TOXICOLOGIC EFFECTS OF REDROOT PIGWEED (AMARANTHUS RETROFLEXUS) IN SWINE

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by

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A Thesis Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
MASTER OF SCIENCE

Major Subject: Veterinary Pathology

Signatures have been redacted for privacy

Iowa State University
Of Science and Technology
Ames, Iowa

1968

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TABLE OF CONTENTS

INTRODUCTION

A disease syndrome of swine characterized by a consistent lesion of perirenal edema has for several years been recognized clinically and upon post mortem examination. Laboratory and field investigations have established a number of factors common to the condition. The disease occurs in young swine only during the summer and early fall months. Onset of the disease is associated with access of swine to pastures containing Amaranthus retroflexus L. (redroot pigweed) and Chenopodium album L. (lamb's quarters). After five to ten days of ingestion of suspected plants, typical signs of weakness, trembling and incoordination develop. These signs progress rapidly to knuckling of tarsal-metatarsal joints, weakness in the hindquarters, sternal recumbency, flaccid paralysis and death within 48 hours after onset of clinical signs. The characteristic lesion is retroperitoneal edema of the perirenal connective tissue. Edema of the mesorectum, mesometrium and lateral ligaments of the bladder is observed. Subcutaneous and intermuscular edema of the abdominal wall may be pronounced. Kidneys are pale brown with petechial or ecchymotic hemorrhages beneath the capsule.

While circumstantial evidence indicated that both pigweed and lamb's quarters might be involved, experimental confirmation had not been successfully attempted.

The purposes of this research were twofold: 1) to establish experimental confirmation that the weeds incriminated were or were not the etiologic agent of perirenal edema, 2) to characterize the disease more fully as relates to clinical signs, lesions, clinical chemistry changes and the probable cause of death.

The characterization of the disease will add to basic information useful in further study of toxic renal diseases. Knowledge of the pathologic effect will also suggest more meaningful areas of investigation concerning the toxic principle contained within the plants.

REVIEW OF LITERATURE

A distinct disease syndrome of swine called perirenal edema has been recognized by veterinarians in recent years (Buck et al. 1965; 1966; Larsen et al. 1962). Clinical signs are described (Buck et al. 1966) as characterized by weakness, trembling and incoordination. These signs progress rapidly to knuckling of the pastern joints and paralysis of the hind limbs. Sternal recumbency is a characteristic posture of affected pigs. When stimulated, such pigs try to walk by dragging their hind limbs which may appear partly or completely paralyzed. Caudal-ventral swelling and enlargement of the abdomen is frequently seen. Temperatures generally remain normal and the eyes are bright. Death commonly occurs within 24 hours after signs of illness are apparent (Buck et al. 1965; 1966; Osweiler 1966).

In field studies of ten naturally occurring cases of the disease Buck et al. (1966) studied the pathologic changes associated with characteristic clinical signs of the syndrome. Gross necropsy findings consistently included edema of the connective tissue around the kidneys. The amount of perirenal fluid varied, sometimes occupying a large portion of the abdominal cavity. In animals with

a clinical course longer than 24 to 36 hours a substantial amount of blood was found in the edematous fluid. Upon section, the lesion was found to be perirenal in nature and a normal-sized, pale brown kidney was found within the edematous or hemorrahagic mass. Edema of the ventral abdominal wall, the perirectal area, and in one instance, the stomach wall was reported (Buck et al. 1965; 1966). Other lesions reported (Buck et al. 1966) as associated with the disease were the presence of large amounts of clear, straw-colored fluid in the thoracic and abdominal cavities. Grossly, the kidneys of affected pigs were normal in size and pale brown with ecchymotic hemorrhages in the cortex.

Christensen (1955) reported a syndrome characterized clinically by acute illness with signs of ataxia, dyspnea, cyanosis and edema. Surviving animals were affected with signs of uremia, polydipsia, polyuria and proteinuria. At necropsy, lesions observed were those of fluid in the body cavities, edema in the subcutaneous tissues and edema in the mesentery. Constant findings were edema and hemorrhage around the kidneys.

McNutt (1953) studied edema disease of swine and reported an occasional lesion characterized by a thickened and edematous renal capsule separated from the ischemic kidney by considerable amounts of blood-stained fluid.

Perirenal edema was listed as a synonym for edema disease.

Larsen (1962) reported on a disease involving perirenal edema which differed from edema disease because of the tendency of edema to accumulate around the kidney. Initial symptoms of the condition were reported as depression, anorexia and ataxia, especially of the hindquarters. Pigs became increasingly weak and apathetic and progressed to general paresis and recumbency. Tremor and clonic convulsions were frequently noticed. Death generally followed in less than three days. Pigs recovering from the acute disease sometimes died of uremia several days later. Post mortem lesions of affected pigs revealed edema in the subcutaneous tissue of the abdominal wall and distention of the abdomen as well as the characteristic perirenal edema.

The occurrence of edema in swine and other livestock, particularly the localized or specific lesion of perirenal edema has been ascribed to a number of causes. The lesions of edema disease or enterotoxemia have been well described. Bennett (1964) in a complete chapter summarized the clinical, pathologic and etiologic factors considered relevant to edema disease. The salient clinical features of edema disease were reported as listlessness, reduced appetite and a weak, wobbly gait. Aimless circling, blindness, generalized tremors, prostration, running

movements and convulsions were also described. Affected animals did not generally have a rise in temperature. Death usually occurred within 48 hours after onset of clinical signs.

The pathologic changes in edema disease are often quite variable. Bennett (1964) reported edema of the stomach wall as the most prominent lesion, while edema was also common in the mesenteric folds of the spiral colon, the eyelids, ears, subcutaneous tissues of the face and the ventrolateral abdominal wall. Pulmonary edema, hydrothorax and hydroperitoneum were also described. Occasionally edema of the capsule of the kidney is observed, with the capsule separated from the kidney by a substantial amount of blood-tinged fluid. In such instances the kidney appears quite ischemic and the perirenal fluids gel upon exposure to air (Bennett 1964; McNutt 1953).

Bennett (1964) and Coulter (1965) have reviewed various hypotheses concerning the etiology of edema disease of swine. The number of possible etiologic conditions suggested include toxins, anaphylactic reaction, nonspecific stress, a virus and nutritional or psychic factors. The most general agreement favors the role of toxins elaborated by hemolytic strains of Escherichia coli under proper conditions in the intestinal tract.

Other workers have reviewed the etiology and pathology of edema disease (Erskine et al. 1957).

Reports of poisoning from deadly nightshade (Hyoscyamus niger L.) include perirenal edema and perirenal hemorrhage as characteristic lesions. Betts (1938) and Quin (1938) have observed blood clots around and adjacent to the kidney in cases of suspected deadly nightshade poisoning. Hofferd (1937) described extensive infiltration of blood and serum around the kidneys, gelatinous material in the abdominal fat and a similar substance around the gall bladder in pigs poisoned by belladonna alkaloids. Breed (1945) stated that if nightshade poisoned swine live for a few days and then die, they may have large amounts of straw-colored fluid around the kidneys and in the peritoneal cavity.

The clinical signs of nightshade poisoning include stupefaction, muscle trembling, incoordination, dilatation of the pupils, vomiting, nervousness and convulsions (Smith et al. 1956; Kingsbury 1964). Carey (1955), Casselberry (1939) and Hubbs (1947) reported field cases of nightshade toxicity due to Solanum nigrum L. However, none of these authors reported perirenal edema or gross evidence of kidney damage as a lesion. Oehme (1963) stated that a problem in differential diagnosis existed

between pigweed and nightshade poisoning.

Rutqvist and Persson (1966) conducted experiments in which pigs were injected with aflatoxin in varying dosages. One injected animal died within 90 minutes while five died in four to seven days. Clinical signs seen in affected swine were arching of the back, muscle trembling and difficulty in rising and standing. Upon necropsy, gross lesions observed included edema in the perirenal region, hydrothorax, pinpoint renal hemorrhages and anemia. Histopathologic examination of the kidneys revealed necrosis of the proximal convoluted tubules, a P.A.S. positive material in the distal tubules and lack of any consistent changes in the glomeruli. A pathologic change attributed to mycotoxins described by Forgacs and Carll (1962) and Sippel et al. (1953) was the presence of a large hematocyst beneath the peritoneum near one kidney and extending from the diaphram to the pelvis. Straw-colored fluid was also found frequently in the thoracic and abdominal cavities. The kidneys were pale and edematous and a gelatinous infiltration of the peritoneal covering of the colon was observed (Forgacs and Carll 1962). Icterus, generalized hemorrhage and yellow-colored livers were other commonly described lesions.

Microscopic renal lesions described for mycotoxin poisoning included glomerular atrophy, tubular dilatation,

edema and necrosis of convuluted tubules (Forgacs and Carll 1962; Sippel et al. 1953). Burnside et al. (1957) experimentally produced lesions of liver damage, icterus, renal capsular congection and swollen, edematous and hemorrhagic kidneys by feeding a water suspension of an Aspergillus flavus corn substrate.

Acorn poisoning of ruminants has been reported to cause some post mortem lesions similar to those described in swine by Buck et al. (1966). Kingery (1960) reported the lesions of acorn poisoning to include edema of the underline, petechia on the kidneys, edema of the loose sublumbar connective tissue and perirenal fat, pulmonary edema, hydroperitoneum and hydrothorax. This agrees with lesions described for oak poisoning by Boughton (1936) as edematous swellings of the body wall, masses of edematous jelly-like material in the abdominal cavity, edematous lymph glands, and pale brown kidneys studded with pinpoint hemorrhages. Smith and Jones (1966) ascribed the ventral edema to renal origin and have described polydipsia and polyuria as a result of the renal damage. Towers (1950) reported on a field case of acorn poisoning in which edema of the renal fat was a prominent lesion. The edematous fat also contained extensive ecchymotic hemorrhage. Smith (1959) has described the microscopic lesion of oak poisoning as characteristic and not duplicated by any other disease. Many proximal

convoluted tubules are necrotic and contain dense albumin casts which may be intimately mixed with the necrotic epithelial cells to form a dense homogeneous mass limited only by the basement membrane. Tubules adjacent to such necrotic tubules may appear normal and glomeruli are not affected. In a few kidneys examined, small greenish, rosette-shaped crystals appeared in some of the tubules. Mullins (1955) found lesions in acorn poisoned cattle consisting of necrosis of proximal convoluted tubules. In examining kidneys of sheep experimentally poisoned by acorns, Fowler and Richards (1965) report hyaline casts, necrosis of proximal tubular epithelium, dilatation of tubules and oxalate crystals in various parts of the tubules.

After extensive post mortem examination of swine characteristically affected with perirenal edema, combined with field trips to investigate the disease, Buck et al. (1966) determined several factors common to the disease. Cases of perirenal edema described invariably occurred during the summer months of July, August and September. The most commonly affected group of swine were those weighing between 30 and 125 pounds. The clinical history usually included sudden access to pasture or green plants after a period of drylot or concrete confinement, usually involving pigs which had never been on pasture before. Clinical signs of the perirenal edema condition usually appeared from five to ten

days after access to pasture. Identification of the flora involved in ten field outbreaks revealed that pastures contained good growth of Amaranthus retroflexus (redroot pigweed) or Chenopodium album (lamb's quarters) or both.

Histopathologic changes in affected swine kidneys examined by Buck et al. (1966) were those of tubular degeneration of varying degree. The proximal tubules were involved with cloudy swelling, hyaline droplet degeneration and necrosis. In some areas tubular lumens were occluded, while in others the renal eptihelium was sloughed. Some tubular lumens contained proteinaceous casts. Perivascular and interstitial edema was frequently observed. The major changes were observed in the renal cortex. A less constant finding included the presence of oxalate-like crystals within the tubular lumens.

The plant most often incriminated by Buck et al. (1966), A. retroflexus, is a member of the Amaranthaceae. It is a common weed of cultivation (Kingsbury 1964) and tends to grow in abandoned hog lots, fence rows, or waste areas. The coarse stem reaches a height of three to five feet by late July and is topped by a large rough inflorescense. Pigweeds have been shown to accumulate dangerous levels of nitrate (Case 1957; Gilbert et al. 1946; Kingsbury 1964; Marshall et al. 1967; Muenscher 1951; Olson and Whitehead 1940; Whitehead and Maxon 1952; Woo 1919). Olson and Whitehead

(1940) reported values as high as 6.10 percent KNO_3 in A. retroflexus from various South Dakota counties. Bradley et al. (1940), from experience with nitrate accumulating plants, arbitrarily set 1.5 percent KNO_3 as a minimum toxic level in forage.

Whitehead and Maxon (1952) showed that a number of environmental factors may influence the nitrate content of Amaranthus sp. and other potential nitrate accumulators. Those environmental factors reported as significant are: (1) high nitrate soils tend to produce crops high in nitrate content; (2) drought, especially if occurring during the time when plants are immature may increase the nitrate levels; (3) deficiency of certain soil micronutrients essential to enzyme function may tend to produce increased nitrate accumulation; (4) increased light intensity or longer photoperiod favor the assimilation of nitrate by plants; and (5) spraying with herbicides may result in higher nitrate content in those plants surviving treatment. Gilbert et al. (1946) reported that nitrate accumulation was favored by high nitrate soils and by shading of the plants. Muenscher (1951) and Kingsbury (1964) also report an increase in nitrate content in plants treated with 2, 4-D herbicides.

Several reports of acute poisoning in cattle due to ingestion of A. retroflexus are available (Bradley et al.

1940; Brakenridge 1956; Cursack and Romano 1967; Egyed and Miller 1963; Kingsbury 1964; Muenscher 1951). These workers have associated the acute death in ruminants with the high nitrate content of Amaranthus sp. One report of poisoning in cattle from eating A. retroflexus has included lesions of perirenal edema (Jeppesen 1966). Cursack and Romano (1967) also reported perirenal edema and ascites in subacute poisoning from A. hybridus L. var. quitensis.

The second weed incriminated as a cause of perirenal edema in swine (Buck et al. 1966) is Chenopodium album (lamb's quarters). The nitrate content of C. album has also been reported to approach dangerous levels (Gilbert et al. 1946; Kingsbury 1964; Muenscher 1951; Olson and Whitehead 1940; Whitehead and Maxon 1952). Gilbert et al. (1946) found the nitrate content of C. album as high as 6.5 percent KNO_3.

Some implication of the possible role of oxalates as a factor in the production of perirenal edema has been suggested (Buck et al. 1966). Oxalate crystals were observed by microscopic observation of kidney sections from field cases of perirenal edema. At least two members of the genus Amaranthus have been reported high in oxalate content. Srivastava and Krishnan (1959) reported the total oxalate content of leaves from Amaranthus gangeticus to be 15.41

percent of the plant on a dry weight basis. Those same workers reported only 4.41 percent water soluble oxalate on a dry weight basis. Marshall et al. (1967) found oxalate levels varying from 12.61 percent to 30.75 percent of the dry weight in A. retroflexus collected in Iowa. These are comparable or higher oxalate levels than those reported for Halogeton glomeratus (Bieb.) C. A. Mey (Kingsbury 1964) and for Oxalis cernua Thunb. (Dodson 1959).

Halogeton and other oxalate poisonings have been described (Clarke and Clarke 1967; Kwatra and Khera 1965). A common effect of acute oxalate poisoning has been the lowering of blood calcium due to formation of insoluble calcium oxalate. Oxalate crystals are observed in renal tubules during histopathologic examination. Anderson (1957) experimentally produced Halogeton poisoning in a ewe by feeding the dried plant. Lesions described included excessive fluid in the peritoneal cavity, congestion of the liver and kidney and edema between the rumen and abomasum. Histologic examination revealed casts and oxalate crystals in tubular lumens. Dodson (1959), in studying Oxalis cernua, produced poisoning in sheep by direct introduction of oxalic acid into the abomasum. Post mortem lesions were those of hemorrhagic and edematous kidneys. Microscopically, renal tubules appeared blocked with calcium oxalate crystals. Stewart and MacCallum (1944) reported large rises in serum

non-protein nitrogen in horses poisoned with various oxalate salts. Kwatra and Khera (1965) fed potassium oxalate to cattle. No gross lesions were observed at post mortem. Microscopic examination revealed increased cellularity of glomerular tufts, variable numbers of eosinophilic globular masses in Bowman's capsules, and presence of eosinophilic masses and crystals of calcium salts and triple phosphate in the tubular lumina. Mild interstitial connective tissue proliferation was seen in later stages. Degenerative changes in the renal tubules generally involved the entire kidney, not being confined to the tubules that showed the presence of calcium oxalate crystals. Intratubular calcium oxalate crystals were demonstrated in only a few cases.

EXPERIMENTAL PROCEDURE

Procurement and Care of Swine

The swine used were purchased from the Iowa State University Swine Nutrition Herd. All pigs were of Yorkshire-Landrace and Poland China parentage and weighed 20 ± 3 kg. No effort was made to select for bloodline, sex or litter origin.

The pigs were given a ration supplied by the Iowa State University Animal Science Department. The ration was identical to that supplied to the pigs before purchase and consisted of the following ingredients:

Ground yellow corn	78.25 lb.
Soy bean oil meal (50% protein)	18.50 lb.
Calcium carbonate	0.90 lb.
Dicalcium phosphate	1.25 lb.
Iodized salt	0.50 lb.
Trace mineral premix	0.10 lb.
Vitamin premix	0.50 lb.
Total	100.00 lb.

The vitamin premix and ration supplied the following levels of vitamins:

	Premix	Ration
Vitamin A	750 I.U./lb. diet	782 I.U./lb. diet
Vitamin D	300 I.U./lb. diet	----
Riboflavin	2.00 mg./lb. diet	0.61 mg./lb.
Pantothenic acid	4.00 mg./lb. diet	2.83 mg./lb.
Niacin	9.50 mg./lb. diet	9.19 mg./lb.
Choline	10 mg./lb. diet	397.00 mg./lb.
Vitamin B_{12}	10.00 mcg./lb. diet	----

All animals were clinically normal. All swine used were given 40 cc. of anti-hog cholera serum, subcutaneously, prior to the initiation of the experiments. The pigs were allowed to spend one week in the holding pens prior to initiation of feeding trials in order to acclimate them to the new surroundings.

Design of the Experiment

The pigs were divided into groups of six each and each group kept together in six-foot by ten-foot concrete-floored pens. After the one-week acclimatization period, blood samples were drawn from the anterior vena cava of each pig for hematologic and clinical chemistry examination. After the initial blood sample was drawn, pigs were subjected to the various weed feeding trials. All animals in each group were allowed free access to weeds for five days, during which time no other feed was made available. After five days

access to weeds, pigs were returned to a diet consisting only of the original complete ground-mixed feed. During the entire experiment, fresh water was available daily. Five days after being returned to feed, the swine were either euthanatized or discontinued for that experiment.

During the entire ten days of each trial, blood samples were drawn initially and at the fifth and tenth day via anterior vena cava venipuncture. Evaluations made upon the various groups to determine the effects of weeds upon the pigs were as follows:

1. Clinical signs characteristic of naturally occurring perirenal edema
2. Gross lesions at necropsy
3. Histopathologic lesions
4. Clinical chemistry and hematologic changes
5. Electrocardiographic (EKG) alterations

During August and early September of 1966, the feeding trials were conducted using three weeds and certain other modifications of the weeds. The following data indicate the identification of the pigs and the type of weed or treatment used:

Pig number	Type of weed	Disposition of weed
1	Amaranthus retroflexus	
2	" "	Fed ad lib.;
3	" "	fresh, cut
4	" "	twice daily
5	" "	
6	" "	

Pig number	Type of weed	Disposition of weed
7	Kochia scoparia Schrad.	
8	" "	Fed ad lib.;
9	" "	fresh, cut
10	" "	twice daily
11	" "	
12	" "	
13	Chenopodium album	
14	" "	Fed ad lib.;
15	" "	fresh, cut
16	" "	twice daily
17	" "	
18	" "	
19	Amaranthus retroflexus	
20	" "	Fed ad lib.;
21	" "	fresh, cut
22	" "	twice daily
23	" "	
24	" "	
25	Amaranthus retroflexus	
26	" "	
27	" "	Water extract
28	" "	
29	" "	
30	" "	
9	Amaranthus retroflexus	Swine retained from trials with C. album and K. scoparia, subjected to fresh A. retroflexus
10	" "	
11	" "	
14	" "	
16	" "	
18	" "	
10	Amaranthus retroflexus	Survivors from the previous group were given fresh A. retroflexus after a two-week recovery period
16	" "	
18	" "	
31	Amaranthus retroflexus	Fed ad lib. the solid residue from the water extraction procedure
32	" "	
35	" "	
33	Amaranthus retroflexus	Fed ad lib. a 30 to 1 concentration of water extract
34	" "	
36	" "	

Additional trials conducted during August and September of 1967 were as follows:

Pig number	Type of weed	Disposition of weed
913	Amaranthus retroflexus	Fed ad lib., fresh, cut twice daily
914	" "	
915	" "	
916	" "	
917	" "	
918	" "	
919	Amaranthus retroflexus	Fed ad lib. a dried and ground preparation of Amaranthus retroflexus leaves
920	" "	
921	" "	
922	" "	
923	" "	
924	" "	
919	Amaranthus retroflexus	Fed fresh Amaranthus retroflexus ad lib. after a two-week waiting period from the previous trial
921	" "	
922	" "	
923	" "	
924	" "	

Collection and Preparation of Weeds

All weeds fed fresh were hand cut and gathered twice daily from farmyards near Ames, Iowa. All pigs used in 1966 were fed with weeds from two locations. In both 1966 and 1967 the weeds gathered were from abandoned pig lots or cattle lots. Weeds were identified and sorted to insure homogeniety of the samples. Pens were cleaned and fresh weed was supplied twice daily.

Preparation of the water extract was accomplished by grinding the fresh leaves of Amaranthus retroflexus in a sausage mill and then soaking the ground preparation in water

for 14 to 16 hours. A filtrate was then made by passing the material through successive layers of cheesecloth and finally filter paper until a clear greenish-colored liquid was obtained. Twice the estimated daily intake of weeds was extracted in the calculated water needs of a group of six 22 Kg. pigs. The animals were then given access only to the water extract for the five-day period.

The concentrated water extract was fed to three pigs. A dilute extract was prepared as above. The fluid volume was then reduced thirty times by low temperature vacuum distillation.[1] The resultant concentrated water extract was stored at 37°F (4°C) until its use.

Amaranthus retroflexus collected in 1966 was dried, ground and fed to six pigs the following year.

Characterization of Clinical Signs

Swine were observed at least four times daily and clinical abnormalities noted. Changes characteristic of field cases of perirenal edema were recorded and given a numerical classification as follows:

0 Clinically normal

1 Mild depression, lethargy, decreased activity

2 Disturbance in gait, mild ataxia or knuckling

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[1]Vacuum evaporator, courtesy Dept. of Dairy Industry, Iowa State University, Ames, Iowa.

3 Unwilling to rise, but can if stimulated

4 Unable to rise even if stimulated; flaccid paralysis

5 Death

E Euthanasia

Necropsy and Histopathologic Procedures

Necropsy examinations were performed after death or after euthanasia on the tenth day of the trial. Portions from the brain, stomach, duodenum, ileum, colon, lung, aorta, renal artery, liver, kidney, spleen, adrenal gland, heart, skeletal muscle and lymph nodes were fixed in ten percent buffered formalin solution. They were dehydrated in ethyl alcohol, cleared in xylene and embedded in paraffin. Sections were cut at six microns and stained with hematoxylin and eosin.

Hematology and Clinical Chemistry

Blood and serum specimens collected during 1966 were analyzed and processed for the following:

(1) Serum calcium mg./100 ml.

(2) Serum magnesium mg./100 ml.

(3) Serum sodium mEq./L.

(4) Serum potassium mEq./L.

(5) Serum inorganic phosphate mg./100 ml.

(6) Serum glutamic oxalacetic-transaminase-sigma units

(7) Blood urea nitrogen mg./100 ml.

(8) Leucocytes/cubic mm.

(9) Packed cell volume percent

(10) Hemoglobin grams/100 ml.

In 1967, all tests performed utilized serum. Those analyses included the following:

(1) Serum calcium mg./100 ml.

(2) Serum magnesium mg./100 ml.

(3) Serum sodium mEq./L.

(4) Serum potassium mEq./L.

(5) Serum inorganic phosphate mg./100 ml.

(6) Serum chloride mEq./L.

(7) Serum urea nitrogen mg./100 ml.

(8) Serum creatinine mg./100 ml.

(9) Serum total protein grams/100 ml.

(10) Serum albumin grams/100 ml.

(11) Serum globulin grams/100 ml.

(12) Serum glutamic oxalacetic-transaminase-sigma units

All serum cations were determined using atomic absorption spectrophotometry.[1]

The determination of serum inorganic phosphorous was made according to the colorometric procedure described by Fiske and Subbarow (1925). Chloride values were found

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[1]Model 303 Spectrophotometer, Perkin-Elmer Corporation, Norwich, Connecticut.

according to the method of Schales and Schales (1941).[1] Blood urea nitrogen levels were obtained following the determination reported by Chaney and Marbach (1962). Serum creatinine was measured by a modification of the Folin-Wu technique as described by Davidsohn and Wells (1963). The colorometric determination of serum glutamic oxalacetic transaminase was accomplished by a modification of the method of Reitman and Frankel (1957).[2]

The improved Biuret Ferro-Ham modification was employed for determination of total protein and albumin-globulin ratios.[2]

Hemoglobin determinations were by the cyanmethemoglobin method (Benjamin 1961). Packed cell volume was measured using micro-hematocrit tubes according to the procedure described by Benjamin (1961). Leucocyte counts were done according to a standard method (Benjamin, 1961).

Electrocardiographic Studies

Electrocardiographic (EKG) recordings were made from pigs clinically affected in various stages of the perirenal edema syndrome. Recordings were made, with the exceptions noted, while swine were suspended in an upright position with a canvas or muslin sling. Standard limb

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[1]Sigma Reagents Kit, Sigma Chemical Co., St. Louis, Mo.

[2]Dade Reagents Inc., Manual of Clinical Chemistry Procedures, Miami, Florida.

leads I, II and III were employed using 27 gauge steel needle electrodes.[1] Calibration for amplitude was at 1 millivolt per centimeter. A paper speed of 2.5 cm. per second was used. When pigs were extremely flaccid or when death was imminent, lateral recumbency was the position allowed.

Statistical Analysis

Clinical chemistry changes were tested for statistical significance.[2] Swine fed Amaranthus retroflexus were compared to composite values for those fed Chenopodium album and Kochia scoparia. Thus the latter two groups served as controls, receiving a diet similar to those fed pigweed. Numerical values for each group were computed from a least square analysis which took into account missing data due to death of pigs. Significance of variance was determined using the F test method (Wine 1964). Only those values significant at the 0.05 level or less were considered.

Correlations between clinical chemistry variables were determined using Student's T test (Wine 1964). Only those correlations showing more than a ± 0.40 level of relationship were considered of value for this work.

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[1] Sanborn Model 51 Viso Cardiett, Sanborn Corp., Waltham, Massachusettes.

[2] Statistical Laboratory, Iowa State University, Ames, Iowa.

RESULTS

Five primary categories of information were included in the data recorded from this project. Evidence of perirenal edema was based upon (1) clinical signs exhibited in affected pigs, (2) gross lesions at necropsy, (3) microscopic lesions under hematoxylin and eosin staining, (4) clinical chemistry changes at specified times, and (5) electrocardiographic changes in affected pigs compared to normal swine.

Clinical Signs

Fifty-two pigs were used in the various trials. Of a total of 24 swine fed fresh Amaranthus retroflexus, all 24 developed some degree of clinical signs within a ten-day period. Eight of these 24 swine died within the ten-day period. Of 12 pigs allowed to live past the ten-day limit, a total of 8 died within 20 days. All swine fed various preparations of A. retroflexus, including dried weed, water extracted weed, water extract residue and concentrated water extract appeared clinically normal with respect to signs relating to perirenal edema for the entire observation period. Of 12 swine fed Chenopodium album or Kochia scoparia, none were affected clinically with signs similar to those fed A. retroflexus. The results of trials conducted

with various weeds and preparations are summarized in Table 1. At the end of the trial for K. scoparia and C. album, three of the unaffected pigs from each group were fed A. retroflexus. All six developed clinical signs of perirenal edema and two of that group died. Five swine unaffected clinically by a dried preparation of pigweed, were poisoned after five days ingestion of fresh pigweed.

The clinical signs and course of experimental perirenal edema commenced from three to seven days after initiation of a trial. Prior to onset of observable signs, intake of the plant (A. retroflexus) or feed decreased markedly. Generalized mild depression was commonly observed or occurred concurrently with a mild ataxia or knuckling of the tarsal-metatarsal joints, most prominent in the posterior quarters. The backs of pigs were often arched and a noticable slump or depression occurred posterior to the scapulae. Early mild ataxia often progressed to posterior paresis characterized by a crouching gait with flexion of the femoral-tibial and tibial-tarsal joints. Pigs would occasionally drag their posterior portions along the floor by means of the relatively unaffected front legs. Muscle tremors were common, particularly when the animals first arose. However, neither convulsions nor hyperesthesia were observed in any affected swine. Affected swine were generally alert and aware of their environment.

Table 1. Incidence of clinical signs and death in swine fed various weeds

Type of trial	Duration of observation in days	Number clinically affected	Number of deaths within 10 days	Number of deaths within 20 days
Amaranthus retroflexus	10	6/6	2/6	
A. retroflexus	20	6/6	3/6	6/6
A. retroflexus after *K. scoparia* and *C. album*	10	6/6	2/6	
A. retroflexus	20	6/6	1/6	2/6
A. retroflexus- after dried weed trial	10	5/5	4/5	
A. retroflexus- refed after previous pigweed	10	0/3	0/3	
A. retroflexus- dried	20	0/6	0/6	0/6
A. retroflexus- (water extract)	10	0/6	0/6	
A. retroflexus- concentrated water extract	10	0/3	0/3	
A. retroflexus- residue of water extract	10	0/3	0/3	
Kochia scoparia	10	0/6	0/6	
Chenopodium album	10	0/6	0/6	

Seriously ill pigs preferred to lie in sternal recumbency and often could not be aroused from that position (Figure 1).

The course of the disease from onset to death was quite variable. There was often spontaneous remission of severe clinical signs, while other swine in apparent good health would terminate within four to six hours. The time sequence of clinical signs and death in pigs fed A. retroflexus is given in Table 2. The nature of the paralysis seems best described as nearly complete muscle atony or weakness. Severely diseased animals lacked muscle tone and body strength. The appearance of many swine was similar to the effects seen from general anesthesia.

All swine fed K. scoparia and C. album remained active and in apparent good health. A mild greenish diarrhea was observed from the second to fifth day of the trial. This looseness of stool stopped when swine were returned to the grower ration.

No clinical signs of perirenal edema were seen in swine fed water extracts or extract residue of A. retroflexus Dried pigweed was fed with no observable clinical effects upon pigs.

In those groups fed pigweed and allowed to live longer than ten days, the majority either died or made an apparent recovery within an additional ten days. Only one pig

Figure 1. Characteristic posture and attitude of swine fed *Amaranthus retroflexus*

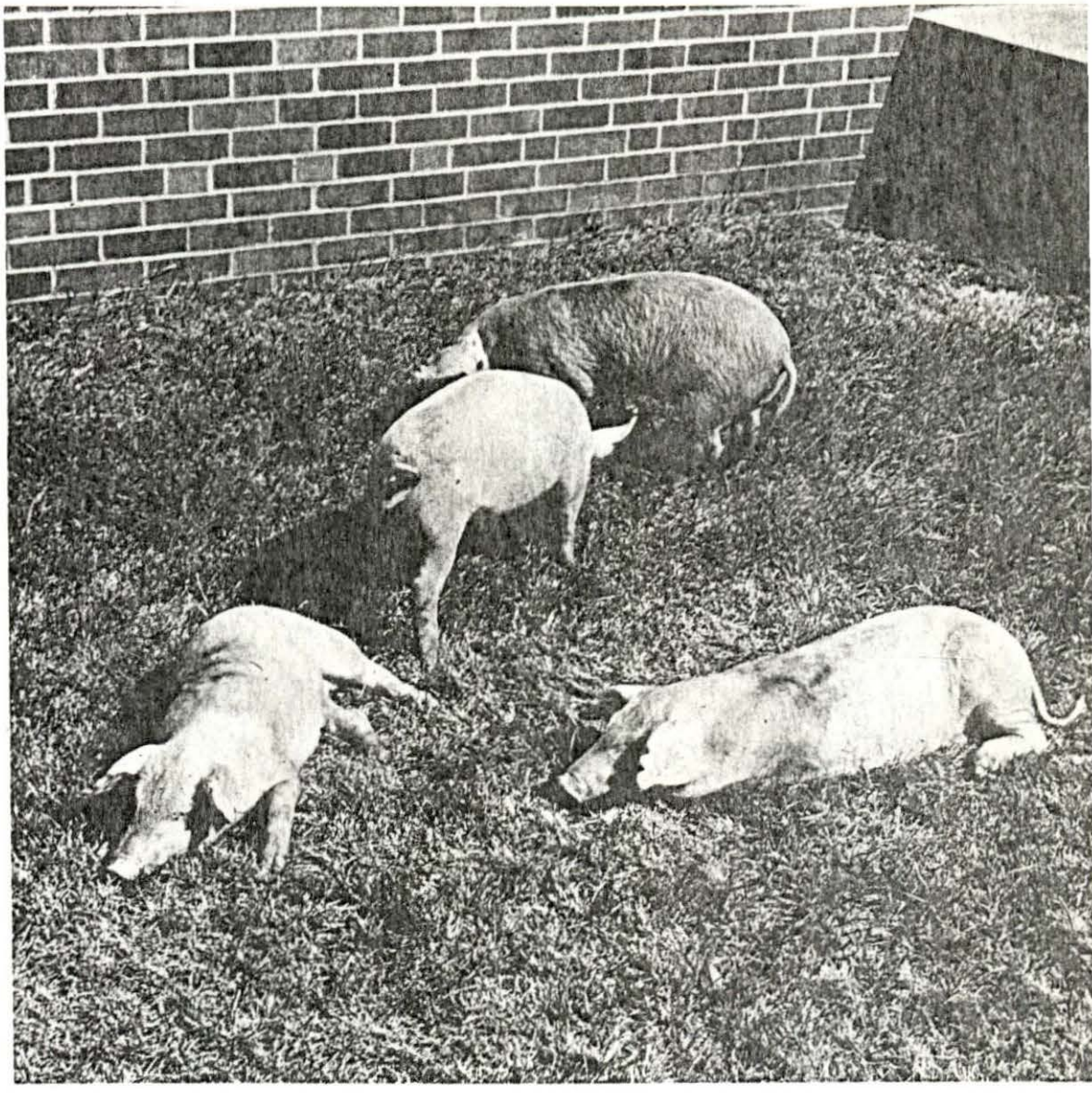


Table 2. Onset of clinical signs and death in swine fed *Amaranthus retroflexus*

Treatment	Pig number	Day of trial 1	2	3	4	5	6	7	8	9	10
Fresh *A. retroflexus*	1	0[a]	0	0	0	1[b]	3[c]	2[d]	2	1	5[e]
	2	0	0	0	2	1	2	0	0	0	0-E[f]
	3	0	0	0	3	4[g]	5				
	4	0	0	0	0	2	1	2	0	0	0-E
	5	0	0	0	0	0	1	0	0	0	0-E
	6	0	0	0	2	3	1	2	2	2	5
A. retroflexus refed after *K. scoparia* and *C. album*	9	0	0	0	1	4	0	1	0	0	0-E
	10	0	0	0	1	4	3	4	0	0	0
	11	0	0	0	2	4	0	0	0	5	
	14	0	0	0	0	4	5				
	16	0	0	0	0	0	0	1	0	0	0
	18	0	0	0	0	0	0	1	0	0	0
A. retroflexus - allowed to live	19	0	0	0	0	0	2	0	0	0	0
	20	0	0	0	0	2	1	0	0	0	0
	21	0	0	0	0	4	4,5				
	22	0	0	0	0	3	2	3	5		
	23	0	0	0	0	0	3	2	0	0	0
	24	0	0	0	0	2	1	0	4,5		

[a] 0= Clinically normal
[b] 1= Mild depression, lethargy, decreased activity
[c] 3= Unwilling to rise, but can if stimulated
[d] 2= Disturbance in gait, mild ataxia or knuckling
[e] 5= Death
[f] E= Euthanasia
[g] 4= Unable to rise even if stimulated; flaccid paralysis

Table 2. (Continued)

Treatment	Pig number	Day of trial 1	2	3	4	5	6	7	8	9	10
Fresh A. retroflexus	913	0	0	0	2	1	1	0	4	3	5
	914	0	0	0	2	4	2	1	1	0	0
	915	0	0	0	2	3	1	0	0	0	0
	916	0	0	0	0	0	0	0	4	0	0-E
	917	0	0	0	1	2	4	1	2	0	0
	918	0	0	0	0	0	0	0	4	1	0-E
Fresh A. retroflexus following dry A. retroflexus	919	0	0	0	0	0	2	3	5		
	921	0	0	0	0	0	2	3	5		
	922	0	0	0	0	0	1	1	5		
	923	0	0	0	0	0	2	3-5			
	924	0	0	0	0	0	1	2	3	2	0-E

(Number 914) developed evidence of chronic sequelae to the disease. This pig developed a very enlarged and distended abdomen and continued to excrete large amounts of dilute urine.

Gross Lesions at Necropsy

The gross pathologic changes considered as evidence of the toxic effect of the various weeds were easily recognized at necropsy. When present, gross lesions were invariably severe and extensive in nature. Only swine fed fresh A. retroflexus or the residue of a water extract of pigweed developed recognizable gross lesions compatible with those observed in field cases. The K. scoparia, C. album, water extract, and dried pigweed groups did not have gross lesions.

The most common gross tissue changes and their relative frequency of occurrence in individual swine are summarized (Table 3). The characteristic lesions observed included large amounts (150-400 ml.) of clear, straw-colored thoracic fluid and moderately increased amounts of pericardial fluid (Figure 2). The heart was generally in diastole, with dilatation of ventricles both of which were filled with clotted blood. Anterior ventral atelectasis was commonly observed in swine with hydrothorax. The liver was normal in appearance but moderately congested. Subcutaneous and intermuscular abdominal edema was marked and sometimes extended

Table 3. Incidence and distribution of gross lesions in swine fed *Amaranthus retroflexus*

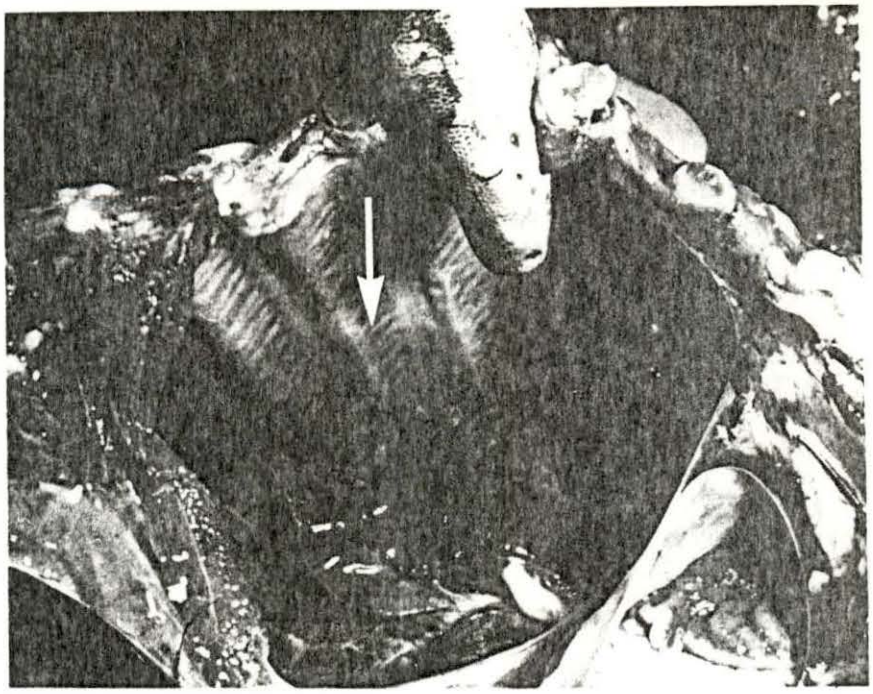
Type of trial	Pig number	Hydrothorax	Ascites	Edema of abdominal wall	Perirenal edema	Renal hemorrhage	Edema of urinary bladder and ligaments	Edema of mesorectum or mesocolon	Edematous or hemorrhagic renal lymph nodes
Amaranthus retroflexus	1		+	+	+	+			
	2			+	+	+	+	+	
	3	+	+	+	+		+		
	4	+		+	+	+			
	5				+	+			
	6	+		+	+	+	+	+	
A. retroflexus after *K. scoparia* and *C. album*	9			+	+				
	11			+	+		+	+	+
	14				+				+
A. retroflexus	19				+	+	+	+	
	20				+	+	+	+	+
	21	+	+	+	+	+	+	+	
	22	+		+	+	+	+	+	+
	23				+	+			
	24			+	+	+	+	+	+

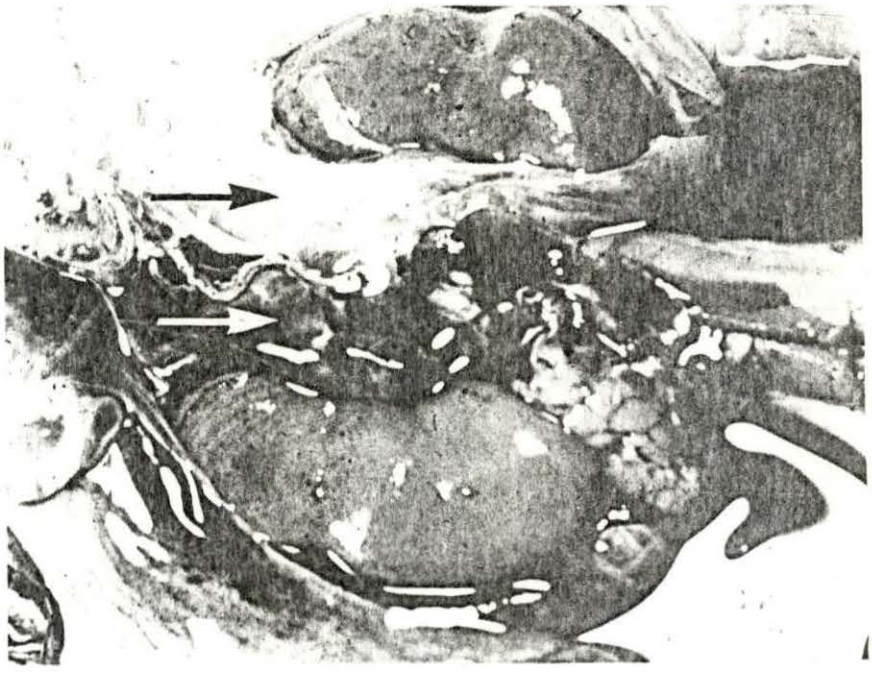
Table 3. (Continued)

Type of trial	Pig number	Hydrothorax	Ascites	Edema of abdominal wall	Perirenal edema	Renal hemorrhage	Edema of urinary bladder and ligaments	Edema of mesorectum or mesocolon	Edematous or hemorrhagic renal lymph nodes
A. retroflexus	913	+	+	+	+	+			
	914					+			
	915					+			
	916				+	+			
	917			+	+	+			
	918				+	+			
A. retroflexus	919			+	+		+		
after dried A. retroflexus	921	+	+	+	+	+	+	+	+
	922		+	+	+	+	+	+	
	923	+	+	+	+	+			

Figure 2. Thoracic cavity of pig fed Amaranthus retroflexus, illustrating large amount of thoracic fluid

Figure 3. Perirenal edema and retroperitoneal hemorrhage in a pig fed Amaranthus retroflexus





posteriorly to the inguinal area and anteriorly to the axillae. Upon entry of the abdominal cavity, ascites was commonly encountered. In no instance was the abdominal fluid tinged with blood.

One or both kidneys were surrounded by from one to five cc. of gelatinous edema (Figure 3). The location of the edema was retro-peritoneal, but exterior to the capsule of the kidney. The consistency of the edema varied from clear fluid contained in a retro-peritoneal sac to firm jelly-like coagulated material interspersed with numerous trabeculae of fibrin-like material. The perirenal edema was often extensive and encompassed the renal pelvis, adrenal glands, and ureters. Edema also extended to the urinary bladder involving the walls of that organ and its suspensory ligaments. Subserosal edema of the rectum, mesorectum and terminal colon was common. In females, mesometrial edema was regularly observed. Gross edema was found in inguinal, iliac and renal lymph nodes. The edema present was found to be blood tinged in a number of swine. In general, those swine living a more protracted course contained blood-tinged fluids in the edematous areas.

The affected kidneys appeared pale and ischemic. Petechial or ecchymotic hemorrhages were present in many cases.

Histopathologic Lesions

Microscopic renal lesions were present in all swine fed fresh A. retroflexus. Milder but similar lesions were observed in swine fed water extracts of pigweeds, dried pigweed, and the residue from water extraction procedures. Evidence of histologic changes was not found in swine euthanatized from the K. scoparia and C. album groups. Consistent and pertinent microscopic lesions were not observed in other tissues saved for examination. Edema was recognized microscopically in those tissues observed as edematous grossly, but lesions relating to specific damage in organs other than the kidneys were not seen.

The pattern of histologic renal damage in swine fed A. retroflexus is summarized in Table 4. In those animals dying after a clinical course of less than four days, the microscopic lesion was characterized by tubular coagulative necrosis, intratubular hyaline casts and sloughing of proximal and distal tubular epithelium. The damage to tubular epithelium was characterized by many degrees of degenerative changes, including cloudy swelling, hydropic degeneration, hyaline droplet degeneration and finally coagulative necrosis (Figure 4). Islands of necrotic tubules could be observed in the midst of relatively normal convoluted and collecting tubules. Necrotic tubule cells were often detached from the basement membrane and clumped together in an

Table 4. Distribution and severity of histopathologic renal lesions in swine fed *Amaranthus retroflexus*

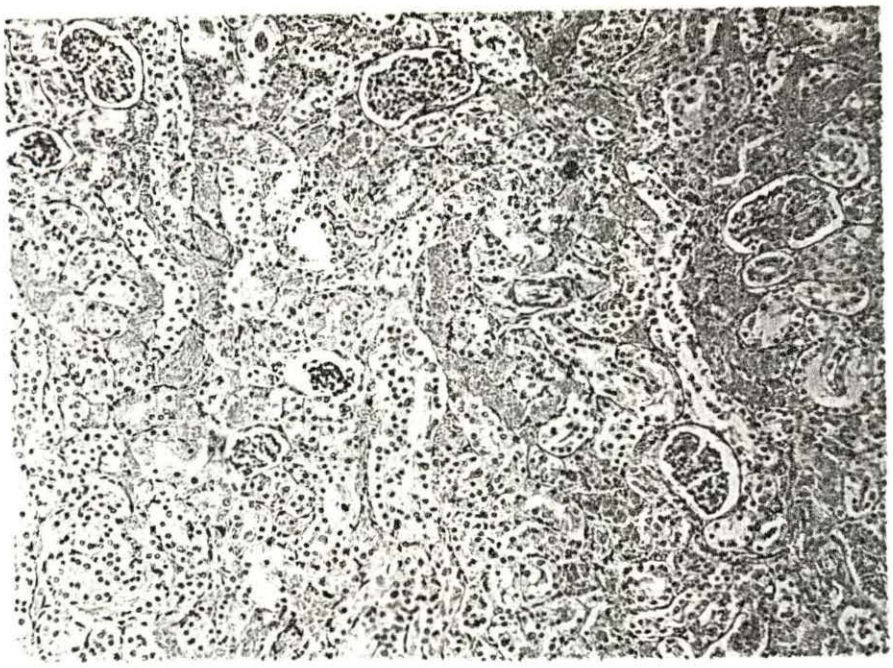
Pig number	Tubular degeneration and necrosis	Hyaline intratubular casts	Sloughing of tubular epithelium	Disruption of basement membranes	Dilatation of tubules and Bowman's capsule	Interstitial inflammatory response	Regeneration of tubular epithelium	Interstitial fibrosis
1	+	+			+	+	+	+
2	+	+	++	++	++	+		
3	++	+	++					
4	+	+	++	++	++		+	
5	+	+	++	++	++		+	
6	+	+	+	+	++		+	
9							+	++
11	+		++	++	++		+	
14	+++	+	++					
10					+++		++	+++
16					+++		++	+++
18					+			++
19	+	+			++			+
20	+	+		+			+	+
21	+++		+					
22	+++		+					
23	++	+	+					
24	++	+	+			+		

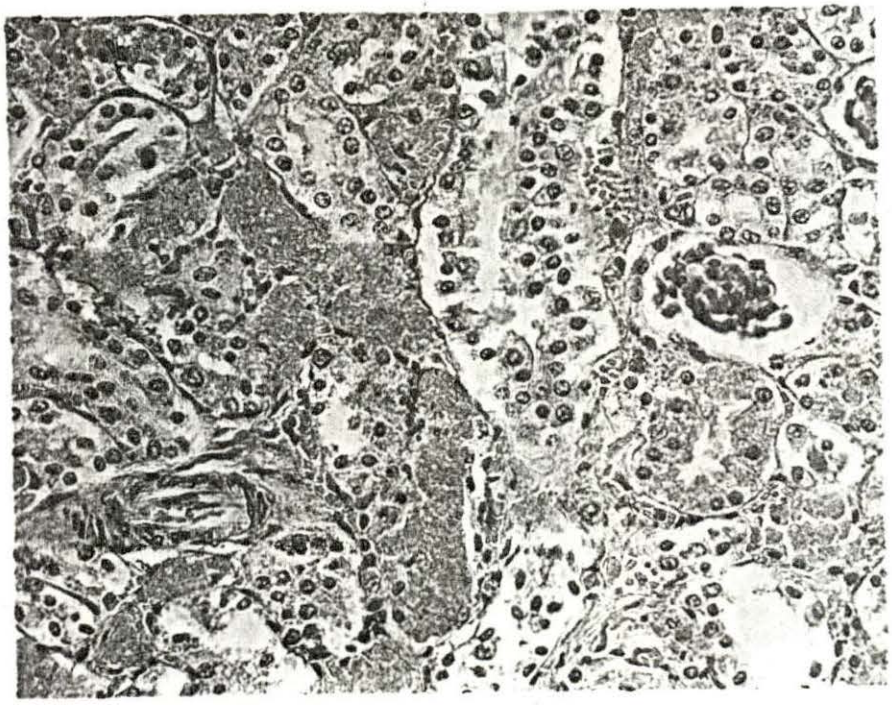
Table 4. (Continued)

Pig number	Tubular degeneration and necrosis	Hyaline intratubular casts	Sloughing of tubular epithelium	Disruption of basement membranes	Dilatation of tubules and Bowman's capsule	Interstitial inflammatory response	Regeneration of tubular epithelium	Interstitial fibrosis
913	+	+	++		+	+		+
914			+		+	+	+	+++
915		+			++	++	+	++
916	+	+	++	++	++		+	
917	+		+		+	+	+	
918	+	+	+++	+++	++		+	
919	+	+	++	+		+	+	
920					+	+		+
921	++	+	++	+		+		
922	++	++	++			+	+	
923	++	++	+++	+		+		
924						+	+	+

Figure 4. Appearance of renal cortex with foci of necrotic tubules in swine fed Amaranthus retroflexus. H & E. X 140

Figure 5. Renal cortex of pig fed Amaranthus retroflexus, showing tubular coagulative necrosis and desquamated epithelial cells. H & E. X 440



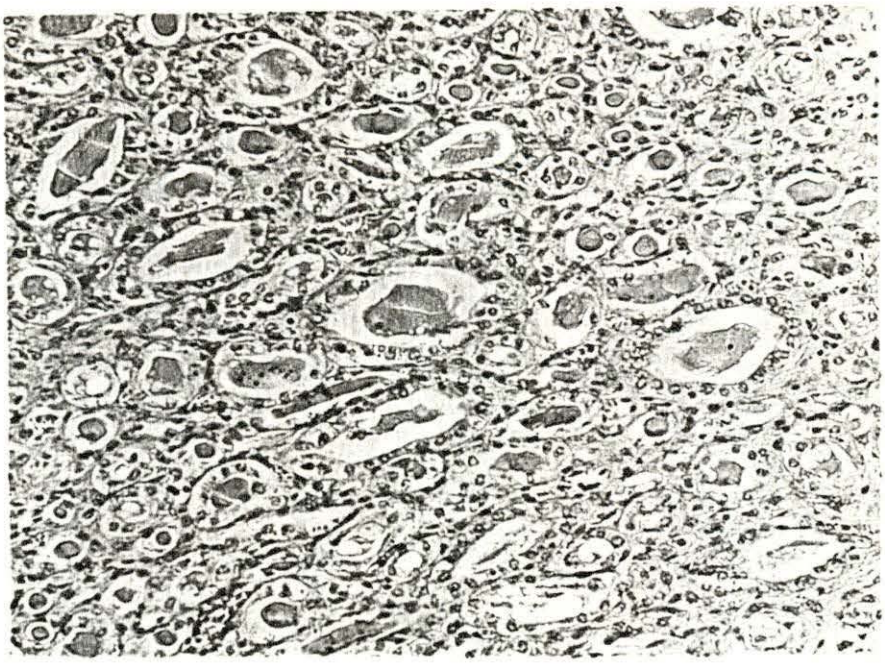


amorphous, eosinophilic mass (Figure 5). Numerous hyaline casts were present within the lumens of the collecting tubules and ducts (Figure 6). Droplets of eosinophilic staining material could also be found within the glomerular space. Interstitial inflammatory response and tubular dilatation were not characteristic lesions in swine dying less than four days after onset of clinical signs.

Characteristic changes were observed in swine living a clinical course longer than four days. In subacute or chronic stages there was little evidence of acute tubular necrosis. Large foci of tubular epithelium were denuded, leaving only the basement membrane of the nephron. In many cases the basement membrane was ruptured so that many tubular lumina were coalesced to form one large cystic space (Figure 7). Commonly, these cystic areas could be observed leading directly to the surface of the renal parenchyma. Cysts could be observed beneath the capsule of the kidney, often in direct communication with the dilated tubules and ruptured basement membranes (Figures 7, 8 and 9). Pink staining material often filled the subcapsular cystic areas. Subcapsular hemorrhage was also commonly observed. Those tubules not denuded of epithelium were markedly dilated as were the periglomerular spaces (Figure 10). The basement membranes of many tubules were lined with a flat squamous epithelium which appeared to be a regenerative stage of the

Figure 6. Intratubular hyaline casts in kidney of pig fed Amaranthus retroflexus. H & E. X 220

Figure 7. Section of renal cortex demonstrating tubular dilatation and disruption of basement membranes with development of subcapsular cysts. H & E. X 140



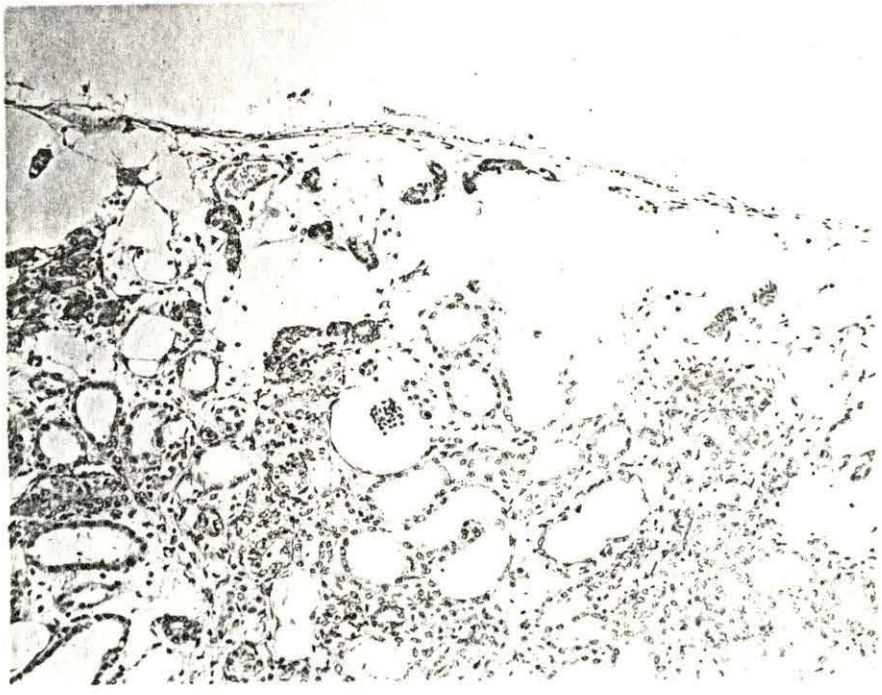
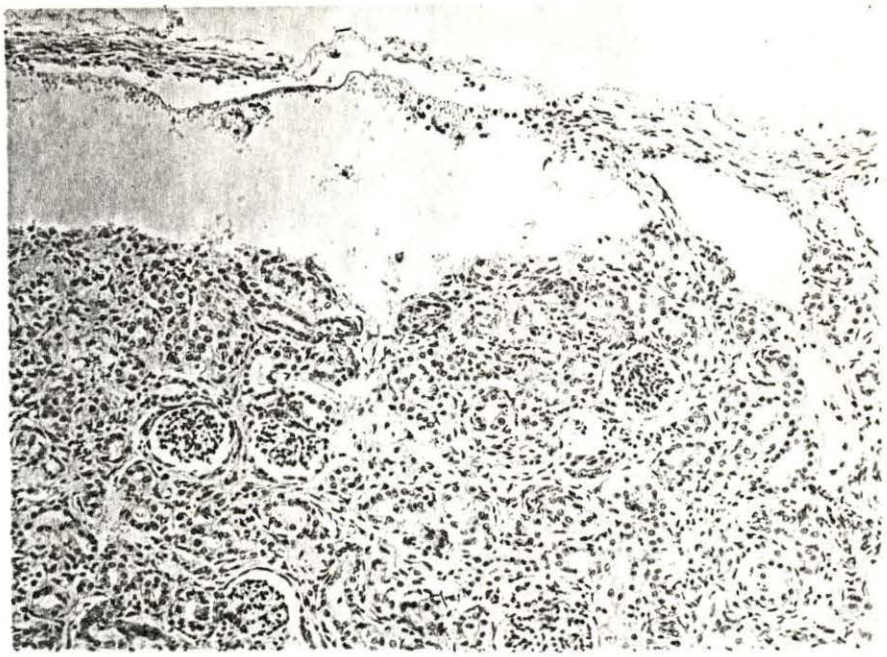
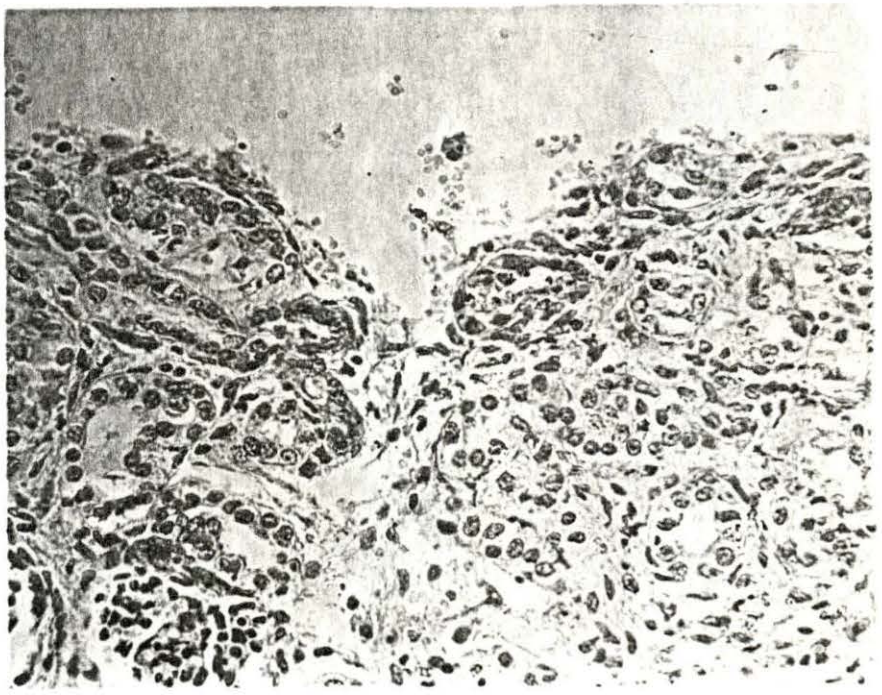


Figure 8. Section of renal cortex containing large subcapsular cystic areas. H & E. X 140

Figure 9. Section of renal cortex with evidence of fluid and erythrocyte passage to a cystic space. H & E. X 440

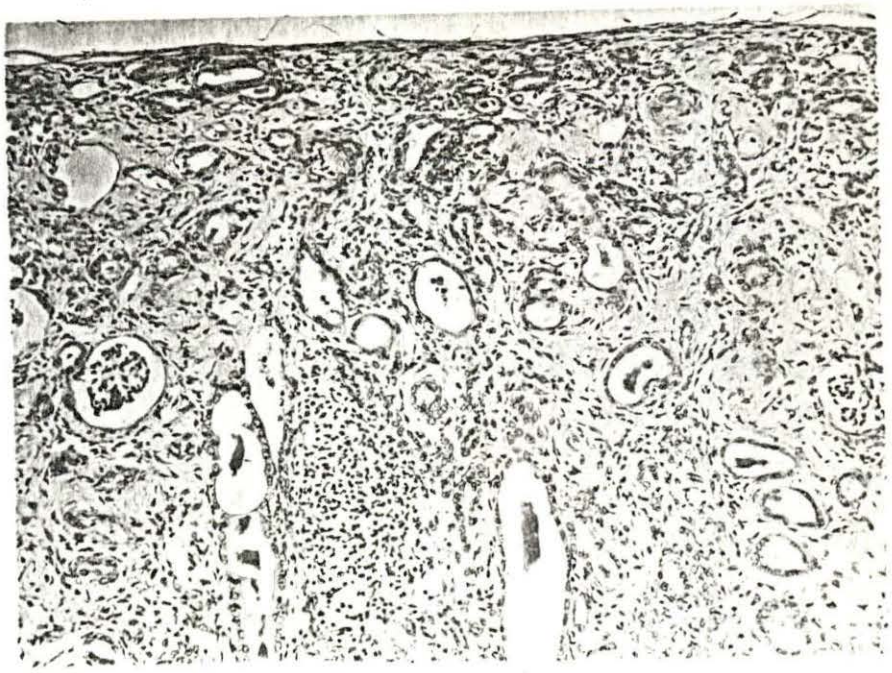


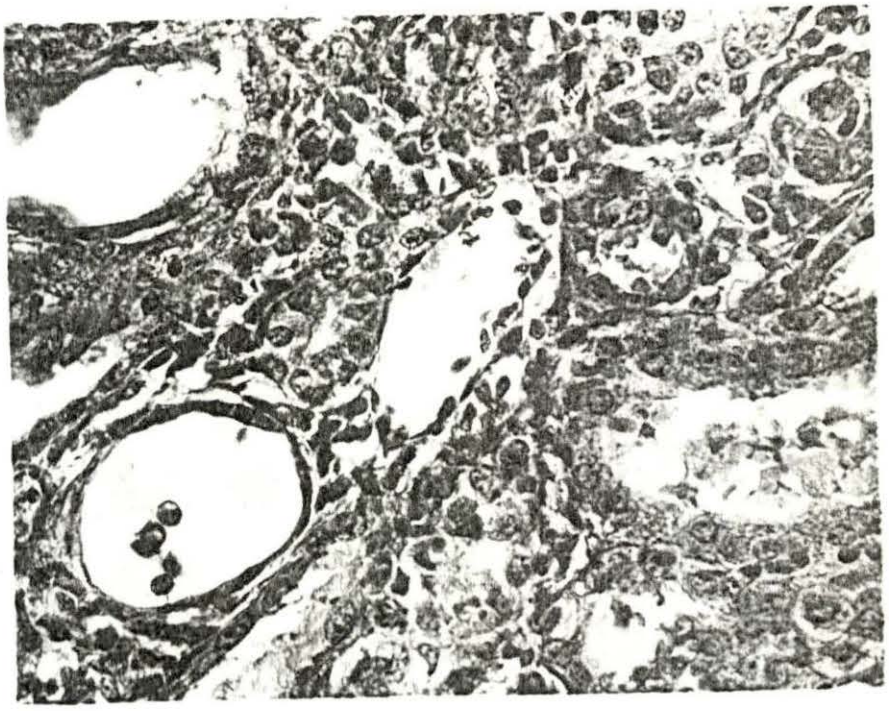


E.

Figure 10. Section of renal cortex demonstrating tubular dilatation, focal inflammatory response and fibrosis in kidneys of swine fed Amaranthus retroflexus. H & E. X 140

Figure 11. Section of renal cortex with dilated tubules and flat regenerating tubular epithelium in kidneys of swine fed Amaranthus retroflexus. H & E. X 560





tubular epithelium (Figure 11). Multiple focal mononuclear cell accumulations characterized the interstitial inflammatory response associated with a more protracted course of disease (Figure 10). Fibroplasia was evident in kidneys of those animals recovered from the acute disease.

Microscopic lesions were seen in kidneys of one pig fed a water extract of A. retroflexus. There was mild tubular dilatation, necrosis and sloughing of tubular epithelial cells. Moderate fatty change was observed in the liver of this pig.

Lesions of tubular coagulative necrosis and intratubular hyaline casts were present in the kidneys of swine fed dried A. retroflexus. Some sloughing and subsequent regeneration of tubular epithelium was observed. Similar lesions were found upon microscopic examination of kidneys from swine fed the residue of the pigweed water extraction. Additional lesions present in the residue group were an interstitial inflammatory response and subcapsular hemorrhages.

Clinical Chemistry

Clinical chemistry and hematologic studies were followed in all groups fed various diets in this project. Serum electrolyte values and serum constituents indicative of renal function were determined prior to beginning a trial, at five days and at ten days or termination where possible.

Serum sodium

Serum sodium values consistently were depressed in swine fed fresh A. retroflexus. Sodium levels were consistently lower in swine fed A. retroflexus than those fed K. scoparia and C. album. The lower levels of serum sodium were usually evident by the fifth day of a trial. The effect of various trials upon serum sodium is summarized in Tables 5, 6 and 7. K. scoparia, C. album and dried A. retroflexus did not cause significant decrease in serum sodium values.

Serum potassium

Swine affected clinically with signs of the perirenal edema condition experienced large increases in serum levels of potassium. All groups fed A. retroflexus in the fresh state had significantly higher (0.05 level) serum potassium levels than those swine fed K. scoparia, C. album, or grain ration. A marked rise in serum potassium was observed in the group fed a water extract of the pigweed. Tables 5, 6 and 7 list the mean values of serum potassium for swine fed various diets.

Serum calcium

Significant changes in serum calcium values were not recorded for the groups fed various diets. The K. scoparia

Table 5. Mean serum electrolyte values in swine fed *Amaranthus retroflexus* - 1966

Type of trial	Day of trial	Number of pigs	Na mEq/L.	K mEq/L.	Ca mg./100 ml.	Mg mg./100 ml.	PO_4 mg./100 ml.
Amaranthus retroflexus	0	6	144.0	5.55	11.68	2.90	10.25
	5	6	137.2	8.66	11.53	4.48	9.25
	10	5	138.6	10.62	12.32	3.68	8.45
A. retroflexus after *K. scoparia* and *C. album*	0	6	147.0	6.70	11.34	2.79	9.90
	5	6	139.6	14.98	11.66	3.80	9.03
	10	5	139.6	9.48	13.10	3.20	9.20
A. retroflexus	0	6	154.2	6.10	10.90	2.61	9.71
	5	6	129.7	11.61	12.11	2.78	11.43
	10	3	131.2	14.26	10.49	3.56	10.26
A. retroflexus - water extract	0	6	154.0	6.41	11.97	2.57	12.48
	5	6	151.2	7.42	12.24	2.67	8.63
	10	6	144.2	8.61	12.16	2.48	9.13

Table 6. Mean serum electrolyte values in swine fed Amaranthus retroflexus - 1967

Type of trial	Day of trial	Number of pigs	Na mEq/L.	K mEq/L.	Ca mg./100 ml.	Mg mg./100 ml.	PO_4 mg./100 ml.	Cl mEq/L.
Amaranthus retroflexus	0	6	144.2	6.23	10.72	2.96	9.31	105.3
	3	6	143.7	6.62	11.62	3.84	6.93	97.5
	5	6	132.3	9.04	11.79	4.41	6.68	84.9
	8	6	134.9	10.74	10.70	4.60	6.60	84.1
	10	5	140.9	7.93	9.85	4.10	7.22	87.9
Amaranthus retroflexus - dried	0	6	145.4	5.31	10.36	2.81	9.18	107.4
	3	6	143.2	6.71	11.54	3.27	7.85	98.5
	5	6	142.1	6.42	11.66	3.13	7.80	97.0
	8	6	147.1	5.88	11.33	3.14	6.38	102.3
	10	6	145.1	6.19	11.29	3.12	7.61	103.9
Amaranthus retroflexus after dried plant	0	5	150.5	6.45	11.95	2.91	6.66	106.0
	5	4	131.3	7.33	10.40	4.12	6.78	94.6
	8	2	129.4	14.40	12.63	5.61	5.35	79.7
	10	1	137.0	9.22	14.25	4.45	4.70	77.5

Table 7. Mean serum electrolyte levels in swine fed various diets

Type of trial	Day of trial	Number of pigs	Na mEq/L.	K mEq/L.	Ca mg./100 ml.	Mg mg./100 ml.	PO_4 mg./100 ml.	Cl mEq/L.
16% protein all grain ration	0	6	149.0	5.88	11.33	2.90	11.0	103.7
	5	6	147.1	5.86	10.45	2.87	10.2	108.1
	10	6	148.1	5.76	10.83	2.83	9.1	108.8
Kochia scoparia	0	6	149.7	6.63	13.13	2.90	8.99	--
	5	6	141.8	6.75	13.33	2.91	6.93	--
	10	6	142.8	7.15	13.13	2.68	8.85	--
Chenopodium album	0	6	144.3	7.13	10.88	2.86	8.41	--
	5	6	140.8	7.45	13.46	3.10	7.81	--
	10	6	138.5	7.77	13.30	3.14	9.23	--

and C. album groups tended to have higher serum calcium values than did the other groups studied (Table 7).

Serum inorganic phosphorus

Inorganic phosphorus serum levels varied greatly among groups. However, trends in levels of serum phosphorus and significant changes could not be demonstrated.

Serum chloride

Marked decreases were observed in serum chloride levels for 12 pigs fed A. retroflexus (Table 6).

Hematologic changes

Leucocyte counts were significantly different (0.05 level) in swine fed A. retroflexus when compared to those fed K. scoparia and C. album. Leucocyte numbers tended to increase markedly in the K. scoparia and C. album groups (Table 9). However, values for leucocytes in those two groups remained within normal values for swine of that age (Benjamin 1961). Packed cell volume (PCV) decreased moderately in swine fed A. retroflexus (Table 8) while the PCV for swine fed K. scoparia and C. album increased slightly (Table 9). A similar relationship of decreasing hemoglobin values in swine fed pigweed as compared to increasing hemoglobin levels in swine fed K. scoparia and C. album was observed (Tables 8 and 9).

Table 8. Mean hematologic and serum non-electrolyte values in swine fed *Amaranthus retroflexus*

Type of trial	Day of trial	Number of pigs	SGOT sigma units	BUN mg/ 100 ml.	Leucocytes /mm^3	PCV(%)	Hemoglobin gm/100 ml.
Amaranthus retroflexus 1-6	0	6	56.0	10.7	13,900	43	13.8
	5	6	89.0	206.0	12.500	38	12.5
	10	5	21.0	187.0	16,800	34	10.8
Amaranthus retroflexus after *Kochia scoparia* and *Chenopodium album*	0	6	48.0	9.4	12,600	37	11.6
	5	6	97.0	42.3	15,200	38	11.4
	10	5	73.0	134.0	15,000	33	10.9
Amaranthus retroflexus 19-24	0	6	21.0	12.6	14,700	37	10.8
	5	6	48.0	87.2	13,600	35	10.6
	10	3	28.0	260.3	14,500	36	9.6
Amaranthus retroflexus water extract	0	6	49.7	11.8	13,400	36	11.3
	5	6	51.3	56.8	16,800	39	12.6
	10	6	60.0	52.5	16,000	36	12.0

Table 9. Mean hematologic and serum non-electrolyte values in swine fed various diets

Type of trial	Day of trial	Number of pigs	SGOT sigma units	BUN mg./100 ml.	Crea-tinine mg./100 ml.	Total protein gm./100 ml.	Leuco-cytes /mm^3	PCV(%)	Hemo-globin gm/100 ml.
All bran, 16% protein grower ration	0	6	54.0	9.8	1.0	4.7	12,100	36	10.9
	5	6	49.0	13.6	1.1	5.3	13,200	39	11.3
	10	6	44.0	17.7	1.1	5.2	14,500	37	11.1
Kochia scoparia	0	6	51.7	15.4	-	-	11,000	37	10.8
	5	6	50.6	9.9	-	-	15,800	36	12.2
	10	6	64.4	12.4	-	-	19,800	38	11.8
Chenopodium album	0	6	41.6	7.5	-	-	10,900	37	10.6
	5	6	41.0	16.6	-	-	13,800	37	12.3
	10	6	42.5	17.0	-	-	21,600	40	12.3

Serum non-electrolytes

Four serum non-electrolytes were followed in various groups of swine. They were Blood Urea Nitrogen (BUN), creatinine, serum glutamic oxalacetic-transaminase (SGO-T) and serum total protein. Very large, significant rises in blood urea nitrogen occurred in each group fed fresh A. retroflexus for the first time (Tables 8 and 9). A significant (0.05 level) but smaller rise in blood urea nitrogen was recorded for swine fed a water extract of pigweed (Table 8).

Serum creatinine levels increased greatly in two groups of swine fed fresh A. retroflexus. Swine fed dried pigweed did not experience significant rises in serum creatinine.

Serum glutamic oxalacetic-transaminase levels were found significantly higher (0.05 level) on day five in two groups fed A. retroflexus than in pigs fed K. scoparia and C. album. No significant rise was found in pigs fed dried or water extracted pigweed.

Total serum proteins appeared to drop slightly in two groups of swine fed A. retroflexus. In one group followed, the drop was seen primarily as a decrease in serum albumin (Table 10).

Statistical significance of serum constituents

Electrolyte, non-electrolyte and hematologic values were tested for significance at the 0.05 level. Swine fed A.

Table 10. Mean levels of some serum non-electrolytes in pigs fed Amaranthus retroflexus - 1967

Type of trial	Day of trial	Number of pigs	SGOT sigma units	BUN mg/ 100 ml.	Creatinine mg/100 ml.	Total protein gm/100 ml.	Albumin gm/100 ml.	Globulin gm/100 ml.
Amaranthus retroflexus	0	6	48.0	12.0	1.8	5.9	3.3	2.6
	3	6		12.4	1.8			
	5	6	71.0	39.4	4.7	5.5	2.9	2.6
	8	6		68.6	11.6			
	10	5	31.4	118.1	11.4	5.1	2.7	2.4
Amaranthus retroflexus dried	0	6	43.3	12.9	1.8	5.5	3.2	2.3
	3	6		6.8	1.6			
	5	6	35.0	8.6	1.7	5.6	3.2	2.4
	8	6		9.2	1.7			
	10	6	41.1	10.5	1.7	5.5	3.1	2.4
Amaranthus retroflexus after dried plant	0	5	30.1	19.5	1.2	6.5		
	5	4	38.0	43.2	5.3	5.8		
	8	2		147.5	11.1			
	10	1	37.0	197.0	14.6	6.1		

retroflexus were compared to those fed K. scoparia and C. album. For comparative purposes, values from the latter two groups were combined and used as controls. The following variables were found to vary significantly at the 0.05 level:

Serum potassium

Serum magnesium

Serum glutamic oxalacetic-transaminase

Blood urea nitrogen

Serum creatinine

Total leucocyte counts

Hemoglobin

Correlations among different variables were determined. The greatest degree of correlation was found as shown in Table 11.

Table 11. Correlation of some variables in groups of swine fed fresh Amaranthus retroflexus

Variables	Amaranthus retroflexus (12 swine)	Amaranthus retroflexus (6 swine)	Amaranthus retroflexus (6 swine)
Sodium-Potassium	-0.59	-0.44	-0.71
Sodium-B.U.N.	--	-0.24	-0.19
Sodium-Creatinine	--	-0.16	-0.17
Potassium-B.U.N.	--	+0.23	-0.01
Potassium-Magnesium	+0.36	--	--
B.U.N.-Creatinine	--	+0.93	+0.80

The most obvious correlations were those of a negative nature between sodium and potassium and of a strongly positive trend between blood urea nitrogen and serum creatinine.

Electrocardiographic Recordings

Electrocardiograph tracings were recorded from 14 swine clinically affected by ingestion of A. retroflexus. Six normal swine of the same age, weight and breeding were also used for comparative purposes. Not all standard limb leads were used, but 12 animals were examined and recordings were made from at least two leads.

Six clinically normal swine had heart rates from 120 strokes per minute to 180 strokes per minute, the mean value being 140 strokes per minute (Table 12). The heart rate of clinically affected swine varied from 70 strokes per minute to 140 strokes per minute with a mean value of 104 strokes per minute (Table 13).

A recording taken from a clinically normal pig is shown illustrating the prominent P wave, tall and narrow QRS complex, and low T/R ratio (Figure 12).

Abnormal patterns in the electrocardiograph tracings were observed in clinically affected swine fed A. retroflexus. The characteristic changes seen were (1) a decrease in amplitude of the P wave, (2) increased duration of the QRS complex resulting in a wide and slurred QRS complex and (3) an

Table 12. Electrocardiographic characteristics of clinically normal swine fed commercial grower ration

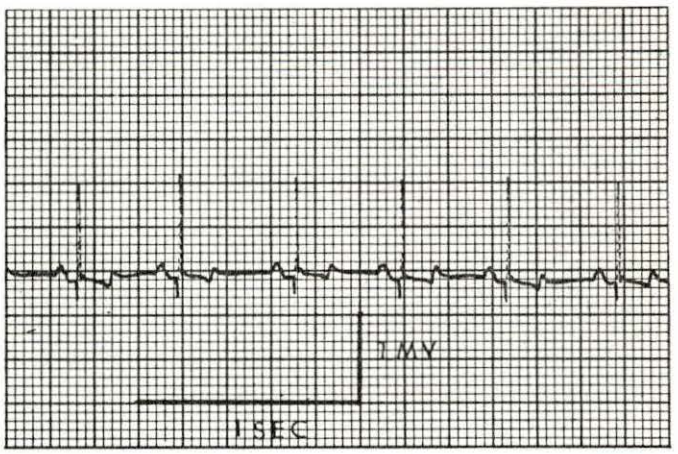
Pig number	Heart rate beats/ minute	P wave amplitude in millivolts			QRS duration in seconds	T/R ratio in percent		
		Lead I	Lead II	Lead III		Lead I	Lead II	Lead III
C-1	140	0.10	0.13	0.05	0.02	12	14	09
C-0	140	0.12	0.15	0.05	0.03	20	07	12
C-2	180	0.12	0.15	0.05	0.03	11	12	14
C-4	120	0.12	0.15	0.05	0.02	11	07	08
C-5	135	0.10	0.12	0.02	0.02	33	12	20
C-6	130	0.15	0.20	0.05	0.02	18	16	40

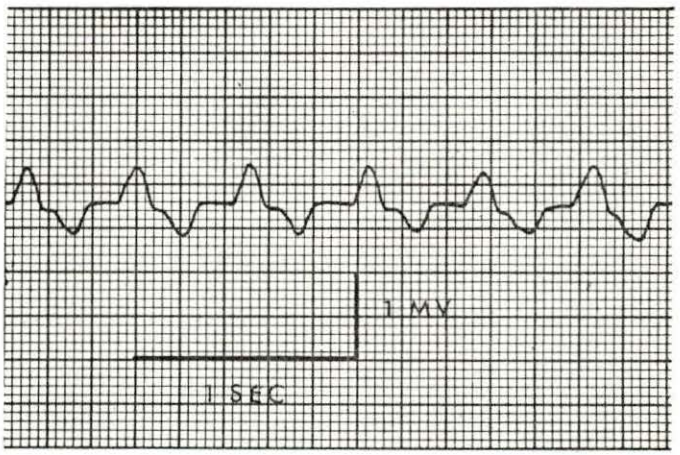
Table 13. Electrocardiographic characteristics of swine fed *Amaranthus retroflexus*

Pig number	Heart rate beats/ minute	P wave millivolts			QRS duration in seconds	T/R ratio in percent		
		Lead I	Lead II	Lead III		Lead I	Lead II	Lead III
3	100	0.05	0.05	0.04	0.08	63	58	262
6	108	0.06	0.09	0.10	0.08	60	50	121
9	140	-	0.00	0.02	0.05	-	67	75
10	100	0.01	-	-	0.08	50	-	-
11	70	0.02	0.00	-	0.10	75	140	-
20	105	0.03	0.05	-	0.05	75	44	-
21	140	0.10	-	0.08	0.04	30	-	33
22	95	0.10	0.08	-	0.05	67	70	-
23	110	0.05	-	-	0.06	150	-	-
24	90	0.05	0.02	0.05	0.08	100	43	33
913	105	0.05	0.10	0.05	0.10	67	175	38
914	120	0.08	0.10	0.10	0.05	67	75	59
915	120	0.03	0.03	0.0	0.06	84	100	180
923	75	0.00	0.00	0.00	0.20	500	400	-

Figure 12. Electrocardiographic recording from a clinically normal pig

Figure 13. Electrocardiographic recording from a pig fed Amaranthus retroflexus showing absence of P waves, abnormal QRS complex, and increased amplitude of T waves


1 MV
1 SEC


1 MV
1 SEC

increase in the amplitude of the T wave relative to the QRS complex (Figure 13). The rise in height of the T wave was the first abnormality recorded. This was followed by changes in the QRS complex and eventually by a decrease in P wave amplitude. In some cases P waves disappeared completely (Figure 13). In severely affected swine, the tracings were so distorted as to be difficult to distinguish as specific parts of the electrocardiograph. Recordings from severely affected pigs resembled a sine wave pattern with little similarity to normal tracings (Figure 14).

Numerical values for heart rate, P wave amplitude, QRS duration and T/R ratio in affected and normal pigs are shown in Tables 12 and 13.

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Figure 14. Electrocardiographic recording from a pig fed Amaranthus retroflexus illustrating the sine wave pattern occurring prior to death

1MV
1SEC

DISCUSSION

A major objective of this work was to substantiate or clarify reports from field investigation indicating Amaranthus retroflexus (redroot pigweed) and/or Chenopodium album (lamb's quarters) as possible etiologic agents for perirenal edema. The elimination of factors such as extraneous plants available, variation in previous ration and environment, and lack of past history were considered important. Twenty-nine of 29 pigs fed A. retroflexus at various times were affected with some degree of clinical disease during a part of the ten-day trial period. No evidence of clinical signs relating to the perirenal edema situation (Buck et al. 1966) was observed in swine fed other weeds or other preparations of A. retroflexus. A feeding trial with C. album gave no evidence of producing clinical signs. The fact that swine were not affected by being fed C. album but were subsequently made ill with A. retroflexus substantiates further that A. retroflexus is a cause of perirenal edema in swine. This also strongly suggests that C. album may not be an etiologic agent of porcine perirenal edema.

The onset and progression of clinical signs appeared most generally related to the muscle tone and strength of affected swine. Ataxia, paresis and paralysis were of a flaccid nature suggesting problems in either neuromuscular

transmission or muscle contraction. Evidence of convulsions, hypersensitivity, abnormal posturing or spastic motor movements was not observed. This suggests a lack of involvement of the central nervous system. Those pigs which died typically reached a crisis or terminal point within three or four days. Only uncommonly did swine linger for many days with severe clinical signs which terminated in death. Those animals able to reestablish relatively normal clinical bearing for several days commonly survived the clinical disease. A characteristic situation was one in which a pig was acutely ill, apparently recovered slightly and then was unexpectedly found dead or recumbent within a matter of hours. This clinical pattern is reported in human patients who have suffered severe renal damage (Leiber and Davidson 1961). The characteristic muscle weakness or flaccid paralysis seen in affected swine is observed in humans with severe acute renal disease and hyperkalemia (Merrill et al. 1950; Finch et al. 1946).

The depressive effect of uremia related to kidney failure is recorded in man (Hoffman 1963). High urea nitrogen values in swine could result in the same biochemical lesion and similar clinical signs.

The gross lesions similar to those reported by Buck et al. (1966) in investigating field cases of porcine perirenal edema supports the role of A. retroflexus as a cause of the disease. The complete lack of such gross lesions in

swine fed C. album is further evidence that lamb's quarters may not be toxic to swine. Gross lesions were not seen in swine fed dried pigweed or a water extract of the pigweed. This was felt to be due to some change in the active principle, rendering it less toxic. Intake of dried plant and water extract was considered adequate to provide enough pigweed to supply the toxic principle if present.

All swine fed fresh A. retroflexus had some degree of perirenal edema or evidence of previous renal damage as shown by gross fibrosis of kidneys.

The histopathologic renal lesions from experimental A. retroflexus poisoning were similar to those described by Buck et al. (1965) and Buck et al. (1966). The characterization of the experimental histologic lesions and their comparison with those described by Buck et al. (1966) was another major objective of this work. All of the histopathologic lesions described by Buck et al. (1966) were observed in kidneys of swine fed A. retroflexus. The only exception to the above was the lack of demonstrable oxalate crystals in the tubules of experimental swine. In addition to tubular degeneration, and necrosis with epithelial sloughing, an additional important lesion was observed. This lesion was a disruption or breaking of the basement membrane. Oliver (1953) considers the integrity of the basement membrane to be an important factor in the severity of renal

damage. Thus, a single break or occlusion in the lumen renders the entire nephron useless for excretion no matter how much tubular epithelial regeneration occurs. Oliver (1953) has extensively studied the pathogenesis of renal failure from nephrotoxic agents by use of microdissection techniques to examine the structure and lesions in individual nephrons. She states that nephrons suffering disruption probably never become functional units again. When repair cannot bridge the gap, an atresia persists in spite of relining of the tubule. The tubule proximal to the point of attempted repair undergoes dilatation and later atrophy. This explanation would seem logical reasoning for the characteristic dilatation of tubules and disruption of the basement membrane seen in swine fed A. retroflexus.

The histologic lesions characterized by dilatation and basement membrane rupture were those from swine living longer than three days after onset of clinical signs. Renal lesions in swine terminating from acute disease were those of cloudy swelling, hyaline droplet degeneration, and coagulative necrosis. These swine had apparently not had time to develop the tubular dilatation described by Oliver et al. (1951). Further studies by Oliver (1953) in rats poisoned with sublimate of mercury demonstrated renal lesions similar to those described for subacute perirenal edema. Kidneys of rats studied by Oliver (1953) at four days post

exposure revealed tubules in all stages of damage from cloudy swelling to necrosis. Many tubular epithelial cells were swollen and granular, but nuclei appeared normal and alive. By seven days, lesions had progressed to an overall general dilatation of tubules with many lined by flat immature epithelium. Again, the pattern and time sequence of lesions appears quite similar to those observed in kidneys of A. retroflexus fed swine. The flat regenerating epithelium lining tubules in kidneys of affected swine is further evidence of the attempted regeneration and repair described by Oliver (1953).

The period of several days required for tubular function to return is mentioned by Bull et al. (1950) as a critical period. If the oliguria of this phase does not cause the animals demise, the second phase, diuresis, occurs. During the diuretic phase, urine flow is re-established but tubular selectivity is subnormal. The lack of adequate electrolyte control is suggested by Oliver (1953) as due to the lack of mitochondrial elements in regenerating tubular epithelium.

The histopathologic renal lesions described by Smith (1959) for oak poisoning in ruminants bear striking resemblance to the lesions observed in acute poisoning by A. retroflexus. Lesions common to both are intermittent islands of coagulative tubular necrosis and numerous hyaline

casts in tubular lumens. Lesions of a similar nature are described by Troen et al. (1951) for bichloride of mercury poisoning in man. Kugel (1947) states that acute toxic nephroses appear quite similar in clinical manifestations, laboratory findings and pathology despite varied etiology. Thus, evidence indicates that the renal lesion is due to a possible common cellular dysfunction.

The correlation of gross lesions with histopathologic renal damage is an interesting prospect. The resultant edema as a sequel to both physical and biochemical abnormalities must be considered. The physical predisposition to perirenal edema could well be related to the disruption of basement membranes and tubules described earlier. Numerous lesions were observed in which several disrupted tubules coalesced to form large cystic spaces. These cystic spaces commonly led to and directly communicated with subcapsular cysts filled with fluid or blood. Interstitial edema was observed also. Thus, numerous conduits for glomerular filtrate were formed which allowed fluids and electrolytes to move to the renal subcapsular area and then filter into the retroperitoneal perirenal connective tissues. Since the perirenal area is anatomically related retroperitoneally to the mesentery, mesometrium, ligaments of the bladder, and mesorectum, the fluid was able to move via a path of least resistance into these areas. Edema of the abdominal wall can also be related to the perirenal

fluid since lamina of fascia and muscle form routes for fluid migration from the sublumbar area to the ventral abdominal wall.

The presence of mild histologic renal lesions in swine fed dried A. retroflexus suggests that the plant retains at least a portion of its toxic principle after drying. It is known that certain oxalate containing plants such as beet tops are less toxic when wilted (Clarke and Clarke 1967). A. retroflexus has been reported high in oxalates (Marshall et al. 1967, Srivastava and Krishnan 1959). While the histologic renal lesion of A. retroflexus intoxication does not appear to be a classical oxalate nephrosis, the presence of oxalates in the plant could be a clue to an unknown toxic principle present in oxalate containing plants.

The correlation of histopathologic lesions with biochemical changes was a third important objective of this work. In its entirety, such an undertaking would be a project in itself. However, serum clinical chemistry examinations were selected on the basis of simplicity and uniformity of sampling which would suggest the primary biochemical and electrolyte alterations.

The serum electrolytes most consistently altered were potassium, sodium and magnesium. Numerous authors attest to alterations of these serum electrolytes during renal

insufficiency (Iseri 1952; Merrill 1956; Merrill 1960; Sirota and Kroop 1951). The early phases of renal damage, including toxic nephrosis, includes a period of oliguria (Bull et al. 1950; Elkinton and Danowski 1955; Kugel 1947; Partenheimer and Citron 1952; Pitts 1963). Patients able to survive the period of oliguria often recover from the renal disease. It is well known that the selective reabsorption of sodium and excretion of potassium is maintained by the renal tubular epithelium, particularly the distal portions (Davidson et al. 1958; Pitts 1963; Smith 1947; Taggart 1958). As suggested by Oliver et al. (1951) and Oliver (1953), any break or blockage in the continuity of the tubule results in a loss of urine flow. The lack of urine elimination (anuria) interrupts the only significant route for loss of potassium from the body (Schwartz et al. 1951). The association of oliguria or anuria with hyperkalemia is also recorded by other workers (Bradley et al. 1950; Elkinton et al. 1949; Hoff et al. 1941; Merrill 1960). The problem of hyperkalemia is further compounded by intake of foods containing potassium salts (Derow 1954; Merrill 1960). Hoffman (1950) and Kolff (1950) state that tissue breakdown in the presence of inadequate renal function can enhance potassium excess in the extracellular fluids. The clinical signs and histologic lesions seen in swine fed A. retroflexus agree with the conditions stated

above. Clinically, oliguria was evident in affected pens. The intake of potassium was substantial due to high levels of potassium in the plant material, and some tissue breakdown occurred due to renal necrosis and muscle wasting in severely affected, anorectic pigs.

The problem of lowered serum sodium values in affected swine may be related to two factors. Gartner (1962) found that dogs with chronic interstitial nephritis had diminished tubular reabsorption of sodium. The tendency for decreased reabsorption of sodium in renal tubular disease in man is also recorded (Pitts 1963; Platt 1950). Since approximately 99 percent of the filtered sodium is reabsorbed via the renal tubules (Guyton 1966; Platt 1951), it is logical that tubular damage could result in a net sodium loss. Because the intracellular stores of sodium are small (Guyton 1966; Pitts 1963), the loss of extracellular fluid sodium is poorly replaced. In perirenal edema the extracellular fluid compartment is increased due to the copious edema, thus diluting even more the extracellular sodium. The lowering of extracellular sodium may serve to increase serum and interstitial fluid potassium levels. Hoe and O'Shea (1965) in studies of nephritic dogs did not find a correlation between hyperkalemia and hyponatremia. In swine fed A. retroflexus a high degree of correlation between high serum potassium levels and low serum sodium levels was found.

A significant rise in serum magnesium was observed in swine fed A. retroflexus. This agrees with the finding of Bradley (1946) who reported an accumulation of magnesium in the blood during renal insufficiency. The hypermagnesemia of renal failure is also recorded by Elkinton and Danowski (1955) and attributed to the same general causes as hyperkalemia.

Bradley (1950), Hoe and O'Shea (1965), Pitts (1963), and Platt (1951) report increased serum inorganic phosphates in renal damage and insufficiency. A significant rise in phosphate levels was not observed in pigs fed A. retroflexus. The increase was less marked than that reported by the authors just cited. Pitts (1963) explains hyperphosphatemia on the basis of reduced glomerular filtration. Thus, once renal blood flow and filtration return, the elevated phosphate levels drop toward normal.

Serum chloride levels were found to decrease markedly in swine fed A. retroflexus. This generally followed the decrease in values for serum sodium. The levels of serum chloride are generally considered related to sodium and to follow the movement of that cation (Elkinton and Danowski 1955; Guyton 1966; Pitts 1963).

Serum glutamic oxalacetic-transaminasse levels were significantly increased on day five to the A. retroflexus

feeding trials. Cornelius and Kaneko (1963) and Benjamin (1961) consider SGO-T significant in myocardium, skeletal muscle and hepatic tissue of swine. With the exception of two animals no histologic evidence of damage to muscle, myocardial or liver tissues was found in swine fed A. retroflexus. Thus, there may be some suggestion for moderate levels of SGO-T in renal tissue of swine. Further assessment of renal damage was made from serum urea nitrogen and serum creatinine levels. Very large increases in both urea nitrogen and creatinine were found in swine with renal damage. A very high correlation between levels of these two constituents was observed. Creatinine excretion is dependent upon tubular function and is not influenced by dietary protein intake, protein catabolism, or exercise (Benjamin 1961; Hoffman 1963). Thus, Hoffman (1963) considers creatinine to be a more reliable index of renal damage than urea nitrogen. However, Hoe and O'Shea (1965) in studying canine nephritis believed that urea nitrogen was a more reliable index of renal damage than was creatinine. This author's experience with renal damage due to A. retroflexus suggests that high serum urea nitrogen levels can occur in the absence of clinical signs or with only mild renal lesions. This effect of elevated serum urea nitrogen values was particularly evident in swine fed a water extract of A. retroflexus. Even though histologic lesions were mild,

the pigs in this group failed to receive adequate energy intake. The loss of body tissue and muscle mass for energy may have resulted in the increases in serum urea nitrogen seen in the extract group. Elevations in both serum urea nitrogen and serum creatinine are considered diagnostic of renal damage (Benjamin 1961; Elkinton and Danowski 1955; Hoe and O'Shea 1965; Hoffman 1963; Pitts 1963).

Significant decreases in hemoglobin concentration and markedly lowered packed cell volume (PCV) were observed in swine fed A. retroflexus. Two possible explanations of these decreases are offered. First, the extracellular fluid volume expansion evidenced as edema may have diluted the constituents of the circulating blood. A second possibility is that the renal damage due to A. retroflexus may have impaired the renal erythroprotein factor associated with stimulation of erythropoesis (Guyton 1966; Pitts 1963).

A marked increase in leucocyte counts was observed in the pens of swine fed C. album and K. scoparia. No information or explanation concerning this effect could be found. However, even though the absolute rise was significant statistically (0.05 level), the increase was still within the normal ranges given for swine (Benjamin 1961).

A logical task to follow the determination of electrolyte and non-electrolyte changes in swine fed A. retroflexus is the demonstration of the physiologic effect of those

changes upon the animal. Numerous reports of the effects of hyperkalemia in man are available. Two major effects upon the organism are described. A change related to hyperkalemi is the occurrence of paresthesia of the extremities and flaccid paralysis of the voluntary musculature (Finch et al. 1946; Hoffman 1950). Hoffman (1950) states that even when the extracellular potassium level is elevated, the intracellular potassium stores may be severely depleted. Thus, the imbalance between intracellular and extracellular potassium can alter the membrane potential of muscle cells sufficiently to prevent proper contraction (Guyton 1966).

Hyperkalemia is associated with abnormal cardiac function and cardiac failure. Numerous authors consider excessive levels of serum potassium to be the cause of cardiac failure in acute renal failure (Bradley 1946; Darrow 1950; Hoff et al. 1941; Keith 1944; Merrill 1956; Partenheimer and Citron 1952; Winkler et al. 1940). The progression of electrocardiographic changes leading to fatal cardiac arrest are well documented (Derow 1954; Hoff et al. 1941; Hoffman 1963; Maher and Schreiner 1962; Merrill 1960; Pitts 1963; Winkler et al. 1940; Wolff 1956). Merrill (1960) and Hoffman (1963) described the characteristic changes. There is development of tall, pointed T waves with depression of the S-T segment. The duration of the QRS complex is increased and the P wave amplitude is diminished.

Arrhythmia is observed. The ventricular complexes disintegrate culminating in a baseline having the appearance of a continuous sine wave. This is followed by ventricular standstill.

These characteristic EKG changes are described for swine in experimentally induced hyperkalemia (Kronberger et al. 1964). The EKG changes seen in swine fed pigweed correspond to the abnormalities described in hyperkalemic human beings and swine. The most prominent EKG alterations in swine fed pigweed were decreased or absent P waves, a wide and slurred QRS complex, and an elevated T wave. The T/R ratio for the EKG recordings of hyperkalemic swine were markedly higher than those of six clinically normal swine.

EKG recordings were taken from swine while suspended in a canvas sling, or occasionally while in lateral recumbency. According to Seidel and Bornert (1964) the variation in left lateral, right lateral and sternal positions of swine did not significantly alter the EKG.

While hyperkalemia may be the major factor in cardiac changes, other cations must be considered in their effect upon the EKG. Merrill (1960), Schwartz et al. (1951), and Pitts (1963) state that concurrent hyponatremia may enhance the EKG changes caused by hyperkalemia. Finch et al. (1946) and Merrill (1956) found that administration of sodium-containing solutions to hyperkalemic patients temporarily improved

the EKG, even though extracellular potassium did not decrease. Anderson and Laragh (1958) felt that cardiac toxicity was directly related to the extracellular potassium concentration in sodium depleted animals. Merrill (1956) felt that the concentration of sodium and calcium, acting as potassium antagonists, may play a role in the total effect upon cardiac function and the EKG. According to Merrill (1960) the EKG records the totality of electrolyte effects on cardiac muscle. Thus, hyperkalemia may not always be associated with the clinical syndrome of potassium intoxication. The EKG recordings from swine fed A. retroflexus could in most respects be associated with hyperkalemia. T/R ratios did not correlate closely with potassium levels. However, P wave amplitude and QRS duration were more closely tied to variations in potassium levels. It is also interesting that as potassium levels increased, there was a high degree of correlation with increased magnesium concentration. Thus, the antagonistic effects of potassium and magnesium were always at work (Merrill 1956; Smith 1949). The net effect, as measured by EKG recordings and clinical observation, appeared to be potassium intoxication with cardiac failure.

SUMMARY

An experimental situation was designed in which 52 pigs were fed various weeds. The weeds fed were Amaranthus retroflexus (pigweed), Chenopodium album (lamb's quarters) and Kochia scoparia.

All swine fed pigweed developed clinical signs and all displayed characteristic gross lesions of perirenal edema. Of the 12 pigs fed Kochia and lamb's quarters, and of 8 pigs fed varying concentrations of water extract of pigweed, none developed either clinical signs or gross lesions. Lesions, but no clinical signs, were observed in pigs fed residue from the water extraction procedure. Three pigs given pigweed after recovery from the previous feeding of that plant did not develop acute perirenal edema but had lesions of severe interstitial fibrosis, evidence of kidney damage from the previous trial.

Blood chemistry and electrolyte changes were seen in pigs fed pigweed and included large and constant increases in serum potassium and smaller increases in serum magnesium. Blood urea nitrogen and serum creatinine were more markedly increased in pigs fed pigweed than for any other trials.

Histopathology of the affected animals revealed microscopic kidney lesions. Most prominent were tubular degeneration and necrosis in a majority of the kidney tubules, dilatation of the convoluted and collecting tubules and

large numbers of proteinaceous tubular casts.

EKG changes were monitored in 14 affected pigs being fed pigweed. The changes were suggestive of hyperkalemia, as evidenced by a slowing of heart rate, a wide and slurred QRS complex and an increase in magnitude and duration of the T wave. In effect this raised the T/R ratio abnormally high.

The cause of death in swine fed pigweed was shown to be associated with cardiac arrest due to hyperkalemia resulting from renal failure.

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ACKNOWLEDGMENTS

The author wishes to express his sincere appreciation to Dr. Wm. B. Buck for providing the stimulus and counsel which greatly enhanced the completion of this research; to Dr. Frank K. Ramsey for the opportunity to pursue graduate study and research and for advice in the writing of this thesis; to Dr. Edward J. Bicknell for valuable assistance in evaluation of histologic preparations; to Dr. F. L. Hembrough, Dr. R. L. Engen, and Dr. Gary Van Gelder for suggestions and assistance in the electrocardiographic studies; to Dr. Vaughn A. Seaton for his cooperation in the conduction of research activities; to Dr. David F. Cox for assistance and preparation concerning statistical analysis; to Mr. James Hurd and Mrs. David Ver Steeg for dependable and cooperative conduction of clinical chemistry procedures; and to my wife, Sue, for her valuable typing and unending patience and understanding during the completion of this work.