above-mentioned oxidation-reduction has been stopped in the quinoid stage. The same explanation may be applicable to low-temperature injuries of other tropical fruits, although our results have been obtained only with pineapples. The fact that immature fruits are more susceptible to low-temperature injuries than mature fruits tends to confirm the theory, because of the larger content of phenols in the form of soluble tannins in the immature fruits.

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Experimental Production of Hyperkeratosis ("X Disease") of Cattle with a Chlorinated Naphthalene[1]

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The baffling and costly malady known as X disease of cattle was first recognized in New York state and described by Olafson (*1*) in 1947. It has been recognized since that time in all states east of the Rocky Mountains, and the Southeastern states seem to have a higher incidence of diseased herds than any other section of the country. In Tennessee alone more than 2300 head of cattle have been affected since 1947. Valuable purebred herds have been affected, and the raising of calves in some herds became impossible over a three-year period. Such diseased herds were slaughtered.

Olson and Cook (*2*) produced the disease in cattle by using a commercially prepared feed that had been incriminated in an outbreak of the disease in a herd in Nebraska. Wagener (*3*) produced it in Germany by exposing cattle to a complex wood preservative used in the construction of a new barn. Olafson and McEntee (*4*) also produced the disease by feeding cattle a processed concentrate, and Bell (*5*) infected calves by feeding them a lubricant. None of these workers has identified the specific chemical compound or compounds that produced the disease.

This experiment was designed to use a known chemical compound, which may be used on many farms in many different ways, and the effect of which was unknown on the bovine. There is no reference in the literature to its having been administered to cattle. Thus the experiment, in the early stages, was one of trial and error to find a toxic dose which would not produce immediate death but which would make the animal ill.

[1] A contribution from the interregional project entitled "X Disease (Hyperkeratosis of Cattle), a Cooperative Study Participated in by the Agricultural Experiment Stations and the Bureau of Animal Industry, U. S. Department of Agriculture."

Two grade Hereford females, one year old and weighing about 500 pounds each, and one Jersey Hereford crossbred female, eight months old and weighing about 400 pounds, were used in the tests. Pentachloronaphthalene was used in the experiment and administered *per os* in capsules each day. The control animal of comparable size and age remained healthy throughout the experiment.

TABLE 1

No. days dosed	Dose/day (g)	Grams pentachloronaphthalene for entire period
10	2	20
10	4	40
10	6	60
10	8	80
Total 40		200

Hereford No. 748 was used as a pilot test to try to find the amount necessary to cause death when administered over a two-week period. This animal received 15 g/day for 13 days and was sacrificed on the 17th day because of its morbid condition. With this acquired knowledge of the toxicity and the amount necessary to cause death in 17 days, the other two animals were dosed according to Table 1.

Symptoms observed were identical with those seen in naturally occurring field cases. They included excessive lacrimation, diarrhea, polyuria, marked salivation, and a serous discharge from the nostrils. A chronic cough, poor appetite, and numerous red macules in the buccal cavity developed later. Some of the macules became 30 mm in diameter, with proliferations of the underlying tissues. By the 35th day hyperkeratosis of the skin had developed on the sides of the neck, across the withers, and around the mammary gland. The skin was dry, hard, stiff, and thrown up in rolls, which later developed fissures (Fig. 1).

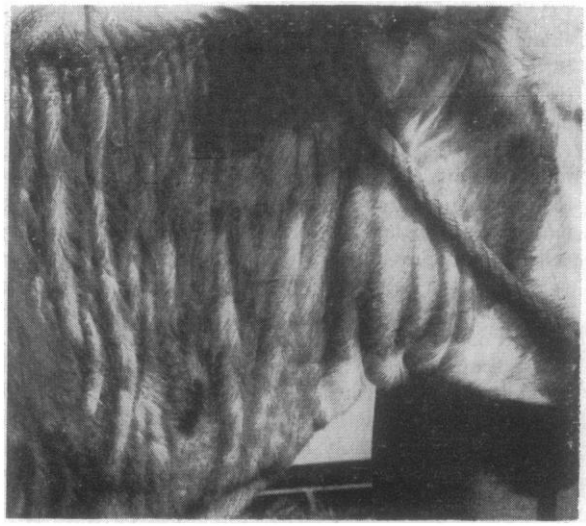

FIG. 1. Note rolls of skin with fissures on side of neck of animal No. 766.

At autopsy there were numerous proliferative areas on the gums, lips, and hard palate. The abomasum had numerous superficial ulcers 10–20 mm in diameter in the pyloric region. The pancreas was swollen, hard, and firm. The liver edges were rounded and slightly thickened. The distended gall bladder was filled with a dark, sticky, viscid bile, and the walls were thickened. Numerous mucous cysts were observed in the large bile ducts. The kidneys were enlarged, and numerous small subcapsular, clear cystlike structures were seen in the cortical portion.

Microscopically the cellular changes observed are similar to those seen in field cases and those reported by other workers. Marked keratinization of the hair follicles, with an excessive accumulation of keratinized material, along with a prolongation of the papillae of the skin, was noted. Central lobular degeneration of the liver cells, with bile duct proliferations, was evident. Dilation of the glands in the wall of the gall bladder was pronounced. In the kidneys, cystic dilation of the collecting tubules of the cortex, with a moderate degree of fibrosis, occurred. In the pancreas numerous areas of degenerating cells in the acini were also noted. A more complete and detailed report concerning these and other pathological changes is to be published later.

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Effect of Renin on Diuresis in Rats

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Croxatto *et al.* (*1*), using renin obtained from rat kidney, confirmed in this species the diuretic effect of renin that had been observed in rabbits by Pickering and co-workers (*2*) and under other conditions by Brandt *et al.* (*3*), Hughes-Jones *et al.* (*4*), Addis *et al.* (*5*), Mason *et al.* (*6*), Sellers *et al.* (*7*), and Barnafi (*8*). This study was undertaken to investigate the conditions that affect the influence of renin in the rat—e.g., the route of administration, the ingestion of NaCl, and adrenalectomy. Some of the experiments were carried out in normally hydrated animals with free access to water. In others the animals were hyperhydrated by forced administration of water, as described by Burn (*9*).

The normally hydrated animals (a total of 160), distributed in groups of 3 or 4 animals, were placed in metabolism cages, and the fluid consumption and the volume of urine excreted were measured every 12 hr. The results were recorded for periods of 10–40 days, depending on the experiment. The drinking fluid was either water or a 1% solution of NaCl. Renin and the other solutions administered were injected once a day intraperitoneally or subcutaneously, as indicated in Table 1.

The hyperhydration of rats was carried out under the conditions required for the Burn test (*9*). One group of rats was fasted with free access to water and then hyperhydrated by administering water through a gastric tube; the volume administered was 5% of body weight. The urine volume was recorded every 15 min. The injection of renin or other solutions was simultaneous with the hydration or preceded it by 1, 2, 3, 4, or 5 hr (Table 2).

Renin was extracted from pig, rat, or human kidney according to the techniques of Dexter (*10*) or Braun-Menéndez (*11*); 12.5–25 u of renin contained in 0.5–1 ml of solution was injected/100 g body weight. An inactive preparation (Ser. B) from pig kidney, as shown by its lack of pressor effect and its inability to produce hypertensin when incubated with hypertensinogen, was also tested. In some experiments (Ser. D, Table 1) hypertensin, at a dose of 1.5–9 u/rat, was injected in place of renin. Animals submitted to this treatment for more than 30 days were killed, and the hypertensinogen content of their blood was determined.

In normally hydrated rats drinking tap water (Ser. A, Table 1) the intraperitoneal administration of renin considerably increased urinary excretion, whereas the same dose of renin given subcutaneously modified it slightly or not at all (Fig. 1).

The stimulating effect on diuresis is observed after each injection of renin, but it decreases with repeated injections. This behavior could be explained by the formation of antirenin on prolonged administration of renin. In agreement with this assumption, we found that the serum of these rats does not produce hypertensin when incubated with renin, but produces pepsitensin when incubated with pepsin. This indicates that there is no lack of substrate (hypertensinogen), but that an inhibitor of renin is present.

Inactive kidney extracts never stimulated diuresis, no matter what the dose or the route of administration (Ser. B, Table 1).

The diuretic action of renin is considerably increased in animals drinking 1% NaCl (Fig. 1). Pronounced effects are observed even when renin is administered subcutaneously (Ser. C, Table 1).

Hypertensin does not show a diuretic effect even at a dose of 9 u; only weak and irregular effects were obtained with larger doses given subcutaneously (Ser. D, Table 1).

Adrenalectomy in rats drinking 1% NaCl considerably decreased or suppressed the stimulating effect on diuresis produced by daily intraperitoneal injections of renin. A dual effect of renin was observed in the polyuria of normal hyperhydrated animals

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