A SURVEY OF THE PREVALENCE OF PORCINE GASTRIC ULCERATION AND GASTRIC CANDIDOSIS

by

WADE LEE KADEL

D. V. M., University of Missouri, 1965

A MASTER'S THESIS

submitted partial fulfillment of the

requirements for the degree

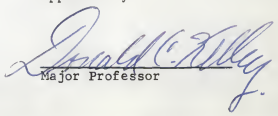
MASTER OF SCIENCE

Department of Pathology, Parasitology, and

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1967

Approved by:



Major Professor

TABLE OF CONTENTS

INTRODUCTION 1

REVIEW OF LITERATURE 1

MATERIALS AND METHODS 20

RESULTS 27

DISCUSSION 51

CONCLUSIONS 54

ACKNOWLEDGEMENTS 55

APPENDIX 56

LITERATURE CITED 69

INTRODUCTION

The etiology of porcine gastric ulcers is incompletely understood as the pathogenesis of this disease has not been established. The yearly economic loss to the swine industry resulting from gastric ulceration has not been confirmed. Reports of controlled experiments indicate that the rate-of-gain and feed efficiency were not adversely affected by this stomach lesion. Descriptions of confirmed field cases indicate that there is a weight loss in animals that ultimately recover and the mortality rate may be economically important.

There remains a lack of agreement among researchers as to the etiology. This is evidenced by the variable reports of the influence of nutritional or environmental factors and Candida albicans. Treatment will continue to be more emperical than rational until the true pathogenesis of this condition is determined.

The purpose of this survey was to gain new knowledge concerning the prevalence of gastric ulcers and gastric candidosis in a swine population maintained under various conditions. Information was collected pertaining to the environmental influences and nutritional programs under which the swine were raised. These data were used to evaluate the relationship between management factors and the occurrence of gastric ulcers.

This survey was conducted to establish the prevelance of porcine gastric ulceration and candidosis and present new information concerning the influence of many management factors and gastric candidosis on the occurrence of esophagogastric ulcers.

REVIEW OF LITERATURE

I. Incidence

There is a difference of opinion among authorities as to the occurrence of gastric ulcers in swine and the significance of these lesions. Smith and

Jones (1966) stated that "chronic indurated ulcers comparable to the human peptic ulcer do not occur naturally in any of the domestic species". A second view point concerning gastric ulcers in swine is taken by Jubb and Kennedy (1965). They state "Ulceration of the gastric mucosa are very common. They are usually acute and heal promptly and may, therefore, be of little significance. Their course depends upon the cause and ulcers of the cardia of swine are quite important. Small superficial defects are termed erosions, but these probably differ only in degree from the ulcer which penetrate to the submocosa. Ulcers of the glandular epithelium are often accompaniments of other diseases and the causes are varied".

The first report of the occurrence of gastric ulcers in swine was by Rosenow in 1923. He described the lesion and stressed the significance of a streptococcus isolated from the lesions.

Streptococci were reported to be associated with human gastric ulcers at that time. Rosenow's description of the microscopic lesion was similar to the peptic ulcers found in man. The ulcers were small, the base and margins were free of necrotic debris and the hemorrhage and leukocytic infiltration were well circumscribed in the submucosa.

The next report of the occurrence of gastric ulcers in swine was the summary of the incidence of ulcers observed at a packing plant by Jenson and Frederick in 1939. Of the 20,000 swine examined, 1,000 (5%) were ulcerated. These workers isolated streptococci of the alpha and viridans group from all active lesions. None of the cultures were beta hemolytic but the oxidative reactions were similar to the streptococci frequently found in the infected teeth and tonsils of man. Jensen and Frederick (1939) believed that these organisms were of primary significance. They also noted a seasonal occurrence. Ulcers were more frequently observed during late winter and early spring. They related this finding to the

fact that ulcers were observed less frequently when swine were on pasture as opposed to being confined in a barn.

Kernkamp (1945) reported on the clinical significance and prevalence of gastric ulcers in swine. He examined the stomachs of 745 swine and observed 18 cases of stomach ulcers. He reported that 2.38% of the examined swine had one or more gastric ulcers. In the description of these ulcers it was evident that most were similar to the peptic ulcer of man. He observed only two cases in which the cardiac region was ulcerated. In none of these cases was the illness ascribed to a gastric lesion. He suggested that the ulcers were the result of nutritional anemia.

A case report by Bullard (1951) reported that a large Chester White boar evidencing anorexia, normal to slight pyrexia, habitual recumbency, frequent constipation, reluctance to move, anemic mucous membranes, and melena. At necropsy this boar was found to have a large, round ulcer, 3½ inches in diameter completely surrounding the cardiac orifice. A large partially organized blood clot was fairly well attached to the ulcerated area.

Curtin et. al. (1963) examined the stomachs of 443 swine subjected to performance studies in a one year study. The seasonal incidence pattern suggested that variations in ambient temperature were a factor in precipitating the clinical disease. The incidence rate of gastric ulcers was 19.6% and the incidence rate of altered keratinization was 86.5%.

In an experiment designed to determine the effects of heat treated corn and gelantinized soybean oil meal on daily gains and feed efficiency for growing finishing pigs, Perry et. al. (1963) found that the swine fed the heat treated corn had a mortality rate of 39% due to esophagogastric ulcers. This group of swine had an ulcer rate of 56% and 73% had excessive cornification. No ulcers were observed in the group of swine fed rations containing raw corn but 50% of

these swine had excessive cornification. In a second experiment in which all pigs received gelantized corn, a 53% prevalence of gastric ulcers (18 of 34) was found.

Kowalczyk et. al. (1960) decribed six different clinical occurrences of gastric ulcers in swine between 1957 and 1959. He described the clinical signs and the observations by gastroscopic examination of a developing gastric ulcer from epithelial proliferation to a true ulcer. They described stomach ulcers found in swine at the University of Wisconsin farms during 1957-59. All cases described involved ulceration of the cardia around the esophageal orifice. Intravenous injection of microorganisms isolated from the base and edges of naturally developing ulcers failed to reproduce stomach ulcers. Although the results of one experiment indicated a relationship between dietary induced parakeratosia and stomach ulcers, another study failed to show this relationship. They suggested that the seasonal factor may play a role.

Berg (1960) and Curtin (1964) reported the occurrence of a gastric ulcer condition of swine as a definite disease entity at the Iowa State and Indiana Boar Testing Stations. They both stated that the condition was first observed at swine testing stations and later observed on the farms when veterinarians have made special effort to necropsy pigs which have died a sudden death.

Thoonen et. al. (1963) reported that 4.6% of 1,332 swine necropsied during the interim 1959-1962 had gastric ulcers. Perforation and formation of pyemia or mediastinal abcessation occurred in 8 of the 62 cases. They observed 4 cases (6.4%) with ulcers in the fundus or pyloris and 9 cases (14.5%) with changes in the distal part of the esophagus. In most cases the esophageal mucosa exhibited an average degree of dyskeratosis and some had hyperkeratosis. In 30 cases (48.4%) there was centralobular fatty change in the liver. Mycelia

were demonstrated in the epithelium of 6 (10%) of the animals. There was no sex prevalence and the average age incidence was 4 months with an average weight of 37 Kg. They observed a seasonal incidence as the largest number of deaths occurred during November, December and January. Dyskeratosis or erosions of the esophagogastric portion of the stomach were observed in 193 or 14.5% of the swine. Ninety of 193 cases of altered keratinization occurred in October and March.

In a study of the incidence and pathology of gastric ulcers in 610 swine from 6 different sources, Griffing (1963) found 131 (21.5%) gastric ulcers. He characterized the epithelial changes as various degrees of thickened keratin or an absence of normal keratin. These epithelial changes were present in 74.2% of the stomachs. As keratinization increased from normal to the thickened keratin the incidence of ulceration also increased.

In a survey of the prevalence of gastric ulcers in swine Muggenburg et. al. (1964) examined 3,753 hogs with the following results: 1,513 (40.3%) were free of gastric ulcers, 1,640 (43.7%) had epithelial changes in the esophageal region of their stomachs and 600 (16%) had gastric erosions, ulcers and scars. Of the 600 stomachs with ulcers 508 (84.6%) had lesions in the esophageal region only, 77 (12.8%) had lesions in the glandular region only and in 15 (2.5%) there were ulcerative changes in both the esophageal and glandular regions.

In a survey between October, 1963, and April, 1964, at 10 bacon factories O'Brien and Connally (1965) found 1,506 stomachs of 5,838 examined (25.8%) were ulcerated. In one farm where the condition was prevalent, 315 stomachs were examined between October, 1963 and March, 1965. Of these, 262 or 85% had some degree of abnormality.

Etiology

Although numerous studies have been conducted to determine the etiology

and pathogenesis of this condition, the exact mechanism remains unknown.

In his address to the 17th World Veterinary Congress, Kowalcyzk (1963) stated that the etiology of gastric ulcers is probably a complex of factors. Some factors thought to be involved in the formation of gastric ulcers are infectious, toxic, traumatic, hormonal, nutritional and psychosomatic conditions such as fear, pain, fatigue and other stress. Although one is reluctant to say that some animal diseases are psychosomatic in origin, more and more often disorders are encountered which result from radical changes in the animal's ecology.

In his book, Diseases of Swine, Dunne, (1959) described gastric ulcers as lesions of poisonings such as salt, red squill, arsenic and nitrates. He also incriminated infestation with Hyostrongylus rubidus and Vitam E deficiency as causes of gastric ulcers.

Dodd (1960) described a relative high incidence of hyostrongylosis and gastric ulceration in swine in a region of New Zealand. These ulcers were most common among breeding sows and were almost exclusively ulcers of the fundus.

Buntain (1961) suggested that a high concentration of copper in the diet could have been the cause of death in 23 fattening pigs in a period of 5 to 6 weeks. At necropsy, these animals had pale anemic carcasses with varying degrees of liver and kidney damage and jaundice together with extensive hemorrhage into the stomach or large intestine. Loss of blood was the immediate cause of death. The stomachs were full of clotted blood, which had apparently originated from large penetrating ulcers surrounding the esophageal opening. The livers of pigs which died contained from 710 to 2,200 ppm copper.

McErlean (1962) reported that he observed a condition in pigs characterized by internal bleeding and sudden death. He described the gastrorrhegia syndrome

in Irish swine and suggested that the disease was less prevalent where skim milk was provided.

Rothenbacher et. al. (1963) presented a detailed description of the gross and microscopic pathology of the cardiac ulcerative gastrorrhagia syndrome. The early and subclinical lesion was found to consist of a parakeratotic proliferative change in the squamous portion of the cardiac region. Histologic changes of the malpighain and basal layers of the squamous mucosa consisted of edema of the intercellular spaces with microvesiculation, hydropic degeneration and lack of keratinization. He suggested that the evidence at that time indicated that an unidentified toxicity was associated with the disease.

Muggenburg et. al. (1964) studied the stomachs of 594 swine. He classified the ulcers into 5 groups: epithelial changes, acute erosions, subacute ulcers, chronic ulcers and scars. He described a progression from an epithelial change to an erosion then on to ulceration. He noted a high correlation between fluid contents and any type of ulcerative lesion.

In studies of the relationship of vitamin E to ulceration of the forestomach in the rat, Harris et. al. (1947) found that a deficiency of vitamin A per se does not produce ulcers of the fore-stomach of the rat. They found that in the regenerative phase from a prior vitamin A pyriodoxine deficiency, if vitamin E is not added with the deficient component, ulceration results. Unless adequate tocopherol is also administered orally the functionally abnormal epithelium of the fore-stomach cannot cope with the acid-pepsin medium with which it is in contact and as a result lesions are produced.

Obel (1953) described hepatosis diaetetica in swine and reported that about 22% of the 77 cases had esophagogastric ulcers. She suggested a relationship between vitamin E and gastric ulcers but also stated that the waxy degeneration of skeletal muscles which is a characteristic lesion of vitamin E

deficiency was not observed in swine with ulcers. The results of her experiments indicated that a vitamin E deficiency is a common factor in spontaneous hepatosis dietetica. The addition of methionine or cystine to a basal ration exerted a preventative action against the development of gastric ulcers.

Jubb and Kennedy (1965) classify stomach ulcers of swine into two varieties, one associated with local mucormycosis involving the glandular mucosa and one of the probable dietary origin involving the pars esophagus.

In their opinion the mucormycotic ulcer occurs in pigs in circumstances similar to those associated with esophageal moniliasis, that is under conditions of artificial feeding and intercurrent debilitating infections. Young piglets are affected. The lesions were found in the diverticulum ventriculi and sometimes the cardiac and fundic mucosa. The most consistent lesions are edematous thickening of all of the diverticulum encompassing large, fairly discrete hemorrhagic areas. The affected mucosa is converted to a thick amorphous layer of necrotic tissue demarcated by a dense rim of inflammation containing giant cells.

They further stated that ulcers of probable dietary origin in swine were strictly confined to the pars esophaga; they rarely encroached on the esophagus and never on the glandular mucosa. In cases which came to post mortem, the squamous mucosa was ulcerated in its entirety. The disease occurred sporadically in groups of pigs after weaning age but it may occur in sucklings in association with some other chronic disease. Death occurs promptly from massive hemorrhage. The carcass was anemic, there was whole or digested blood in the stomach and melaena.

Histologically, it was apparent that the ulceration did not extend beyond the submucosa which is instead the location of acute leukocytic infiltration and in chronic cases of granulation tissue.

Hannon and Nyham (1962) conducted an experiment to determine the influence of various vitamins in preventing gastric ulcers within a herd of swine incurring losses due to gastric ulcers. Observations made on 377 pigs at the slaughterhouse showed that 53% had varying degrees of ulceration in the esophageal zone of the stomach. The use of vitamin E by the intramuscular route or the addition of vitamins A, E and K to the ration at three times the required levels did not alter the incidence of ulcerative gastric hemorrhage in pigs.

Reese et. al. (1966) reported that the addition of thiamine, riboflavin, pyridoxine, calcium pantothenate, niacin, vitamin B_{12} and ascorbic acid or the fat soluble vitamins A, E, D and K to the basal ration did not change the number of stomach lesions observed.

There are numerous reports relating the ration and the incidence of gastric ulcers. The report of Buntain (1961) relating a high copper diet to gastric ulcers was mentioned previously. However, Gordon (1957) failed to produce or observe the lesion in his experimental studies of copper toxiciosis.

Barrow (1963) inferred that the high content of iron in the concrete was more of a factor than confinement in causing ulceration in a group of swine. Those placed on pasture did not develop ulcers. Orfeur (1965) discussed the possibility that the ulcers were caused by sporadic ingestion of high concentration of mineral salts due to the uneven mixing of a mineral supplement in the feed. He did not regard as significant the fact that these animals were very crowded and suffering from pneumonia.

Interest in the effect of the type of grain and physical form of the ration as it relates to gastric ulceration was stimulated by Perry et. al. (1963). He observed an incidence rate of 55% in swine fed a basal ration containing gelatinized corn. However, Reese et. al. (1966) failed to produce ulcers using a similar corn product.

The only difference in the rations was that the ration used by Reese contained 5% alfalfa leaf meal and 3% brewers yeast. Perry's results were interpreted by some as relating the pelleting process to gastric ulcers.

Chamberlain et. al. (1967) reported that their experiments indicated that the process of pelleting was involved in the development of esophagogastric ulcers and also improved the feed efficiency.

Mahan et. al. (1964) also reported that their experiments revealed that the incidence of ulcers in swine fed raw corn was quite low but the incidence among swine fed finely ground raw corn was higher than in swine fed more coarsely ground raw corn. Among the swine fed gelatinized corn, the addition of dietary fiber, dried skim milk, or reduced growth rate failed to reduce the incidence of ulcers.

Experiments by Nuwer et. al. (1964) designed to isolate the ulcerogenic factor or factors in gelatinized corn, revealed that it was associated with the gelatinized endosperm fraction of corn.

Muggenburg (1965) observed sporadic severe death losses due to gastric ulcers in sows near parturition. He reported that antibiotics, protein source, or increased dietary lipids had no influence on the occurrence of gastric ulcers. He did observe a preventive influence of oats and oat hulls and concluded that undetermined management factors and feeding practices contributed to the development of gastric ulcers.

Fugate et. al. (1965) reported on the effects of various methods of corn preparation and fineness of grinding on swine performance. Two experiments were conducted using 420 pigs. In a summer experiment the following rations were fed to growing finishing swine: gelatinized, coarsely ground, medium ground, finely ground, and shelled corn. A winter trial was conducted with the following rations: gelatinized, finely ground, medium ground, pelleted reground corn. In both trials

the finer feeds and the gelatinized corn resulted in more efficient gains than did coarse feeds. There was a greater incidence of esophagogastric ulcers and associated lesions in the swine fed finely ground feeds than in swine fed more coarsely ground corn rations. There were more ulcers in the swine fed pelleted feeds than in those receiving ground or reground rations. Doubling the number of pigs per pen resulted in slower and less efficient gains in both trials. There was little difference in ulcer occurrence in the summer trial but there was an increase in the severity of lesions during the winter experiment. Additional research by these workers confirmed their earlier conclusions. The results of the study by Mahan et. al. (1965) revealed the highest incidence of ulcers occurred in swine receiving gelatinized corn with the lowest incidence among those receiving the more coarse ration. The stomach contents were more fluid in those pigs having ulcers, erosions or cornifications, and the stomach content had a lower pH. The inclusion of plastic cubes and additional vitamins had no effect on the incidence of ulcers.

From surveys and experimental work O'Brien and Connolly (1965) reported that the feeding of cheese whey appeared to be a major factor in the occurrence of gastric ulceration. A measure of control was attained by the combined use of vitamin E and selenium. Selenium alone administered orally or parenterally did not reduce the incidence of the condition.

Reese et. al. (1966) reported that the addition of dried skim milk, ground extracted soybeans which had been heated, and fluid milk did not alter the incidence of stomach lesions when compared to the incidence observed in swine fed a basal corn ration. A ration containing 15% soybean oil also had no significant effect. The addition of thiamine, riboflavin, pyriodoxine, calcium pantothenate, niacin, vitamin B_{12} and ascorbic acid or fat soluble vitamins A, E, D and K to the basal ration did not alter the number of stomach lesions

observed. A significantly greater percentage of normal stomachs was found when a wheat-oat ration was fed instead of a corn ration.

These workers found that feeding a ration containing heat treated corn or corn which was pelleted and reground had no effect on the development of ulcers. Fluidity of the stomach contents was associated with abnormal stomachs.

In another study, Reese (1966) reported the influence of alfalfa meal, oats, wheat, and corn on the development of ulcers. The study reported on the incidence rates of epithelial changes, erosions and ulcers within 104 swine. The feeding of alfalfa leaf meal as 5% of a corn ration had no effect on the prevalence of stomach lesions in swine.

Fewer stomach lesions were observed in swine fed rations containing wheat and oats or corn and oats as the only grains. Swine receiving a ration containing 85% oats had all normal stomachs while the stomachs from pigs fed 76% corn had abnormalities, including 53% with erosions or ulcers.

Riker (1966) indicated that oats had some protective factor, possible fiber content, against esophagogastric ulcers and suggested that oats could be used to replace up to 70% by weight of corn without significantly decreasing weight gains. However, wheat when finely ground did not offer any protective action against esophagogastric ulcers.

Maxwell et. al. (1966) found that swine fed a ration including 25% ground oat hulls had fewer stomach lesions than a group fed a corn ration of the same particle size. When the oat hull ration was finely ground the protective effect was lost. It was concluded that either particle size of the ration or certain ration components was an important factor determining the development of stomach lesions in swine.

The possible role of dietary sugar was suggested as a contributing factor in gastric ulcers in swine by Griffing, (1963). Stedham (1965) postulated that

high-heat treated pellets might allow saliva to penetrate the feed, allowing the salivary amylase to act upon starch for considerable time before being inactivated by stomach acid. This process might produce an increased amount of sugar in the stomach. The resultant sugar would inhance the growth of C. albicans and ulcer production. His experiment involved the feeding of low levels of dietary sucrose and maltose and the results indicated that the growth of C. albicans was not inhanced nor was there any increase in the occurrence of esophagogastric ulcers.

Stedman's hypothesis concerning pelleting and enzyme action was confirmed by Jensen (1965).

Fugate (1965) found that feeding finely ground feeds resulted in a greater number of esophagogastric ulcers than feeding of coarser feeds. He also found that there were more ulcers in swine fed pelleted feeds than in those fed the ground or reground feeds.

Mahan (1965) found that the incidence of ulcers increased with the use of finely ground and gelatinized corn and varied with different groups of swine.

Reimann (1966) found that the average osmotic pressure of a filtrate of stomach content decreased with ration particle size and it was approximately isotonic for the swine fed finely ground feed. It was hypertonic in the group fed coarse feed. This suggests that decreased ration particle size resulted in a greater rate of gastric secretion or greater water consumption. The average pepsin concentration of the filtrate was 3 to 15 fold higher in groups fed finely ground feed than in those fed a coarse feed, however, pH was unaffected, which suggested that the ulcerogenic effect of finely ground rations may have been related to the higher concentration of pepsin in the stomach content.

In a recent series of experiments studying the relationship of various feed components to the occurrence of gastric ulcers in swine Nafstad and

Nafstad et. al. (1967) found that the addition of vitamin B_1, amino acids, and the feeding of low fat rations did not change the number of stomachs lesions observed. A certain degree of protection against development of stomach lesions seemed to be afforded by vitamin E supplement. The feeding of low protein diets resulted in no increase of the total number of stomach lesions, but appeared to increase their severity. Rations containing high amounts of unsaturated fatty acids either in fresh or oxidized condition had strongly ulcerogenic properties. The feeding of saturated instead of unsaturated dietary fats resulted in a reduction of the severity of gastric lesions. A lower incidence of gastric abnormalities occurred when soybean meal replaced casein as a source of protein.

One of the major changes in the management procedures employed in feeding swine has been the increased practice of confining the animals during the growing and fattening period. Some work has been reported in recent years evaluating the influence of confinement as a factor altering the incidence of gastric ulcers.

Griffing reported that the results of a controlled experiment revealed that there was a greater incidence of ulceration in groups of boars confined at a boar testing station with two animals per pen, then in a control group of boars confined with four animals per pen. There was no previous history of Candida infection at the site where the control animals were housed but there was a history of Candida infection at the boar station. He suggested that placement of boars in pens of 2 and environmental contamination with C. albicans contributed to ulceration.

Fugate et. al. (1965) found that doubling the number of pigs per pen did not affect the occurrence of stomach ulcers in a summer feed trial but increased the severity of lesions during a winter experiment.

Reese et. al. (1966) reported that results of seven controlled studies

utilizing 352 pigs indicated that crowding of pigs resulted in no increase in the numbers of stomach lesions, but may have influenced their severity.

Chamberlain (1964) observed that there was a significant reduction in ulcer incidence when pigs were placed on pasture.

LeBars (1964) stated that an external factor may precipitate gastric ulcers in swine and this factor may be transportation.

Rider et. al. (1966) noted a significant increase in stomach lesions when swine were rotated between environmental temperatures of 29.9°C and 18.3°C.

Rothenbacher (1965) reported that the severe stress of prolonged restraint of 2 pregnant gilts did not cause acute erosive or ulcerative lesions in their stomachs.

Methods have been recently developed to experimentally produce esophagogastric ulcers in swine.

Muggenburg et. al. (1966) produced acute ulcers or erosions in the esophageal region of the stomach in 13 of 16 swine by intramuscular injection of reserpine. The administration of reserpine resulted in decreased pH and in increased free acid concentration and pepsin activity.

Huber et. al. (1965) found that the intramuscular injection of repository histamine to starved swine produced acute hemorrhagic esophagogastric ulcers. They observed that food or other material in the stomach apparently inhibited severe ulceration. The results of this investigation suggested that the frequency of feeding and the buffering capacity of the diet may influence the incidence of porcine gastric ulcers.

Baker and Cadman (1963), Griffing (1963, Bixby (1964 and Stedham (1965) suggested that Candida albicans may be of significance in porcine gastric ulcers.

Winner and Hurley (1964) stated that C. albicans was found in numerous sites in man throughout the world, both as a commensal and as a pathogen. They cited

numerous references that related to the recovery of the organism in nature as well as causing spontaneous disease in several animal species. The infrequence of isolating the organism from soil suggested that C. albicans occurred in the soil only by chance contamination from animal feces. In view of the ubiquity of the organism as a commensal and the comparative rarity of disease produced by it, they felt there must be common agreement that the thrush fungus is a micro-organism of low virulence.

They further stated that a physiologic disturbance in the host destroys the equilibrium between the host and parasite of thrush and overt disease results. It was virtually impossible to reproduce oral thrush in the mouths of adult healthy humans but if the buccal mucous membrane was damaged, the disease became reproducable.

Winner and Hurley further stated that clinical and subclinical candidosis has often been observed following the onset of anti-bacterial therapy. They presented both positive and negative evidence that related antibiotics to enhancement of growth and virulence of C. albicans. The balance of their discussion strongly pointed toward a positive relationship of antibiotic therapy and development of clinical candidosis. They also discussed the relationship of C. albicans to steroids and concluded that the susceptibility of the individual to candida infection was enhanced by adrenal steroids.

Quin (1952) reported a case of occulusion of the esophageal-gastric junction in a porcine by a piled-up inflamatory fungus lesion which yielded a pure culture of Monilia.

Van Uden (1960) found that 222 of 250 (88.8%) swine sampled had yeasts in the intestinal tract. In this survey he found that 9.2% had C. albicans and 48.4% had C. slooffii.

A report by Van Uden and Do Sousa (1958) stating the results of culturing the

caeca of various animals found the distribution of the yeasts of any species and for C. albicans respectively was: horses 52.4%, 4.4%, sheep 6.8%, 4.2%, goats 6.4%, .8%, swine 88.8%, 9.2%.

Van Uden (1960) also noted the influence of the diet upon the gut flora. Candida slooffii is an obligate saphrophyte like C. albicans. Swine receiving only a green plant diet had no C. slooffii. Those receiving a mixed diet with kitchen refuse had low numbers of C. slooffii but those receiving an all grain diet had higher numbers of C. slooffii. In another report Van Uden (1958) reported that 22% of wild African wart hogs had C. albicans in the intestinal tract. East Africans on a low animal protein diet had more C. albicans and more (12%) were infected than the people on a high animal protein diet (4%). He concluded that intestinal infection with obligate saphrophytic yeast is enhanced by a grain diet and inhibited by a diet high in animal protein and cellulose.

One of the first reports relating C. albicans to gastric ulcers was by Baker and Cadman (1963). They stated that C. albicans appeared to be prevalent in the stomachs of unthrifty pigs. The organism was isolated from the stomachs of 2 to 8 week old pigs from 8 herds during a two year period. Ulcerative, inflamatory, lesions were observed in the esophageal region of the stomach and the organism had a predilection for this region.

Gitter and Austwick (1959) described a concurrent infection of C. albicans in the oral cavity and esophagus in an outbreak of gastric muromycosis in a litter of young pigs. They isolated C. albicans only in non glandular epithelium and Rhizopus microsporus only from gastric glandular epithelium.

Osborne et. al. (1960) reported a 17.8% mortality in 140 artifically reared pigs fed a semisynthetic diet containing penicillin. Lesions of moniliasis were present in these swine but only half of the fatal cases showed lesions visible in

the mouth so that morbidity well over this figure was assumed. They postulated that the keratolytic properties of the yeast were enhanced by the sugars in the milk substitute.

Even though Curtin (1963) consistently isolated C. albicans from stomach scrapings in swine with gastric ulcers, he did not regard it as a primary etiological agent. He stated the presence of excessive cornification and erosions alter the barriers provided by normal mucosa, and the fungus is able to enter and grow in the superficial layers of tissue.

Griffing (1963) concluded that excessive keratinization contributed to the pathogenesis of esophagogastric ulcers and entrapment of C. albicans contributed to ulcerogensis.

Bixby (1964) found epidemiologic relationships of esophagogastric epithelial denudation and ulceration to the incidence of Candida species, especially C. albicans.

In a case report of thrush in a piglet, McCrea (1957) recovered Candida species from the esophagus and C. albicans from the colon.

Of the 62 cases of esophagogastric ulcers observed at necropsy by Thoonen (1963), mycelia were demonstrated in 10% upon histopathologic examination.

Action of Candida Albicans

Some of the possible actions of C. albicans are presented below to explain how its presence in the tissues will cause pathologic alterations.

Kapica and Blank (1957) demonstrated that C. albicans could utilize keratin as the sole source of nitrogen in the presence of glucose.

The studies of Mankowski (1962) revealed that metabolic products of C. albicans have an inhibitory effect on the growth of new born mice. Increased dosages of filtrates from media containing living C. albicans caused mice to show large areas of baldness. This relates C. albicans to an altered epithelial

metabolism.

Isenburg (1963) found that C. albicans contained an endotoxin-like fraction which caused extensive necrosis of the skin around the sites of injuction. The avirulent stains tested did not produce any ill effects.

Roth (1957) found that a substance released from C. albicans was lethal to mice when the mice were pre-treated with chlorotetracycline. This substance was only slightly active when given in the absence of chlorotetracycline and slightly active after chloramphenicol or streptomycin pre-treatments.

Winner and Hurley (1965) and Baker and Cadman (1963) suggest the promiscous use of antibiotics may promote the development of candidosis.

Huppert (1955) reported that all of antibiotics used in his experiments when administered by the oral route predisposed towards the establishment of C. albicans in the microbial flora of the intestinal tract of mice.

The results of an in vitro study by Huppert (1953) revealed that chlorotetracycline hydochloride stimulates the growth of C. albicans significantly while penicillin chloramphenicol, streptomycin and oxytetracycline do not show a similar effect. However, Seligman (1953) found that the chlorotetracycline and oxytetracycline greatly enhance the virulence of C. albicans to mice. Other antibiotics failed to show this effect. Administration of cortisone shortly before and after infection with C. albicans produced a generalized fatal infection.

In vitro studies by Cormane (1964) indicated that the reason for the apparent increased incidence of C. albicans infection following broad spectrum antibiotic therapy was through the removal of bacteria competing for glucose. Reese et. al. (1966) observed that the feeding of chlorotetracycline or a mixture of chloretracycline, arsanilic acid bacitracin or high levels of streptomycin had no significant effect on stomach abnormalities.

Curtin (1963), Kowalcyzk (1960), and Griffing (1963) stated that hyperkeratosis or parakeratosis of the esophagogastric region was frequently concomitant with ulceration. An understanding of the process of keratinization may offer new insight into the pathogenesis of an ulcer.

Dorland's Medical Dictionary (1965) defines keratinization as the development of or conversion into keratin i.e. the process of becoming horny. Rothman (1954) stated that this process included not only the transformation of cytoplasmic proteins into keratin fibers but also a complete disentegration of the keratinizing cell, including decomposition of both cytoplasma and nucleus. During keratinization, sulfhydryl containing amino acids residues facing each other on neighboring polypeptid chains close to form a disulfide cross-linkage. This conversion of cysteine to cystine is a paramount chemical feature of keratin formation. The higher and more resistant keratinous structures contained a higher cystine content.

From the studies of pathologic keratinization, Van Scott (1954) concluded that in many types of pathological keratinization the sulfhydryl and disulfide contents of the horny scales deviate from normal. The most pronounced alteration was the greatly increased sulfhydryl content.

MATERIALS AND METHODS

Collection and Processing

Specimens were collected at an Arkansas City, Kansas abattoir. Swine were received at this plant from most regions of Kansas, south central Nebraska and northern Oklahoma. Only barrows and gilts weighing between 86 and 104 kg. were included in the survey.

For the purpose of this survey the term lot was defined as any group of animals purchased by the packing plant from a single seller. As a routine procedure, the lot numbered was tatooed on each animal prior to slaughter. This

facilitated identification following depilation and evisceration. Carcasses and viscera were examined and a record was made of the gross lesions of all livers and lungs.

Twenty percent of all lots available and 20% of the animals in each lot were examined. A total of 143 lots and 1,350 swine were examined.

Stomachs were examined and portions of each esophagogastric region were collected at two week intervals beginning August 8, 1965, and ending July 22, 1966 (appendix table 1).

After 10 to 20 stomachs had been tagged with an identifying number and removed from the viscera pans, they were moved to another part of the plant for examination. A maximum time of one hour elapsed between removal of the stomach from the carcass and collection of tissues.

A incision was made on the greater curvature of the stomach which was then everted and the contents removed. The entire stomach was examined and all gross alterations were recorded. Following gross examination, alcohol flamed forceps and scissors were used to collect tissue from the esophagogastric region of each stomach. If a lesion was present, a portion of the lesion as well as a part of the grossly normal epithelium was collected for mycologic determinations. Each piece of tissue was placed in a sterile plastic bag[1] and packed in ice until transferred to media. Tissues were collected for histopathologic examination by removing sections adjacent to the areas removed for culturing. A solution of buffered 10% aqueous formalin was employed as the fixative for the tissues to be stained with Hematoxylin and Eosin as well as for the sections to be stained by the Grocott method. Carnoy's fixative was used for tissues to be stained for glycogen by the Best-carmine technique. A 1% solution of trichloroacetic acid in 80% ethanol was used for tissues to be stained for cystine and cystiene. The method of Barnett and Seligman with the modification of Cafruny (1955) was

[1] Whirl Pack, Scientific Products, North Kansas City, Missouri

used for the histochemical demonstration of cystine and cysteine.

A scoring system was developed in order that numerical values could be assigned to the gross and miscroscopic appearance of the esophageal portion. Listed below are the descriptions representative of each score.

Gross Keratinization Scores

1. Normal to slightly thickened keratin; .5 to .75 mm.
2. Moderately thick keratin; .75 to 1.00 mm.
3. Thick keratin; 1.00 to 1.75 mm.
4. Marked thick keratin; 1.75 to 2.00 mm.

Character of Keratin

1. Soft--delicate to the touch, lacked tensile strength and was easily removed from underlying epithelium.
2. Normal--neither soft nor hard, was well attached to underlying epithelium.
3. Hard--held shape even under pressure, cut with increased resistance.

Gross Ulcer Scores

1. Normal to slight erosion.
2. Moderate erosion.
3. Ulceration.
4. Ulceration with severe inflammation.

After histopathologic examination of several hundred stomachs was completed, it was noted that the lesions could be divided into four groups and all written descriptions were converted to numerical values. This procedure facilitated statistical comparisons. The four miscroscopic grades differed in severity. Severity was indicated by the degree of epithelial loss and the amount of inflammation.

Listed below are the descriptions of each microscopic grade. The descriptions indicate the most frequent combination of microscopic findings in each stomach within a grade. All histologic features were considered before a numerical grade was assigned.

Microscopic Ulcer Scores

Grade I. This grade included normal stomachs and those with slight changes, including loss of the stratum corneum and mild hydropic changes of cells of the stratum spinosum. Although a mild parakeratosis was occasionally observed the stratified squamous epithelium was 20 to 50 cells thick.

Grade 2. The epithelium of these stomachs was 60 to 80 cells thick. Both hyperkeratosis and parakeratosis were often observed. Erosion had extended to the mid point of the stratum spinosum. Acanthosis, spongiosis and vesiculation were frequent alterations. The leukocytic response was mild. There was mild lymphoctyic and eosinophilic infiltration of the propria and papilla. Lymphofollicular hyperplasia of the propria was occasionally observed.

Grade 3. The epithelium was 60 to 80 cells thick. The rete pegs were elongate and irregular. Acanthotic plaques were frequently seen as evidenced by irregular arrangement of the rete pegs. Parakeratosis and hyperkeratosis were frequent findings. Most of the epithelium was eroded, leaving only the base of the rete pegs. The stratum cylindricum, 5 to 10 cells of the stratum spinosum, and half of the papilla were exposed. A moderately severe monomoculear and polymorphnuclear infiltration was noted. These stomachs frequently had a severe eosinophilic infiltration. Marked hydropic degeneration of the stratum spinosum was frequently seen and vesicles coalesced to form bullae which contained an amorphous acidophilic substance. Bacteria were occasionally observed in the bullae and neutrophills filled some of the bullae. Pseudomycelia and blastospores were observed in the epithelium adjacent and superficial to the

degenerating epithelium. Lymphofollicular hyperplasia in the propria and a diffuse infiltration of lymphocytes were frequently observed. Occasionally fibroplasia and increased vascularity were noted in the propria and muscularis mucosa beneath the erosion and in the submucosa of adjacent cardiac glandular epithelium.

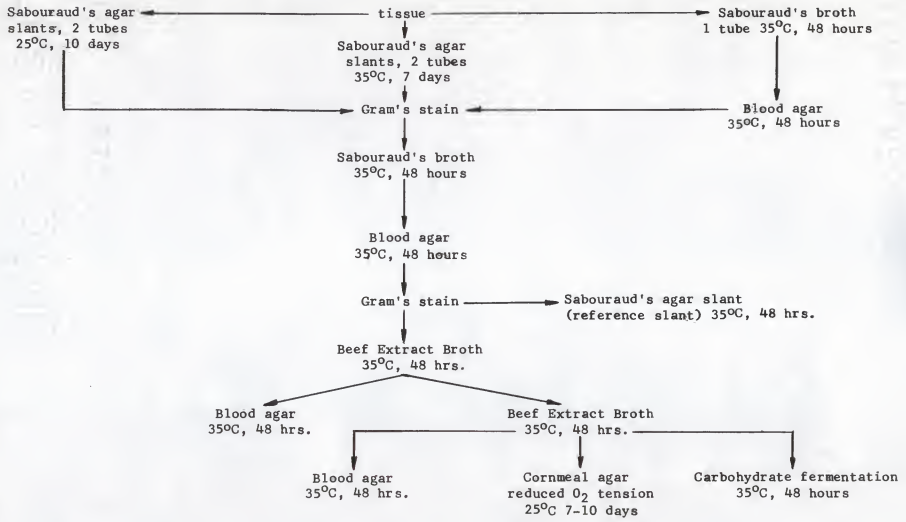
Grade 4. Stomachs in this grade had true ulcers. All of these stomachs had dyskeratotic changes as described in Grade III. The size of the lesions varied in width from a few millimeters to several centimeters. Rarely was the entire esophagogastric region ulcerated. The main criterion for specimens to be included in this grade was severity of the lesion. Stomachs in Grade 4 had lost all epithelium, some or all of the propria and there was necrosis of the muscularis mucosa. The surface of the crater was covered with necrotic tissue and degenerate leukocytes. Severe leukocytic infiltration was present beneath the erosion. Neutrophils numerically exceeded esoinophils and the number of lymphocytes was relatively reduced. Lymphofollicular hyperplasia and arteriolar thrombosis were frequently observed. However, thrombosis of venules was rare. Thickening of the media of small arterioles was occasionally observed and these vessels had a corrugated intima. Interstitial edema was frequent and severe.

Mycology

The flow sheet, Figure 1, outlines the techniques used to determine the presence of fungi in tissue. Sabouraud's dextrose agar and broth were used for initial cultivation. Chloramphenicol (.05 mg/ml) and Cycloheximide (.5 mg/ml) were added to inhibit non pathogenic fungi and bacteria. Addition of these inhibitors may have prevented detection of some saphrophytic Candida sp. but the advantages of using inhibitors out-weighed the disadvantages. A reference culture of Candida albicans* was used as a media control.

*National Communicable Disease Center, United States Public Health Service, Atlanta, Georgia.

FIGURE 1---Flow Sheet Illustrating The Sequence of Procedures Used for Mycologic Examination



Management Data

Letters explaining the purpose of the survey and questionnaires (appendix exhibits 1, 2 and 3) were sent to each farmer-producer whose swine were sampled. The purpose of the questionnaire was to obtain data concerning management practices. These data were prepared for statistical analysis. Chi square values were computed comparing incidence rates of stomach lesions to various management practices.

If swine of a farmer-producer were sampled within 60 days of a previous examination and a questionnaire was received, these data were used for the second sampling. However, if more than 60 days lapsed between examinations, a new completed questionnaire was requested. Data were used from 87 producers (75.5%) of the swine from farmer-producers, representing 521 animals.

A comparison of the prevalence rates of stomach lesions to all combinations of management practices was made in an attempt to determine what factor or combination of factors resulted in the highest ulceration rate.

Seasonal Incidence Data

Climatological data relative to the mean high and mean low temperatures were obtained.* These data were from the Winfield, Kansas weather station, the nearest station to the sampling site and the area from which most swine originated.

Statistical Techniques

Data including gross and miscroscopic lesions were converted to numerical values and the data coded onto cards.** The comparisons were computed.***

* Weather Bureau State Climatologist.

** Programs were prepared by the Kansas State University Statistics Department

*** IBM 1410 Computer.

Erosive or ulcerative changes 280 20.74

The results of the comparisons were reported as row percentages and chi square values. The chi square values were converted to levels of probability.

Twenty-four stomachs were not graded as to character of keratin and 32 paraffin embedded tissues for histopathologic examination were accidently destroyed, therefore, the tables of results report minor deviations but not sufficient to cause changes in significance or trends.

RESULTS

Sampling Rates

Data concerned with the sample size; the number of swine in the sampled population and the sampling rates were as follows:

Total number of swine at abattoir on all sampling days	26,984
Total number of lots available for sampling	659
Number of lots sampled	143
Percent of available lots sampled	21.70%
Total number of swine in lots sampled	6,553
Percent of available swine sampled	20.60%
Number of swine sampled	1,350

The sampling percentages on each collection period are included in Appendix Table 1. The sampling rates for individual lots are in Appendix Table 2.

Gross Examination

Only livers and lungs evidencing marked pathologic changes were included in this summary of data. The total number of swine with gross lesions of stomach, liver, and lungs are presented (Table 1).

TABLE 1--Results of Gross Examination of 1,350 Swine

Lesions	Number with lesions	Per cent of swine with lesions
Liver changes	165	12.22
Lung changes	129	9.55
Altered keratinization	629	46.59
Erosive or ulcerative changes	280	20.74

This summary of data relating to liver and lung lesions were analyzed by statistical techniques and no relationship was found to exist between liver and lung changes separately or together and the occurrence of gastric ulcers. Altered keratinization and ulceration were frequently observed. Altered keratinization occurred at a higher rate.

Gross and Microscopic Examination Comparing the Source of Swine

Prevalence rates of altered keratinization and ulceration in swine from farmers and dealers are presented (Table 2). Swine derived from producers were maintained by the same person who sold them for slaughter. These animals came directly from the farm to the abattoir. Swine derived from dealers were purchased at collection points such as community sales and maintained on trucks or holding pens until sufficient numbers had been purchased to fill a truck. These swine were then transported to market. In many instances these swine were maintained in crowded holding pens or on trucks for periods over 18 hours. Stomachs of these swine were frequently contracted and contained only a brownish-green mucoid fluid. This material had a foul odor and the pH was usually between 7.0 and 8.5. This relatively high pH was probably due to regurgitation of duodenal contents during the processing procedures. Only occasionally were the same findings seen in swine derived from the farmer-producer. The esophagogastric portion was frequently light yellow, bright yellow or yellow-green and the keratin was very hard or very soft. Most of the stomachs from farmer-producers had keratin of normal consistency.

TABLE 2---Prevalence Rates of Altered Keratinization and Ulceration Comparing Ante Mortem Environment in Swine

Source	Total No. Swine Examined	Altered Keratinization		Ulceration	
		No.	Per cent	No.	Per cent
Farmer	665	250	37.59	97	14.58
Dealer	685	379	55.32	183	26.71

$P < .001$

The major factor responsible for the differences in the gross appearance of stomachs derived from traders and farmers was the length of time that the animals were withheld from feed. This was probably more important than other environmental stress factors. This was further emphasized as the prevalence rates of gross lesions were very low in some lots of trader derived swine with full stomachs and high in some lots of farmer-derived swine with empty stomachs.

To facilitate a more detailed comparison of the influence of the source of swine as a factor influencing ulceration, a comparison was made of the microscopic ulcer scores and the source of swine. The results of this comparison are summarized in Table 3.

TABLE 3.---Comparison of the Severity of Esophagogastric Ulcers In Dealer and Farmer Derived Swine

Microscopic Ulcer Score	Farmer Derived Swine		Dealer Derived Swine	
	No. with lesions	% with lesions	No. with lesions	% with lesions
1	412	52.68	370	47.31
2	135	50.37	133	49.62
3	44	36.36	77	63.63
4	38	25.85	109	74.14

$p < .001$

The rates of stomach lesions in the dealer derived swine increased with increased severity.

A comparison was also made of the degree of keratinization in farmer-producers and dealer-derived swine. These comparisons are included in Table 4.

TABLE 4--Comparison of the Prevalence of Various Degrees of Keratinization in Farmer and Dealer Derived Swine

Degree of Keratinization	Farmer		Dealer	
	No.	Per cent	No.	Per cent
1	414	58.31	296	41.69
2	181	41.51	255	58.49
3	55	32.93	112	67.07
4	15	40.54	22	59.46

$P < .001$

The prevalence rates of altered keratinization within the dealer derived swine increased with an increasing degree of keratinization in grades 1 to 3 but the rate decreased from grades 3 to 4. It should be noted that the number of observations in grade 4 is considerably lower than the other grades. The relatively small number of observations may have been responsible for the changes in the trend. However, these data indicate a relationship between dealer swine and altered keratinization.

The high statistical significance of these data and the marked differences in the rates indicate that adverse antemortem environmental factors may predispose swine to gastric ulcers.

Transit Hours as a Factor Influencing Ulceration

Hours in transit was the total time lapsed from leaving the farm until arrival at the packing plant. The results of a comparison of the influence of transit hours in altering the prevalence of stomach lesions in all swine for which data were available are presented (Table 5).

TABLE 5--Hours in Transit as a Variable in Altering the Prevalence of Stomach Lesions in Swine

Hours in Transit	Total No. Sampled	Altered Keratinization No.	Altered Keratinization Per cent	Ulcerative Changes No.	Ulcerative Changes Per cent
0 to 1	161	48	29.81	15	9.31
1 to 2	153	49	32.02	16	10.45
2 to 3	123	48	37.50	19	14.84
3 to 4	100	56	56.00	18	18.00
5 or more	284	190	66.54	88	30.98

$P < .001$

The data in Table 5 clearly indicate a relationship between increasing hours in transit and altered keratinization and ulceration.

Confinement

Confinement was defined as a management procedure of maintaining swine on concrete floors, slated floors, or in a dry lot with less than 18 square feet of floor space per animal. Nonconfinement was defined as the provision of abundant pasture or dry lot area. A comparison of the prevalence rates of gross stomach lesions and the severity of these lesions in swine that were confined during the finishing phase of the feeding period to those that were not confined failed to reveal any significant differences.

Floor Space

The occurrence of stomach abnormalities as influenced by the number of square feet of floor space per pig was determined. No significant differences in the occurrence rates were observed when floor space was considered as a variable.

Pasture Type

The statistical comparisons of pasture types as a factor influencing the occurrence of altered keratinization or ulceration failed to reveal any trends or relationships.

Days of Feed

The number of days the swine were on full feed was considered as a variable influencing prevalence of stomach lesions. These comparisons are recorded (Table 6).

TABLE 6.---Length of Feeding Period as a Factor Influencing the Prevalence of Stomach Lesions In Swine

Length of Period on Full Feed	No. Swine in each Period	Altered Keratinization		Ulceration	
		No.	Per cent	No.	Per cent
90-120 days	214	83	38.78	33	15.42
120-150 days	189	87	46.03	25	13.22
150-180 days	79	15	18.98	8	10.12
180-210 days	31	2	6.45	0	00.00
210-240 days	8	7	87.50	1	12.50
		$P < .001$		$P < .10$	

These results indicate that when the feeding period was less than 150 days the rate of stomach lesions increased. The groups of hogs in the last feeding period can be considered unique. Under modern management practices it is rare to see market hogs kept on feed for 7 months. These data indicate that rapid rate of gain probably was related to an increased rate of stomach lesions.

Ration Type

The data pertaining to ration type is summarized in Table 7. The rations were those fed for the 30 day period prior to slaughter. The returned questionnaires revealed that the producers were using 12 different rations.

The main constituent of the pelleted and meal rations was either corn or

milo. No apparent relationship was observed between the these rations and the development of altered keratinization. However, a strong trend was observed for a high prevalence of ulcers to occur in swine fed a complete ration in pelleted or meal form. The data also indicate that the small grains had a preventative effect.

TABLE 7.---Prevalence Rates of Altered Keratinization and Ulceration in Swine Fed Different Rations

Ration	Number of Swine Receiving Ration	Altered Keratinization		Ulceration	
		No.	%	No.	%
Complete ration pelleted	73	43	58.90	20	27.39
Complete ration meal form	78	33	42.30	15	19.23
Corn, barley, and supplement	6	6	100.00	1	16.66
Corn and supplement	22	8	36.36	3	13.63
Milo and supplement	158	54	34.17	21	13.29
Barley, milo, corn and supplement	8	1	12.50	1	12.50
Wheat, barley, milo and supplement	32	22	68.75	3	9.37
Barley, milo, and supplement	25	3	12.00	1	4.00
Wheat, milo and supplement	28	5	17.85	1	3.57
Corn, milo and supplement	70	11	15.71	1	1.42
Wheat, barley and supplement	19	7	36.84	0	00.00
Corn, milo, wheat supplement	2	1	50.00	0	00.00

$P < .001$

Antibiotics

A comparison of the prevalence of stomach lesions to the use of feeding a ration containing any antibiotic at any concentration is summarized in Table 8.

TABLE 8---The Influence of Rations Containing an Antibiotic on the Occurence of Stomach Lesions in Swine

Antibiotics	Total No. Sampled	Altered Keratinization No.	%	Ulceration No.	%
Ration not containing antibiotic	142	40	28.16	11	7.74
Ration containing an antibiotic	379	154	40.63	56	14.77
		$P < .01$		$P < .05$	

These data indicate a direct relationship between antibiotics and gross stomach lesions.

Anthelminthics

A statistical comparison was made of the use and non use of an anthelmintic to the prevalence of stomach lesions. The results of this comparison were of low statistical significance and no difference was observed in the rates.

Geographical Origin

Data pertaining to the geographical origin of the swine were obtained for 1,325 of the 1,350 examined animals. Statistical examination of this data failed to reveal any relationship between geographical origin of swine and the occurrence of stomach ulcers.

Seasonal Occurrence

The mean high temperature and the mean low temperatures, computed from 50 years of weather data was charted. Superimposed on these curves were the daily high and low temperatures for August, 1965 through July, 1966, and the percentages of ulcers observed during each collection period. This chart was prepared to

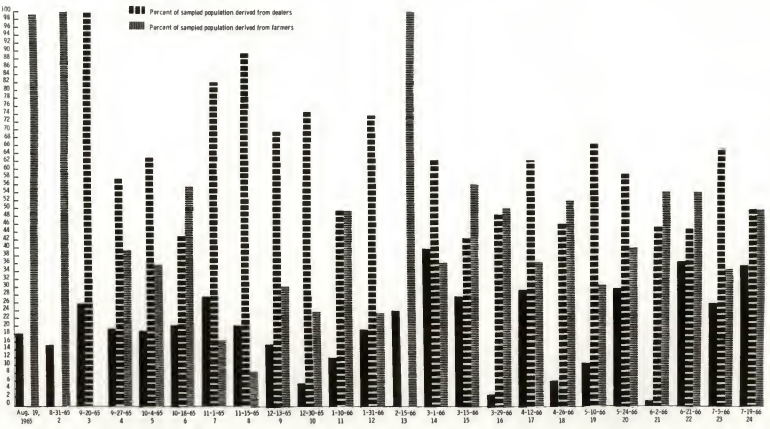
determine if there was a cyclic or seasonal occurrence of gastric ulcers and to learn what influence variations in daily temperatures had on the occurrence of gastric ulcers. Examination of Figure 2 revealed a higher prevalence of ulcers in the late fall and early spring, and the temperature chart revealed a wider range in daily temperatures during these seasons. Figure 2 reveals that the seasonal prevalence pattern was independent of the sampling technique. Figure 3 further confirms the correctness of the seasonal prevalence pattern determined from weather data. It can be seen that the total ulcer rates, ulcer rates of farmer-derived swine and dealer derived swine usually varied together.

Fungi in the Stomach

The rates of isolation of Candida albicans, Candida sp. and Geotrichum sp. for each sample period are presented in Table 3. These data are graphically presented (Figure 4). Altered keratinization always occurred at a higher rate than ulceration. The trend for the rates to change in a similar pattern is quite apparent. These data also strongly suggested that C. albicans, altered keratinization and ulceration were related. Only once did the rate of isolation of C. albicans exceed the ulcer rate and these isolations occurred from dealer derived swine with numerous gastric lesions. Only fair agreement in an increased rate of isolation of Candida sp. and increased rate of ulceration was found. Occasionally there was agreement i.e. high rate of isolation along with an increased rate of ulcers. Since the term Candida sp. includes all species of the genus Candida other than the species albicans it is probable that those instances of agreement occurred when a pathogenic species was present.

Figure 4 also illustrated the poor relationship between isolation of Geotrichum and the prevalence of altered keratinization and ulceration. The reason for the occasional agreement was that an increased rate of isolation occurred with an increased rate of ulceration in the dealer-derived swine with soil

Fig. 2 The seasonal occurrence of esophagogastric ulcers as related to the percent of the total farmer and dealer derived swine population of swine during each sample period.



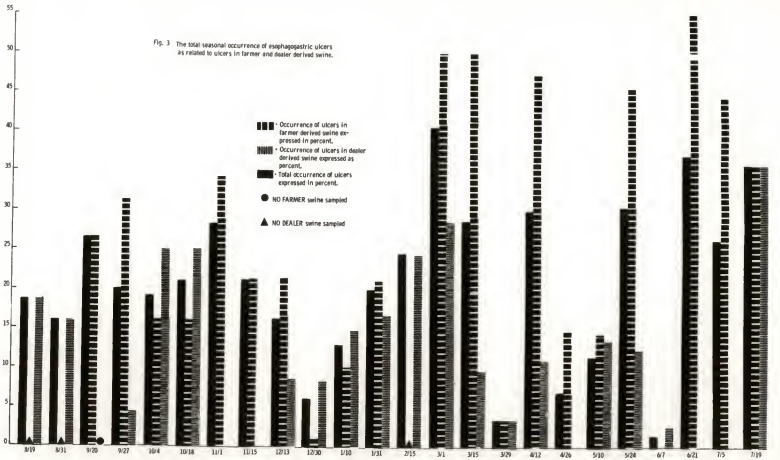


Fig. 3 The total seasonal occurrence of esophagogastric ulcers as related to ulcers in farmer and dealer derived swine.
Occurrence of ulcers in farmer derived swine expressed in percent.
Occurrence of ulcers in dealer derived swine expressed as percent.
Total occurrence of ulcers expressed in percent.
NO FARMER swine sampled
NO DEALER swine sampled
55
50
45
40
35
30
25
20
15
10
5
0
8/19
8/31
9/20
9/27
10/4
10/18
11/1
11/15
12/13
12/20
1/10
1/31
2/15
3/1
3/15
3/29
4/12
4/26
5/10
5/24
6/7
6/21
7/5
7/19

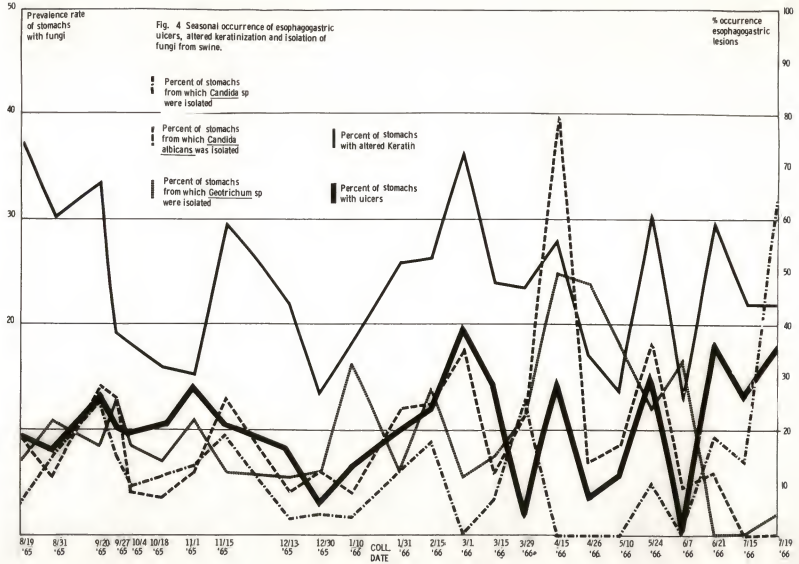


Fig. 4 Seasonal occurrence of esophagogastric ulcers, altered keratinization and isolation of fungi from swine.

stained mucoid contents.

Although the above discussion of the results did point out some significant observations relating mycologic determinations and ulceration no seasonal prevalence patterns in the occurrence of various mycotic organisms was noted.

Figure 4 offers a comparison between the rates of isolation of C. albicans, Candida sp., and Geotrichum sp. In general, the graph indicated good agreement between the changing rates of C. albicans and Candida sp. Only fair agreement is evidenced in the changing rates of isolation of Geotrichum sp. and C. albicans and Candida sp. This indicates that C. albicans and Candida sp. are related and that their isolation may be related to a common factor i.e. altered keratinization and/or ulceration. Isolation of Geotrichum sp. appeared to be independent of isolation of C. albicans and Candida sp. It also appeared to be independent of the occurrence of altered keratinization and ulceration. Its isolation was probably closely related to ingestion of soil.

Degree of Keratinization vs. Miscroscopic Ulcer Score

A comparison was made between the degree of keratinization and microscopic ulcer scores. This comparison is included in Table 9.

Evaluation of these data revealed some interesting relationships between degree of keratinization and ulceration. In the group of swine with an essentially normal keratinization the prevalence rate of stomach lesions decreased as the severity of the lesions increased. The swine which had degree "2" keratinization evidenced an opposite effect. The comparison of degree "1" and "2" reveal the strong relationship between a build up of keratin and ulceration. The swine evidencing degree "3" and "4" keratinization had prevalence rates of microscopic ulcer scores 2, 3 and 4 in excess of 3 times microscopic ulcer score 1. The swine evidencing degree "4" keratinization had the highest rate of prevalence

of microscopic lesions in the most severe catagory. These comparisons were statistically highly significant.

Character of Keratin vs. Microscopic Ulcer Scores

The physical properties of the keratin were compared to the severity of stomach lesions. Histopathologic examination revealed that the soft keratin was thickened epithelium resulting from hydropic degenerative changes and the hard keratin was compact parakeratotic epithelium. Table 10 is a summary of the significant data resulting from a comparison of the occurrence of abnormal keratin observed during gross examination and the rates of prevalence of stomachs with various degrees of ulceration.

TABLE 9---Comparison of Degree of Keratinization and Microscopic Ulcer Scores in Swine

Miscroscopic ulcer score	Degree of Keratinization 1		2		3		4	
	No. with microscopic ulcer score	% with microscopic ulcer score	No. with miscroscopic ulcer score	% with miscroscopic ulcer score	No. with miscroscopic ulcer score	% with miscroscopic ulcer score	No. with miscroscopic ulcer score	% with miscoscopic ulcer score
1	545	69.78	173	22.15	53	6.78	10	1.28
2	95	35.58	104	38.95	55	20.59	13	4.86
3	27	22.15	63	51.62	26	21.32	6	4.92
4	23	15.54	85	57.48	32	21.62	8	5.42

$P < .001$

TABLE 10---Comparison of the Severity of Stomach Lesions to the Occurrence of Grossly Abnormal Keratin

Miscroscopic ulcer score	Character of Keratin: Soft No. stomachs	Soft % stomachs	Normal No. stomachs	Normal % stomachs	Hard No. stomachs	Hard % stomachs
1	84	10.74	664	84.91	14	1.79
2	36	13.43	208	77.61	21	7.83
3	10	8.26	104	85.95	6	4.95
4	20	13.60	114	77.55	13	8.84

P. < .001

The highest rates of prevalence of stomach lesions occurred in the group of swine with normal epithelium. It was noted that stomachs with soft keratin had higher rates of prevalence of lesions of increased severity than the stomachs with hard keratin. The statistical group with the lowest prevalence rate of stomach lesions were the swine with hard keratin and essentially normal stomachs.

Degree of Keratinization vs. C. albicans

The data comparing the presence of C. albicans in tissues of varying degrees of keratinization are included in Table 11.

TABLE 11---Comparison of the Degree of Keratinization and the Presence of Candida albicans as Revealed by Cultural Techniques

Degree of Keratinization	C. albicans not isolated: No. stomachs	C. albicans not isolated: % stomachs	C. albicans isolated: No. stomachs	C. albicans isolated: % stomachs
1	676	95.21	34	4.79
2	387	88.76	49	11.24
3	135	80.84	32	19.16
4	25	67.57	12	32.43

P < .001

Data relating the degree of keratinization and the presence of Candida sp. are included in Table 12.

TABLE 12---Comparison of the Degree of Keratinization and the Presence of Candida sp. as Revealed by Cultural Techniques

Degree of keratinization	Candida sp. not isolated		Candida sp. isolated	
	No. stomachs	% stomachs	No. stomachs	% stomachs
1	686	96.62	24	3.38
2	396	90.82	40	9.17
3	153	91.62	14	8.38
4	37	100.00	0	0.00

$P < .001$

Although these data presented a trend in the relationship between increased rate of occurrence of Candida sp. with increased degree of keratinization the relationship was not as close as C. albicans and keratinization. As explained earlier this phenomenon was probably the result of heterogeneity of this group of organisms.

Character of Keratin vs. C. albicans

The possiblility that C. albicans was more frequently isolated from grossly abnormal keratin than from normal epithelium was investigated. A record was made of all tissues with either very soft keratin or very hard keratin. A summary of the comparison of the isolation of C. albicans in normal, soft, and hard keratin are presented (Table 13).

TABLE 13---Character of Keratin as a Factor Altering the Isolation of C. albicans

Candida albicans	Character of Keratin: Soft No. stomach	Soft % stomach	Normal No. stomachs	Normal % stomachs	Hard No. stomachs	Hard % stomachs
Not isolated	142	90.44	1,014	91.02	43	78.18
Isolated	15	9.56	100	8.97	12	21.81

P .001

The data in Table 13 indicated that C. albicans was isolated less frequently from normal epithelium than abnormal epithelium and that it was recovered at the highest rate of frequency from the hard keratin. This was strong statistical evidence relating C. albicans and abnormal cornification.

Microscopic Ulcer Score vs. C. albicans

One of the most important comparisons made during the study was that of microscopic ulcer scores and the culturing of the organisms from the tissues. A summary of this comparison is included in Table 14.

TABLE 14---Comparison of Cultural Results with Miscroscopic Ulcer Scores

Microscopic ulcer score	C. albicans not isolated No. stomachs	C. albicans not isolated % stomachs	C. albicans isolated No. stomachs	C. albicans isolated % stomachs
1	741	94.87	41	5,37
2	234	87.31	34	12.68
3	102	84.29	19	15.70
4	115	78.23	32	21.76

$P < .001$

These data clearly indicated the rate of isolation of C. albicans increased as the severity of the lesions increased.

Miscroscopic Ulcer Score vs. Candida sp.

Data comparing the severity of miscroscopic lesions and the isolation of Candida sp. are presented (Table 15).

TABLE 15---Comparison of Microscopic Ulcer Scores with Isolation of Candida sp.

Microscopic ulcer score	Candida sp. not isolated		Candida sp. isolated	
	No. stomachs	% stomachs	No. stomachs	% stomachs
1	756	96.67	26	3.32
2	240	89.55	28	10.45
3	108	88.52	14	11.47
4	128	87.67	18	12.32

$P < .001$

These data revealed the rate of isolation of Candida sp. increased with an increasing severity of stomach ulcers.

Miscroscopic Ulcer Score vs. Geotrichum species.

Data comparing the severity, microscopic ulcer score, of stomach lesions and isolation of Geotrichum species are presented (Table 16).

TABLE 16---Comparison of Microscopic Ulcer Scores with Isolation of Geotrichum species

Microscopic ulcer score	Geotrichum sp. not isolated		Geotrichum sp. isolated	
	No. stomachs	% stomachs	No. stomachs	% stomachs
1	690	88.23	92	11.76
2	222	82.83	46	17.16
3	105	86.77	16	13.22
4	125	85.03	22	14.96

P - NS

These data were of low statistical significance and did not reflect any trend. The rate of isolation of this organism was greater in stomachs evidencing pathologic changes than in the normal stomachs but evaluation of these data confirms earlier data stating that the occurrence of Geotrichum sp. is more closely related to some other factor than it is to the presence of a gastric ulcer.

Analysis of Combined Factors

The probability of a combination of certain management factors serving as the cause of gastric ulcers was investigated. To facilitate the comparison, the prevalence rate of gastric lesions and gastric candidosis were determined in each of 26 different combinations of five factors. These data are included in Table 17. This table was prepared by placing the combination of management factors that resulted in the highest prevalence rate of gastric ulcers first on the list and listing the other combinations of factors in a decreasing order of occurrence of ulcers. A code for interpreting what 1 or 2 in the factor columns represent is included in a code sheet I.

Evaluation of the data in Table 17 suggests the following trends and relationships:

1. The combination of factors that produced the greatest occurrence of altered keratinization resulted in the second highest rate of ulceration and gastric candidosis. Previous data related the occurrence of these three factors and these data indicate that the triad was the result of a common factor. This common factor was the management practice of feeding a ration containing corn or milo as the primary grain, feeding antibiotics, and confining the animal to less than 18 square feet of floor space.
2. Previous data indicated that confinement feeding and limited floor

TABLE 17---Analysis of Combined Factors Altering the Prevalence of Esogphagogastric Ulcers, Arranged in Decreasing Rates of Ulceration

Factors*													
Rations	Antibiotics	Transit hours	Floor space	Days on feed	No. Pigs Sampled	Increased Keratinization		Ulceration		C. albicans Isolated		Candida sp. Isolated		Geotrichum sp. Isolated	
						No.	%	No.	%	No.	%	No.	%	No.	%
2	2	1	2	1	25	5	20.0	6	24.0	2	8.0	1	4.0	1	4.0
2	2	2	2	2	27	25	92.6	6	22.2	4	14.8	8	29.6	3	11.1
2	2	2	1	2	60	29	48.3	13	21.7	11	18.3	6	10.0	2	3.3
2	1	1	1	2	27	4	14.8	5	18.5	2	7.4	2	7.4	4	14.8
2	2	1	1	2	33	19	57.6	6	18.2	3	9.1	0	00.0	1	3.0
1	2	1	2	1	6	4	66.7	1	16.7	0	00.0	0	00.0	0	00.0
2	2	1	2	2	20	14	70.0	3	15.0	0	00.0	2	10.0	2	10.0
2	1	1	2	2	37	6	16.2	5	13.5	4	10.8	0	00.0	2	5.4
2	2	1	2	2	126	42	33.3	16	12.7	7	5.6	7	5.6	19	15.1
1	1	1	1	2	10	6	60.0	1	10.0	0	00.0	0	00.0	0	00.0
2	1	1	1	2	21	10	47.6	2	9.5	0	00.0	1	4.7	2	9.5
2	1	2	2	2	14	4	28.5	1	7.1	0	00.0	0	00.0	1	7.1
2	1	1	1	1	15	1	6.7	1	6.7	0	00.0	2	13.4	0	00.0
2	2	1	1	1	35	10	28.6	1	2.8	4	11.4	0	00.0	8	22.9

*Rations

1) Wheat and milo supplement; oats or barley and milo plus supplement; wheat and barley plus supplement; corn, milo, wheat plus supplement; milo and barley plus supplement; barley and milo and corn plus supplement; wheat, barley, milo plus supplement.

2) Complete ration pelleted; complete ration mash or meal; corn plus protein supplement; corn and milo plus supplement; milo plus supplement.

Antibiotic in ration

1) No

2) Yes

Transit hours

1) 1-3 hours

2) 4-5 hours

Floor space

1) More than 18 sq. ft. per pig

2) Less than 18 sq. ft. per pig

Days on Feed

1) 150-240 days

2) 30-150 days

space were not significant factors altering the prevalence of stomach lesions when considered alone. However, these factors become significant when considered in combination with oral antibiotics.

3. These data indicated that the ration and rate of gain may be the most important factors influencing the rates of ulcers and candiosis. The combination in line 4 indicates that the positive factors increasing the ulcer prevalence rate was the ration and a shorter feeding period and yet the ulcer rate was high.
4. Comparison of lines 1 and 2 indicated that altered keratinization may be influenced by transit hours.
5. The feeding of ration 2 (corn or milo) and antibiotics may predispose to gastirc candidosis.
6. Comparison of lines 2 and 3 indicate that the amount of floor space may be a factor influencing the occurrence of altered keratinization.

Comparison of Results of Culture and Histochemic Techniques

The results of cultural procedures for the detection of C. albicans and the histochemic determinations were compared to determine the agreement between these two tests. A summary of this comparison is included in Table 18.

TABLE 18---Comparison of Cultural Results and Histochemic Detection of C. albicans for Which Data Was Available

C. albicans	No. not present in tissues	% not present in tissues	No. present in tissues	% present in tissues
Not isolated	1,073	90.09	118	9.90
Isolated	86	70.49	36	29.50

$P < .001$

The data in Table 19 revealed that cultural techniques were more sensitive in detecting C. albicans in tissues than histochemic demonstration of pseudomy-

celia. C. albicans was observed in less than 10% of the stomachs in which cultural techniques failed to detect the organism. Although C. albicans in tissues forms characteristic pseudomycelia it was possible that some of these were in fact the mycelial phase of one of the pathogenic C. species. Even though culturing detected C. albicans in over 90% of the tissues in which it was not revealed upon histopathologic examinations these data do illustrate the necessity of using both techniques in any effort to determine the presence or absence of C. albicans in tissues. This combined procedure expanded the total prevalence rate from 9.40 to 12.79.

Histochemic Examinations

A randomized sampling of stomachs sectioned and stained demonstrated the relative amounts of cystine and cystiene in the epithelium. Evaluation of all the descriptions revealed the following trends:

1. The stomachs which upon gross examination had soft keratin had increased cysteine content in the stratum corneum.
2. The stomachs which upon gross examination had hard keratin had increased cystine content in the stratum granulosum and stratum corneum.

The sections stained to demonstrate glycogen were shown to have increased quantities of this compound in the epithelium of stomachs with dyskeratotic or erosive changes.

Esophagogastric Ulcers vs. Candida albicans

The results of cultural procedures revealed that 9.40% of 1,350 swine stomachs had C. albicans in the esophagogastric region. Cultural techniques detected C. albicans in 5.37% of the normal stomachs and in 21.76% of the ulcerated stomachs.

DISCUSSION

This survey documents previously suggested relationships between environmental factors and C. albicans to the occurrence of gastric ulcers in swine. The design of the survey required the sampling of a large population of swine over a one year period and enabled the procurement of significant results.

These results indicated that gastric ulcers were not caused by any single factor but probably by several factors. The following factors contributed to the pathogenesis of gastric ulceration: stress, antibiotics, certain rations and gastric candidosis.

The dealer derived swine usually had higher prevelance rates of ulcers than did swine derived from farmers. The factor that was common to most lots with high ulcer rates was withdrawal of feed and confinement in trucks or holding pens for periods over 12 hours. The severity of stomach lesions also increased with increased hours in transit.

Environmental temperature variation was a factor contributing to the seasonal occurrence pattern. Ulcers were observed more frequently during late fall and early spring, the seasons when the animals were becoming aclimatized to a new weather pattern.

The prevalence of ulceration was about twice as great in swine fed antibiotics as it was in swine not fed antibiotics. Most of the swine receiving antibiotics were fed chlorotetracycline. Huppert (1953) revealed chlorotetracycline stimulated the growth of C. albicans and Seligman (1953) demonstrated that chlorotetracycline enhances the virulence of C. albicans to mice. These results gave strong presumptive evidence relating feeds containing antibiotics, gastric candidosis and ulceration. Controlled studies are needed to test this relationship.

The type of ration was a factor influencing the occurrence of gastric ulcers.

Swine receiving pelleted rations had the highest rate of ulceration. Swine receiving a complete ration in a meal form had the second highest ulcer rate. Rations composed of corn or milo and a supplement had an additive influence toward the development of ulcers but the addition of wheat into the ration exerted some preventive influence.

The management practice of strict confinement did not influence the occurrence of ulcers. However, confinement rearing in combination with ulcerogenic factors such as pelleted rations, antibiotic feeds and gastric candidosis resulted in an ulcer rate above the rates in lots with these factors alone.

Rapid rate of gain was related to increased rate of gastric ulcers. Although the nutritional requirements of swine have been fully documented, it is not known how dietary requirements are influenced by maximal growth or environmental stress. Curtin (1963) suggested that enzyme systems may not be able to function at an accelerated rate or the presence of inhibitory substances may interfer with utilization of substrates. The results of this study suggested that the development of gastric ulcers was influenced by an altered metabolism precipitated by stress.

The results indicated that C. albicans was related to the occurrence of gastric ulcers and severity of stomach lesions. The results of this survey did not indicate that it was the primary etiological agent but it must be considered a contributing factor.

Elucidation of the pathogenisis of esophagogastric ulcers in swine is to be found by determing what factors alter the metabolism of the epithelium of the stomach. Even though Huber (1965) and Muggenburg (1966) experimentally produced lesions very similar to clinical gastric ulcers they lacked the thickened stratified squamous epithelium seen in a clinical gastric ulcer. Thus the increased acid production due to histamine stimulation of parietal cells does not com-

pletely explain the clinical occurrence of gastric ulcers.

Maximal growth, environmental stress and gastric candidosis may alter the metabolism of the epithelium and a hyperkeratotic or parakeratotic condition results. Essential components for normal epithelial metabolism may be absent due to a deficiency state. This hyperkeratotic condition may have predisposed the epithelium to infection with C. albicans which through its competition for substrates and production of toxins further altered the metabolism of the epithelium. If the normal buffering capacity of the ingesta was absent or the swine were fed a ration of very small partical size, the osmotic pressure of the contents decreased and the cells underwent hydropic changes. This set of events resulted in the production of an abnormal stratified squamous keratinized epithelium i.e. pre ulcerative condition. If these stimuli persisted an erosion resulted as this epithelium is not an effective barrier to the acid pepsin contents. If the stimuli are removed healing may ensue. However, if during the hyperkeratotic phase the stomach was infected with C. albicans or Candida sp. the condition was not so readily corrected. Confinement rearing increased the prevalence of this organism among the swine.

The histochemic studies were inconclusive but certain trends were observed. The special stain for cystine and cystiene revealed that there was an increased cystiene content in the superficial layers of epithelium in stomachs with soft keratin and an increased quantity of cystine in the hard or warty epithelium. Increased quantities of glycogen were observed in the epithelium of ulcerated stomachs. These observations suggest an abberation in the oxidative and reductive enzyme systems of the epithelium. Although the exact metabolic role of Vitamin E is still unknown, its antioxidant properties are well known. Many of the enzymes systems of C. albicans function at a lower redox potential than mammalian systems and could successfully compete for substrates in the epithe-

lium.

Van Uden (1960) found that 9.2% of the swine he sampled had C. albicans in the intestinal tract. Griffing (1963) recovered C. albicans from 22.12% of 226 selected stomachs. The cultural results of this survey revealed that 9.40% of 1,350 swine had C. albicans in the esophagogastric region of the stomach. Histochemic determinations revealed pseudomycelia in some stomachs for which cultural techniques were negative. When cultural and histochemic techniques were combined a prevalence rate of 12.79% was found. Cultural techniques revealed that 21.76% of the stomachs with severe esophagogastric ulcers were infected with C. albicans.

CONCLUSIONS

The examination of 1,350 swine from a population of 6,553 revealed the esophagogastric region had altered keratinization in 46.59% of the individuals and erosive or ulcerative changes in 20.74%. Cultural techniques detected 9.40% infection C. albicans, 5.77% Candida sp. and 10.29% Geotrichum sp.

Evaluation of management factors revealed that environmental stress, antibiotic feeds, rapid rate of gain, and pelleted rations were ulcerogenic.

A seasonal occurrence pattern was noted. Ulcers occurred more frequently during late fall and early spring.

Altered keratinization was associated with the occurrence of ulceration. Infection with C. albicans was strongly related to the occurrence of altered keratinization. The isolation of C. albicans was directly related to the occurrence of ulceration and increased with increasing severity of stomach lesions. A similar but not as strong relationship was evidenced by the isolation Candida sp. Infection with C. albicans is a complicating factor contributing to the pathogenesis of esophagogastric ulcers of swine.

ACKNOWLEDGMENT

The author wishes to extend his thanks to many people who have assisted and advised in this research project. The entire staff of the Department of Pathology, Parasitology and Public Health was helpful and cooperative to the highest degree. Specific acknowledgment of the always ready advice and assistance of Dr. D. C. Kelley, Associate Professor of Public Health is gratefully made. Dr. E. H. Coles, Head of the Department, offered helpful advice and specific assistance.

The cooperative spirit of the Maurer Neuer Packing Plant, Arkansas City, Kansas, was greatly appreciated. In the interest of brevity further specific thanks, of which many are warranted, will not be given here but will be given personally.

The author is indebted to Kansas State University and the National Institutes of Health for selecting him to work as a research associate on this project and the opportunity to further his education.

APPENDIX

Kansas State University

Manhattan, Kansas 66502

College of Veterinary Medicine
Department of Pathology, Parasitology and Public Health
Burt Hall

Dear Mr. Farmer:

The Research Laboratory of the College of Veterinary Medicine, Kansas State University, is presently studying the causes of gastric ulcers in swine. As part of this study, a survey is being conducted to determine the incidence of ulceration in Kansas pigs.

Pig stomachs are collected at the Maurer Neuer Packing Plant in Arkansas City. Each stomach is studied in an effort to determine the cause of ulceration. The stomachs are chosen by random chance from random lots of pigs which had the same origin.

The stomachs of some of the pigs you sent to slaughter were collected and studied. This does not mean that your pigs have a greater or lesser incidence of ulceration than other pigs; it just means that by random chance your pigs were chosen.

Stomach ulceration can be a very severe disease among pigs and can cause economic loss, so you can do a great service by helping us in this study. We need more information to adequately evaluate our results. Only you can give us some of this very important information by completing the enclosed form and returning it to us.

While your memory is still fresh concerning the pigs you recently marketed, please complete the questionnaire and return it to us as soon as possible.

Sincerely yours,

Wade L. Kadel, D.V.M.
Research Associate

WLK:lh

Enclosure

Owner - Name _____ Address _____

Breed _____ Weight _____ Lot No. _____

Total No. of Pigs Marketed ____ Date Arrived at Market _____ Hours in Transit___

Type of operation:
Home reared pigs ____
Confined after weaning in pens ____
During feeding period confined on concrete ____

Purchased as feeders ____
Semi-confined in small lots after weaning ____
During feeding period confined on slats ____

During feeding period ran loose on pasture ____
if so, what kind of pasture _____

Breifly describe your facilities for handling your pigs if the above operation does not adequately cover your type of operation:

Type of feeding program:
Days on feed: 30-60 ___; 60-90 ___; 90-120___; 120-150___; 150-180___; 180-210___; 210-240___; over 240___.

Type of feed:
Complete ration pelleted ____ Name of feed and % of protein_____

Complete ration mash or meal ____ Name of feed and % of protein_____

Corn plus protein supplement ____ Name of feed and % of protein_____

Grain combination plus supplement ____ Name of feed and % of protein_____
what is the combination?

Antibiotics and/or wormer added to feed ____
Name of antibiotic and concentration used _____
Name of wormer and concentration used _____

Frequency of feeding:
free choice ____
hand fed once per day ____
hand fed twice per day ____
other, please describe _____

Floor space per pig:
6 square feet per pig ____ 12 square feet per pig ____
18 square feet per pig ____ 24 square feet per pig ____
more than 24 square feet per pig ____

Briefly describe anything that you think is unique about your swine management program. You may want to comment on the rapid rate of gains, low death loss or particular health problems you have experienced.

Continued

Data obtained from this study will be used for publication; however, names and management practices of individuals will be kept confidential.

Thank you very much for your cooperation.

Appendix Exhibit 3.

Kansas State University

Manhattan, Kansas 66504

College of Veterinary Medicine
Department of Pathology, Parasitology and Public Health
Burt Hall

Dear

On stomach samples were collected from pigs that you sent to the Maurer-Neur Packing Plant in Arkansas City, Kansas, for slaughter. A letter and questionaire was sent to you shortly after this. We asked you to complete the enclosed questionaire and return it to us. We realize that the responsibilities of the modern hog producer limit his time, and perhaps you did not have time to complete the questionaire when you received it.

Information concerning the management of your pigs is of great value to us in our effort to determine the cause of stomach ulcers in swine.

Would you please complete the enclosed questionaire and return it to us at your earliest convenience. Your help will be greatly appreciated and will help find the cause of a serious disease of swine.

Sincerely yours,

Wade L. Kadel, D.V.M.
Research Associate

WLK:lh

Enclosure

TABLE 1.---A Summary of the Percentages of Lots Sampled from Available Lots and Swine Swine Sampled from These Lots

Period	Number of Lots Available	Number of Lots Sampled	Per cent of Available Lots Available	Number of Swine in Available Lots	Number of Swine Sampled	Per cent of Swine Examined in Sampled Lots
1	27	9	33.33	207	43	20.77
2	38	9	23.68	274	56	20.43
3	24	2	8.33	236	49	20.76
4	27	6	22.22	282	55	19.50
5	23	6	26.08	235	47	20.00
6	31	6	19.35	279	57	20.43
7	22	2	9.09	232	46	19.82
8	26	4	15.38	294	52	17.68
9	28	6	21.42	358	74	20.67
10	16	4	25.00	271	49	18.08
11	21	10	47.61	198	53	26.76
12	21	5	23.80	298	50	16.77
13	32	5	15.62	302	57	18.87
14	33	7	21.21	349	57	16.33
15	27	8	29.62	317	55	17.35
16	33	8	24.24	280	59	21.07
17	18	5	27.77	274	60	21.89
18	38	10	21.05	297	62	20.87
19	39	7	20.51	266	72	27.06
20	28	5	17.85	235	59	25.10
21	30	4	13.33	309	70	22.65
22	22	4	18.18	283	62	21.90
23	28	6	21.42	182	56	30.76
24	27	5	18.51	295	50	16.94
Total	659	143		6,553	1,350	
Average			21.70			20.60

TABLE 2--Sampling Rates of Individual Lots of Swine

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
1	10	2	20.00
2	16	2	18.60
3	28	6	21.50
4	25	5	20.00
5	31	6	19.50
6	35	7	20.00
7	27	6	22.22
8	28	6	21.42
9	7	2	28.57
10	18	3	22.22
11	37	7	18.91
12	59	12	20.33
13	10	2	20.00
14	30	6	20.00
15	28	6	21.42
16	13	3	23.07
17	12	3	25.00
18	67	13	19.40
19	138	29	21.01
20	98	20	20.40
21	161	32	19.87
22	43	10	23.25
23	10	2	20.00

TABLE 2--Continued

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
24	12	2	16.66
25	23	4	17.39
26	33	5	15.15
27	159	30	18.86
28	7	3	42.85
29	5	2	40.00
30	4	2	50.00
31	20	3	15.00
32	40	7	17.50
33	23	6	26.08
34	23	4	17.39
35	34	7	20.58
36	125	25	20.00
37	32	6	18.75
38	42	9	21.42
39	192	38	19.79
40	40	8	20.00
41	80	16	20.00
42	195	31	15.89
43	11	3	27.27
44	8	2	25.00
45	187	37	19.78
46	7	2	28.57
47	13	4	30.76

TABLE 2--Continued

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
48	11	3	27.27
49	71	14	19.71
50	69	14	20.28
51	69	12	17.39
52	161	25	15.52
53	18	5	27.77
54	23	7	30.43
55	131	27	20.61
56	7	5	71.42
57	5	1	20.00
58	9	3	33.33
59	4	2	50.00
60	5	4	80.00
61	13	2	15.38
62	6	4	66.66
63	11	3	27.27
64	7	2	28.57
65	20	5	25.00
66	13	3	23.07
67	104	9	8.67
68	20	4	20.00
69	141	29	20.56
70	100	15	15.00
71	143	27	18.88

TABLE 2--Continued

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
72	9	3	33.33
73	7	3	42.85
74	43	9	20.93
75	59	13	22.03
76	176	23	13.06
77	36	6	16.66
78	11	3	27.27
79	37	6	16.21
80	13	3	23.07
81	17	3	17.64
82	30	6	20.00
83	156	24	15.38
84	21	4	19.04
85	27	5	18.51
86	21	4	19.04
87	24	5	20.83
88	13	2	15.38
89	25	5	20.00
90	143	29	20.27
91	12	3	25.00
92	54	11	20.37
93	10	2	20.00
94	8	2	25.00
95	5	2	40.00

TABLE 2--Continued

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
96	39	8	20.51
97	9	2	22.22
98	187	38	20.32
99	4	1	25.00
100	36	8	22.22
101	35	0	25.71
102	12	4	33.33
103	146	27	18.49
104	14	3	21.42
105	11	3	27.27
106	37	0	24.32
107	10	2	20.00
108	8	2	25.00
109	9	2	22.22
110	10	3	30.00
111	28	6	21.42
112	24	5	20.83
113	9	4	44.44
114	144	29	20.13
115	50	20	40.00
116	24	6	25.00
117	11	4	36.36
118	7	3	42.85
119	21	6	28.57
120	22	8	36.36

TABLE 2--Continued

Lot	Number of swine in lot	Number of swine sampled	Per cent sampled
121	7	5	71.42
122	6	4	66.66
123	24	7	29.16
124	176	35	19.88
125	99	21	21.21
126	9	4	44.44
127	160	32	20.00
128	41	13	31.70
129	177	35	19.77
130	15	6	40.00
131	12	5	41.66
132	79	16	20.25
133	53	22	41.50
134	72	14	19.44
135	19	7	36.84
136	10	4	40.00
137	8	2	25.00
138	20	7	35.00
139	63	15	23.80
140	39	8	20.51
141	100	10	10.00
142	84	14	16.66
143	9	3	33.33
Total	6,553	1,350	20.60

TABLE 3--A Summary of Lesions and Mycologic Determinations for Each Collection Period

Date	Period	Number of swine examined	Liver lesion		Lung lesion		Altered keratin		ulceration		C. albicans		Candida sp.		Geotrichums species	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
8-19	1	43	7	16.27	5	11.62	32	74.41	8	18.60	4	9.30	1	2.32	3	6.97
8-31	2	56	14	25.00	11	19.64	34	60.71	9	16.07	3	5.35	4	7.14	6	10.71
9-20	3	49	6	12.24	5	10.20	33	67.34	13	26.53	6	12.24	6	12.24	4	8.16
9-27	4	55	5	9.09	7	12.72	21	38.18	11	20.00	5	9.09	4	7.27	7	12.72
10-4	5	47	3	6.38	4	8.51	17	36.17	9	19.14	2	4.25	2	4.25	4	8.51
10-18	6	57	11	19.29	7	12.28	18	31.57	12	21.05	2	3.50	3	5.26	4	7.01
11-1	7	46	7	15.21	3	6.52	14	30.43	13	28.26	4	8.69	3	6.52	5	10.86
11-15	8	52	8	15.38	0	00.00	31	59.61	11	21.15	7	13.46	5	9.61	3	5.76
12-13	9	74	9	12.16	14	18.91	33	44.59	12	16.21	3	4.05	1	1.35	4	5.40
12-30	10	49	8	16.32	10	20.40	13	26.53	3	6.12	3	6.12	1	2.04	3	6.12
1-10	11	53	8	14.18	6	11.11	20	37.03	7	12.96	2	3.70	1	1.85	9	16.66
1-31	12	50	2	4.00	10	20.00	26	52.00	10	20.00	6	12.00	3	6.00	3	6.00
2-15	13	57	13	22.81	10	17.55	30	52.65	14	24.56	7	12.28	5	8.78	8	14.10
3-1	14	57	13	22.81	18	31.57	42	73.68	23	40.35	10	17.54	0	0.00	3	5.26
3-15	15	55	6	10.71	5	8.92	27	48.21	16	28.57	3	5.35	2	3.57	4	7.14
3-29	16	59	8	13.55	1	1.69	28	47.25	2	3.38	7	11.86	8	13.55	7	11.86

TABLE 3--Continued

Date	Period	Number of swine examined	Liver lesion		Lung lesion		Altered keratin		Ulceration		C. albicans		Candida sp.		Geotrichums species	
			No.	%	No.	No.	No.	%	No.	%	No.	%	No.	%	No.	%
4-12	17	60	8	13.33	1	1.66	34	56.66	20	30.00	24	40.00	0	0.00	15	25.00
4-26	18	62	8	14.03	4	7.01	19	33.33	4	7.02	4	7.02	0	0.00	14	24.56
5-10	19	72	1	1.42	1	1.42	19	27.14	8	11.42	6	8.57	0	0.00	13	18.57
5-24	20	59	1	1.69	1	1.69	36	61.01	18	30.50	11	18.64	3	5.08	7	11.86
6-7	21	70	4	5.71	0	00.00	18	25.71	1	1.42	3	4.28	0	0.00	12	17.14
6-21	22	62	13	20.96	4	6.45	37	59.67	23	37.08	5	8.06	6	9.67	0	0.00
7-5	23	56	00	00.00	1	1.75	25	43.85	15	26.31	0	0.00	4	7.01	0	0.00
7-19	24	50	2	4.00	1	2.00	22	44.00	18	36.00	0	0.00	16	32.00	1	2.00
TOTAL		1,350	165		129		629		280		127		78		139	
AVERAGE				12.22		9.55		46.59		20.74		9.40		5.77		10.29

REFERENCES

Baker, E. D., and Cadman, L. P.: Candidiasis in Pigs in Northwestern Wisconsin. J.A.V.M.A., 142, (1963): 763-767.

Barrow, N. S. and O'Brien, J. D. P.: White Pig Disease, Vet. Rec., 75, (1965): 100.

Berg, J. N.: A Gastric Ulcer Condition of Swine. Iowa State Coll. Vet., 22, (1960): 77-78.

Bixby, H. R.: The Effects of Candida albicans on the Esophagogastric Area of the Porcine Stomach. A Master's Thesis, Kansas State University, (1964).

Bullard, J. F.: Gastric Ulcer in a Large Boar. J.A.V.M.A., 119, (Aug. 1951): 129.

Buntain, D.: Deaths in Pigs on a High Copper Diet. Vet. Rec., 73, (1961): 707-713.

Cafruny, E. J., D. Stephano, H. S. and Farah, A.: Cryptophotometric Determination of Protein-Bound Sulfhydryl Groups. J. Histo. and Cytochem., 3, (1955): 354-359.

Chamberlain, C. C., Merriman, G. M., and Lidvall, E. R.: Diagnosis and Incidence of Experimentally Induced Gastric Ulcers. J. Anim. Sci., 23, (Aug. 1964): 910.

_____, Gamble, C. T.: Effects of Feed Processing Method and Diet Form on the Incidence of Esophagogastric Ulcers in Swine. J. Anim. Sci., 26, (1967): 72-75.

Cormane, R. H., and Goslings, W. R. O.: Factors Influencing the Growth of Candida albicans (in vivo and in vitro studies). Sabouraudia., 3, (1964): 52-63.

Curtin, T. M., Goetsch, G. D., and Hollandbeck, R.: Clinical and Patho-

logic Characterization of Esophagogastric Ulcers in Swine. J.A.V.M.A., 143, (1963): 854-860.

Dodd, D. C.: Hyostrongylosis and Gastric Ulceration in the Pig. New Zealand Vet. J., 8, (1960): 100-103.

Dorland's Medical Dictionary. 24th Ed. W. B. Saunders Company, Philadelphia and London, 1965.

Dunne, H. W.: Diseases of Swine. Iowa State University Press, Ames, Iowa., 1959.

Fugate, W. H., Pickett, R. A., Perry, T. W., and Curtin, T. M.: Influence of Feed Preparation on Performance and Occurrence of Ulcers in Swine. J Anim. Sci., 24, (1965): 881.

Gitter, M., and Austwick, P. K. C.: Mucormycosis and Moniliasis in a Litter of Suckling Pigs. Vet. Rec. 71, (1959): 6-11.

Gordon, W. A. and Duke, D.: Copper Poisoning in the Pig. Vet. Rec., 69, (1957): 37-41.

Griffing, W. J.: A Study of the Etiology and Pathology of Gastric Ulcers of Swine. Kansas State University, Ph. D. Dissertation (1963).

Hannon, J., and Nyham, J. F.: The Use of Some Vitamins in the Control of Ulcerative Gastric Hemorrhage in Pigs. Irish Vet. J., 16, (1962): 196-197.

Harris, P. L., Hove, E. L., Mellott, M., and Hickman, K.: Dietary Production of Gastric Ulcers in Rats and Prevention by Tocopherol Administration. Proc. Soc. Exptl. Biol. and Med., 64, (1947): 273-277.

Huber, W. G., Wallin, R. F.: Experimental Production of Porcine Gastric Ulcers. Vet. Med. SAC, 60, (1965): 551-558.

Huppert, M., and MacPherson, D. A.: Pathogenesis of C. albicans Infection Following Antibiotic Therapy. J. Bact., 65, (1953): 171-176.

_____Pathogensis of C. albicans Infection Following Antibiotic Therapy. J. Bact., 70, (1955): 440-447.

Isenburg, H. D., Alterhand, J., and Berkman, J. I.: An Endotoxin-Like Fraction Extracted from the Cells of Candida albicans. Nature, 197, (1963): 516-517.

Jensen, A. H. and Becker, D. E.: Effect of Pelleting Diets and Dietary Components on the Performance of Young Pigs. J. Anim. Sci., 24, (1965): 392-397.

Jensen, L B., and Frederick, L. D.: Spontaneous Ulcer of the Stomach in Several Domestic Animals. J.A.V.M.A., 95, (1939): 167-169.

Jubb, K. V. F., and Kennedy, P. C.: Pathology of Domestic Animals. Vol. 2, 1st Ed. Academic Press, New York and London, 1965.

Kapica, L., and Blank, F.: Growth of Candida albicans on Keratin as Sole Source of Nitrogen. Dermatologica, 115, (1957): 81-105.

Kernkamp, H. C. H : Gastric Ulcers in Swine. Am. J. Path., 21, (1945): 111-115.

Kowalcyzk, T., Hoekstra, W. G., Puestow, K. L., Smith, I. D. and Gummer, R. H.: Stomach Ulcers in Swine. J.A.V.M.A., 137, (1960): 339-344.

_____, Muggenburg, B. A., Recent Developments in Gastric Ulcers in Swine. Am. J. Vet. Res., Address to 17th World Veterinary Congress, Hanover, (1963).

LeBars, H.: Production of Gastric Ulcers in Pigs. Comptes. Rednus. Academie Ges. Sci., Paris, 255, (1964): 3501-3503.

Mahan, D. C., Pickett, R. A., Perry, T. W., Curtin, T. M. Beeson, W. M., and Featherson, W. R.: Influence of Ration Partical Size on the Incidence of Ulcers in Swine. J. Anim. Sci., 23, (1964): 883.

_____: Influence of Various Nutritional Factors on Esophagogastric Ulcers in Swine. J. Anim. Sci., 25, (1965): 1019-1023.

Mankowski, Z. I.: Pathological Activity of Metabolic Products of Candida albicans on New Born Mice. Mycopatholigic, et Mycologica Applicata., 17, (1962): 165-175.

Maxwell, C. V., Reinmann, E. M., Grummer, R. H., Hoesktra, W. G., Muggenburg, B. A., and Kowalcyzk, T.: Effects of Oat Hulls and Ration Particle Size on the Development of Gastric Ulcers in Swine. J. Anim. Sci., 25, (1966): 1248.

McCrea, M. R., and Osborne, A. D.: A case of Thrush in a Piglet. J. Comp. Path., 67, (1957): 342-344.

McErlean, B. A.: Recently Recognized Clinical Disease Entities in Pigs in Ireland. Irish Vet. J., 16, (1962): 221-232.

Muggenberg, B. A., McNutt, S. H. Kowalczyk, T.: Pathology of Gastric Ulcers. Am. J. Vet. Res. 25, (1964): 1354-1365.

_____, Reese, N., Kowalcyzk, T., Grummer, R. H., Hoekstra, W. G.: Survey of the Prevalence of Gastric Ulcers in Swine. Am. J. Vet. Res., 25, (1964): 1673-1677.

_____, Kowalcyzk, T., Hoesktra, W. G., and Grummer, R. H.: Experimental Production of Gastric Ulcers in Swine by Reserpine. Am. J. Vet. Res., 27, (1966): 1663-1669.

Nafstad, I., Gastric Ulcers in Swine, 1., Effects of Dietary Protein, Dietary Fat and Vitamin E on Ulcer Development. Pathologia Veterinaria 4, (1967): 1-13.

_____, and Tollersrund, S.: Gastric Ulcers in Swine. 2., Effects of High Fat Diets and Vitamin E on Ulcer Development. Pathologia Veterinaria 4, (1967): 15-21.

_____, and Baustad, B.; Gastric Ulcers in Swine 3. Effects of Different Proteins and Fats on their Development. Pathologica Veterinaria, 4, (1967): 23-29.

Nuwer, A. J., Perry, T. W., Pickett, R. A., Featherson, W. R., Curtin T. M., and Beeson, W. M.: Effects of Heat Processing of Various Corn Fractions on Occurrence of Ulcers in Swine. J. Anim. Sci., 23, (1964): 887.

_____: Value of Various Additives to Ulcer Producing Gelatinized Corn Diets Fed to Swine. J. Anim. Sci. 24, (1965): 113-119.

Obel, A. L.: Studies on the Morphology and Etiology of So-called Toxic Liver Dystrophy (Hepatosis Dietetica) in Swine. Acta. Path. and Microbiol. Scandinav. Suppl. 94, (1953): 5-87.

O'Brien, J. J., and Connally, J. F.: Ulceration of Pars Esophagus of the Pig. Vet. Rec. 77, (1965): 577.

Orfeur, N. D.: Gastric Ulcers in Fattening Pigs, Vet. Rec., 77, (1965): 781-783.

Osborne, A. D., McCrea, M. R., and Manners, M. J.: Moniliasis in Artifically Reared Pigs and its Treatment with Nystatin. Vet. Rec., 72, (1960): 237-241.

Perry, T. W., Jimenez, A. A., Shively, J. E., Curtin, T. M.: Incidence of Gastric Ulcers in Swine. Science, 139, (1963): 349-350.

Quin, A. H.: Newer Problems in Swine Diseases-Control and Treatment. Canad. J. Comp. Med., 16, (1952): 265-270.

Reese, N. A., Muggenburg, B. A., Kowalcyzk, T., Hoekstra, W. G., and Grummer, R. H.: Effects of Corn, Wheat, Oats, and Alfalfa Leaf Meal on the Development of Gastric Ulcers in Swine. J. Anim. Sci. 25, (1966): 21-24.

_____: Nutritional and Environmental Factors Influencing Gastric Ulcers in Swine. J. Anim. Sci., 25, (1966): 14-20.

Reimann, E. M., Maxwell, C. V., Hoekstra, W. G., Grummer, R. H., Muggenburg, B. A., and Kowalcyzk, T.: Effect of Ration Partical Size on Composition of Swine Gastric Contents. J. Anim. Sci., 25, (1966): 1247.

Riker, J. T., Heidenreich, C. J., Perry, T. W., and Pickett, R. A.: Influence of Temperature on Swine Fed an Ulcerogenic Diet. J. Anim. Sci., 25, (1966): 894.

_____, Perry, T. W., and Pickett, R. A.: Influence of Oats or Wheat on the Occurrence of Gastric Ulcers in Swine. J. Anim. Sci. 25, (1966): 894.

Roth, F. J.: Lethality of Cell Free Extract of C. albicans for Chlorotetracycline Treated Mice. Proc. Soc. Exptl. Biol. N. Y., 44, (1957): 530.

Rothman, S.: Physiology and Biochemistry of Skin. Univ. of Chicago Press., 1954.

Rosenow, E. C.: Etiology of Spontaneous Ulcer of Stomach in Domestic Animals. J. Inf. Dis., 32, (1923): 384-399.

Rothenbacher, H., Nelson, L. W., Ellis, D. J.: The Stomach Ulcer Gastrorrhagia Syndrome in Michigan Pigs. Vet. Med., 58, (1963): 806-816.

_____: Esophagogastric Ulcer Syndrome in Young Pigs, Am. J. Vet. Res., 14, (Sept. 1965): 1214-1217.

Runnels, R. A., Monlux, W. S., Monlux, A. W.: Principals of Veterinary Pathology. 7th ed. Iowa State University Press, Ames, Iowa, 1965.

Siligman, E.: Virulence Enhancement of C. albicans by Antibiotics and Cortisone. Soc. Exptl. Biol. and Med., 83, (1953): 778-781.

Smith, H. A., and Jones, I. C.: Veterinary Pathology, 3rd ed. Lea and Febiger, Philadelphia, 1966.

Stedham, M. A.: Relationships Between Dietary Sugar, Candida albicans, and Gastric Ulcers in Swine. Kansas State University, Master's Thesis, (1965).

Thoonen, J., and Hoorens, J: Gastric Ulcers of Pars Esophagus with Fatal Bleeding in Pigs. Deutsche Tierarytliche Wochenschift, 70, (1963): 394-395.

Van Scott, E. J., Flesch, P.: Sulfhydryl Groups and Disulfide Linkages in Normal and Pathological Keratinization. Arch. Dermat. and Syph., 70, (1954): 141-154.

Van Uden, N., Carmo Sousa, L. Do., Farinha, M.: Intestinal Yeast Flora of Horses, Sheep, Goats and Swine. J. Gen. Microbiol. 19, (1958): 435-445.

_____. The Occurrence of Candida and Other Yeasts in the Intestinal Tracts of Animals. Ann. N. Y. Acad. Sci., 89, (1960): 59-68.

Weissman, G. and Fell, H. B.: The Effect of Hydrocortisone on the Response of Fetal Rat Skin in Culture to Ultra Violet Radiation. J. Exptl. Med., 116, (1962): 365.

Winner, H. I., and Hurley, R.: Candida albicans. Little Brown and Co., Boston, 1964.

A SURVEY OF THE PREVALENCE OF PORCINE GASTRIC ULCERATION AND GASTRIC CANDIDOSIS

by

WADE LEE KADEL

D.V.M., University of Missouri, 1965

AN ABSTRACT OF A MASTER'S THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Pathology, Parasitology, and Public Health

KANSAS STATE UNIVERSITY
Manhattan, Kansas

1967

ABSTRACT

A randomized survey of 6,553 swine over a 1 year period which included the gross and microscopic examination of 1,350 stomachs was conducted. The prevalence rate of stomachs with altered keratinization was 46.59% and 20.74% of all stomachs evidenced erosive or ulcerative changes.

Data obtained from questionnaires were examined by statistical methods employing the use of an IBM computer. The evaluations of the influence of environmental factors revealed the occurrence of ulcers increased when feed was withheld and the swine were confined in trucks or holding pens for periods exceeding 12 hours. The severity of stomach lesions increased with increasing hours in transit. Rapid rate of gain was found to be associated with the occurrence of ulceration. A higher prevalence of stomach ulceration was found in swine fed a complete ration in pelleted or meal form and the addition of wheat to any other ration exerted some preventive influence. Swine fed a ration containing antibiotics had a prevalence rate of ulceration almost twice as great as those not fed an antibiotic.

Studies of the seasonal incidence pattern revealed that esophagogastric ulcers occurred most frequently during the late fall and early spring.

An analysis of combined factors revealed that the highest prevalence of ulcers occurred in swine that were fed a ration composed of corn or milo with added antibiotics, with limited floor space, making rapid gains and in transit over 4 hours. Swine maintained with these factors also had high prevalence rates of altered keratinization and gastric candidosis.

Cultural techniques revealed that 9.40% of all swine had C. albicans in the esophagogastric region of the stomach. A prevalence rate of 5.77% was found for Candida sp. and 10.29% for Geotrichum sp. The prevalence rate of infection with C. albicans in swine with ulcerative lesions was 21.76%.

The occurrence of ulcers and the severity of the ulcers was directly related to the isolation of C. albicans. Isolation of Candida sp. was similarily but not as strongly related to the occurrence of lesions. Isolation of Geotrichum sp. was independant of the occurrence of lesions.

The results of histochemic studies suggested an alteration occurred in the concentration of cystine and cysteine in the epithelium of stomachs with altered keratinization.

The results of the survey do not indicate that C. albicans is the etiological agent of esophagogastric ulcers in swine. However, the close relationship between the presence of C. albicans, altered keratinization, and ulceration indicates that it is a serious complicating factor.