in the warmer months, and should either be sent to slaughter or treated to destroy the carrier state.

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Hyperkeratosis

AUBREY M. LEE

A NEW and strange disease of cattle was first seen and reported by Dr. Peter Olafson, of the New York State Veterinary College, in 1941. It was called hyperkeratosis, or X-disease—"X" being a symbol for the unknown and "hyperkeratosis" indicating the increased amount of keratin, or horny material, that develops on skin of the neck, shoulders, and withers in chronic cases.

This ailment was reported in 10 States in 1946. A year later it was known to exist in 27 States. Officials of the Department of Agriculture and of Southeastern States in 1948 investigated 26 affected herds in 20 counties in Alabama, Florida, Georgia, Tennessee, and Virginia. They found an average loss of 4,200 dollars per herd.

The disease was causing an estimated loss of 2 million to 4 million dollars a year by 1949. Deaths were highest—up to 80 percent—in calves less than 6 months old. About 50 to 60 percent of older calves died. The mortality in adult cattle was 10 to 35 percent.

In Texas the disease was diagnosed in 53 counties by 1950. In Wisconsin in June 1952 we had reports of 1,085 cases among cattle on 268 premises; an estimated 10,000 calves died in the winter of 1952. In Illinois 33 herds were affected. Tennessee reported more than 3,000 cattle had died or had to be slaughtered before 1952 because of the hyperkeratosis. About 20,000 animals were affected in Texas and 5,000 in Oklahoma in the winter of 1952-1953.

The disease then had been diagnosed and reported in 35 States, and in 4 more States it had been suspected in a herd or two. No new cases of hyperkeratosis of cattle were reported to the Department of Agriculture in 1954 or 1955—an indication that it had been
eradicated or reduced to the extent that it was no longer important to the livestock industry.

Symptoms usually start with listlessness, depression, excessive secretion of tears, drooling of saliva and a watery discharge from the nose, and loss of flesh. A rapid drop in blood plasma vitamin A often to very low levels may occur.

Often there also develops loss of condition, emaciation, a variable appetite, intermittent diarrhea, and a dry, scurfy skin. Raised areas, or wartlike lesions, often are found on the floor of the mouth and on the dental pad, hard palate, lips, tongue, gums, and the inside of the cheeks. They have been found also on the muzzle, the margins of the nostrils, and the lining of the esophagus.

If the animal survives those systemic effects and does not die from secondary bacterial infection, pneumonia, or inflammation of the intestines, the typical skin hyperkeratosis develops slowly. Then there develops gradually an accumulation of hard, keratinous material, which makes the skin thick, inelastic, and wrinkled. The deep fissures and bold folds formed in the skin become so hard that they are not reducible by stretching with the hands. The skin feels more like a hide than a skin. Hair on the affected skin gets thin or disappears entirely. The sides of the neck, shoulders, and withers are affected most commonly. Skin on the inner surface of the thigh, the udder, and scrotum, the convex surface of the ear, the dewlap, and the sides also may be affected. Almost all the skin of the body and sometimes the skin of the legs may be affected in extreme chronic cases.

A few herds, free of brucellosis but severely affected with bovine hyperkeratosis, have had abortions and still-born calves and greatly reduced milk secretion. In some experimentally produced cases of hyperkeratosis in pregnant cows, abortion took place and milk flow dropped markedly. The extreme lowering of blood plasma vitamin A in hyperkeratosis could predispose to secondary bacterial infections, such as abscess formation, and inflammations of some of the internal organs.

The symptoms vary according to the amount of the toxic or poisonous substance the animal eats or touches and the duration of the exposure. The concentration of the toxic substance in the feed or in the compound that the animal comes in contact with will also cause variations in some symptoms. Other factors, such as age, individual differences, rations, and the material in which the toxic principle is suspended, may determine which symptoms are shown and which form the disease takes.

Research workers applied known hyperkeratosis-producing substances in diluted form locally to the skin of cattle. Little or none of the general systemic effects were produced, but a typical definite hyperkeratosis of the skin developed. The scientists found, however, that the systemic effects developed if the material were fed or given internally and that the skin hyperkeratosis developed from this internal administration, although usually it took 6 weeks to 2 months or longer. Calves died with the acute—rapid—form of the disease before skin changes appeared.

The internal changes or lesions in the internal organs that are most characteristic of hyperkeratosis are swellings on the inside lining of the gall bladder, gall duct, and the large bile ducts. Characteristic changes of the small bile ducts of the liver commonly occur. The pancreas, liver, kidneys, and reproductive organs may be affected. The intestines, may become inflamed, and the inside lining of the fourth, or true, stomach, especially near the intestinal opening, may have reddened areas, flat erosions, and small ulcers.

Scientists in 18 States in 1949–1953 undertook research in a cooperative
project with the Department of Agriculture to find the cause of hyperkeratosis. They had to start from scratch. They had only a few theories to begin with.

They had to study practically the whole environment of the affected cattle—soils, plant life, fertilizers, bacterial flora of the rumen, livestock feeds, viruses.

Drs. A. G. Johnson and W. O. Robinson, of the Department of Agriculture, established that soil, plants, and fertilizers were not factors.

Dr. W. O. Gibbons, of Alabama Polytechnic Institute, did extensive survey work and proved that DDT did not cause the disease.

Dr. William Sippel, of the Georgia Coastal Plain Experiment Station, Dr. Dennis Sikes, of the University of Tennessee, and Dr. Hubert Schmidt, of the Texas Agricultural and Mechanical College, demonstrated that the disease was not caused by a virus and was not infectious. They also proved that road oils and American wood preservatives did not cause it.

Dr. Carl Olson, Jr., of the University of Nebraska, in 1950 produced hyperkeratosis experimentally in cattle with a pelleted feed that had been suspected because of being connected with an outbreak.

Dr. Peter Olafson, of Cornell University, produced it by feeding a particular lot of suspected breadcrumbs from the slicers in a commercial bakery which were being fed to cattle and found the toxic substance was eliminated in the milk.

Dr. R. C. Miller and Dr. A. L. Bortree, of Pennsylvania State University, induced the disease by feeding a certain cutting of timothy hay that had been fed to cattle on a farm where the disease had caused heavy losses.

All the experiments were made under rigid controls, so there was no question but that each particular lot of the three products contained something that caused or brought on the disease.

Dr. H. W. Schoening, of the Department of Agriculture, at a conference in Europe in May 1950 learned of a disease condition in cattle produced experimentally at the Hannover Veterinary College in Germany. It seemed to be like the bovine hyperkeratosis in the United States. In Germany the condition had been caused by a particular tank carlot of a commercial wood preservative. Some of the wood from a barn at Hannover and some of the preservative with which it had been treated 2 years previously were taken to Cornell University and Pennsylvania State University for study.

Dr. William Hansel, Dr. Olafson, and Dr. Kenneth McEntee, of Cornell University, and Drs. Bortree and Miller produced hyperkeratosis with both the wood preservative and the wood in April 1951. They found the disease produced was the same as existed on farms in this country and as had been produced experimentally with pellets, breadcrumbs, and timothy hay.

Drs. Olafson, Hansel, and McEntee began studies of the place of vitamin A in hyperkeratosis produced experimentally by breadcrumbs and by the German wood preservative. They found that the blood plasma vitamin A was lower than had previously been produced experimentally—as low as 3 and 4 micrograms per 100 milliliters. Dr. Miller and Dr. P. H. Phillips, of the University of Wisconsin, later confirmed the finding, which was of value in studies in nutrition and in the research program to determine if a suspected causative agent should be studied further.

Cattle will eat grease from machinery and grease cans. Dr. Wilson B. Bell, of Virginia Polytechnic Institute, found in 1951 that a lubricant or grease recovered from a farm on which the disease had occurred and a similar product purchased on the market produced hyperkeratosis. With the cooperation and help of the company that made it, he fed this serial number of grease minus its various chemical additives.
Soon afterwards he found the item in the grease that made it produce hyperkeratosis was highly chlorinated naphthalene. Dr. Sikes, at the University of Tennessee, at the same time was feeding several chemicals used in greases and also found that highly chlorinated naphthalene produced hyperkeratosis.

N. R. Ellis, R. E. Davis, and Ivan Lindahl, of the Department of Agriculture at Beltsville, Md., investigated a feed mill of the kind that is commonly used in this country. The directions for operating it called for the use of grease every 2 hours of operation. The grease lubricated the bearings of the rollers that force the feed against the die plate. The end of the shaft is in contact with loose feed, and provision is made that the grease will work out from the bearing in order that feed and dirt will not get into the bearings. The workers concluded that the grease used as replacement every 2 hours went into the pellets.

The men at Cornell University started working on the breadcrumbs in an effort to find the chemical as soon as they proved the breadcrumbs would produce hyperkeratosis. The test itself had to be developed and perfected. It required expensive equipment and much time. They developed a testing method and identified highly chlorinated naphthalene as the contaminant in the breadcrumbs and also in the German wood preservative. They later cooperated and worked closely with several industries concerned in the production of pellets that were causing hyperkeratosis in Texas. One large corporation bought expensive special equipment and set a large staff of chemists to work on the problem. Highly chlorinated naphthalene was found and identified in the pellets and in the grease used to lubricate the pellet machines. Dr. Roger P. Link and Dr. E. F. Reber, of the University of Illinois, later identified this chemical in pellets that produced hyperkeratosis in Illinois.

Dr. Bell prepared a good livestock feed. He pelleted one-half of it in a machine greased with a lubricant that did not contain highly chlorinated naphthalene. For the other half the pellet machine was lubricated with a grease that contained 3 percent of highly chlorinated naphthalene. The pellets made when the machine was greased with the lubricant that did not contain highly chlorinated naphthalene were not toxic to the calves to which they were fed. The pellets made when the machine was lubricated with a grease which contained highly chlorinated naphthalene produced hyperkeratosis in calves. The first pellets made following the lubrication were highly toxic, but the ones made just before lubrication were only slightly toxic.

Oil companies and feed manufacturers, warned of the danger, did what they could to keep the damaging additive away from livestock and livestock feeds.

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For further reading:
Wilson B. Bell: The Relative Toxicity of the Chlorinated Naphthalenes in Experimentally Produced Bovine Hyperkeratosis (X-Disease), Veterinary Medicine, volume 48, pages 135–140. 1953.