INTRODUCTORY REVIEW.

1.—Definition and Historical Notes.

Lamsiekte is the name originally given by the South African pioneering farmers to a fatal disease of cattle, characterized by symptoms of paralysis and paresis, principally of the locomotor system, but in many cases also of the muscles of mastication and deglutition. Now that its etiology is clearly established as an intoxication produced by an anaerobic saprophyte infecting protein substrates, it may be described as *Parabotulismus bovis*.

There are no definite pathognomonic anatomical changes, and unless the case is observed during life, diagnosis is exceedingly difficult.

Although, as a devastating naturally occurring disease, it primarily affects cattle, it can be produced experimentally, and occasionally occurs accidentally, in other animals. Goats, sheep, guinea-pigs, and rabbits are very susceptible to the toxin, horses less so, and poultry comparatively resistant. Dogs and pigs are practically immune (page 1108).

Historically (page 843), lamsiekte has been known and feared as a disease of cattle as far back as records of the sub-continent go. The French naturalist, Le Vaillant, in his "Travels into the Interior Parts of Africa," in the years 1780-1785, describes "lam-sikte" in Cape Colony. He also describes what is now called "osteophagia" with remarkable accuracy, although his explanation is wrong, and he does not connect it with lamsiekte.

About twenty years later, Lichtenstein, in his "Travels in Southern Africa in the years 1803, 1804, 1805, and 1806," records the disease in Rietvalley, near St. Helena Bay, and in the Goudinie District. About the same time (1805), i.e. well over a century ago, a commission appointed by the Government of the time to tour the Cape and induce sheep owners to improve their flocks by the introduction of woolled rams, observed lamsiekte amongst the cattle of fifteen different farms, mostly in the territory of the "Twenty-four Rivers."

Half a century later (1858), the disease is referred to in a "Settler's Guide to the Cape of Good Hope and Natal" with the words: "Lamsickness; no one knows the cause or seat of, and yet it is one of the oldest and most destructive cattle diseases we have."

Towards the latter end of last century the disease came under more scientific observation, and Hutcheon, Colonial Veterinary Surgeon in the Cape, records data from 1884 to 1903. Hutcheon correlated it with the "perverted appetite" shown by cattle in the lamsiekte areas, and regarded the disease as due to deficiency of lime and phosphorus in the soil. This view was strongly supported by the work of Borthwick in 1895, who showed that regular feeding with large quantities of bonemeal greatly reduced the incidence of lamsiekte; also supported by the soil analyses of Juritz, which revealed a wide-spread deficiency of phosphorus in the soils of the Colony. The mineral deficiency theory, however, as an explanation of the cause of the disease, broke down when it was shown quite conclusively that the incidence of the disease was independent of the food supply, in the sense that one batch of cattle might be *recovering* from the disease at the very time, and in the very paddock, that other members of the same herd were *sickening* of it; also, that a wire-fence arbitrarily dividing two farms with similar soil formation might divide a diseased herd from a herd in which no lamsiekte occurred.

Various alternative theories were therefore put forward. Spreull, in 1907, described a " pasteurella," isolated from the intestinal canal, as causing the disease. Keeling Roberts, in 1909, provided limited support for this view, and unquestionably produced lamsiekte experimentally, although he failed to find the correct explanation for his own results. Walker, 1909-1911, and Mitchell, 1911-1912, effectively dismissed the " pasteurella theory," and, indeed, demonstrated that the disease was neither infectious nor contagious in the ordinary sense. Both, however, like Keeling Roberts, produced what may, in the light of present knowledge, be definitely regarded as genuine cases of lamsiekte by injection or forcible oral administration of decomposing material from animals which had died of the disease; but both were puzzled by the irregularity of their results, and preferred to diagnose their stray cases as non-specific toxaemias due to absorption of septic material.

Walker also considered the possibility of the disease being due to a poisonous plant, and fed various suspects to cattle, but with negative results.

Theiler and Burtt-Davy investigated the poisonous plant theory in considerable detail, the latter classifying suspected plants according to geographical distribution and the former undertaking feeding experiments with such as were common to lamsiekte areas. The results were entirely negative, but Theiler remained so convinced that some form of intoxication best explained the known facts, that he advanced what he termed the " Accumulative Vegetable Poison Theory " and made an ingenious attempt to fit all the recorded observations of the time into it.

In 1913, Stead, in South Africa, and Funk, in Europe, propounded the " Vitamine Deficiency " theory; a view which was dismissed by Theiler, Green, and Viljoen the following year.

In 1915, Hedinger advanced the view that lamsiekte was a sarcosporidiosis, but the work of Theiler and Viljoen directly contradicted this.

In the same year (1915) Theiler dismissed the remote possibility of the disease being caused by an ultra-visible virus transmitted through accidental ingestion of insects, but in the course of the relevant experimental work did actually produce two ambiguous cases of lamsiekte by forcible oral adminstration of blow-fly pupae collected from the carcass of an animal which had died of the disease and sent to him at Pretoria. It was, however, not until four years later, in the course of personal investigations on the lamsiekte farm Armoedsvlakte, near Vryburg, that he realized the full significance of these earlier experiments; then only after actual observation of a natural case of lamsiekte following the *deliberate* ingestion by cattle of skeletal carcass débris, and experimental demonstration that this same débris was capable of producing typical lamsiekte when forcibly administered by mouth.

The idea of a *toxicogenic saprophyte* at once leaped into the foreground, and the true significance of the " depraved appetite," so frequently associated with lamsiekte in the past, but also so frequently recorded as occurring quite independently of it, became suddenly apparent. A flood of light was thrown upon all the conflicting observations of the previous quarter of a century, and the enigma of years was solved in a few days. There only remained the elaboration of the proof and the investigation of the problem in all its ramifications.

2.—Cause of the Disease and Experiments upon its Production in the Lamsiekte Area.

The records concerned will be found on pages 851-1051 of the text.

For brevity sake the complete explanation may be offered in the form adopted in the popular article of June, 1920, already referred to; that is, as an "etiological chain of six links," expressed diagrammatically on page 825.

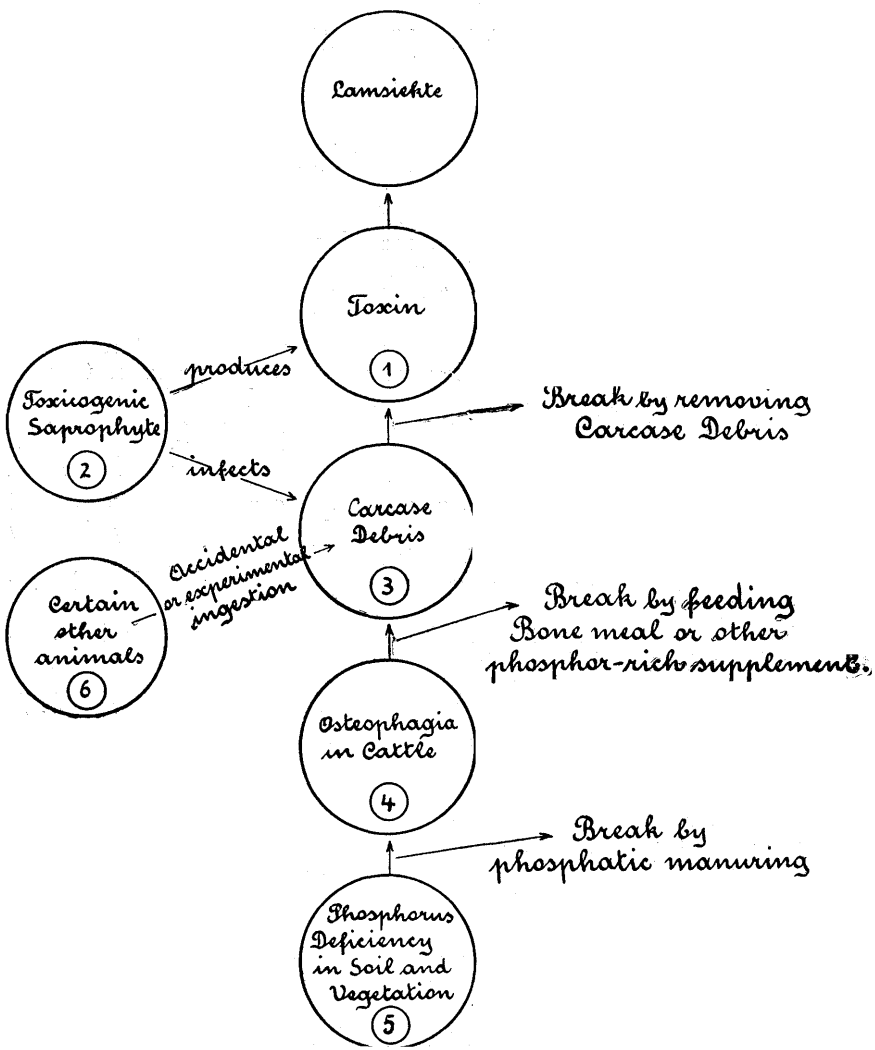
(1) The toxin which poisons the animal.
(2) The toxicogenic saprophyte (parabotulinus type) which produces the toxin.
(3) The carcass débris acting as substrate for the saprophyte, and from which the toxin is elaborated.
(4) The depraved appetite (pica, or more specifically *osteophagia*) which impels the animal to eat carcass débris which it would otherwise shun.
(5) The phosphorus-deficient vegetation which produces the depraved appetite, the soil upon which the vegetation grows, and the climate of the district.
(6) The susceptibility of the animal concerned towards osteophagia and towards the toxin.

Reversing the order and beginning with the soil, the sequence of events would be expressed as follows:—

Phosphorus deficiency in the soil leads to phosphorus deficiency in the pasture, and thence to phosphorus deficiency in the animal. In cattle, a specific form of depraved appetite, "osteophagia" or "bone craving," is developed as one manifestation of aphosphorosis. Such cattle then eat any carcass débris which happens to be lying about the veld. Animal débris is usually abundant on wide areas of cheap ranching land (often containing game), where shortage of labour militates against proper disposal of carcasses. If this débris happens to be infected with the specific anaerobe *Parabotulinus bovis*, in addition to the ordinary putrefactive bacteria, it becomes violently poisonous and the cattle die of *lamsiekte*.

All six links of the etiological chain are concerned in the production of the naturally occurring disease. The animal must be susceptible to the toxin (link 6). Cattle are, but dogs are not. Hence dogs never die of lamsiekte, although they undoubtedly eat toxic carcass débris. The depraved appetite (link 4) is essential since normal cattle will not touch such débris. The carcass débris itself (link 3) is essential since without it no toxin (link 1) would be developed by the toxicogenic saprophyte (link 2). The phosphorus deficiency of soil and vegetation (link 5) is the direct cause of the osteophagia (link 4). If in any given area any one link is missing, lamsiekte will not occur.

In considering lamsiekte only as a naturally contracted disease of *cattle*, the last link (6) of course falls away, since all cattle are susceptible to the toxin and nearly all cattle are susceptible to osteophagia, although the degree of abnormal appetite is partly a question of individual idiosyncrasy, and some few animals may not develop it at all. As explaining the rare sporadic cases of the disease reported in goats, sheep, equines, ostriches, and poultry, however, the question of species susceptibility becomes important. With ostriches and poultry, link 4 of the chain is unnecessary since they do not need to display osteophagia, but may pick up fragments of toxic bones or



Lamsiekte.] [*Theiler and Others.*

DIAGRAM ILLUSTRATING THE CAUSATION AND PREVENTION OF LAMSIEKTE.

carrion in the ordinary course of events. Birds, however, are very refractory towards the toxin as compared with cattle, and a farm with a bad reputation for lamsiekte has carried ostriches without serious disaster. Goats have occasionally been observed to eat " pensmist " or rumenal contents of lamsiekte carcasses, and so contract the disease without necessarily showing depraved appetite. That osteophagia is rare in goats is indicated by the fact that, although they are highly susceptible to the toxin, the mortality recorded for goats—on farms over which a high mortality prevails for cattle—is small. Sheep are also very susceptible to the toxin, and the only reason why they do not contract lamsiekte naturally is that they do not develop osteophagia to any appreciable extent, and so do not ingest the toxin, even although exposed to the same veld conditions as the cattle. The growing practice of stocking the lamsiekte areas with sheep simply because cattle could no longer be reared profitably, now finds its explanation not in the fact that sheep are immune to the disease (as formerly supposed) but in the fact that they are not " bone eaters." In this connexion it may be mentioned that the practice of rearing sheep *along with cattle* on the lamsiekte areas in the past increased the incidence of lamsiekte amongst the cattle. The sheep, though they do not naturally contract the disease themselves, die from other causes, and since the farmer has rarely troubled to remove dead sheep or lambs from the veld, they have supplied one of the commonest sources of toxic carcass material. Now that the etiology of the disease is known, the danger can, of course, be easily guarded against by taking special precautions to bury dead animals and by feeding bonemeal to the cattle to obviate osteophagia.

Horses and donkeys are susceptible to the toxin in less degree (page 1105), but do not contract natural lamsiekte because, like sheep, they do not develop osteophagia. The susceptibility to pica is therefore an important link in explaining why lamsiekte is dominantly a disease of cattle and why it is so rarely reported in other animals. Other animals only get it by accident. The relative susceptibility of different animals will be discussed presently in dealing with experiments carried out with the toxin.

Of the various links in the etiological chain, the most important from a practical point of view are naturally those which can be most easily and most cheaply *broken*. Any one effective break is sufficient to eradicate lamsiekte, and the reason why the disease is not rampant over greater areas in South Africa than is actually the case, is simply that there are many places in which the chain happens to be naturally broken. It is a well-known fact that over the last half-century lamsiekte has been steadily spreading over the Union, and appearing on farms where it was formerly unknown. This is because one or other of the missing links is supplied by the operation of some other cause—most commonly by the spread of infected débris. Dogs, for instance, can readily carry infected bones from one farm to another. Vultures may carry still farther, and since the organism is a sporulating one, the droppings of carnivorous birds is a factor which cannot be overlooked.

Whether the control of lamsiekte in the known lamsiekte areas will be sufficient to prevent its spread to areas now healthy depends largely upon the method of control adopted. Thus, if the method adopted were the burning or burying of all carcass material (link 3), the disease could never spread. But if the chain were only broken by

an immunizing process (link 6), it would not completely prevent the spread. It would only protect the individual animal without removing the cause. As will be seen presently, however, this latter method is not a practicable one in any case since only a feeble transient immunity against the toxin can be experimentally conferred.

To break link 2 of the chain without breaking link 3 is practically impossible since the organisms are sporulating ones and infect the soil. Once into the soil, there is no practicable method of dealing with them, although they may die out of their own accord in the course of years if, by removing all carcass material, they are prevented from multiplying.

It may well happen, however, that link 2, the toxicogenic saprophyte, is naturally absent in certain areas in which all other links are present. Exposed carcasses then undergo the ordinary non-toxic type of putrefaction occasioned by harmless bacteria, and the rotten bones, bits of hide, flesh, and other animal fragments do not produce the disease even if the cattle display pica and eat the obnoxious material. This is a state of affairs which does exist in many parts of South Africa, and presumably exists in those countries where pica is reported but where lamsiekte is unknown. But if an animal leaves a lamsiekte area either by sale or in "trekking" for fresh pasture, and dies soon after in a clean area, its own carcass (link 3) may serve as a pabulum for the multiplication of the toxicogenic saprophyte (link 2) introduced into its own intestine (as harmless spores) while previously grazing in the lamsiekte region. Toxic material (link 1) may then be produced and a large number of organisms scattered around the immediate vicinity. If this happens in a district where conditions (link 5) are such that pica (link 4) is prevalent, a new focus of lamsiekte may be set up and the disease so appear in an area in which it was previously unknown.

It does not necessarily follow that an animal so dying will reproduce large numbers of the toxicogenic saprophytes, but it may, and occasionally certainly does. Other factors, however, as yet not fully understood, also govern the decomposition of carcasses and regulate the ease of spread of the causal organism. Climatic factors play a part, and it has been experimentally shown that an animal killed by dosing with toxic material rich in spores, and deliberately exposed in a non-lamsiekte area, does *not necessarily* develop a toxic carcass or set up a fresh focus of infection. It may or it may not, according to circumstances not yet completely investigated. If it does, the organisms so introduced into the new area may remain in the soil for some time after the carcass has decomposed, but if they get no chance of perpetuating themselves by infecting a fresh carcass they apparently die out in time under competition with the normal soil bacteria and protozoa. This seems to have happened within a few years in the case of soil in a particular paddock at Onderstepoort, Pretoria, into which infected carcasses were introduced experimentally in 1918, but from which infection seems now to have disappeared, or at least to remain negligibly small. If, on the other hand, animals are dying in the new area from other causes, such as drought or epidemic disease, at the time of introduction of a lamsiekte infection (by any means whatever) fresh carcasses may become infected and the toxicogenic saprophyte thus be multiplied. If the extent of phosphorus deficiency and osteophagia in the new area is only slight, the

subsequent mortality from lamsiekte may remain low, appear in some seasons and not in others (link 5), and possibly even disappear altogether.

In regard to the general mode of scattering infection, it is considered that for short distances blow-flies, dogs, jackals, and wind-born dust are important; and for longer distances birds, trekking animals, and accidental transport of infected material.

With this short illustration of the interaction of the various factors involved, a brief summary of the experimental work recorded in the main text may be given.

On pages 851-1051 will be found the detailed protocols of the experiments upon the production of the disease in the lamsiekte areas. A great variety of carcass débris was " drenched " to cattle, i.e. forcibly administered by mouth, and the toxicity of various materials so determined. The larvae and pupae of blow-flies collected from the carcasses of animals which had died from lamsiekte generally proved highly toxic, although certain exceptions were noted. Larvae were generally found more toxic than pupae. For pycnosoma pupae the minimum toxic quantity observed for cattle was half an ounce. Larvae and pupae collected from carcasses of animals dying of other causes, but left to decompose upon the veld, were sometimes toxic and sometimes not. The results, however, show quite clearly that no constant relation exists between the cause of death of any animal and the toxicity of blow-fly larvae or pupae derived from its carcass. The carcass may become infected by dust or by the very blow-flies whose larvae are afterwards tested, and once infected anything associated with the carcass may prove toxic. With larvae and pupae of the ordinary house-fly collected from the vicinity of putrefying carcasses, negative results were obtained in the four cases tested. This fly, however, breeds on the rumenal contents of carcasses rather than on the putrefying flesh, and since such contents only become toxic by percolation from the cadaver proper, the negative results are not surprising. Drenching of putrefying flesh of cadavers exposed to infection produced typical lamsiekte, irrespective of the cause of death of the animal from which the material was derived. Of fifteen head of cattle " drenched " with crushed bones (page 884) from putrefying carcasses, and exposed on the veld for periods varying from five to thirty days, seven contracted the disease; the period between ingestion and death varying from twenty-four hours to sixteen days. In general, the larger the amount of material the more rapid was the death; and the shorter the interval between exposure of the carcass and the collection of putrefactive material the more toxic was that material. Apparently carcass débris may develop high toxicity in a few days, retain that toxicity for long periods, but finally lose it through " weathering," and the ultimate stages of dominantly aerobic change. Since skeletal débris is the material most favoured by cattle showing the ordinary form of depraved appetite, and cattle only ingest desiccating flesh and hides when the specific " osteophagia " has passed over into an indiscriminating " allotriophagia," it is interesting to note that the smallest quantity of veld bones actually shown to produce lamsiekte was 4 oz. (page 884.)

The protocols recorded for bones scraped free from adhering flesh (page 885) and then exposed to natural infection on the veld are of special interest. In no case was toxicity developed. The explana-

tion is, of course, simple. Such bones are moderately permeable to air and a dominantly aerobic flora tends to control decomposition. Since the toxicogenic saprophyte is an obligate anaerobe, it tends to be suppressed. On the other hand, when bones are undergoing natural decay in the intact carcass, or are associated with adhering flesh, conditions allow both of anaerobic bacterial development and of permeation of toxin from dense flesh undergoing anaerobic putrefaction, and natural skeletal débris may therefore be highly toxic; quantities of 4 oz. per 1,000 lb. bovine live weight being fatal in some cases.

The experiments conducted to determine the toxicity of *ingesta* of carcasses are interesting in view of the fact that although goats, and even donkeys, have been reported to contract natural lamsiekte, they do not develop a sharply defined osteophagia. They have, however, been observed to consume rumenal contents or "pensmist" of decomposing carcasses, and it is therefore interesting to note that contents of the alimentary tract of putrefying cadavers *can* become toxic; more probably by permeation from the flesh than by actual utilization of alimentary débris as substrate for toxin production. Of sixteen cattle "drenched" (enforced oral administration) with the contents of the alimentary tract of carcasses exposed to infection, or derived from animals dying of lamsiekte, the disease was reproduced in five cases (page 889). The experiment recorded on page 890, in which the spleen of an animal, removed twenty hours after death, proved toxic, is of interest as demonstrating the rapidity with which toxin production can occur in some cases, and as representing a clear instance of infection of carcass through the alimentary tract. The unusual brevity of the period, and the fact that the animal was exposed in the post-mortem room and not on the open veld, practically excludes infection of the spleen from the outside through the intact skin, and throws the weight of evidence in favour of infection from the intestinal contents of the carcass immediately after death. Intestinal contents themselves could, of course, easily be infected by the ingestion of infective but non-toxic material without producing death, and the experiment therefore also serves to indicate that an animal moved from a lamsiekte area in a healthy state, but dying immediately afterwards in a clean area from any cause whatever, may develop a toxic carcass and set up a new centre of infection.

Partially bleached bones from which the toxicity has disappeared, but which still harbour spores of the toxicogenic saprophyte, are very common on the veld, and such material would infect the intestine without necessarily doing any harm to the animal. Another source of harmless infection of the intestine may be particles of infected soil, and grass infected by spore-laden dust from the site of an old cadaver. The experiment, at any rate, demonstrates invasion from the *inside* of the carcass.

An experiment showing infection wholly from the *outside* is of special interest. A full-time foetus was removed from a cow which died on the eve of calving. Since there is no direct intercourse between the blood of the mother and that of the foetus, it may be accepted that the unborn calf was not infected with saprophytic bacteria from the cow. The calf was excised immediately after death of the cow and exposed to infection on the open veld. Material subsequently collected from it promptly produced lamsiekte, so indicating infection either by spore-laden dust or by blow-flies from distant toxic carcasses.

In regard to experiments upon the forced administration of carcass débris from animals other than cattle, data concerning the dog, fowl, lamb, horse, meerkat, steenbuck, and ostrich are recorded on pages 892-898.

They show that any sort of carcass material undergoing putrefaction on infected veld is liable to be toxic. Both acute and chronic cases of lamsiekte were produced, the time elapsing between dosing and death depending simply upon the toxicity of the particular sample of material used. In some cases small doses did not prove fatal, but upon repeating the dose every day for a week or a fortnight the disease finally developed. This observation is of interest as indicating that under natural conditions lamsiekte may be produced by repeated ingestion of sub-toxic débris until the point is reached at which the total toxin ingested is sufficient. In some cases carcass material proved altogether non-toxic (page 895), showing that not all carcasses become infected even when exposed on an infected veld. Of still greater interest is the observation that material obtained from different parts of the same carcass was not uniformly toxic, thus indicating a localized infection of putrefying débris, or localized conditions favouring the dominance of the toxicogenic saprophyte.

A decaying carcass must, of course, be regarded as a battle-ground for all putrefying bacteria with which it happens to become infected. If *Parabotulinus bovis* establishes itself at any particular point the segments of the carcass concerned will be toxic. If the veld infection of this organism is low in the vicinity of the carcass, the ordinary putrefying organisms which do not produce toxin will naturally control decomposition, and the carcass will either not be toxic at all or may only show a patchy development of toxin.

The fact that the cadavers of small wild animals, such as meerkats, become toxic explains why it is that even when good hygiene is practised and the carcasses of farm stock buried as soon as they are found, lamsiekte may still occur. Hares, squirrels, small game, birds, and even lizards and tortoises may be minor sources of danger; and although carcasses of the larger animals constitute the greatest source of danger, any small "protein substrate" is sufficient to account for sporadic cases. Only when systematic cleaning of the farm by native searchers is practised can lamsiekte be kept down to negligible proportions by hygienic measures alone.

The observations upon the extent to which a naturally grazing herd contracted lamsiekte when offered toxic-veld bones, and left to eat voluntarily instead of being forcibly fed, are recorded on pages 936-949. A small herd of forty-five cattle, including heifers, young steers, and cows, was selected as showing systematic osteophagia when tested with relatively sweet bones (page 949). These were allowed to graze in a paddock cleared of bone débris, and brought to the homestead every morning. After the morning drink they were placed in a small paddock containing bones collected from putrefying carcasses. Of the forty-five animals, observed over a period of seven weeks, sixteen contracted lamsiekte. Of these, ten died and six recovered, the recoveries being all chronic cases lasting from twelve to thirty days, probably produced by ingestion of successive small quantities of toxic bones. Of the ten which died, four were acute cases, succumbing within a few days. Of the whole forty-five, only two refrained altogether from eating the displayed bones, although several only ate on occasional days throughout the

period of observation. Of the two which regularly refused the bones displayed in troughs, one was then transferred to an experiment in which bones were scattered in a paddock. Here it commenced to eat bones, and subsequently died of lamsiekte.

These experiments are of interest in showing that although lamsiekte can always be produced by forced administration of crushed toxic bones in suffiicent amount, the proportion of natural cases ascribable to bone-eating depends upon a variety of factors: the toxicity of individual whole bones; the suceptibility of individual animals; and the varying degree of osteophagia as influencing the frequency of bone-eating, the quantity eaten, or the selection of bones according to stage of weathering.

In the experiment in which cattle were left to look for bones in a paddock (page 993) instead of having them presented in troughs, the incidence of lamsiekte was rather lower and the disease generally milder. This might be explained by assuming that a certain degree of resistance was acquired by animals regularly eating small quantities of bones of relatively low toxicity; also by the fact that the opportunity for bone-eating was less obvious in the paddock than in the troughs.

On pages 1021-1031 will be found the experiments conducted by subcutaneous injection of putrefactive débris, and of bouillon cultures of the mixed flora derived therefrom. The later experiments on toxic cultures prepared in minced liver media are recorded on page 1102.

On page 1039 spontaneous cases of lamsiekte, contracted by picking up toxic material before systematic cleaning of the veld reduced the incidence to negligible proportions, are recorded. The symptomatology and pathology of the natural cases differed in no respect from the cases produced experimentally.

3.—Experiments Outside the Lamsiekte Area.

While the main investigations were in progress at Armoedsvlakte, Vryburg, a few experiments were carried out at Onderstepoort, Pretoria, an area on which lamsiekte never occurred and on which osteophagia was absent, or at most very mild. Briefly, the object was to ascertain whether toxin production occurred in carcass débris of non-lamsiekte areas, and, if so, whether the toxin was of the same type as in the lamsiekte areas investigated; also, whether introduced infection would give rise to toxin production in exposed carcasses or whether other factors determining putrefaction would inhibit it.

The results are given on pages 1051-1099. No positive cases of lamsiekte were produced with débris from normal carcasses allowed to putrefy around Onderstepoort, thus showing that natural infection of the veld with the toxicogenic saprophyte was at most very low. Toxic material from Armoedsvlakte was then forcibly administered to Onderstepoort cattle, and after ensuing death from lamsiekte the carcasses were exposed on the veld. These cadavers generally developed toxicity as a result of infection through the intestine. Toxic material taken from them could be used to produce lamsiekte in fresh cattle, and the carcasses of these again developed toxicity in the same way when allowed to putrefy. The disease could therefore be readily maintained on the Onderstepoort paddock by carrying the infection through successive animals, although the proportion of failures to develop toxicity suggested that the local conditions (climate, nature of competitive putrefactive flora) were less favourable to toxin production than at Armoedsvlakte.

Fly larvae collected from cadavers of animals which had died of experimentally produced lamsiekte were sometimes toxic and sometimes not. Once the infection had been established in the Onderstepoort paddock it remained for a considerable time, and fresh uninfected carcasses frequently developed toxicity some months later if exposed in the vicinity of the original experimental camp. In one experiment (page 1053) a horse carcass was cut open and exposed in a small wire enclosure a mile and a half away from the nearest lamsiekte carcass. Larvae collected from it four days later promptly produced lamsiekte, thus showing that at this time the infection was fairly widely distributed. Whether the infection had spread by means of flies, kaffir dogs, and wind-borne dust from the original lamsiekte cadavers, or whether it existed independently of these, could not be determined with certainty. The earlier negative experiments (February to December, 1919) with carcasses exposed before the introduction of infection from Armoedsvlakte might be explained by assuming that, with a low level of natural veld infection, the toxic type of putrefaction is more likely to occur under certain seasonal conditions than under others. On the other hand, the distance of 1½ mile is not so great as to exclude spread of infection from the original experimental paddock.

The absence of natural lamsiekte at Onderstepoort can, of course, readily be explained without assuming absence of infection. The degree of osteophagia is so low that cattle do not ordinarily touch carcass débris.

That infection does not always spread with certainty, even over short distances, is indicated by an experiment (page 1055) in which the intact carcass of a horse was placed about 20 yards away from a highly toxic lamsiekte carcass. Decomposing material and fly larvae subsequently taken from it did not prove toxic. The opportunity for infection was abundant, but it would appear that the intact skin protected the interior long enough to allow the ordinary putrefactive flora, invading the cadaver from the intestine, to dominate decomposition so completely that infected flies from neighbouring carcasses no longer set up toxin production when the opportunity for their entry arose.

On pages 1066-1069 are recorded the results obtained by forced administration of carcass material obtained from seven different farms in Natal, on none of which had lamsiekte been definitely shown to exist, but on some of which it had been suspected. In none of these cases was lamsiekte produced experimentally from the material sent. In most of the farms considered, osteophagia was shown by the cattle, and the absence of lamsiekte was therefore due to absence of the toxicogenic saprophyte, or to local conditions which favoured a non-toxic type of putrefaction.

Records of data obtained with mixed cultures, derived by inoculating toxic bones into minced raw liver, are given on pages 1062-1066. Exceedingly toxic material could be obtained in this way, in one case (Jar V) 3 grms. proving sufficient to kill a large heifer when given per *os*. This jar was sent to Vryburg, and formed the basis of subcultivation in experiments which fixed the minimum lethal dose by subcutaneous injection as one-tenth of a milligram per kilo bodyweight, or one-twentieth of a gram per thousand pounds weight.

4.—Lamsiekte Toxin and Experiments on Immunity.

The major work on species susceptibility and attempts at producing immunity will be found on pages 1099-1201. The method adopted to prepare large quantities of highly toxic material, of more or less uniform character, consisted in inoculating the mixed flora of a previous toxic culture into jars of pasteurized minced liver tissue and incubating at 37° C. In about a week the jar contents reached their maximum toxicity, were then suitably diluted, filtered through a Berkefeld candle, and used as "toxin." Whatever the dilution used for actual experiments, the "toxin" was expressed in terms of "jar contents," standardized if necessary by testing on guinea-pigs.

Species Susceptibility.—The minimum lethal dose for *Cattle*, of toxin prepared in this way, was found to be about 0.02 c.c. per kg. body-weight when administered per *os*, but only 0.0001 c.c. per kg. by subcutaneous injection. A direct relation is shown between quantity of toxin administered and duration of the disease; the larger the dose the more rapid the death. Acute, subacute, or chronic cases of lamsiekte could be produced at will by varying the dose and method of administration; and it was found possible to predict with fair certainty when the first symptoms would appear after injection and when death would supervene. A very large dose frequently killed within eighteen hours.

In *Horses*, the M.L.D. by subcutaneous injection was found to be 0.005 c.c. per kg., or roughly fifty times as large as for cattle. Donkeys are still more resistant, but die if large quantities are injected.

Goats and *Sheep* show about the same susceptibility as cattle. For *Rabbits* and *Guinea-pigs* the M.L.D. is about 0.001 c.c. per kg., or ten times as high as for cattle. Rats are practically insusceptible and are only killed by enormous doses. For *Mice*, the dosage is still very large, but lower than for rats.

Dogs and *Pigs* are entirely insusceptible; even 150 c.c. for a medium sized animal, or about a hundred thousand times the fatal dose for cattle, failed to produce any symptoms.

Of the domestic birds, the *Ostrich* is the most susceptible, but relatively enormous doses (50 c.c. or more per ostrich) are required to kill. *Turkeys* appear to be very resistant, and of all the birds tested only one showed a doubtful reaction. Amongst *Ducks* two typical cases were produced by giving large doses per *os*, but several others remained unaffected. Pigeons are very resistant and can generally stand fifty thousand times the M.L.D. for cattle (per kg.).

Attenuation of Toxin.—The numerous experiments upon attenuation of the toxin by physical and chemical means will be found on pages 1115-1128.

Heat treatment at 70° C. for twelve hours was found to give satisfactory attenuation, in the sense that the M.L.D. for cattle was raised 1,000 to 5,000 times. Heating to higher temperatures for any length of time rendered the toxin altogether non-toxic. The degree of cold produced by surrounding with solid carbon dioxide produced no effect on the toxin. Neither did exposure to sunlight or to desiccation. Toxin kept under sterile conditions for two months showed no appreciable diminution of virulence, but after six months appeared less toxic.

Mixing with iodine effected attenuation. Berkefeld filtrate mixed with three times its volume of Lugol's solution reduced the toxicity to such an extent that quantities corresponding to 1,000 to 10,000 M.L.D. could be safely injected. Phenol, alcohol, ether, chloroform, and boric acid had apparently no attenuating effect. Toxin occluded in agar was still fatal when injected.

Immunity.—The behaviour of cattle under natural conditions demonstrates that the order of immunity is at best small. A beast which recovers from a mild attack of lamsiekte may contract the disease a second, third, or fourth time within relatively short periods, although it is rare for it to survive a third or fourth attack. Nevertheless it was considered possible that larger amounts of anti-bodies might be produced, and a useful measure of immunity possibly conferred, by the injection of very large doses of attenuated toxin or so-called "toxoid."

A number of cattle were therefore treated (pages 1129-1138) with toxin heated to 70° C. for twelve hours, in quantities varying from 1,000 to 10,000 M.L.D. of original filtrate. These animals were then tested with unheated filtrate in carefully graduated doses, and it was found that although a certain degree of immunity had been established, it was rarely sufficient to protect against 10 to 50 M.L.D. of virulent toxin. No better immunity could be established either by toxic cultures heated to higher temperatures for shorter periods, or by toxin attenuated with Lugol solution. Animals so immunized might stand from 3 to 10 M.L.D. of virulent toxin, with or without showing symptoms; then stand a second injection of 10 M.L.D.; but when again injected with doses of 100 M.L.D., promptly succumb in as short a time as untreated control animals.

Another attempted method of immunization consisted in injecting virulent toxin *into the tail* of the animal, on the analogy of the method formerly practised against pleuro-pneumonia in cattle, the underlying idea being that slow absorption from the hard fibrous tissues near the tip of the tail might produce better results than rapid absorption by other channels. The results indicated that a certain degree of immunity could be produced in that way, but the method proved neither safe nor sufficiently effective to justify continuance. Several animals contracted lamsiekte after the injection of 10 M.L.D. into the tail for immunizing purposes, while the immunity of the survivors broke down under subsequent subcutaneous injection of 10 to 25 M.L.D.

A further attempt was made to confer active immunity by repeated subcutaneous injection of gradually increasing sub-lethal doses of virulent toxin (pages 1141-1147). A moderate degree of success was obtained, a few goats finally withstanding 16 M.L.D., but unfortunately succumbing to twice this dose. From a theoretical point of view, observations in this direction appear worth extending, but even if the method could be improved upon, it would be too cumbersome for general application in practice.

In regard to *passive immunity*, attempts are recorded on pages 1147-1152. Injections were made with serum obtained from animals after recovery from lamsiekte, or after active immunization with large doses of heated toxin. Serum of cattle, horses, goats, dogs, and pigs was tried, but no satisfactory results were obtained.

Summarizing the work on immunization, it may be stated that the immunity conferred was neither great enough nor lasting enough to render this method of controlling the disease a practicable proposition under South African Conditions.

5.—Isolation and Description of the Toxicogenic Saprophte.

The early work, up to the date of the publication of the article upon "Cause and Prevention of Lamsiekte" in May, 1920, was fragmentary, and owing to the fact that even the most toxic cultures used for the work on species susceptibility and immunity were invariably dominated by a mixed putrefactive flora containing the actual toxicogenic organism in relatively small numbers, actual isolation and description were left until later. This later work is recorded on pages 1201-1211, and may be summarized by describing the organism as *Parabotulinus bovis*. It is a sporulating anaerobe of the *Clostridium botulinus* type, 5μ to 8μ in length and 0.8μ to 1μ in breadth, generally showing short chains in young cultures and long filaments of 15 to 20 organisms in old cultures. The oval spores are terminal, generally slightly wider than the vegetative rod and 1.5μ in length. Young cultures are gram positive, but gram-negative forms dominate in old cultures. No motility has been observed. Growth occurs in most of the conventional media used for the cultivation of strict anaerobes. In chopped meat media gas is produced in three or four days, but the supernatant fluid above the meat particles remains clear and the meat itself does not appear to be broken down, however long the medium is incubated. The cultures develop a pleasant sweetish smell and are highly toxic.

In Hibler's brain medium growth is good, with abundant gas production but without blackening. No sporulation and relatively little toxin formation appear in this medium. In serum broth, growth occurs as fine suspended flakes sedimenting after a few days, and toxin production is good. In ordinary broth, growth is poor, with slight cloudiness. In glucose broth the growth resembles that in serum broth. In Tarozzi cultures and in liver broth, growth resembles that in meat mash medium. Turbidity is visible in Tarozzi medium.

Colony formation does not ordinarily occur on the surface of agar, blood or serum agar, or glucose agar, even under the best anaerobic conditions, but is good in deep cultures. In Vignal tubes of glucose agar, colonies are of a fluffy type without a central nucleus, appearing after twenty-four hours at 37° and finally growing to about 3 mm. in diameter; are greyish white and never dense in any portion; apparently formed of filaments without spores; and do not give rise to gas production or fragmentation of the medium. In Vignal tubes of liver agar, gas production may occur, and the woolly colonies show denser centres and hair-like projections. In gelatine stab cultures, growth occurs along the track of the needle, with fine projecting outgrowths. No liquefaction occurs within ten days. In milk, coagulation may sometimes occur, but without material change of reaction. Growth is best at 37° C., but also good at room temperature.

Toxin is present in all suitable media after three days incubation. The toxin is thermolabile and toxicity of cultures generally disappears after twenty minutes at 70° C. Toxin production occurs over a Ph range of 6 to 8, but is best on the alkaline side.

The susceptibility of various animals towards the toxin in general confirms the observations given under the previous section on the "toxin," the apparent order of species susceptibility being cattle, goats, guinea-pigs, rabbits, horses, fowls, mice, rats. The symptoms produced in cattle were indistinguishable from those of natural lamsiekte, and hence no doubt exists concerning the identity of the organism with that producing the toxin in the carcass débris from which it was isolated.

6.—Osteophagia in Relation to Lamsiekte.

The data upon the origin of "perverted appetite," or "pica," or more specifically *bovine osteophagia*, will be found on pages 1211-1248.

The fact that over large areas of South Africa, cattle show an "abnormal craving" or "pica" has been recognized as far back as records of the sub-continent go (page 843). Indeed, so widespread is the habit that farmers brought up in many districts look upon it as a natural thing, and only pay attention to it when it becomes so pronounced as to constitute a public nuisance, i.e. when the cattle congregate around the homestead or kaffir huts, devour bags, clothes, skins, cinders, and miscellaneous rubbish, and persistently return when driven away. Such acute manifestations of "allotriophagia" are what is understood by the term "depraved appetite" in the worst districts, and a man brought up in such districts may quite ignore the subdued craving or "osteophagia" manifested only for bones, which is common on farms where pica is comparatively mild.

That some connexion existed between pica and lamsiekte had been surmised for many years, but the fact that depraved appetite was so widespread over the whole country, while lamsiekte was often so strictly localized, created the impression that the correlation was fortuitous rather than essential (page 847). It is true that Hutcheon, of the old Cape Veterinary Service, definitely explained bone-eating as a definite premonitory symptom, and indeed formulated a deficiency theory in which lack of lime and phosphate was held to be the *cause* of lamsiekte (page 845); a theory which led Borthwick and Spreull to demonstrate (page 845) that the feeding of bonemeal materially reduced the incidence of the disease. But the Hutcheon hypothesis failed to explain the symptoms shown or to throw any light upon the immediate cause of death, and was therefore generally abandoned when it was found that on some very bad pica farms, lamsiekte was quite unknown. The "toxicogenic saprophyte" was not suspected and the "bone paradox" was not grasped, i.e. that the giving of sweet bonemeal merely prevented the ingestion of toxic-veld bones.

Furthermore, the psychological circumstance, already referred to, obscured the truth. Most observers were so familiar with pica that they took no notice of mild bone-chewing, but regarded it as normal; treated it rather as a harmless pastime indulged in by the cattle to pass eternity upon an uninteresting veld. This lead to the constant reiteration that lamsiekte occurred independently of pica. Obviously, if this had been true, and lamsiekte and pica occurred independently of one another, there could be no essential relation between the two.

It was not until the real nature of lamsiekte had been grasped and the chain of causation visualized as a whole (page 825) that the full distinction between "allotriophagia," the non-specific extreme

form of pica, and " osteophagia," the highly specific general form, became apparent. Once the idea of the toxicogenic saprophyte was brought in as etiological link, it became obvious that although pica could quite well occur without lamsiekte, and lamsiekte perhaps occur accidentally (as it does experimentally) without pica, the disease could only be prevalent in areas where depraved appetite was fairly pronounced.

The various degrees of perverted appetite shown by different cattle under different circumstances are most striking. A " mild craver " is fastidious in its selection of clean weathered skeletal débris, but an " extreme craver " has even been seen crunching a living tortoise, with the blood dripping from its jaws, or eating pieces of hide with adherent putrefying flesh.

This recognition of the specificity of craving led to the introduction, for experimental purposes, of a simple method of expressing both the degree and prevalence of osteophagia on a definite chartable basis. Bones at various stages of putrefaction were offered in troughs and the behaviour of the cattle noted. It was found quite easy to pick " stinking bones " which only the worst cravers would touch, and perfectly sweet bleached bones which even the mildest craver would at least toy with. Intermediate degrees of perverted appetite could be identified by intermediate bones, but for routine testing two grades were found sufficient—" sweet or bleached " and " distinctly rotten." The latter were picked out as veld bones which would produce lamsiekte if dosed in sufficient amount, but were then autoclaved to destroy the thermolabile toxin. They served to indicate a degree of craving dangerous from a lamsiekte point of view. The former (bleached) were selected so as to be quite unobjectionable to any beast which showed any clearly definable craving at all, and therefore served to reflect the appearance and disappearance of osteophagia. Two sets of troughs, placed at opposite ends of a large enclosure, were provided with these two grades of " test bones." The cattle to be tested were admitted first to the rotten bones, and the number which picked and chewed these were recorded as " marked cravers." Those which refused to touch the rotten bones were then driven over to the sweet bones. The cattle which would eat these were recorded as " mild cravers," and the remainder, which refused even the bleached bones, entered up as " non-cravers."

At the experimental farm Armoedsvlakte all the cattle were tested once a week as a matter of routine, so that the effect of treatment and seasonal variation of craving could be plotted in the form of curves showing the effect of the particular factor under consideration.

The general results, recorded on pages 1211-1248, may be summarized as follows:—

(1) Osteophagia is definitely produced by the natural veld grasses, and is definitely due to phosphorus deficiency and to nothing else.

(2) Although different botanical species varied somewhat in phosphorus-content, all the grasses examined were phosphorus-deficient in the final stages of growth, and osteophagia is therefore attributable to the veld as a whole and not to particular grasses (page 1315). This is due to deficiency of phosphorus in the soil, the " available P_2O_5 " of which ranged from 0.0005 to 0.002 per cent. in various parts of the farm (page 1358).

(3) The degree and prevalence of osteophagia varies with the season of the year and the stage of growth of the grass. The very young grass of spring generally contains for a short period sufficient phosphorus for prevention of osteophagia, but as the grass matures, carbohydrate formation in the plant proceeds so much faster than phosphorus absorption from the soil that the percentage of phosphorus in the "dry matter" of the grass rapidly falls. After the seed has fallen the phosphorus-content of the winter grazing (standing hay) is so low that osteophagia becomes universal in the herd. The phosphorus-content of the first green blades of spring (September-October) showed 0.5 per cent. phosphorus oxide, expressed on the dry matter, and as the cattle successfully obtained appreciable quantities of this to supplement the residual standing hay of the preceding year, the extent of osteophagia in the herd steadily fell. By the middle of November it practically disappeared, but returned rapidly as the summer rains (December-February) brought on relatively abundant rapidly growing grass of falling phosphorus-content. By the time the seed had fallen from the mature grass (about April) the phosphoric oxide content had fallen to 0.08 per cent., and osteophagia was then shown by 80 per cent. to 90 per cent. of the entire herd throughout the long rainless autumn and winter. The curves plotted throughout the year for phosphorus in the grass closely reflected the curve showing osteophagia in the cattle (page 1216).

(4) Osteophagia can be rapidly removed by feeding any material rich in digestible phosphorus compounds, and in most cases complete disappearance can be effected in a few weeks if the amount is large enough. Bran, bonemeal, precipitated calcium phosphate, sodium phosphate, and even phosphoric acid, are all effective (page 1231). The experimental efficacy of this last compound disposes of the possibility of any other mineral deficiency being involved under ordinary circumstances, although for obvious reasons its use is not practicable. Rock phosphate is of very little value owing to its refractory character and low utilization in digestion (page 1233). Bonemeal is the cheapest product available when compared upon the basis of efficacy in preventing osteophagia. From this point of view 1 oz. of bonemeal is about as effective as 1 lb. of bran, although the latter has, of course, its independent high ordinary feeding value.

(5) Simple compounds containing sodium, potassium, calcium, magnesium, iron, chloride, and sulphate, have no effect in relieving osteophagia (pages 1230-1231). Indeed, carbonates of the alkalis or alkaline earths may aggravate the craving. Whatever compound be administered, reduction of osteophagia is only effective if sufficient phosphorus is present, and lack of phosphorus is the common factor in the production of osteophagia under various conditions.

(6) The effect of supplementary foodstuffs depends upon their phosphorus-content and upon the amount fed, and negative results may be obtained with apparently valuable supplementary feeds. Quantities of maize up to 3 lb. per head

per day do not necessarily effect disappearance of osteophagia, nor do moderate quantities of lucerne-hay if this happens to have been grown on phosphorus-poor soil. Conditions of soil and water supply, however, prevent growth of supplementary feeds upon the ranching areas over which lamsiekte is most rife, and since importation of foodstuffs from other areas is too expensive, the only practicable way of correcting the phosphorous deficiency shown by the cattle is to feed a " phosphorus concentrate " such as bonemeal.

(7) Rectification of phosphorus deficiency in the animal by feeding bonemeal or other phosphorus-rich supplement, effects remarkable improvement in growth and condition of stock, although weight records were not available at the date on which the protocols of pages 1307-1361 were prepared for the Press (1919), and are therefore left for a later article. In general, an average of 3 oz. of bonemeal per head per day was found sufficient to prevent osteophagia in a mixed experimental herd, but actual demands of individual cattle obviously depend upon size, age, sex, period of lactation, and any other factors which influence the physiological requirements for phosphorus. Data in this direction are in course of preparation.

(8) Although the development of osteophagia under phosphorus shortage is characteristic for cattle and is reflected by nine-tenths of an ordinary herd, some individual animals never develop osteophagia, even although phosphorus deficiency is indicated by the fact that they respond by improved condition to bonemeal-feeding. Conversely, some few individual animals do not lose osteophagia even when abundantly supplied with bonemeal. Intercurrent sickness of any sort, or a period of starvation, may frequently effect temporary disappearance of osteophagia.

(9) Osteophagia can be artificially produced away from the lamsiekte areas by feeding upon synthetic rations of sufficiently low phosphorus-content (page 1242). The process, however, is slow in comparison with the rate of production in naturally grazing animals. It would appear that some " psychological factor," so far uninvestigated, plays a part.

(10) Phosphorus deficiency in the vegetation can be removed by phosphatic manuring (pages 1243-1245) of the veld; and cattle allowed to graze over such veld, rapidly lose osteophagia and improve in condition. Phosphatic manuring, however, is impracticable over the greater proportion of the lamsiekte areas owing to the fact that the cost of fertilizer required to produce the desired effect is higher than the capital value of the land (10s. per acre), and the fact that the shallow soil, and low strictly seasonal (few summer months) rainfall, militate against adequate return in the form of increased growth of grass. In areas of higher rainfall and more arable land, nearer to centres of consumption, direct phosphatic manuring is profitable. In the ranching areas, however, it pays to feed the phosphorus (bonemeal) directly to the animal. The greater proportion

of the phosphorus fed is, of course, returned to the land in the excreta of the animal, but the benefit of this is only slowly felt on land so poor that its carrying capacity for cattle is only reckoned at about "20 acres per head."

7.—Symptomatology of Lamsiekte.

The symptomatology of lamsiekte is discussed on pages 1248-1292 It varies considerably according to the course taken by the disease—typical or atypical.

For the typical form it has been customary in the past to recognize four degrees, based upon the onset and sequence of symptoms: peracute, acute, subacute, and chronic.

An incubative period, or rather a latent period before symptoms are noticed, is a common feature of all forms, and in artificially produced cases this varied from about eighteen hours to about fourteen days according to the amount of toxin administered and the mode of administration. The average period in natural cases is usually two to six days.

Absence of fever is characteristic, and examination of the blood shows no definite changes in the normal blood picture. The duration of illness bears a definite relation to the length of the "incubation period," a short latent period between ingestion of toxin and onset of symptoms being usually succeeded by a short duration of illness and early death. There are, however, exceptions to this rule.

Cases are generally termed peracute if the period between onset of symptoms and time of death is within one day; acute if within two days; subacute if lasting three to seven days; and chronic if lasting longer. Recoveries may occur in all forms of the disease, and although more frequent in subacute and chronic cases, have also been observed after alarmingly acute symptoms.

The order of appearance of symptoms usually follows the same succession in all four forms, the rapidity of succession decreasing from peracute to chronic cases. The first symptom is generally a disturbance of the locomotor system, manifested as a stiff or clumsy walk and an inclination to lie down. This is followed by increasingly impaired muscular action and a difficulty in rising, beginning in the hindquarters and proceeding forwards. Finally, the animal is altogether unable to rise. The costo-sternal position is frequently adopted, and inability to support the head in this position often results in doubling back of the head upon the flank. In many cases the animal falls over into the lateral position. Death usually supervenes in the lateral or costo-sternal position. Recovery, if it occurs, may take place at any stage.

The less common accompanying symptoms affect the muscles of deglutition and mastication. Increased salivation, pointing to paresis of the pharynx, is common. This condition need not be associated with paralysis of the masticatory apparatus, and food can then be chewed but not swallowed, leaving masticated boluses of food at the root of the tongue. It may be complicated with paresis or paralysis of the tongue, the tip of which may then hang out or rest upon the incisors. The mandible may also be paralysed and the animal unable to close its mouth. These various conditions are first indicated by difficulties in prehension of food or in subsequent slow mastication.

Anorexia and adipsia may be noted throughout the whole course of the disease. Failure to feed is usually regarded as an alarming symptom, but the converse is not necessarily hopeful.

Under natural conditions peracute cases may never come under observation, the animal being simply found dead on the veld. In the acute and subacute cases, disturbances of the digestive organs may be noted, but are often overshadowed by extensive paralysis of the locomotor system. The paralysis of the tongue, however, is not easily missed. In chronic cases the animals continue to feed normally, but slowly, if food is within reach, steadily losing condition and remaining in the costo-sternal position. Death in this position may then ensue quite suddenly. Disturbance of the intestinal tract shows itself as constipation or discharge of dry black faeces coated with mucus; more rarely as diarrhœa.

Sensitiveness of the skin and the eye reflex are generally maintained until the comatose stage is reached. In the last stages, animals still respond to pricking, but the defensive action is purposeless. Death generally supervenes without agony; rarely with prolonged agony, accompanied by grunting, bellowing, struggling, and kicking.

In the exceptional atypical course of the disease, paresis or paralysis of the muscles of mastication and deglutition occurs without corresponding paralysis of the muscles of locomotion; or the onset of symptoms in the latter muscles follows later than in the former. There is also an intermittent form of lamsiekte, in which the symptoms noted may occur at intervals of a few days with normal appearance between, or the intervals may be shorter with several mild attacks within a few days.

Unusual symptoms, rarely observed, may include nervous excitement, aggressiveness, and charging. Rarely, also, tympany is noted during the course of the disease.

8.—Pathology of Lamsiekte.

There are no changes in the internal organs which can be regard as pathognomonic (page 1305). Indeed, the absence of definite lesions is characteristic, and normal post-mortem appearance is the rule. The tissues show their normal colour, and the blood coagulates and stains well. Ecchymoses are sometimes found in the epicardium and endocardium. No changes are noted in the lungs or in the large glands. Alterations found in the intestinal tract are confined to a mucous catarrhal gastro-enteritis, sometimes slightly haemorrhagic. The reticulum frequently contains bones, tortoise shells, cinders, stones, fragments of china, or other foreign débris swallowed during life in consequence of the perverted appetite which led to the ingestion of the toxic material causing death.

In chronic cases a cachectic condition is frequently noted. Microscopically, fatty degeneration of the muscles is often observed in chronic or subacute cases, but not in acute or peracute cases.

Prevention and Therapy.

From what has been already written, the measures for control will be obvious. An effective break in any one of the links of the etiological chain indicated on pages 824-828 is sufficient to prevent lamsiekte, but for practical economic purposes only two points of weakness can be successfully attacked. The toxicogenic saprophyte leaves comparatively resistant spores; and once a farm is infected, it may remain infected for a long time. Natural or artificially induced immunity is neither strong enough nor durable enough to offer noteworthy protection under the conditions of South African cattle

ranching. Serum therapy is impracticable, and no drug has been found which materially affects the course of the disease. The only lines of attack are therefore removal of the substrate upon which the toxicogenic saprophyte multiplies, and in which it produces the toxin; and removing the perverted appetite which induces ingestion of the toxin. For economic reasons, correction of phosphorus deficiency by manuring the soil is impracticable, excepting on arable areas close to markets, and phosphorus feeding therefore remains the only practical procedure.

The measures for prevention therefore are—

(1) cleaning the farm of all carcass débris; and
(2) feeding bonemeal in amount sufficient to prevent osteophagia.

Both are recommended; the former, not only because it protects against lamsiekte, but because it is a general hygenic measure which also reduces the incidence of other diseases, particularly anthrax; the latter, not only because it offers a sound insurance against lamsiekte, but also because the cost of the treatment is amply repaid by the improvement in condition and growth of the cattle. Either measure alone is effective if thoroughly carried out, but both together are certain. Their introduction at Armoedsvlakte led to a reduction of mortality from lamsiekte in a herd of 500 cattle from 30 per cent. down to 2 per cent. within twelve months, and to a complete disappearance of the disease amongst the bone-fed animals in the ensuing year. The use of only one method can never be completely relied upon. A small proportion of a herd may continue to show osteophagia in spite of a liberal ration of bonemeal, and however carefully the cleaning of a farm is carried out, minor carcass substrates, such as hares, tortoises, lizards, snakes, and the like, are apt to be overlooked.

The cost of cleaning a farm of major carcass débris and of keeping it clean is not so great as would be expected. Using the cheap labour of the native women and children of the farm, it may be assessed at very few shillings per annum per head of grazing cattle. The cost of bonemeal at the average rate of 3 oz. per head per day works out at about five shillings per head per annum, but the return in the form of improved condition of the stock is several times this figure. Exact data in this direction are now being acquired by the use of a recently introduced weigh-bridge. The actual cost of bonemeal can be kept down to the minimum by periodical testing of the cattle for osteophagia, and adjusting the ration according to the needs of individual animals and according to season of the year. In general, however, it pays to err on the liberal side in feeding bonemeal.

In regard to the best method of feeding the bonemeal, each farmer has to make his own experience and adapt his procedure to his local conditions. The method so far found best at Armoedsvlakte consists in using a large number of small wooden troughs placed in a kraal erected at the approach or exit of the watering-places (windmills). The herd is divided into lots, each lot containing not more animals than the number of troughs available. If this is not done, and too few troughs are used, the weaker animals do not get a chance of consuming their ration, and osteophagia is not removed. The appropriate ration is measured into each trough with a spoon, or tin cut to the required dimensions, and as one lot passes through the kraal, the troughs are replenished for the lot behind. The animals soon learn

what the troughs are for, finish their ration in a few seconds, and can be driven on by the native herd-boy. The process goes very quickly and, properly managed, it can be conducted very cheaply. Daily feeding of bonemeal is recommended as most effective. The "lick method," i.e. mixing the bonemeal with salt and offering *ad libitum*, involves less trouble, but is more expensive in bonemeal, and is not recommended owing to the fact that the craving for salt and bonemeal do not run parallel. If the mixture is adjusted according to the estimated salt requirements, some animals may get too little bonemeal and others too much. If this method is used, however, the mixture should contain excess of bonemeal; two or more parts of bonemeal to one part of salt, varying according to the degree of phosphorus deficiency prevalent over the farm. Other methods of administration of bonemeal are now being worked out.

SECTION 1.—DEFINITION AND HISTORICAL NOTES.

Definition.

Lamsiekte, also known as gal-lamsiekte, and spelt lam-sikte in the earliest records, is a fatal disease of cattle, rarely of other animals, caused by the ingestion of carcass débris containing a toxin produced by an anaerobic toxicogenic saprophyte and characterized by symptoms of paralysis and paresis, principally of the locomotor system, but in many cases also of the muscles of mastication and deglutition.

There are no gross pathognomonic anatomical changes, and unless clinical observations are made during life, diagnosis is difficult. Pathological lesions of fatty degeneration and Zenker's degeneration are common in the muscles.

Lamsiekte may now be described as *Parabotulismus bovis.*

Occurrence.

Lamsiekte has been recorded as causing serious losses in the South Cape Province, being most severe in the coastal districts south of East London; on the Cape plateau, where it is popularly believed to have originated; in the western Transvaal, in the Bloemhof, Wolmaransstad, and Lichtenburg Districts; in the Orange Free State, in the Boshof and Hoopstad Districts; over the greater part of Griqualand West; and in many parts of Bechuanaland. Occasional outbreaks, however, have been reported or suspected at one time or another from nearly every area of the Union, and since the disease is liable to occur wherever *Phosphorus deficiency* of the soil and the presence of *Parabotulinus bovis* coincide, no region can be regarded as safe. Certain uninvestigated conditions of climate and soil, however, seem to affect the survival of an introduced infection, and the occurrence of the disease is not so universal as is the phosphorus deficiency of the pastures of South Africa.

Historical Notes.

Lamsiekte is not a new disease in South Africa, but is noted as far back as historical records of the sub-continent go. Le Vaillant, in his "Travels into the Interior Part of Africa," in the years 1780-1785, referring to Cape Colony, writes on page 78 (English translation, second edition, London, 1796):—

"It is then also that the season most dangerous for these animals commences; and when they are subject to four destructive maladies which occasion dreadful devastation among the herds. The first, called