout was reported in commercial layers naturally exposed to SB toxicity [12]. Moreover, some outbreaks of visceral gout in poultry have been attributed to sodium bicarbonate toxicity [13].

Gout is a common metabolic disorder which results in abnormal accumulation of urates (monosodium and calcium urates) in domestic birds [14]. It occurs as two distinct forms, namely visceral (visceral urate deposition) and articular gout [15,16]. Birds form uric acid rather than urea as the end product of nitrogen metabolism and therefore they are susceptible to hyperuricaemia sub-sequent to renal damage [13,17].

As far as we aware, no experimental work has been conducted to focus on the visceral gout induced by SB toxicity. Therefore, the purpose of the present study was to investigate the toxopathological changes of gout induced in laying pullets by SB toxicity. Trial was also made to elucidate some aspects of the pathogenesis of gout in birds.

EXPERIMENTAL :

Materials and Methods :

Experimental design:

A total of sixty, 3-weeks- old, laying pullets of mixed native breeds obtained from governmental farm were used in the present study. The experimental birds were acclimatized for one week in cages and during this period they had access to feed (commercial starter laying ration) and water (normal tap water) ad libitum. At the 4 th week of age, the birds were divided randomly into 5 groups of 12 each and designated groups 1,2,3,4 and 5. The first four groups received sodium bicarbonate in their drinking water at the rates of: 2g/L (0.2%), 7.5 g/L (0.75%), 20 g/L (2%), and 40 g/L (4%), successively. The fifth group served as control and had access to normal tap water. At days 3, 10, 20 and 35 post-exposure, 3 birds from each exposed group and 3 birds from the control group were bled and sacrificed. Birds died during the course of the experiment were also necropsied. The experiment was terminated when the birds were 9 weeks of age. Sodium bicarbonate (SB) was obtained from Sigma Company.

Clinical pathology:

Blood obtained from either exposed or control birds were drained into tubes containing EDTA (1 mg/ml blood) as anticoagulant or into tubes containing no anticoagulant. Serum was harvested from all collected blood samples. Erythrocytic (RBCs) count was determined using a haemocytometer

and blood diluent according to the method described by Natt and Herrick [18] . Packed cell volume (PCV) was measured using haematocrit tubes. Cyanmet-haemoglobin method as described by Benjamin [19] was used to estimate haemoglobin (Hb) levels.

Blood Chemistry:

Serum levels of sodium (Na^+) and potassium (K^+) were estimated by using Carl-Zeiss flame photometer (M7D, Germany) according to Williams and Twine [20]. Level of (Cl^-) in the serum samples was measured by $AgNO_3$ titration method as descrbied by Jackson [21]. Serum uric acid was estimated by employing the enzymatic colorimetric test (uricase-PAP) using the diagnostic kits (Diamond, Diagnostics) according to Fossati [22]. Blood pH was determined using "Whatman" indicator papers.

Statistical analysis:

Student's "t" test was used to calculate the significance between control (non exposed) birds and exposed ones. Probability values of 0.05 and 0.01 were considered statistically significant.

Histopathology:

Tissue samples from kidneys, lungs, heart, liver, spleen, proventriculus, gizzard, intestine and other tissues and organs were collected from treated and control birds and fixed in 10% neutral-buffered formalin. Tissue samples were processed routinely for paraffin embedding technique, sectioned at 3μ and stained with haematoxylin and eosin (HE). Selected tissue sections were stained also with periodic acid Schiff reagent (PAS). Staining procedures were done according to the methods described by Bancroft and Stevens [23].

Electron microscopy:

Immediately after necropsy, tissue samples from the kidneys of exposed and control birds were fixed by immersion in 2.5% buffered glutaraldehyde. Samples were then post-fixed in 1% osmium tetroxide, dehydrated in ascending grades of ethanol and embedded in Epon 812. Semithin sections were prepared and stained with 1% toluidine blue. Ultrathin sections were double stained with uranyl acetate and lead citrate and examined using transmission electron microscope (Jeol,100 CXII) operated at 80 Kv.

RESULTS :

Clinical signs and mortality :

From the third day post-exposure, birds of groups 2, 3, and 4 were depressed and their water intake was increased while their feed intake was decreased and they had watery dropping. The mostly depressed and emaciated birds were those of group 4. Birds of group 1 manifested no clinical signs and their feed and water intake was relatively normal. No mortalities were recorded in group 1 (0.2%). In group 2 (0.75%) two birds were died, while three birds in group 3 (2%) and six birds in group 4 (4%) were died. By the tenth day post-exposure, all birds in group 4 were either died or necropsied. No clinical signs or mortalities

were recorded among the control birds all over the experiment.

Haematological parameters:

RBCs count, PCV and Hb levels of the exposed birds were increased at all times post-exposure compared with that of the corresponding control birds. However, the increments were not steady and showed some fluctuations.

Blood chemistry:

Serum levels of Na^+ in all exposed birds were increased in comparison with that of control birds. However, fluctuation was noticed at the different intervals post-exposure. At any time post-exposure, serum level of Na^+ in birds of group 4 (4%) was higher than that of the other exposed birds. Compared with control birds, serum levels of Cl^- and K^+ were decreased in all exposed groups. Serum level of uric acid was increased in all exposed birds. The measured blood pH values in all exposed birds were shifted towards the alkaline side and ranged from 6.7 to 8.1. Tables 1 and 2 show the haematological parameters and other parameters of blood chemistry measured in both control and exposed birds. The various parameters were expressed as mean values for the different groups at each time interval.

Gross pathology:

Four birds in group 2 and six in group 3, successively showed gross signs of visceral gout. These birds had whitish metalic urate deposits in the kidneys and white chalky urate coating on the serous surfaces of liver, heart and lung. Deposits of urates were also detected on the mesentry, peritoneum and spleen. Air sacs with urate deposition were thick and opaque. Pericardium was also thickened and adhesed to myocardium. Kidneys of the gouty birds were pale and swollen and had clear tubular markings. Ureters were distended with urates. Two birds in group 3 showed picture of both visceral and articular gout. Beside the visceral urate deposits, these birds had whitish chalky material deposited on the articular surfaces (Fig. 1).

Histopathology:

In birds which manifested the gross picture of visceral urate deposits (0.75% and 2% groups), the most prominent histological changes were noticed in the kidney. In some cases, only intraluminal amorphous eosinophilic urate material was noticed distending many cortical renal tubules and the associating inflammatory cell reaction was minimal (Fig. 2). The intraluminal urate material, in some cortical tubules, was in the form of basophilic spherules. In some other cases, many cortical areas showed crystalization of the urate material which appeared to be deposited on the partially necrosed cytoplasm of cortical tubular cells. This was accompanied by the increased interstitial heterophil cell reaction. With progression of the tubular necrosis, the birfringent nature of the deposited urate material became more apparent. The feathery shape of the deposited urate material was noticed when it had been free in some

interstitial locations. The local tubules in these cases were destructed. With increasing the number of cortical discrete foci of crystalized urate deposits, the associating areas of tubular necrosis were also increased. Confluent areas of urate deposition were seemed to be formed by the coalescence of adjacent focal crystalized urate deposits which attained the starburst appearance (Fig. 3). The interstitial inflammatory cell reaction, mainly heterophilic, was distinct and more diffuse with increasing the size of urate deposits (Fig. 4).

Frequently, the cortical glomeruli showed proliferative changes with thickening of the glomerular basement membranes (GBMs) (Fig. 5). Deposition of the crystalized urate material was also noticed on some cortical glomeruli which showed marked proliferative reaction. Some of these glomeruli disclosed advanced necrotic changes with disruption of their architecture (Fig. 6). At sites of urate deposition and beside the interstitial heterophil cell infiltration, intraluminal heterophils were also seen within the dilated cortical tubules. Birds of 2% group at the last two intervals, showed the presence of varied sized renal urate granulomas (tophi). The interstitial urate granulomas were build up from central amorphous eosinophilic material surrounded by giant cell reaction and bordered by heterophils and lymphocytes (Fig. 7). At some locations, the giant cell reaction was observed in the presence of little deposited urate material (Fig. 8). In some granulomas, the central urate material was crystalized and feathery-shaped. Both cortical and medullary urate granulomas were seen in some cases.

Interstitial fibrosis was the feature of the renal tissue where considerable areas were occupied by urate granulomas. Accompanying the picture of interstitial urate nephritis, features of chronic proliferative glomerulitis were detected. Both mesengial and epithelial components of cortical glomeruli were proliferated. The proliferated glomerular visceral epithelium was adhesed to the parietal epithelium. The chronic glomerular changes were associated by periglomerular fibrosis. Some other glomeruli had atrophied tufts and some showed cuboidal change of their parietal epithelium.

Kidneys of birds in group 4 (4%) revealed tubular necrotic changes and fewer interstitial urate deposits. No significant renal changes were detected in birds of group 1. Microscopic examination of heart, liver and lungs of birds in groups 2 and 3 revealed amorphous eosinophilic urate deposits on their serous surfaces. Subjacent to the pericardial urate deposits, the examined hearts showed edema, hyperaemia and myodegeneration. Other tissues and organs showed edematous and degenerative changes. No comparable changes were noticed in the control birds. Table 3 shows scoring for the renal pathological lesions in the exposed birds.

Electron microscopy:

Examination of kidney samples with gross urate deposits revealed intraluminal amorphous moderately electron-dense urate material in many convoluted and collecting tubules (Fig. 9). Needle-shaped urate crystals deposited on the tubular basement membranes

were also observed (BMs) (Fig. 10). This was associated with tubular cell necrosis evidenced by disintegration of nuclear chromatin and disruption of cell organelles with loss of cell outlines. The neighbouring renal tubular cells had degenerated mitochondria and dilated rough endoplasmic reticulum (RER). Glycogen rossettes were frequently seen in these cells. Loss of microvilli and blebbing of the apical cytoplasmic membrane of convoluted tubular cells were frequent findings.

Some glomeruli had thickened basement membranes which manifested swelling of foot processes of podocytes on one side and degenerated swollen endothelial cells on the other side (Fig. 11). Some degenerated endothelial cells contained glycogen rossettes and showed blebbing or indentation of the nuclear membrane. No comparable fine changes were detected in the control birds.

Table (1): Mean values of RBCs, Hb, Packed cell volume (PCV),and blood pH in laying pullets expsoed to sodium bicarbonate (Mean ±S.E.M.)

Group	RBCs (x10^{12}/L)				Hb (g/L)				PCV (%)				Blood pH			
	Time post-exposure (days)				Time post-exposure (days)				Time post-exposure (days)				Time post-exposure (days)			
	3	10	20	35	3	10	20	35	3	10	20	35	3	10	20	35
control	1.799 ± 0.039	2.11 ± 0.55	2.17 ± 0.06	2.29 ± 0.04	10.3 ± 0.14	9.4 ± 0.218	10.2 ± 0.031	9.9 ± 0.025	28.4 ± 0.167	28.3 ± 0.152	28.1 ± 0.231	29.2 ± 0.227	6.7 ± 0.125	6.5 ± 0.131	6.7 ± 0.001	6.8 ± 0.002
0.2%	1.93 ± 0.046	2.21 ± 1.15	2.39 ± 0.08	2.45 ± 0.01 *	10.8 ± 0.11 *	11.25 ± 0.027 **	11.5 ± 1.244	11.8 ± 0.145 **	28.8 ± 0.190	28.4 ± 0.036	28.0 ± 0.707	29.2 ± 0.473	6.7 ± 0.021	6.8 ± 0.001	6.9 ± 0.012 **	6.9 ± 0.115 **
0.75%	1.920 ± 0.310	2.35 ± 0.46	2.47 ± 0.05 *	2.70 ± 0.04 **	10.7 ± 0.44	10.0 ± 0.471	10.6 ± 0.071 **	10.5 ± 0.018 **	29.9 ± 0.276 **	29.5 ± 0.071 **	29.4 ± 0.073 **	31.6 ± 0.055 **	7.1 ± 0.52 **	7.3 ± 0.056 **	7.4 ± 0.015 **	7.8 ± 0.021 **
2 %	2.1 ± 0.031 **	2.85 ± 1.15	2.9 ± 0.16 **	2.95 ± 0.08 **	11.2 ± 0.11 **	11.0 ± 0.047 **	11.5 ± 0.235 **	11.67 ± 0.072 **	30.2 ± 0.612 *	30.5 ± 0.008 **	30.7 ± 0.402 **	31.8 ± 0.032 **	7.2 ± 0.132 *	7.5 ± 0.018 **	7.7 ± 0.012 **	8.1 ± 0.032 **
4 %	2.3 ± 0.068 **	2.95 ± 0.03	ND	ND	11.1 ± 1.06	13.0 ± 0.071 **	ND	ND	30.7 ± 0.668 *	31.5 ± 0.084 **	ND	ND	7.2 ± 0.171	7.7 ± 0.027 **	ND	ND

* Significant at P < 0.05 ** Significant at P < 0.01 ND = not detected

Table (2) : Mean values of Na^+, Cl^-, K^+, and uric acid in serum of laying pullets exposed to SB (Mean ± S.E.M.).

Group	Na^+ (mg/ml)				Cl^- (mg/ml)				K^+ (mg/ml)				Uric acid (mg/dL)			
	Time post-exposure (days)				Time post-exposure (days)				Time post-exposure (days)				Time post-exposure (days)			
	3	10	20	35	3	10	20	35	3	10	20	35	3	10	20	35
control	5.1 ± 0.31	5.2 ± 0.16	5.1 ± 0.15	5.0 ± 0.13	5.5 ± 0.07	5.3 ± 0.01	5.2 ± 0.15	5.1 ± 0.01	156.0 ± 0.31	140.6 ± 0.65	144.5 ± 0.15	147.5 ± 1.53	5.3 ± 0.04	5.4 ± 0.09	5.1 ± 0.04	5.7 ± 0.04
0.2%	5.3 ± 0.21	6.5 ± 1.03	6.2 ± 2.19	6.3 ± 0.02 **	5.2 ± 0.12	5.2 ± 1.18	5.0 ± 0.35	5.1 ± 0.05	142.0 ± 0.36 **	143.3 ± 1.36	144.2 ± 0.03	145.0 ± 0.07	5.4 ± 0.37	5.6 ± 0.14	7.1 ± 0.33 **	8.7 ± 0.71 **
0.75%	5.5 ± 0.30	6.9 ± 0.13 **	6.8 ± 0.16 **	6.6 ± 0.14 **	5.4 ± 0.06	5.1 ± 0.06 *	4.8 ± 0.38	4.9 ± 0.08	146.7 ± 0.42 **	136.5 ± 1.15 *	142.1 ± 0.03 **	141.7 ± 1.92	9.5 ± 0.31 **	14.5 ± 1.60 *	16.1 ± 2.96 *	23.8 ± 0.04 **
2 %	5.6 ± 0.58	7.3 ± 1.33	6.9 ± 0.08 **	6.8 ± 0.26 **	4.9 ± 0.13*	4.7 ± 0.23	4.5 ± 0.03 **	5.3 ± 0.08	131.8 ± 0.73 **	139.5 ± 0.09	141.3 ± 0.84 **	140.0 ± 0.06 **	9.6 ± 0.63 **	13.2 ± 0.49 **	18.3 ± 2.61 **	28.3 ± 2.33 **
4 %	5.8 ± 0.08	7.9 ± 0.15 **	ND	ND	5.1 ± 0.43	5.2 ± 0.24	ND	ND	143.3 ± 0.60 **	142.0 ± 0.07	ND	ND	9.7 ± 0.40 **	21.1 ± 0.80 **	ND	ND

*** Significant at P < 0.05** **** Significant at P < 0.01** **ND = not detected**

Table(3) : Kidney lesion scores in birds exposed to various levels of sodium bicarbonate .

Days post-exposure	Exposed groups							
	0.2%		0.75%		2%		4%	
	Gross lesions [A]	Mic. Lesions[B]	Gross	Mic.	Gross	Mic.	Gross	Mic.
3	-/4[C]	-/4	+/4	+/4	--/4	++/4	++/4	++/4
10	-/4	-/4	++/4	++/4	+++/4	+++/4	+++/12	+++/12
20	-/4	-/4	++/4	++/4	+++/4	+++/4	ND	ND
35	+/4	+/4	+++/4	+++/4	++++/4	++++/4	ND	ND

A Gross scoring:
-= negative; +=congested kidneys; ++ = swollen & pale kidneys; +++= pale-colored kidneys with urate deposits; ++++=urate deposits in kidneys & distention of ureters with urates associated with visceral urate deposits.

B Microscopic gradings:
-=negative; +=edema & hyperaemia of peritubular capillaries; ++=tubular degeneration & swollen glomeruli;
+++ = tubular degeneration, proliferative glomerulitis & urate material in tubular lumina, ++++ = interstitial urate granulomas, interstitial fibrosis, tubular necrosis & chronic glomerulitis.

C Score / No. of chickens showing lesions.

Fig. (1): SB- exposed bird (2%, 35 days post-exposure) showing marked visceral urate deposits in the kidneys and on mesentry. There is urate coating on the pericardium (large arrow). Ureters (arrowhead) are distended with urate material. Note the chalky urate material deposited on the bony articulations (small arrow).

Fig.(2):Kidney showing intraluminal eosinophilic urate material (arrow) distending a cortical convoluted tubule. One focus of intersitial urate deposition (I) can be also seen. The interstitial inflammatory cell reaction is minimal. SB-exposed bird (0.75%, 10

Fig.(3): Coalesced focal crystalized urate deposits accompanied by local tubular destruction and interstitial heterophil cell infiltration. SB-exposed bird (2%, 21 days post-exposure). HE. X 320.

days post-exposure). HE. X 200 .

Fig.(4): Distinct and more diffuse interstitial heterophil cell infiltration accompanying larger areas of urate deposition in the renal cortex. SB-exposed bird (2%, 21 days post-exposure). HE. X 320 .

Fig.(5): Kidney showing cortical glomeruli with proliferative changes and thickening of the glomerular basement membranes (GBMs). The proliferative glomerular changes mainly involve the mesengial cells. SB-exposed bird (2%, 21 days post-exposure). PAS.X 320 .

Fig.(6): Crystalized urate material (arrow) deposited on a glomerulus which is destructed and it's architecture is lost. The neighbouring tubule contains amorphous urate material and heterophils. Note the accompanying interstitial fibrosis. SB-exposed bird (2%, 35 days post-exposure). HE. X 280 .

Fig.(7): Urate granuloma (tophus) (T) in the renal cortex of SB- exposed bird (2%, 35 days post-exposure). The tophus is built up from central amorphus material (urate and tissue debris) surrounded by giant cells and bordered by heterophils and lymphocytes. HE. X 280 >

Fig.(8): Kidney showing giant cell reaction (arrow) in the presence of minimal urate deposition and marked tubular cell destruction. SB- exposed bird (2%, 35 days post-exposure). HE X 280 .

Fig.(9): Electron-micrograph showing intraluminal amorphus urate material (U) in a collecting tubule. Blebbing of the apical cytoplamic membrance (arrow) and swelling of mitochondria (m) can be seen. SB- exposed bird (0.75%, 10 days post- exposure). X 4500 .

Fig.(10): Electron-micrograph showing deposition of urate crystals (arrows) on the tubular basement membranes and on the necrosed cytoplasm of tubular cells. The tubular cells are disrupted and their organelles are disintegrated. SB- exposed bird (2%, 21 days post-exposure). X 4500 .

Fig.(11): Gradually thickened glomerular basement membrane (g) in the kidney of SB-exposed bird (2%, 35 days post- exposure). The foot-processes of podocytes (P) are swollen and nucleus of the endothelial cell (e) is indented. Electron-micrograph. X 8000 .

DISCUSSION :

The present study was conducted to investigate some aspects of the toxopathogenesis of gout in laying chickens. The practical significance of this work comes from the fact that gout is a common finding during necropsy of domestic birds with various disease conditions [13]. Laying pullets were used in this experiment as they are more susceptible for the development of gout [24]. Exposure of birds in this experiment started when they were 4 weeks of age. Thus, these immature birds were more succeptible for SB toxicity. It is known that young birds are more susceptible for nephrotoxic agents as their kidneys are not fully developed [25].

Our results recorded that all birds of 4% - group were died within 10 days post-exposure and they showed acute renal changes. This conformed with the finding that birds at high level of sodium salts develop acute kidney damage which contributes to death of birds [13]. Birds which received 2% SB in the present work survived for the whole experimentation period and hence they developed the picture of chronic gouty nephritis.

No signs of toxicity or visceral gout were observed in the first group (0.2% SB), this is in accord with the reported range of SB toxicity (0.6-1.2%) [1,26]. In the present study birds which received 0.75% SB developed visceral gout while previous studies [7,27] revealed that the broiler chickens did not manifest visceral gout at the same level of SB. This contradiction may be related to differences between meat-type chickens and laying birds concerning the renal function of both.

Clinical signs of increased water consumption and watery dropping observed in the present SB intoxicated birds are similar to those reported by Davison and Wideman [12] in commercial layers spontaneously intoxicated by SB. Also, mammals exposed to SB toxicity manifested the same clinical signs [28].

RBCs counts, Hb and PCV values of the exposed birds were increased at all time intervals compared with that of controls. Similar result was reported in the previous studies of sodium intoxication [7,27,29]. We propose that these increments of haemato-logical parameters may be ascribed to increased erythropoietin activity. On the other hand these increments may be untrue and related to fluid loss due to watery dropping manifested by the exposed birds.

Serum levels of Na^+ measured in the exposed birds in our study were increased and the increments were dose-related. This result indicates that laying pullets are unable to adequately increase their renal excretion of sodium [13]. Subsequenly, the birds become vulnerable to the renal damage exerted by excess sodium. Decreased serum levels of K^+ and Cl^- may ascribed to increased excretion of these elements due to renal dysfunction. Loss of these elements in the watery dropping of the treated birds may also contributes to their decreased serum levels. The dose-related increments of uric acid in exposed birds were most probably related to the resultant renal damage which is known to lead to hyper-uricaemia [15,30]. The measured blood pH in the present exposed birds was shifted toward

the alkaline side. This was related to a state of metabolic alkalosis created by the bicarbonate overload in the exposed birds.

Similar changes of blood parameters, including metabolic alkalosis, hypernatremia, hypokalemia and hypochloremia, were reported in commercial layers exposed spontaneously to SB toxicity [12]. Also other animals and even human beings exposed to SB toxicity showed similar changes of blood chemistry [9,31].

In the present work, all exposed birds that developed visceral gout had increased serum level of uric acid. We assume that visceral urate deposition in the present birds is mostly linked to the state of metabolic alkalosis induced by SB overdosing. Undoubtedly, visceral urate deposition was preceeded by a state of hyperuricaemia which is strongly related to renal dysfunction as indicated from the present renal histological changes. All renal functions evaluated in birds and mammals exposed to SB toxicity were found to be greatly compromised [12,31].

Uric acid in birds is chiefly excreted by glomerular filtration and active tubular transport [16]. Therefore, it is likely that the present pathological glomerular and tubular lesions exacerbated the state of hyperuricaemia. It has been stated that not all cases of hyperuricaemia are associated with visceral urate deposition and disturbance of the constitution of the intercellular fluid is needed to initiate urate deposition [15]. Blood chemistry of the present experimental cases indicates significant changes in electrolyte balance involving the levels of Na^+, Cl^- and K^+. The composition of the intercellular fluid was thus significantly altered in the exposed birds to allow the precipitation of urates in the presence of hyperuricaemia.

It was shown that the two distinct forms of gout, visceral and articular, are different as regard to their pathogenesis [13]. The development of both forms in the same bird in the present work may indicate common pathway(s) in their pathogenesis. The finding of both visceral and articular urate deposition in the same bird may be related to the higher degree and long duration of hyperuricaemia as reported in some cases of mycotoxicosis [32]. However, the finding of both forms of gout as demonstrated here in the same bird was not reported previously in SB toxicity.

Siller [31] described two forms of urate deposition, acute urate deposition without inflammatory cell reaction and chronic form which is associated with granulomatous reaction. The author also demonstrated that the acute cellular reaction against the deposited urate material ensuses by 72 hrs and this acute reaction progresses to granulomatous form by 96 hrs. In the present exposed birds, the renal chronic granulomatous reaction was likely arised when the deposited crystalized urate material was free in interstitial locations associated with renal tubualr necrotic changes.

Some of the demonstrated glomerular changes, especially the thickening of GBMs are probably related to intoxication by sodium ion. Similar findings were reported in chickens intoxicated with salt [34,35]. Hyperuricaemia

may be also a contributor to these changes. Mortalities in the present study are most likely ascribed to renal failure and also to the state of hypokalemia which is known to compromise the cardiac performance [36]. Potassium has a major function in regulation of potentials across cells and it is necessary for the cellular sodium pump system by which Na^+ is extruded from the cell [37,38]. In this respect, the role of hypokalemia in causation of mortalities is approved by the finding that potassium has a protective effect in cases of sodium bicarbonate toxicity [33].

The present work indicates that development of gout in birds is related to electrolyte imbalance and also to aetiologies which can lead to renal damage and metabolic alkalosis. Future studies should pay attention to these aspects for more accurate invest-igation of the pathogenesis of avian gout. Conclusively, the present study may be considered as a good model for studying of gout in domestic birds.

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التغيرات السمية الباثولوجية للنقرس فى كتاكيت انتاج البيض المتعرضه لبيكربونات الصوديوم

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استخدم فى هذه الدراسة عدد ٦٠ كتكوت بياض عمر ثلاثة أسابيع حيث قسمت إلى خمس مجموعات متساوية. عند عمر شهر تمت إضافة الصوديوم بيكربونات لمياه الشرب للأربع مجموعات الأولى حسب النسب التالية: ٠,٢% ، ٠,٧٥%، ٢%، ٤% أما المجموعة الخامسة فاستخدمت كضابط للتجربه.

أظهرت النتائج أن الطيور فى مجموعتى ٠,٧٥%، ٢% شوهد فيها نقرس الأحشاء أما طيور مجموعة ٤% فشوهد فيها إصابات كلوية حادة. عدد كرات الدم الحمراء والحجم الخلوى المضغوط والهيموجلوبين إزداد فى كل الطيور المعاملة.

كذلك سجلت هذه الدراسة زيادة فى نسبة الصوديوم فى أمصال الطيور المعاملة وعلى النقيض فقد انخفضت نسبة كل من الكلوريد والبوتاسيوم مقارنة بالطيور الضابطة . أما مستوى حمض اليوريك فقد لوحظ به ارتفاعا ارتبط بوثوق بالجرعة المعطاه وقد كان الدم قلوياً فى ألاس الهيدروجينى.

ودلت نتائج الفحص المجهرى وجود تغيرات كلوية كان من أهمها ترسيبات من اليوريات مع تكسير فى ألانابيب الكلوية . كما شوهد فى طيور المجموعه الثانية (٢%) التهابات كلوية مزمنة .

وقد تبين من النتائج أن هناك ارتباط وثيق بين نشوء النقرس فى الدجاج والأس الهيدروجينى وعمليات ألايض الغذائى والتى تأثرت كثيراً فى الوسط القلوى وصاحبها تغيرات هامه فى توازن العناصر وخاصة ألاملاح بالجسم.