

To obtain best results in treatment, an adequate concentration of the drug must be maintained in the udder for a period of time. Best results are usually obtained when the drugs are administered once or twice daily over a period of 2 to 4 days, depending upon the causative agent and the nature of the case. Most staphylococcal infections must be treated longer than streptococcal infections. Clinical cases must be treated longer than cases not showing symptoms to produce a cure.

Many of the antibiotics are available in various vehicles, such as ointments and water-in-oil emulsions, that are designed for infusion into the udder. The vehicles aid in maintaining an adequate therapeutic level of the antibiotic in the udder for about 24 to 48 hours after 1 injection. Because antibiotics can persist for several days in the udder, the milk from the treated cows should not be marketed during the period of treatment or for at least 72 hours after the last treatment. The antibiotics interfere with the growth of the bacteria necessary for the production of cheese.

The drugs are administered by infusion into the infected quarter through the teat canal. First, though, the teat must be washed thoroughly and the teat orifice cleansed with a pledget of cotton wetted with alcohol.

Because drugs do not cure all infections caused by some of the bacteria and yeasts, the danger exists of introducing these resistant micro-organisms into the udders while treating for another type of organism and of allowing a more severe form of mastitis to develop. Faulty technique in preparing the teat for injection and contamination of the instruments, drug, or vehicle may be to blame.

In treating acute mastitis, it is desirable to have the drugs administered intravenously or intramuscularly, in addition to infusing them into the udder.

Frequent milking of the quarter and application of icepacks at the beginning of the attack often are helpful in preventing excessive swelling until veterinary treatment can be obtained. After the cow no longer shows marked symptoms, the application of hot packs to the udder, along with gentle massage, may hasten recovery.

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## *Ketosis in Cattle*

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KETOSIS in dairy cattle is not a specific disease but a metabolic disorder. It is an imbalance between the nutritive intake and the nutritive requirements of the animal.

The lack of balance is indicated by several associated disturbances: Low

blood glucose levels (hypoglycemia); depletion of liver glycogen (glucose stores); mobilization of body proteins, as amino acids, to the liver for new production of glucose (gluconeogenesis); mobilization of storage fat; fatty infiltration of the liver; increased pro-

duction of ketone bodies; increased ketone bodies in the blood and urine; loss of body weight (emaciation); lower milk production; and dehydration.

One may compare ketosis to a bank account. At the beginning one may assume that the account is in balance and the reserve is big enough to draw on in an emergency. If the income falls below the expenditures and if the emergency is prolonged or is severe, however, the condition may become serious.

THAT GENERAL REASONING may be applied to the high-producing dairy cow, which is metabolically a delicately balanced milk-producing "machine."

At the time of calving and onset of lactation, the animal's nutritive and metabolic requirements are increased about 100 percent—partly because of the loss of sugar, protein, and fat in the milk and partly because of the increased metabolic work associated with the production and secretion of milk.

For every 20 pounds of milk produced, approximately 1 pound of glucose, 0.8 pound of fat, and 0.7 pound of protein are withdrawn from the animal. Those withdrawals are from the animal's available resources. If the dietary intake is adequate, the animal remains normal. If the diet is too poor to maintain approximately normal levels of blood glucose and liver glycogen, an imbalance in metabolism develops.

This upset is indicated by the existing anorexia (loss of appetite), hypoglycemia, and depletion of liver glycogen. In response to these disturbances, compensatory metabolic adjustments are initiated and tend to correct the imbalance.

The adjustments are triggered primarily by the hypoglycemia via specific physiological mechanisms. Some of the mechanisms are nervous in character. Others are linked to hormone actions. The hormones include primarily ACTH and possibly growth hormone of the anterior pituitary gland and hormones produced by the

adrenal cortex such as cortisone and 17-hydroxycorticosteron.

The important physiological effects are an increased mobilization of depot fat and fatty infiltration of the liver and an increased mobilization of amino acids from body protein to the liver, in which some are converted to glucose and glycogen. Fatty infiltration of the liver tends to produce a temporary increase in ketogenesis (the production of ketone bodies). Glucose or glycogen tends to prevent it.

Small doses of these hormones of the adrenal cortex may cause a temporary increase in ketogenesis, but as the glucose production by the liver is sufficiently increased, ketogenesis is checked. Glucose acts to prevent ketogenesis from fatty acids by the liver by maintaining a small supply of "oxalacetate," which has to combine with fatty acid fragments if they are to be oxidized. If fatty-acid oxidation in the liver is blocked by a deficiency of oxalacetate, the metabolism of fatty acids is incomplete and ketogenesis may occur.

A SECOND FACTOR that may lead to the development of ketosis in dairy cattle is the unique nature of rumen digestion. The microbial fermentation of carbohydrates in the rumen leads to the production of large amounts of the lower fatty acids. A high percentage of them is ketogenic, and about 20 percent—propionic acid—can be converted to glucose by the animal body.

The true dietary intake of carbohydrate, compared to that of carnivores, therefore is relatively small, and the intake of potential formers of ketone bodies is large. If, however, the blood glucose and liver glycogen levels can be maintained, both glucose and fatty acids are oxidized and ketosis does not occur.

On the contrary, when the blood glucose is low, the carbohydrate stores in the liver tend to become depleted in an attempt to maintain the level of blood glucose and, in turn, the carbohydrate requirements of other tissues. Ketogenesis and ketosis tend to develop

under those conditions. An abnormal amount of ketone bodies in the blood, body fluids, and tissues characterizes ketosis.

The liver is the principal organ in which ketone bodies are produced. They are normal intermediary metabolites, associated chiefly with the metabolism of fatty acids under conditions of relative deficiency of the carbohydrates. The intensity of the ketosis is directly related to the level of the deficiency.

Ketone bodies cannot be metabolized further by the liver but are passed into the blood and to the other tissues, where they can be oxidized. Ketosis develops only when the rate of ketone body production (ketogenesis) exceeds that at which they are utilized. There is no inability of the tissues, other than the liver, to oxidize either glucose or ketone bodies under those conditions. Although the concentration of ketone bodies in the blood is high, only a fraction of those produced is excreted by the kidneys, the mammary glands, and expired air.

**KETOGENESIS** and ketosis are not due to an initial or absolute deficiency in the hormonal secretory capacity of the anterior pituitary or adrenal cortex—in fact, such deficiencies would make ketogenesis nearly impossible.

Because of the increased metabolic requirements of the animal under the stress of high milk production, starvation, disease, and other single or multiple conditions, the anterior pituitary and adrenal cortex and various available body resources are mobilized to meet the immediate metabolic requirements. The resources include the mobilization of depot fat and muscle proteins as amino acids. The former is associated with fatty infiltration of the liver. The latter leads to an increased conversion of amino acids to glucose in the liver and an increased urinary nitrogen excretion. Both lead to emaciation of the animal.

Under those conditions, a relative anterior pituitary or an adrenal cortex

secretory deficiency, or both, usually develops.

The hormonal mechanism for stimulation of the adrenal cortex by a specific hormone (ACTH) from the anterior pituitary may induce an enlargement and increase in number of cells of the adrenal cortex. Within wide limits, this is a physiological process; if it were followed by cellular degeneration or complete exhaustion, however, the results might be fatal. That occurs rarely.

VARIOUS CLINICAL CLASSIFICATIONS of bovine ketosis have been used.

Lactation ketosis includes cases that suffer from a simple imbalance between the nutritive intake and the nutritive requirements to maintain the increased demands of the lactating animal. This type occurs most frequently 14 to 28 days after parturition, but may occur as early as the seventh day and as late as 40 to 70 days after calving. The cases often are classified as uncomplicated, primary, and digestive ketosis, which occur in most countries where ketosis is prevalent. The terms "small-farm acetonemia" (in which the nutrition may be inadequate) and "estate acetonemia" (in herds apparently in good nutrition, but in which the acetonemia is frequently severe) are used in the British Isles.

Complicated or secondary ketosis may occur in varying intensities in lactating or nonlactating cattle—even in steers—and include cases in which the metabolic disturbance is precipitated or aggravated by infections, exposure, foreign bodies (hardware) in the rumen or reticulum (traumatic gastritis), peritonitis, mastitis, cystic ovaries, vaginitis, displacement of the abomasum, indigestion, and starvation. The treatment and correction of the complicating factor or factors in such cases is imperative if the animal is to recover.

**DIGESTIVE KETOSIS** INCLUDES the cases we listed that do not develop the so-called nervous symptoms.

In nervous ketosis the animals usually are reported to be excited and

show signs of neuromuscular incoordination. They keep looking around and are disturbed if someone enters the stall. The condition is occasionally described as a semiconscious state and one indicating a depression of the cortical nerve centers of the brain. The manner of walking of the animal is often staggering, swaying, and more or less parietic and listless. Other symptoms are frequent licking of the stanchion walls, sucking, biting, salivating, and hyperesthesia of the skin. Those disturbances probably are due to a progressive depression of the higher nerve centers in the brain, which in turn progressively releases the subcortical centers in the brain stem.

Nervous symptoms of ketosis have been produced in fasting pregnant ewes by relatively severe hypoglycemia and in normal ewes and cows by the intravenous administration of isopropanol (an alcohol). Isopropanol is present in appreciable amounts in rumen liquor, blood, and milk of ketotic ruminants. The isopropanol concentration is greatest in the rumen, and is believed to be formed from acetone by the ruminal micro-organisms. The combined effects of hypoglycemia and isopropanol may act in an additive or synergistic manner to produce the effects. Similar effects occur in various species of animals under incomplete anesthesia and in intoxicated persons.

KETOSIS IN CATTLE occurs in practically every country in which dairying is practiced. Only a few cases occur in some regions, but in others its incidence may be 15 percent or more.

It develops primarily in high-producing dairy cows and seldom in low-producing cows, steers, or bulls, except those suffering prolonged starvation and protracted diseases. In many areas the number of recognized cases of ketosis has increased greatly since 1940. The first described case of ketosis in cattle in the United States is reported to have been in 1929.

Ketosis may occur in dairy cattle of

all ages, but is more prevalent during the years of greatest milk production—after the second, third, and later lactation periods.

A million cases of ketosis occurred in 1950 among the 24,577,000 milking cows in the United States, an incidence of approximately 4 percent.

Mortality from ketosis in dairy cattle is low, ranging from 1 to 5 percent. Lactation ketosis is rarely fatal even if untreated—not more than 1 or 2 percent. Reports for “estate ketosis” indicate a somewhat higher death rate.

Statistics from the ambulatory clinic of the New York State Veterinary College for the year that ended July 1, 1950, showed only 6 deaths out of 284 treated cases, a little more than 2 percent. Appreciably greater financial losses from ketosis in dairy cattle arise from the associated drop in milk production and removal of animals from the milking line to be slaughtered prematurely.

UNDER CONDITIONS of ketogenesis, the primary metabolic defect in the liver (the principal organ of ketone body production) is a deficiency of oxalacetate. This metabolite must be present so as to combine with the two-carbon fragments of fatty acids and other ketogenic substances in order that they may be oxidized to carbon dioxide and water. In its absence, the fragments are converted to acetoacetic acid, beta-hydroxybutyric acid, and also acetone—the well-known ketone bodies. The main metabolic sources of oxalacetate are from carbohydrate and glycogenic amino acids.

PREVENTION of ketosis in dairy cows is the ultimate objective. We know of no perfect preventive regime, but the following suggestions may help:

Be alert to recognize conditions of infections, disease, injury, exposure, or disturbance that might subject the animals to unnecessary stress.

The diet should contain enough of the right kind of nutrients for maintenance and lactation.

A marked decrease in the intake of feed just before calving is not advised.

Stimulate the appetite by suitable rations. The addition of molasses or glucose to the ration frequently increases its palatability, stimulates the appetite, and increases feed intake. The reliability of the practice of feeding molasses or sugar to augment the blood sugar and liver glycogen has been questioned.

Feed an adequate quantity of high-quality hay and roughage.

Assure the maintenance of a proper balance between roughage and grain.

After calving, it is desirable to bring the cow up to maximal grain feeding as rapidly as seems justifiable.

The metabolic requirements of protein for the lactating cow should be met. The glucogenic amino acid content of the dietary protein is important.

The silage, especially if it is grass silage, should be checked for its content of butyric acid, which, if high in concentration, would tend to increase the incidence of ketosis.

Increase the facilities for comfort, ample pasture, exercise, and ventilation for the animals.

SEVERAL PRACTICES have been used successfully in treating ketosis in dairy cattle.

The administration of glucose, preferably by the continuous infusion method or by repeated intravenous injections of 50-percent glucose solutions at relatively short intervals of 2 or 3 hours until the animal responds, has given excellent results. Unless frequently repeated injections are made, the liver glycogen is neither increased appreciably nor is maintained for a sufficient time to correct the oxalacetate deficiency. The amount of oxalacetate required is not large at any given time, but these small amounts must be maintained if ketosis is to be cured.

Intravenous injections of fructose in the same manner and for the same purpose as that of glucose are also satisfactory. Some investigators have reported fructose to be more effective

than glucose for alleviating ketosis. These two sugars are metabolized similarly in the animal body, but fructose metabolism is independent of the action of insulin, while glucose is not. The specific identity of these sugars is lost in the metabolic pathways.

Propionic acid, as sodium propionate, gives good results when administered with the feed or by drench. This acid is a normal end product of ruminal digestion and when absorbed can be converted to glucose by the liver. The intravenous administration of solutions of glucogenic amino acids or solutions of glucose and glucogenic amino acids combined (Aminosol) by methods similar to those for glucose also gives good results.

Gloconate or lactate may be used in the same way.

Similar to sodium propionate, glycerol or propylene glycol is satisfactory when administered orally in the feed or by drench.

Frequently lactation ketosis in high-producing dairy cows can be successfully treated by an increase in feed alone, especially the grain ration.

The feed intake of cows just before calving should not be limited, as some dairymen do with the aim of checking edema.

Any existing complicating disease, condition stress, or disturbance afflicting the animal must first be treated and corrected if the usual method of treating the accompanying ketosis is to be effective.

ACTH (adrenocorticotrophic hormone of the anterior pituitary) and the so-called glucocorticoid hormones of the adrenal cortex have been administered with good results. ACTH has no direct effect on carbohydrate, protein, or fat metabolism and ketogenesis; it acts by stimulating an increased output of adrenal cortex hormones. The specific corticoadrenal hormones involved are cortisone, 17-hydroxycorticosterone (compound F), and corticosterone. Their specific responses are the mobilization of amino acids from body protein and fatty acids from depot fat

to the liver. The interaction of growth hormone of the anterior pituitary and corticoadrenal hormones is necessary for body fat mobilization. As we stated earlier, the primary functions of these hormones are to mobilize the body resources to meet the metabolic needs of the animal body. They thus serve as a compensatory mechanism.

Ketosis, with or without complications, increases the metabolic requirements roughly proportionately to the magnitude of the combined stresses associated with lactation and other disturbances.

Because of the increased requirements, the animal's own pituitary and adrenal mechanisms have been brought into increased functional activity, but the mechanisms may be unable to cope with the physiological needs. A relative pituitary or corticoadrenal insufficiency then exists. Supplementary administrations of commercial corticoadrenal or ACTH hormones are indicated and have been found to be good.

Functional exhaustion of the anterior pituitary or of the adrenal cortex has not been satisfactorily demonstrated. That the latter is not exhausted or degenerated is indicated by the fact that ACTH is effective when administered. Furthermore, exhaustion of the pituitary would tend to eliminate ketosis.

Experiments have demonstrated that

ketosis is produced by an increased output of hormones of the pituitary and adrenal cortices and not by a deficiency of one of both of these systems. Ketosis can be experimentally terminated by removal of the pituitary or the adrenal cortices.

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## Shipping Fever

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BOVINE shipping fever is an infectious respiratory disease. It is somewhat comparable clinically to influenza in man, but it has a longer incubation period and is primarily a disease of the lungs.

It has been a major disease of cattle

for at least half a century. In some years it probably has caused the death of more young cattle than any disease.

Yet, because its primary cause has not been determined, it has never been given a fully satisfactory name.

Shipping fever, or the shipping-