

THE SO-CALLED "STAGGERS" OR "PUSHING DISEASE" OF CATTLE IN NATAL.

AN INTOXICATION DUE TO THE INGESTION OF *MATRICARIA NIGELLÆFOLIA* D.C.

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FROM time to time outbreaks have occurred in Natal, and probably in some other provinces of South Africa, of a peculiar bovine disease characterised by symptoms indicating some affection of the central nervous system, and liable to cause very serious losses in the affected herds. The disease has received a number of popular names, such as "Brain Disease" and "Brain Staggers," but the most commonly used name, derived from a symptom which is a prominent feature of a typical case, is "Pushing Disease."

In the earlier years of colonial history in Natal the great majority of outbreaks were not reported, and it is most probable that very few cases, if any, came under the observation of veterinarians. Even during more recent years the vast size of the country controlled by comparatively very few officials, and the preoccupation of the latter with a succession of newly introduced diseases of outstanding importance have rendered it inevitable that many by no means unimportant diseases should escape observation and detailed description. It is therefore not surprising that the first written record of the disease which I have been able to trace dates back only to 1902 (1), although outbreaks are known to have occurred much earlier than that. About the year 1885 or 1886 there was an outbreak which caused losses of such severity that it is still remembered by all the older farmers of the Balgowan district. It is reported that there was another outbreak near New Hanover about thirty years ago, and the disease is known to have appeared from time to time during the past twenty years in the various affected districts. Most of these outbreaks have been very localised, and in many instances they have been confined to one or two farms, so that their occurrence has not become widely known. During the summer season 1902 to 1903 a more extensive outbreak occurred in the Howick area, and a number of cases came under the observation of Mr J. L. Webb, the District Veterinary Surgeon, to whom we owe the first description of the disease.

The *Report of the Principal Veterinary Surgeon for the Colony of Natal* for 1902 gives a description of the symptoms of the disease, which is there stated to appear periodically in the vicinity of Howick, and usually during the winter months, although in 1902 the majority of the cases occurred in the middle of the summer. The report states that the disease usually appeared when the cattle were running on old mealie fields, but that cases had occurred amongst cattle on grass land, and that removal to fresh grazing ground was found always to stop the disease. It is also recorded

that cows in milk were chiefly (and sometimes exclusively) affected, although mixed cattle had been running on the same pasture. The report contains notes by Lieut.-Col. H. Watkins-Pitchford, Government Bacteriologist, on morbid specimens taken from two cows affected with "staggers" and sent to him by Mr J. L. Webb. In a brain which was sent to him Col. Pitchford noted the occurrence of an extensive hyperæmia of the pia mater, without any inflammatory exudation. No definite effects were observed as a result of the performance of a few inoculations, and, although a small coccus was obtained in pure culture from a trace of liquid in the lateral ventricle, the author did not feel justified in ascribing to it any etiological importance.

Subsequent to this more widespread outbreak in 1902-3, various localised outbreaks occurred from time to time, and it is probable that at least a few isolated cases occurred every year. It appears that there was no further extensive outbreak, however, until the winter and spring of 1919, when not only were cases reported almost simultaneously from a very much larger number of farms than had ever previously been affected, but the actual losses sustained were in most cases greatly in excess of any previously recorded.

My attention was first drawn to the disease in August 1918 by Mr G. L. Harber, Government Veterinary Officer at Mooi River, and shortly after examining a case of the disease at St. Ives I received notification of a similar outbreak near Ixopo from Mr J. L. Webb. Two months later I was consulted by Mr F. J. Carless, M.R.C.V.S. in connection with an outbreak of particular severity (although confined to one farm) in the Balgowan area.

In the first instance I was led to interest myself in the disease for almost purely theoretical reasons, and after the above-mentioned outbreaks had been investigated it was still considered that the disease, however interesting, was only a "minor local affection," as stated in the Natal report for 1902; but the events of the winter and spring of 1919 proved that the condition, under certain circumstances, could become of primary importance throughout a considerable area, including some of the best stock-breeding districts of Natal, and that it was liable to cause most serious and widespread losses. The outbreaks personally investigated, and those reported to me with fairly complete and reliable data, showed by the end of 1919 a total number of 570 cases, of which certainly more than 450 ended in death. Moreover, it was considered by the Senior Veterinary Officer that one could very safely estimate the actual losses which occurred in Natal during the period involved (of a little more than one year) to be quite double the known losses, the majority of the remaining cases being reported under some such vague description as "vegetable poisoning," "death from drowning," or "accident," and some, of course, not being reported at all. Losses of twenty, thirty, and even fifty head of cattle were known to have occurred on several different farms, and on one farm eighty head succumbed within a period of a couple of months; a number of native labourers and squatters lost every member of their small herds. It was therefore decided to undertake a more thorough and systematic investigation than had previously been attempted.

I must express my indebtedness to Mr W. G. Raw of St. Ives,

who first aided me considerably by the accurate information which he was able to furnish with respect to the symptoms of the disease and the conditions under which it had appeared on his farm. Subsequently he not only allowed me to conduct experiments on his farm, and freely gave me all the required facilities, but he personally supervised a number of experiments during my absence and gave me much valuable assistance.

I.—DESCRIPTION OF THE DISEASE AS OBSERVED UNDER
NATURAL CONDITIONS.

(A)—*Geographical Distribution.*

During 1918 and 1919 I was able personally to investigate outbreaks and observe cases of the disease in five of the Magisterial districts of Natal, viz., Lions River, Ixopo, Umvoti, New Hanover, and Pietermaritzburg. In addition to these outbreaks, others were reported from certain farms situated in the districts of Camperdown, Dundee, Paulpietersburg, and Vryheid. The heaviest losses and the greatest number of affected farms were reported from the Lions River district, and in some other districts only one or two farms were known to have been affected.

There is much reason to believe that the disease is considerably more widespread in Natal than is at present known with certainty, and that it occurs in Zululand also. Moreover, Mr R. Paine, F.R.C.V.S., has informed me that the disease undoubtedly occurs in East Griqualand. It may be noted that all the affected areas in Natal lie within the Thorn Veld of Pole Evans (2), and most of the farms involved are situated in the Natal Midlands, at an altitude of from 2000 to 4000 feet above sea-level.

(B)—*Conditions under which Outbreaks have Occurred.*

1. *Locality.*—All the farms on which the presence of the disease has been definitely established have one feature in common—the presence of vleis or swamp grazing, generally associated with some river or stream. Thus many of the known affected farms in the Lions River district are actually bordered or traversed by the Lions River, while others are on the Karkloof and the Umgeni. Similarly, other affected farms are found along the Ixopo and Umvoti rivers, but in some cases the farm is traversed only by some small unnamed stream, or has within its boundaries only a small area of swampy ground.

In only a few instances does the connection between swamp grazing and the disease appear to have been suspected or realised. It was well appreciated, however, by Mr Raw of St. Ives; his farm includes a very large vlei—a comparatively flat and low-lying area that is liable throughout most of its extent to periodical inundation from the Lions River, and also a large area of comparatively high and well-drained land on the slopes of a range of hills. He informed me that he never had cases of “pushing disease” amongst cattle which had grazed for some time on the hills, but that the outbreaks always occurred when the cattle were in the vlei. He had found that the disease was stopped by moving the animals back to the

hill pasture, but that further cases were liable to develop for a month, and even exceptionally six weeks, after the movement had been effected.

In most of the other natural outbreaks that were investigated, it was difficult or impossible to draw any definite conclusions from the history recorded, nor had the owners themselves formed any definite opinion on the matter. Although all of these farms included a larger or smaller area of vlei grazing, in these particular districts of Natal the same might be said of a very large number of farms on which the occurrence of the disease has never been recorded.

In August 1919, after the performance of a partially successful experiment designed to reveal the relation, if any, between the nature of the grazing and the appearance of the disease, a natural outbreak occurred under circumstances that lent the strongest support to the working hypothesis which had been based on the facts supplied by Mr Raw. On the farm separated from St. Ives by the Lions River the belt of vlei along the river is very much narrower, and it is separated completely by a public road (fenced on both sides) from the remaining and very much larger portion of the farm, which is practically all well-drained hill pasture, with only a minimum of vlei. The owner had allotted this conveniently separate (vlei) portion of the farm to his native labourers, and towards the end of the winter of 1919 these natives lost some fifty head of cattle, practically all they possessed, whereas the European owner, with a much larger herd, had only one case.

2. *Annual Incidence.*—On some farms the disease has appeared for a number of years in succession, although the number of cases has in most instances varied considerably from year to year. On the other hand, there are known instances in which there have been very long intervals between the outbreaks. On one farm near Ixopo the owner, who lost cattle from "staggers" in October 1918 and again in the spring of 1919, informed me that the only previous outbreak had occurred twelve years earlier; and on a farm in the vicinity of New Hanover it was stated that there had been a severe outbreak about thirty years previously, followed by a period of twenty-four years' freedom from the disease, another outbreak in 1913, and a third in November 1919. It is very possible that in many of these instances at least there have been a few odd cases developing during the prolonged periods of supposed freedom from the disease, but that these cases have been incorrectly diagnosed, or that they have failed to attract any particular attention.

In a number of instances the disease is stated to have disappeared entirely from farms on which cases formerly occurred, and repeated outbreaks of the disease are known to have occurred in the past on some areas now alleged to be free from it.

In view of the considerable periods of time which are reported to have elapsed between successive outbreaks on some farms, it is of course impossible to feel at all certain that the disease has definitely disappeared from an area. On the other hand, the absence of cases on previously affected farms during such a period as the winter of 1919, when in some instances the disease was active on all the surrounding farms, suggested strongly that some factor favouring the appearance of the disease had then ceased to operate on those

farms, although it had formerly affected them quite as much as, or in some cases even more than, it had affected the adjacent areas. From the evidence afforded by the few cases of this kind that could be investigated, it was not found possible to determine the probable nature of this factor, and it appeared to be reasonable to suppose that the same factor was not necessarily involved in the different cases. There is no doubt that during the years 1918 and 1919 losses were sustained on many farms on which the disease had never previously been known to occur.

3. *Seasonal Variations.*—From the records of past outbreaks which I was able to collect, it appeared that the disease was especially liable to appear in the early spring, soon after the veld had been burned.

The owner of St. Ives, who had kept records for a number of years, considered the spring to be the critical season, although some cases had also occurred in the autumn, whereas until 1918 he had always found it perfectly safe to graze his cattle in the vlei during the middle of the summer and of the winter. On his farm, however, the disease appeared in July 1918, and the heaviest losses on record from this cause occurred on many farms during the winter months of 1919.

My records show that at least some naturally-contracted cases were seen, on one farm or another, during every month of the period August 1918 to February 1920, with the exception of the two months March and April 1919.

4. *Rainfall.*—In the absence of accurate records it was impossible to obtain any indication of the possible influence of either excessive rainfall or drought on the production of past outbreaks. Of the outbreaks which I was able to investigate personally, the majority occurred under conditions of drought, but this factor was certainly lacking in several instances.

5. *Over-stocking a Paddock or Farm.*—Here again the evidence relating to past outbreaks was too meagre and vague to allow any deductions to be drawn. With respect to the more recent outbreaks which have come under closer observation, it may be said that the number of cattle allotted to a particular grazing area was undoubtedly excessive in many instances on account of the particular conditions of drought then prevailing, but in certain cases over-stocking appeared to play no part at all.

(C)—*Animals Affected.*

1. *Species.*—In no instance were any animals other than bovines reported to suffer from the same or any similar disease on the farms on which cattle contracted it and died. Some of the farms on which the bovine disease has appeared are situated in districts in which the equine disease known as Dunziekte occurs, and the two diseases clinically have many features in common, but, as far as I was able to ascertain, they have never appeared on the same farm.

In most instances investigation showed that the area grazed by an affected herd was reserved entirely for cattle, or that it was shared with only a relatively very small number of horses, which in most cases would graze it far less constantly; but Mr Raw had found that the vlei could be grazed at all seasons with impunity by horses

and sheep, and in this case comparatively large numbers of both horses and sheep were involved.

2. *Breed*.—The available evidence did not suggest that any particular breed of cattle was either more or less susceptible to the condition than others.

Serious losses were known to have occurred amongst pure-bred Shorthorns, Lincoln Reds, Frieslands, etc., and amongst grade cattle sired by bulls of such breeds, but equally severe and fatal outbreaks appeared amongst nondescript Kaffir cattle.

3. *Age and Sex*.—There is no doubt that any bovine animal, of either sex and of any age, may contract the disease when grazing; no case has ever been recorded to have occurred in a calf before it had commenced grazing. Considerable numbers of yearling heifers and steers are known to have died from this disease, and numerous cases have been recorded in adult working oxen, but on the whole the experience of the outbreaks of 1918-20 was similar to that of 1902, by far the heaviest losses occurring amongst milch cows. On one farm only cows were affected, although several spans of working oxen were running in the same paddock when not actually in yoke and working elsewhere on the farm, and were kept there without loss many weeks after the cows had been removed on account of the occurrence of nineteen cases amongst them. The comparative rarity of a case in a bull is, of course, easily explained.

4. *Comparative Susceptibility of Native and Imported Cattle*.—It appeared to be of some interest to ascertain whether cattle bred on affected farms were either more or less susceptible than cattle introduced from other parts of South Africa or from European countries. During the worst part of the extensive outbreak of 1919 there appeared to be no difference in this respect; the majority of the affected animals naturally belonged to the most numerous class, that of cattle born on the farms concerned or on neighbouring farms. Records of some small isolated outbreaks, however, certainly suggest that cattle bred in the affected areas are less liable to contract the disease than newly-introduced animals. In one instance six newly-introduced Cape cows all died from the disease, although a number of locally-bred cattle had been running on the same small pasture for some time previously without mishap, and they continued for years to graze over the same ground with impunity.

(D)—*Symptoms of the Disease.*

The symptoms which first attract attention vary considerably in different outbreaks and in individual cases, and this is due partly to the occurrence of different clinical types of the disease, and in part to differences in the experience possessed by the owner or attendant or to the care exercised by him. It was found that certain farmers who had had considerable experience of the condition were able to detect cases at a remarkably early stage by a change in the expression of the eyes. This symptom can usually be appreciated very easily at a later stage of the disease, when it is well developed; the eyeball then appears to protrude abnormally from the orbit, the cornea acquires a peculiar glaze, and the pupil may be considerably contracted, the animal appearing to glare or stare wildly. In many

cases this change is not at all obvious, at least to the average observer, until many other symptoms of the disease have become manifest.

It may be stated here that this wild glare of the eye is certainly deceptive, for amongst the hundreds of cases of which the details have been observed by or reported to me there has not been one in which the animal gave any evidence of a desire to attack or injure another animal or an attendant. On the contrary, vicious and nervous animals become quiet and docile at a very early stage of the disease, and such a change in behaviour may be one of the earliest signs of the condition.

As in many other diseases, isolation from the herd may be an early symptom, and attention may first be attracted by the fact that the appetite is impaired or lost, or by constant grinding of the teeth. In certain outbreaks the majority of cases have first been detected by a quivering motion of the ears.

The commonest early signs, however, are a tendency to restless wandering, often with the head carried abnormally low; a clumsy or uncertain gait, with a liability to stumble at very small elevations or depressions of the ground; and perhaps a difficulty in drinking, although this often passes unnoticed for some time under natural conditions. Finally, the course of the disease is sometimes so acute that cases, when first seen, present some of the more serious symptoms to be described.

In the second stage of the disease the best-known and most striking symptom, which, moreover, is present in the great majority of cases, is the "pushing" to which the disease owes its popular name. The animal exhibits a peculiar tendency to press the head against some solid and immovable object, such as a tree, a wall, a post in a fence, or even another bovine or a man. A considerable amount of variation is seen in connection with this tendency. In some cases very little force is exerted, and the animal may be said to rest or lean the head against the object; but more commonly the pressure is considerable, as is shown by the attitude adopted by the animal and by the tension of the muscles, the weight of the body being thrown forward. In some instances the "pushing" may be described as violent; in addition to throwing the weight forward, the animal may attempt to advance by the aid of forcible movements of the legs, and the ground on which this occurs may be considerably cut up by the scraping of the hoofs. In the stable an animal in this state frequently places the forefeet in the manger and appears to be attempting to climb. When thrust against an object, the head is generally placed at a low level, but occasionally it is stretched up in such a way that the inferior maxillary region, rather than the horns or the frontal region, is in contact with the object.

The attacks of moderate intensity are generally terminated by a gradual relaxation of the muscles involved, and the animal may move away more or less normally, or it may, after attacks of longer duration or greater severity, appear to be considerably exhausted and go down, lying in a normal position. In the more violent cases there may also be gradual relaxation of the muscles, and the animal may stagger away or lie exhausted, or again it may merely relax to the stage of moderate or light pressure, and after a variable time pass suddenly again into the violent

phase, until the stage of exhaustion supervenes. In the very violent cases another termination to a bout of "pushing" is not uncommon: owing to the low position in which the head is held, or possibly in some cases owing to fatigue of the muscles of the neck, the animal loses its balance and turns a more or less complete somersault on to the back. The shock of such a fall appears to cause a temporary abatement of the symptoms.

In all but the mildest cases external stimuli tend to prolong and intensify the "pushing" action, and if in a severe case the stimuli are applied whenever the animal relaxes the "pushing" is instantly resumed, and it can be maintained in this way until fatigue causes the animal to go down. In some of these cases a sudden blow or noise will cause an immediate response in the form of such a violent effort that the animal loses its balance and falls over.

Successive bouts of "pushing" may be separated by intervals of a few minutes, of some hours, or even days, and the duration of an attack may be a matter of only one or two minutes, but more commonly is from ten minutes to half an hour. Many cases occur in which an animal keeps the head against an object (particularly in a corner of a byre or shed) for several hours or even for a day or longer. During these prolonged attacks the animal, having adopted an attitude that throws the weight forward against a fixed object, remains almost passively in this position for the greater part of the time, and exerts pressure actively only at considerable intervals, or (and especially if free from interference) not at all.

Generally speaking, either the frequency and violence or the duration and violence increase as the case progresses, but this is not always so.

Besides the characteristic "pushing," or in its absence, animals may exhibit a number of other abnormalities in connection with muscular movements, and these may be conveniently described in two classes, viz., forced or involuntary movements and inco-ordinated movements.

Forced or involuntary movements may affect single muscles or only small portions of them, smaller or larger groups of muscles, or even apparently the entire skeletal musculature; they include mere fibrillation, tremor, clonic spasms (which may occur at quite irregular intervals or with a remarkable regularity), tonic spasms, and generalised tetaniform convulsions. Cases have been seen in which the twitching appeared to be confined to the panniculus on one side of the neck or over one shoulder, and in one case the movement was noted only on one side of the face beneath the orbit, the wing of the nostril being very noticeably affected by the contractions. In some cases the twitching is most noticeable in the muscles of the ears, which may move backwards and forwards so rapidly that the movement might be described as a vibration.

In one not very common type of case a rhythmic contraction involving larger groups of muscles, and of greater intensity, produces a constant extension and flexion of the head on the neck—a nodding of the head. In one such case that I was able to examine the rate or frequency remained very constant, the movement being repeated from thirty to thirty-two times in a minute. After a

variable time, generally about fifteen minutes, the movements would cease, and the termination was usually very gradual, the amplitude of the movement constantly decreasing although the frequency remained practically unaltered. The animal, after periods of quiescence which were of very variable duration, would suddenly make a few restless movements and recommence the nodding with the same frequency as before, and during the quiescent phase a bout of nodding could usually be provoked by the application of various external stimuli. In a number of cases, and generally at a later stage, ordinary clonic or tonic spasms may affect one or more limbs, the trunk, or the head and neck, and towards the end of many acute cases general tetaniform convulsions may occur; in such cases these spasms may usually be provoked by ordinary external stimuli.

Inco-ordination of movement is often shown first by irregularities of gait, but in a number of cases the first sign is a difficulty experienced in drinking. In some cases the gait alters very little up to the time that the animal goes down in an exhausted condition, but in the majority of cases it becomes increasingly abnormal. At first one usually notices a tendency to stumble wherever the ground is uneven; later the animal may sway irregularly from side to side, it may drag the forefeet somewhat and stumble frequently, and in a few cases the feet are lifted abnormally high. The animal may deviate irregularly from its course and fail to arrive at a desired goal (such as a water-trough), or attain it only with obvious difficulty, even in cases in which there does not appear to be that impairment of vision which is noted in many other cases. In some cases the gait becomes increasingly uncertain, and the animal appears to have difficulty in preserving its balance. It may then assume a variety of strange and abnormal attitudes when standing, and in walking it may reel and stagger from side to side, at times abducting the legs widely and at times crossing them. The general tendency is to carry the head very low, and even before the gait is at all obviously affected an animal may wander restlessly with the head at such a level that the muzzle barely clears the ground. In the later stages the head may be held so low, and be so strongly flexed on the neck, that the horns actually come into contact with stones or other projections from the ground surface, and this may cause the animal to turn completely over.

Difficulty in drinking may appear very early in a case, but in many cases the animal appears to drink normally until it becomes comatose, in the final stage of the disease. Where this interference with drinking occurs it is usually first observed that an animal exhibits a keen desire for water, drinking eagerly and particularly noisily, but that the level of the water, if the latter be contained in a bucket or other small vessel, subsides only very slowly. As a rule only little, if any, water is returned by the nostrils, and the animal appears to be unable to draw the water into the mouth with normal ease and rapidity, although the water that can be obtained appears to be swallowed without difficulty. At a later stage the head may be inserted into the bucket only with some difficulty, and the muzzle is often plunged below the surface of

the water to an excessive depth. It is of interest to note that an animal may still appear to eat quite normally although drinking has become a slow and difficult process; inco-ordination in connection with the process of eating may appear later, but in most cases the desire to eat is lost before any abnormality in the performance of the act can be detected.

In a number of cases an animal may be seen to retain food in the mouth for a long time without any effort at mastication or deglutition, and it may wander about or lie for hours with a bunch of hay held between the jaws; normal feeding may be resumed quite suddenly.

Occasional fits of grinding the teeth are commonly noted in the earlier stages, and later this may become a prominent symptom, the animal grinding the teeth at very frequent intervals or for quite prolonged periods, and sometimes with the exertion of considerable force.

Salivation may be a very early symptom of the disease, and may continue to be observed throughout its course; in the later stages of some cases the flow of saliva is very profuse.

Lachrymation is also noticeable in most cases, although often only in the later stages. A serous discharge from the nostrils is noted only in a minority of cases, and in the later stages of those cases. Apart from the lachrymal discharge that is usually present, the eyes generally show the abnormal protrusion and the glazed appearance of the cornea to which reference has already been made. The pupils may appear normal but are usually somewhat contracted; in all cases which have come under observation the pupils have been equal. At a later stage of the disease, and particularly during phases of violent muscular activity, the pupils are very markedly contracted; in cases in which the nervous symptoms are only occasionally displayed the pupils in most instances appear during the quiescent periods to be almost or quite normal, at least until the case is nearing its end. In many cases the sight is very considerably affected.

Constipation is practically always present, and the *fæces* tend to be abnormally dry and firm, with an excessive admixture of mucus; quite small hard spherical masses may be passed.

The urine is always quite clear when first passed, and of a light yellow colour. Throughout the greater part of the attack the animal will generally micturate in a normal manner during the quiescent phases, and in no case has an animal been observed to pass urine at all during a phase of abnormal muscular activity. In the majority of cases micturition is suspended altogether during the final stage of the disease.

The application to the urine of the ordinary sugar tests of Fehling and Nylander shows that it may contain a reducing substance, but the latter is frequently absent. The presence of protein material can be detected occasionally by the application of the ordinary tests, but the amount is very small.

During quiescent phases of the disease the pulse may be quite normal in frequency and strength, and perfectly regular; during the periods of violent movements it may be almost impossible to feel the pulse or to form an opinion as to the character of the heart-beat,

but these appear at such times to show only those changes which would normally be expected to occur during the course of very violent muscular activity.

In the majority of cases the respiration also is very little if at all affected, except during and immediately after phases of great muscular activity and when the final stage of coma is approaching.

The temperature has never been found to be affected to any significant degree, and the occurrence of an abnormally high temperature, especially if associated with any alteration in the respiration, points to the development of some complication, such as a "drenching" pneumonia.

An exceedingly rapid loss of condition is seen in practically all cases, but it is uncommon for any particular loss to be observed before the onset of definite symptoms, and in acute cases animals displaying the most violent symptoms of the disease may still be in excellent condition. In all sub-acute cases the animals before death are more or less emaciated.

In the majority of cases the animal becomes progressively weaker, and it finally lies on the side in a semi-comatose condition that gradually passes into deep coma. In acute cases the animal, even in the later stages, may be very violent, and before going down finally it may repeatedly turn somersaults, or fall on its side, and rise again; the head may then be injured by the repeated falls and by violent contact with the solid obstacles against which it is thrust. When down finally these animals may continue for many hours to have phases of violent movement. In a considerable number of acute cases there are wild convulsive struggles, during which the head is repeatedly struck against the ground, or against any neighbouring wall or post, with great force. These animals, unless quickly destroyed, soon present a pitiable sight, with horns torn off or broken, horn-cores fractured and lacerated, and numerous contusions and lacerations, particularly about the head but also on the limbs and even the trunk; there is often considerable hæmorrhage, especially from the horn-cores.

The final stage of a gradually deepening coma, whether interrupted by phases of violent movement or not, may be quite prolonged, and animals that appear likely to die within a few hours will often exist for four or five days. Indeed, it may be said that under natural conditions very few animals actually die from this disease, although from humane motives large numbers are slaughtered in what appears to be a hopeless and incurable condition.

Experience has shown that animals may recover after displaying a number of the earlier symptoms, such as the wild staring eye, impaired vision, grinding of the teeth, an irregular stumbling gait, and even a slight or very moderate amount of pushing. Only very rare recoveries have been recorded, however, after these symptoms had developed to any considerable degree, and after any of the more severe symptoms had been shown, and no case has been recorded of the recovery of an animal which had reached the third stage of the disease (semi-coma or convulsions).

Taking the duration of the disease to be the time that elapses between the appearance of recognisable symptoms and the attain-

ment of that stage at which slaughter is considered desirable or necessary, the disease may be said to last for any period from a few days (probably never less than three or four) to many weeks; cases ending fatally after two months are known to have occurred. The majority of cases probably end in compulsory slaughter between the tenth and twentieth days.

Cool cloudy weather has a most favourable influence on the course of the disease, whereas clearing of the sky and renewed exposure of the animal to strong direct sunlight may precipitate the re-appearance of nervous symptoms even within fifteen or thirty minutes.

During the earlier stages of the disease symptoms may be shown only at intervals, and during the earlier intervals, which may be of many hours or even of several days' duration, the animal may present very few, if any, signs of disturbed health. It is not uncommon to see an animal displaying quite severe nervous symptoms, including hard pushing against a wall or post and apparent disturbance of consciousness, and yet an hour or less later to see the same animal walking about or feeding quietly.

Under natural conditions many cases end quite early in accidental death, or in the receipt of injuries which necessitate immediate slaughter, and the accident may occur miles from the starting-point, the animal forcing its way through wire fences, and over many obstacles in spite of repeated falls, temporary checks, and painful contusions and lacerations. A number of affected cattle ultimately walk or fall into rivers and are drowned; others are caught finally in strong wire fences, and may remain quietly in the same position until they fall exhausted, or they may renew at intervals their fruitless efforts to advance, but they practically never attempt to retreat from the entanglement.

It may be remarked that on one farm a particular type of the disease may be seen to predominate, and on an adjoining farm, or even on the same farm at another period, quite a different type of case may be most common.

(E)—*Macroscopic Lesions of the Disease.*

The appearances which were found in a series of more than fifty *post-mortem* examinations may be summarised as follows:—

1.—*Lesions almost Constantly Present.*

(a) Poor condition or emaciation (except in a few very acute cases) and most of the usual features associated with such a condition.

(b) Some petechiæ or ecchymoses in connection with the heart, and usually under the left endocardium; much less commonly under the right endocardium or the epicardium.

(c) A flabby consistence of the myocardium, which generally was distinctly paler than normal, and had a somewhat opaque appearance; occasionally a slight tinge of yellow was noted.

(d) The liver showed some degree of change in every case. The organ was very often of normal size, but in about one-third of the cases it appeared to be somewhat enlarged. On section it appeared

to contain a normal, or even somewhat sub-normal, amount of blood, and only occasionally appeared to be slightly congested in parts. On the other hand, subcapsular hæmorrhages, forming circular black spots up to 2 mm. in diameter under the capsule, and extending to a depth of about 1 mm., were noted in about one-tenth of the cases. In such cases there were usually only three or four of these hæmorrhages, and they were never numerous. The parenchyma was generally paler than normal, the colour being usually a yellowish-brown, but in a few instances it was of a pale chocolate hue. The lobulation of the organ was almost always abnormally indistinct. The elasticity was usually reduced, in a number of cases not very noticeably; the cohesion of the tissue was practically always reduced, although to varying degrees, the parenchyma being friable.

2.—*Lesions less Constantly Found.*

(a) In acute cases the horns, the muzzle, and the cutaneous surface sometimes showed various signs of trauma, and the subcutaneous tissue was the seat of hæmorrhages, or was infiltrated in patches with clear liquid, or with a serous liquid tinged with blood.

(b) In acute cases (about 40 per cent.) the lungs were affected with emphysema, particularly at the apices and along the lower borders. This lesion was usually bilateral, although very often unequally developed on the two sides, and it was sometimes very extensive. It appeared to be essentially an interstitial emphysema, arising during the respiratory movements accompanying, or immediately succeeding, the more violent convulsions.

(c) The renal cortex was generally seen to be pale, sometimes with a distinctly yellowish tinge, but exceptionally it was somewhat darker than normal, and traversed by a number of narrow radial streaks of dark red colour.

(d) In nearly one-half of the cases the contents of the omasum were abnormally hard and dry, but in many cases they were found to be quite as soft, finely divided and moist, as in the normal carcase.

(e) The abomasum, in about one-fifth of the cases, was the seat of a number of ulcers, which varied from small points of the size of a large pin's head to lesions of 1 cm. diameter; exceptionally some of them had a diameter of 3 or 4 cm. In most cases they were circular or broadly oval in shape; much less commonly, but especially when of larger size, they were of irregular shape, and in a few instances, in which an active process of healing appeared to be occurring, they were distinctly stellate. The erosion extended down to the sub-mucous tissue in fully developed ulcers, but in no instance did the serosa and muscular coats show any change at all. The borders were always very sharply defined, and a mixture of *débris* and coagulated blood practically always adhered to the edge, and frequently covered entirely the flat base of the ulcer. These lesions were often found only at or near the summits of the loose folds in the mucous membrane, and several adjacent folds were usually affected. The number of ulcers found in different cases varied from three to more than twenty, the average number being from four to six. Occasionally the abomasum contained an excess of mucus, and in

some cases the mucous membrane showed a considerable amount of diffusely-scattered whitish deposit, which appeared to consist of epithelial *débris* and mucus.

3.—*Lesions Present only Occasionally.*

In a small proportion of cases the lungs showed a slight degree of œdema, and exceptionally a broncho-pneumonia was found, affecting the inferior portion of one or both middle lobes.

In some cases the mucous membrane of the small intestine showed a very slight diffuse hyperæmia and the presence of a slight excess of mucus.

In many cases firm parasitic nodules were present in the sub-mucosa, and in a number of instances one found fairly thick clusters of nodules, many of which had discharged contents; and over them the mucous membrane, besides showing a number of perforations, was often thickened and roughened, infiltrated with clear liquid, and covered by a number of small blood coagula. The number of free œsophagostomes present in the lumen of the ileum was sometimes very large.

The large intestine usually showed little abnormality other than the presence of an increased amount of mucus, and an unusually desiccated condition of the contents, particularly in the rectum. Patches of moderate congestion were only occasionally noted, more especially in the region of the anus.

Submucous parasitic nodules were often present, and in some cases they were very numerous. The bowel frequently contained many free nematodes, and in some cases the number was extremely large.

The bladder was usually found to be moderately distended with clear yellow urine, and in some cases it was greatly distended; in a few cases the mucosa showed a considerable number of petechiæ.

On certain farms practically all the autopsies revealed the presence in the rumen of numerous *Amphistomum conicum*, and on some farms the livers were generally infested to some extent with flukes (apparently the common *D. hepaticum*), although no heavy infestations were noted. The presence of *Hæmonchus contortus* in the abomasum, or of cestodes in the small intestine, was noted only in a few isolated cases.

The cerebro-spinal fluid was always perfectly clear and transparent, and almost colourless or of a very light yellow colour. In most instances it was not practicable to measure the total quantity present, but such measurements would have had little value, in view of the great variations in size shown by the subjects (most of which could not be weighed) and the comparatively wide limits within which the amount of the fluid may vary in apparently normal animals. It appeared that the amount of liquid was very little, if at all, affected in this disease. In one case the vessels of the pia mater appeared to be distinctly engorged, but in no other instance could any abnormal appearance whatever be detected in the meninges by naked-eye inspection.

With respect to the brain itself, I was not able to detect any macroscopic lesions which could be attributed to this disease, and

no changes in the appearance or consistence of parts were found on section in any region of the central nervous system.

The lesions observed microscopically are discussed briefly on p. 300.

(F)—*Mortality.*

The average mortality, calculated from data concerning all the outbreaks of which fairly complete details are available, is rather less than 80 per cent. On many farms comparatively small outbreaks were observed in which all the visibly affected animals eventually succumbed, and in the majority of outbreaks the cases ending in recovery amounted to about 10 per cent. (or less) of the total number.

The average given above is considerably affected by the figures relating to four or five farms on which outbreaks involving a mortality of only about 50 per cent. occurred. In some at least of these outbreaks there is reason to suppose that the character of many of the cases was affected by the fact that the grazing ground was changed almost immediately after the development of the first cases.

In outbreaks of a severe character, the few cases that recover are commonly some of those which have been the last to develop, and in most instances they develop after a change of grazing ground has been effected, but that has not always been the case.

In a number of outbreaks all the animals in a herd have been attacked, but in some instances only one or two animals out of a large herd have been affected.

(G)—*Sequelæ.*

It has generally been found that animals which recover from an attack of this disease are only very slowly restored to a normal condition, and complete recovery is not established for a period of months, except in very mild cases.

On a few farms it was reported that certain cows which had recovered from an attack of the disease four or five years earlier were still affected by any excitement. These cows appeared to be in good health; they had had several calves without difficulty, and they gave an excellent supply of milk. Under all ordinary conditions they behaved normally, but anything causing excitement, and especially driving them, caused them to lose their heads and become clumsy and unmanageable.

(H)—*Immunity.*

In no instance was it recorded that any animal had been known to suffer from two or more attacks of the disease, but this evidence was purely negative, and it was difficult to trace any cases in which it was possible to be reasonably certain that recovered animals had been exposed to reinfection.

The history of one small outbreak suggested that some protection was conferred by an attack of the disease. In this case nine cows and one calf were running together under identical conditions; seven cows and the calf contracted the disease, and only one cow and the calf recovered. The two cows which were not affected at all had both passed through an attack of the disease some five years pre-

vously, and whenever driven or excited they were still liable to display the symptoms already mentioned.

II.—EXPERIMENTAL DETERMINATION OF THE CAUSE OF THE DISEASE.

When this enquiry was instituted the available information relating to the disease allowed very few conclusions to be drawn with regard to its probable cause. The symptoms appeared obviously to arise from the action on the central nervous system of a toxin or poison, but there was little to indicate whether the hypothetical toxic substance was elaborated by some living organism which had gained access to the animal body, or whether it was present normally in some species of plant ingested by the cattle, or was formed in such a plant as a result of the invasion of its tissues by a parasite.

Throughout the course of the investigation it was attempted, as far as practicable, to explore simultaneously all the more probable hypotheses, and several more or less independent lines of enquiry were being carried on up to the time that one particular method yielded a positive result.

With respect to all the experiments to be described it is well to state here: (1) That the experimental animals in most cases were purchased specially for this purpose from farms on which the disease had never been known to occur, and that were not in the vicinity of any affected farms. Most of the remaining animals had been bred at the Veterinary Research Laboratory near Pietermaritzburg, at which the disease has never been known to appear spontaneously, and the balance had been purchased from various sources but had been at the laboratory, under constant supervision, for several years. (2) That where additional rations were given these were known to be above suspicion; throughout the whole period of these experiments many other cattle, utilised for experiments of a totally different nature, were being fed on the same food-stuffs.

The procedures that were adopted may conveniently be divided into direct and indirect (or, at any rate, less direct) methods of investigation.

(A)—*Direct Methods.*

As the methods mentioned under this head gave no positive results, it is proposed only briefly to indicate the nature and scope of the work done.

1.—*Attempts to Transmit the Disease by Inoculation.*

In a number of the earlier experiments the materials were taken on farms from naturally arising cases and transported to the laboratory, with a consequent interval before inoculation of from twelve to twenty-four hours; at a later date living cases of the disease were transported to the laboratory and the interval was reduced to an hour or less, or even, in the case of blood, to a few minutes.

Material was taken from animals which had been killed in various stages of the disease, and the following inoculations were performed,

the inoculated subjects being of the bovine species except where it is otherwise stated:—

(a) Blood, both citrated and defibrinated, was inoculated subcutaneously and intravenously, in quantities varying from 10 cc. to a litre. Later, direct transfusion of blood from the jugular vein of a living case to that of a healthy animal was tried.

(b) Portions of heart, liver, kidney, and spleen were finely minced and mixed thoroughly with normal saline solution; after sedimentation the supernatant liquid was inoculated both subcutaneously and intravenously.

(c) Rabbits were inoculated with 3 and 4 cc. respectively of cerebro-spinal liquid, and bovines received as much as 20 cc.; both subcutaneous and intravenous channels were tested.

(d) Brain tissue was ground into a fairly smooth emulsion with normal saline solution, and the emulsion inoculated.

(e) Portions of the wall of the abomasum and of the intestine were minced and mixed with normal saline solution, the supernatant liquid being withdrawn after a time and administered *per os* and subcutaneously.

(f) Ingested material taken from the various portions of the gastro-intestinal canal was mixed with water or normal saline, and administered by the mouth.

No positive results were obtained.

2.—*Bacteriological Examinations.*

(a) Many preparations, made from practically all the important fluids and tissues of the body, were examined microscopically, both in the fresh state and after fixation and staining by a variety of methods.

No micro-organisms of any kind were found in any preparations, other than those made from such regions as the olfactory mucous membrane and various parts of the alimentary canal. Examination of films made from these particular regions revealed what appeared to be the usual mixture of organisms.

(b) Attempts to cultivate micro-organisms from many different organs and tissues were made, and in all cases from animals killed for the purpose, subjects being chosen in different stages of the disease; many different media were utilised. Owing to pressure of other work and lack of convenient apparatus little was done with anærobic cultures, although more or less anærobic conditions were produced in a number of instances by such methods as that of Smith and Tarozzi, and by the use of glucose, shake-cultures, great depth of medium, and the action of a supernatant layer of paraffin.

All tubes and plates remained sterile after inoculation with blood or cerebro-spinal fluid, or with material taken from such organs as the brain, cord, liver, spleen, and kidney, except in a minority of cases in which obvious contamination had occurred.

3.—*Examinations for Macroscopic Parasites.*

The several different helminths encountered at *post-mortem* examinations appeared here, with one possible exception, to have no particular significance.

With respect to *Cæphalogostomum radiatum*, it appeared at one

stage of the enquiry that these worms were present in every case of the disease, and that not only were the nodules in the intestinal submucosa very numerous, but that the number of worms free in the lumen of the bowel was generally large, and sometimes really huge. Moreover, in many cases the intestinal mucosa showed considerable hæmorrhage and evidence of local inflammation, in areas displaying numerous perforations from the underlying nodules. It was felt that these worms merited some attention, although the available literature lent no support to the suggestion that they might be directly connected with the causation of such a disease. It appeared to be conceivable that an abnormally heavy infestation might reveal the existence of a toxin, the action of which was masked when only small quantities were absorbed, or that the worms were of some importance on account of the opportunity afforded to some micro-organisms to invade the animal tissues through the numerous injuries to the intestinal mucosa.

Large numbers of the free parasites were obtained from the contents of the ileum and large intestine by repeated washing and sedimentation, and various extracts were made and inoculated without definite result.

Young larvæ in large numbers were obtained from the excreta of heavily infested animals, and, when no further development appeared to be occurring in the larvæ, attempts were made to infest young bovines with very large numbers of them. In one instance a yearling bovine received by the mouth a suspension in normal saline solution of thousands of such larvæ, and in another instance a similar suspension was applied on the surface of a compress to a large shaved area of skin. In both cases no developments were noted, and this work was suspended, further observations having shown that on certain farms it was difficult or impossible to find any *œsophagostomes* in cattle affected with "pushing disease."

Of macroscopic parasites other than helminths, only certain ectoparasites (ticks and flying insects) were found or known to infest the animals, and there seemed to be little chance of obtaining results in this direction.

4.—*Botanical Investigations.*

It appeared to be desirable that botanical surveys should be made of a number of affected farms, and particularly of the more limited areas that could be associated fairly definitely with the appearance of the disease. I therefore approached Mr A. O. D. Mogg, Plant Ecologist to the Division of Veterinary Research, who readily undertook to make such surveys whenever possible, and to point out any species which should be regarded with suspicion.

Even in connection with the flora of Great Britain and other European countries, our knowledge of poisonous plants is still in a very unsatisfactory stage, and reference to almost any work dealing with poisonous plants shows that the majority of the species mentioned have never been definitely shown to possess the properties of which they are accused. The evidence on which they have been associated with cases of poisoning (or supposed

poisoning) appears often to have been of the flimsiest character. It is therefore only to be expected that our knowledge of the South African flora, from the toxicological point of view, should still be very superficial and imperfect; some interesting and important discoveries have been recorded, but the workers in this vast field have been comparatively very few.

In this particular case Mr Mogg very naturally found many plants that could be classed as suspected on account of their botanical affinities with other plants known or alleged to have proved poisonous, but the number of such plants was far too large for direct feeding tests to be made at all. Similarly, a list of the plants common to all the various affected areas would have provided far too many species which, for divers reasons, might be regarded as inviting suspicion. It was not found possible to obtain any useful guidance by comparing the flora of the vleis on affected and unaffected farms, and eliminating all common factors. It was therefore considered that direct botanical investigations offered little hope of an early solution to the problem, apart from the fact that there were no grounds for assuming that the disease was necessarily caused by the ingestion of any particular plant. It was decided to make a few plant-feeding tests, however, in the hope that by good fortune the right plant (if such a plant existed) might be included. Cattle were made to ingest considerable quantities of several plants selected by Mr Mogg, and also a few plants suggested by different farmers, but no positive results were obtained. It may be remarked that on various occasions European farmers and also natives pointed out plants which they believed to be poisonous, but that in no case was *Matricaria nigellæfolia* considered to be other than a common and quite harmless weed.

(B)—*Indirect Methods.*

1.—*Experiments to determine the Channel of Entrance of the Cause of the Disease.*

Field Experiment I.—This work, which was commenced in October 1919, after the association of the disease with vleis had been fairly definitely established, was carried out at St. Ives, in the very large Lions River vlei to which reference has been made.

For this purpose thirty-five young cattle were taken by train from an area free from the disease, muzzled (with ten exceptions) as they were taken from the trucks, and driven to the St. Ives homestead. The ten unmuzzled cattle were driven to the vlei paddock and left there as free-grazing control animals, and the muzzles were removed from the remaining twenty-five animals, which were then allowed to graze in a hill paddock. From the beginning of November seventeen of these animals were caught in a kraal early each morning, muzzled, and turned into the vlei camp for the day; each evening they were driven to the kraal, and after removal of the muzzles were turned into a hill camp to graze during the night. The muzzles did not interfere with drinking, but prevented grazing almost completely; it was only very occa-

sionally that an animal was seen to succeed in securing a few stiff blades of grass.

It was hoped in this way to determine whether the disease was acquired during the process of grazing, or whether it was independent of this factor. Should the sequence of events indicate the advisability of such measures, it was proposed to institute further muzzling experiments in which the method would be modified in various ways, and also experiments designed to test the possibility of the entrance of the causal organism or toxic substance through the skin.

No results were obtained in this first muzzling experiment, but this line of enquiry would doubtless have yielded positive information had it been pursued for a sufficient length of time.

The muzzled animals were kept in the vlei by day for only a few weeks, and on 1st December the experiment was abandoned, the results obtained by other methods having rendered it unnecessary. The animals were then allowed to run entirely in the hill paddock unmuzzled, and no cases of the disease developed amongst them.

The grazing control animals were left in the vlei for some weeks longer, and when removed to a hill paddock they had been in the vlei for more than sixty days. One of the animals had died from acute tympanites within a day of its arrival on the vlei, but the other nine animals had remained healthy, and they showed subsequently no symptoms of the disease.

2.—*Localisation to Definite Areas.*

(a) *Localisation to Vleis or Swamps.*

Field Experiment II.—This experiment was instituted at a farm on which a very severe outbreak had occurred during the period November 1918 to January 1919.

The history of this outbreak, in conjunction with that of outbreaks at St. Ives and elsewhere, suggested that the disease in all cases had probably been contracted in one particular paddock, a strip of ground enclosed on three sides by ordinary wire fences, and of a shape approximating to that of a long narrow wedge. At the narrow end of the wedge the unfenced boundary was formed by the bank of a stream of water of sufficient size to form an efficient barrier to cattle under ordinary conditions. The stream was bordered by a belt of marsh or streambank vegetation which varied considerably in breadth and character, and succeeding this there was a strip of more or less flat and low-lying ground with vegetation differing from that of the actual marsh, and also from that of the higher ground. Finally, the greater part of the paddock was high ground.

A fence, with a gate in it, was erected along the summit of the first more or less abrupt ridge, so as to divide the camp into an upper portion, containing only hill grazing, and a lower portion with the two belts of vlei vegetation and a small amount of hill grazing; it was not practicable to make the division absolute.

Eighteen cattle from a clean area were divided into three lots of six animals, and it was arranged that one set should remain continuously in the hill division, another set in the vlei portion,

and that the third group should graze in hill and vlei camps on alternate days.

Owing to the distance of the farm from Pietermaritzburg I was able to inspect the animals only at rather long intervals, and I had to rely on the owner to carry out my instructions, and to notify me of any developments requiring my presence.

On account of the abnormally dry season that followed, the experiment was somewhat complicated by the fact that after a time the animals, especially in the small vlei camp, were unable to obtain a reasonable maintenance diet, and they were losing condition rapidly. As a matter of fact this circumstance was really favourable to the end in view, and represented an unusually extreme degree of the conditions which most commonly lead to the appearance of the disease; moreover, the position could have been met by giving the animals rations of artificial foodstuffs, sufficient to prevent actual starvation, but not so liberal as to discourage close grazing.

Unfortunately the owner of the farm, without awaiting my instructions, decided to remove the cattle and to burn the veld in the paddock, in order to provide early spring vegetation for a resumption of the test. This was done on 11th August, and on the following day two of the cattle were found to be showing early symptoms of the disease. Unfortunately the cattle had been transferred to a large paddock that was bordered by the same stream, and, although the cultivation of crops had here reduced the vlei grazing to a very small area, the presence of the latter could not be ignored. The cattle had to be left in this second paddock for eleven days (*i.e.*, until 22nd August), and were then removed to a farm known to be free from the disease.

The course of events, as regards the incidence of the disease, may be summarised thus: (*a*) Of the six animals grazing in the vlei, two died from the disease, three were distinctly affected and recovered, and one was slightly affected for a few days. (*b*) Of the six animals with access to both paddocks, one died from the disease and two suffered from very mild attacks and recovered. (*c*) Amongst the six animals grazing in the hill paddock, no cases occurred.

It may be remarked that, subsequent to the first two cases developing on 12th August, three further cases had developed by 22nd August, the day on which the animals were removed to a clean area, and four cases developed subsequent to their arrival on that area. Two cases developed on 25th August, three days after their arrival and fourteen days after the removal from the experimental camp.

It appeared to be almost certain that the disease had been contracted only in the vlei portion of the experimental paddock, and that one could probably assume that no cases should be attributed to anything acquired during the sojourn in the second paddock. This assumption involved the existence of a period of incubation which might be as long as fourteen days. These conclusions agreed well with the evidence previously furnished by Mr Raw, and they were supported by further evidence (from natural outbreaks) which became available during August and September 1919.

I now decided to attempt to localise the disease far more narrowly, and to endeavour to obtain cases amongst animals tethered in a vlei.

(b) *Localisation by the Method of Tethering.*

Field Experiment III.—The first tethering experiment was carried out on the large Lions River vlei at St. Ives. On 6th September six young cattle from the Allerton laboratory were sent by train to a station close to the farm, and on the following day they were muzzled (while still in the railway truck) and then driven to the vlei.

The animals were then secured by ropes to stout iron pegs about 2 feet in length, the pegs being driven firmly into the ground. The ropes had a length of rather more than 30 feet, and in all instances they were attached to the horns, but in a few cases it was afterwards found necessary to secure them to a collar. In this way an animal was forced to graze down a circular area with a radius of from 28 to 29 feet, and when it became necessary the peg was moved so as to allow another circular area to be grazed, the untouched space between the successive areas having generally a minimum breadth of only a few feet. Special emphasis was laid on the necessity for the very close grazing of each patch, and no animal was moved until it was quite evident that a longer stay on that spot would involve suffering and excessive loss of condition without any commensurate gain with respect to close grazing.

Owing to the distance from the laboratory my supervision was limited to fairly frequent visits of inspection, but the owner (Mr W. G. Raw) superintended all movements and kept the necessary records. The strict enforcement of the closest possible grazing was so well observed that the grazed circular patches were most clearly demarcated for months after grazing on them had been discontinued.

The details of the animals, and of the selected sites, are as follows:—

Animal A. Cow. On grass-land, with access to temporary swamp, which later dried up, necessitating watering with a bucket.

Animal B. Cow. Started close to A, but was moved gradually in the opposite direction, and later had access to permanent swamp with tall reeds.

Animal C. Heifer. On the border of a permanent reed swamp from the first.

Animal D. Yearling ox. On drained vlei, and receiving river water from a bucket.

Animal E. Heifer. On the border of a small swamp, with less coarse type of reed vegetation (at the commencement).

Animal F. Bull. Started close to E, and was moved in the opposite direction; later it was on natural vlei, partially drained, and had to be watered from a bucket.

Of the six tethered animals, only one contracted the disease under the conditions described above. On 1st November animal D showed the first signs of general malaise, and "pushing disease" could be definitely diagnosed on the following day. When the first symptoms of the disease were shown animal D had been

in the vlel for fifty-five days, and during this period it had been tethered on seven different areas (which in subsequent references are designated areas D1 to D7).

Animals B, C, and E were removed entirely from their original areas on 13th November (*i.e.*, eleven days after D had developed the disease), and their subsequent history is described in connection with Experiment III. a.

Animals A and F were kept on their original grazing grounds, being moved when necessary in the directions originally intended, until 23rd December (*i.e.*, for a total period of 107 days. They were then removed and turned loose in a hill camp, and they subsequently remained perfectly healthy.

Experiment III. a.—On 13th November it was arranged to enquire further into the distribution of the causal agent, whatever its nature, by tethering a few cattle around the grazing areas of D, and at a short distance from them. Accordingly animals B and C were taken from their previous grazing zones and tethered about 20 yards from the position of D, one on each side, while E was tethered on the river bank a little beyond the new position of C.

This brought these animals into the Matricaria zone (*see* Experiment III. c), and seventeen days later, when the importance of the plant had been demonstrated, the new sites for the tethering pegs were deliberately chosen so as to induce the maximum amount of grazing on it. Both C and E had become infected, however, before this special precaution was taken. Early signs of the disease were observed in C on 13th December, thirty days after the rearrangement of the grazing areas, and the animal was in a state of deep coma, and was slaughtered nine days later.

On 19th December animal E displayed signs of uneasiness and difficulty in drinking, and on the following day pronounced quivering of the ears was seen; the animal was destroyed in an advanced stage of the disease after a course of ten days.

The facts in connection with the contraction of the disease by C and E were perfectly in accord with the deductions based on the results of Experiments III. b and III. c.

It may be noted that animal B was kept in the danger zone for forty days, and during that period it must have consumed a very considerable amount of the above-mentioned plant, but at no time subsequently were any signs of ill-health observed. As this was the only resistant animal encountered during the course of these investigations, it was intended to perform further tests quantitatively, but I was unable to arrange the test before leaving Natal.

Experiment III. b.—The object of this test was, by having the various circular areas of D grazed down separately, to ascertain whether the disease was connected with some factor present on only one or two of those areas, or whether the factor was distributed more or less equally among them. It was quite possible that a purely negative result would be obtained, and that would have pointed most probably to the merely temporary (or possibly cyclical) presence of the causal factor at the time when D had become affected. It was decided to ignore areas D6 and D7, at least temporarily, as they had been grazed only during the twelve days preceding the appearance of symptoms in animal D,

and there were grounds for assuming the occurrence of an incubation period of several weeks.

Five yearling bovines grazing in a hill paddock were caught, muzzled, and led to the vlei; one animal was then tethered on each of the areas D 1 to D 5, and the muzzles were removed. Each animal was kept on its area until the latter had been grazed down very closely. It was then muzzled, led to the hill camp, and allowed to graze freely day and night.

The results were as follows:—

Animal 265. Tethered on D 1 for 20 days—remained healthy.

Animal 247. Tethered on D 2 for 10 days—remained healthy.

Animal 240. Tethered on D 3 for 20 days—Showed early symptoms 22 days after its removal from D 3, and was killed 20 days later after a very characteristic attack.

Animal 268. Tethered on D 4 for 10 days—remained healthy.

Animal 271. Tethered on D 5 for 18 days—early symptoms 18 days after removal from D 5, soon developed into a typical case of violent type, and had to be destroyed after a course of 10 days.

The results of this experiment would have provided a certain clue to the solution of the problem had not the solution itself been attained some weeks earlier through the performance of Experiment III.c. In any case they abundantly confirmed the results of Experiment III.c.

The only outstanding difference between areas D 3 and D 5 on the one hand, and areas D 1, D 2, and D 4 on the other, was connected with the distribution of one particular plant (*Matricaria nigellæfolia*), which was very abundant on D 3 and D 5, relatively scarce on D 2, still more so on D 1, and represented on D 4 only by one tuft.

Experiment III.c.—After it had been decided to perform Experiments III.a and III.b, it was felt that additional work, possibly capable of yielding valuable information very quickly, might be based on the assumption that there is a period of incubation of approximately four weeks.

This provisional assumption was based in the first place on the evidence supplied by Mr Raw, and no facts had come to light which were in any way in conflict with it.

Reference to the records of animal D (Field Experiment III.) showed the following position:—

D was on area D 1 for 9 days, *i.e.*, from the 55th to 46th day before early symptoms appeared.

D „ D 2 „ 11 „ *i.e.*, from the 46th to 35th day before early symptoms appeared.

D „ D 3 „ 11 „ *i.e.*, from the 35th to 24th day before early symptoms appeared.

D „ D 4 „ 6 „ *i.e.*, from the 24th to 18th day before early symptoms appeared.

D „ D 5 „ 6 „ *i.e.*, from the 18th to 12th day before early symptoms appeared.

D „ D 6 „ 8 „ *i.e.*, from the 12th to 4th day before early symptoms appeared.

D „ D 7 „ 4 „ *i.e.*, during the last 4 days before early symptoms appeared.

The above-mentioned assumption would indicate that animal D had most probably contracted the disease while grazing on area D 3, and that by taking the areas D 2 to D 4 into consideration one should be making sufficient allowance for any probable variations in individual cases.

It was therefore attempted to observe some difference between area D 3 on the one hand (as a positive area), and areas D 1 and 2 on the other hand (as negative areas), and also between areas D 2, 3, and 4 (positive) and area D 1 (negative). Further negative controls were furnished by the first three, four, or five areas (according to the dates of movement of animals A, B, C, E, and F). When areas D 1 to D 4 were examined from this point of view, it appeared that, apart from any differences in the composition of the vegetation, there were no other factors which could be seen or expected to vary, and that, unless the cause of the disease was necessarily connected with some particular species of plant, its occurrence on only one or two of these areas was most probably quite accidental, and might be only temporary.

With respect to the vegetation on the four areas there was one very striking quantitative difference that could hardly fail to attract attention. A considerable portion of the area of D 3 was occupied by a luxuriantly-growing plant with a very strong and fragrant odour, and this plant had obviously been well grazed down. Inspection of the four areas revealed differences in the distribution of the plant which are expressed very roughly in my field notes in the following terms: "D 1—only a few tufts seen; D 2—rather more than in D 1; D 3—very much; D 4—only one large tuft seen."

Inspection of all the earlier grazing areas of animals A, B, C, E, and F, failed to reveal any of this plant at all (although subsequently further search showed the presence on one area, A 2, of two small tufts that appeared not to have been touched).

On this evidence it was decided at once to institute a feeding test with the plant, of which I then knew nothing apart from its distribution in these small areas; at a later date flowering specimens were identified for me, by the Division of Botany at Pretoria, as *Matricaria nigellæfolia* D.C.

On 4th November two yearling bulls, numbered 238 and 243 respectively, were selected from the herd in the hill paddock, and confined together in a loose box. Here they received daily an unweighed quantity (approximately 10 lbs) of freshly cut *Matricaria nigellæfolia* from the vlei, supplemented by the requisite quantity of grass freshly cut in a small home paddock, which was high and well-drained, and known to be free from infection.

Bull 243 undoubtedly consumed considerably more than half of the daily ration of *matricaria*, being very much stronger and heavier than No. 238, and very aggressive.

The feeding was continued for ten days, and the two animals were then turned out to graze again in a hill paddock, where they were kept under daily observation while developments were awaited.

On 29th November No. 243 was noted by Mr Raw to be showing vague signs of ill-health, and on the following day typical symptoms developed. I was unable to visit the farm until the third day (1st December), and, although earlier in the morning the animal

had been "pushing" violently, by the time that I was able to inspect the case it was unable to stand and rapidly becoming comatose.

On the same day No. 238 was found to be grinding the teeth excessively and salivation was noticeable; two days later it was seen to be wandering restlessly throughout the greater part of the day, the gait was clumsy and languid, and there were signs of impaired vision. Symptoms of muscular inco-ordination developed rapidly, and later the animal repeatedly displayed the "pushing" symptom; it was ultimately destroyed on 13th December when comatose.

In both cases *post-mortem* examination revealed the presence of the usual naked-eye features observed in natural cases of the disease.

The disease appeared therefore in both of the animals fed on *Matricaria nigellæfolia*, and in No. 238 the duration of the disease and the symptoms shown were such as are very commonly seen in natural cases; in No. 243 some very characteristic symptoms were noted, but the course of the disease was quite exceptionally acute. In the two cases the first symptoms were observed respectively twenty-five and twenty-seven days after the commencement of the special feeding, and fifteen and seventeen days after its suspension.

There was no reason to suppose that the disease might have been contracted in the hill paddock either before or after the period of special stable feeding. In addition to the long negative history furnished by the owner, and the other facts in this connection that have already been mentioned, there was the fact that throughout the period of these experiments the hill paddocks were grazed with impunity by twenty-two control animals of the same age, type, and origin as the two concerned, and a very much larger herd of cattle belonging to the owner of the farm was also grazing there.

Field Experiment IV.—A second tethering experiment was commenced on 16th October in the small vlei subdivision described in connection with Experiment II. Six animals were tethered, and two loose controls were allowed to run freely over the vlei area.

No cases of the disease developed. Owing to the distance of the farm from the laboratory, I was able to inspect the paddock only rather infrequently, and the failure of these animals to contract the disease may, in my opinion, be attributed to the fact that was quite obvious throughout the course of the experiment, viz., that the animals were not kept sufficiently long on one area and compelled to graze down the less attractive plants. It was found that all the tethered animals had had access to at least a small quantity of *matricaria*, and that in two cases the quantity was considerable; but on most of the patches examined the tufts of *matricaria* showed few or no signs of having been bitten off at any time, and in no case had they been at all extensively fed down, as was the case at St. Ives.

When Experiment III.c had given such definite results, which shortly afterwards were supported very fully by those obtained in Experiments III.a and III.b, it was decided to conduct all future work at the Allerton Laboratory, near Pietermaritzburg. Confirmation of the feeding test (Experiment III.c) by another carried out in a clean area was clearly desirable, but, while arrangements were

being made for such further experiments, it was thought desirable to visit as many as possible of the known affected farms.

Matricaria nigellæfolia was found easily enough on all of the affected farms that could be visited, and no facts inconsistent with the suggestion that the disease is due to the ingestion (probably long-continued) of the plant came to light. Specimens of the plant were sent or exhibited to many owners of affected farms that I was unable to visit personally, and also to several Government Veterinary Officers in affected districts. In only one case was it reported to me that there was any difficulty in finding the plant on an affected farm, and in that instance there had been no cases of the disease for months previous to this search.

I believe that it would be wrong to attribute much importance to this one case, partly because it was not certain that the disease which had occurred on the farm (situated far from the areas in which I had worked) was identical with the one investigated, but more particularly because a considerable quantity of the plant may be concealed in midsummer by the vigorous growth of other plants. Moreover, the area over which *matricaria* grows is subject to constant fluctuations (related to changes in the humidity of the soil), and I have on occasions found it very difficult to discover the plant in places in which I had myself noticed an abundance of it only a few months earlier.

On the other hand, there was no doubt at all that the plant occurred, in some instances abundantly, on many farms on which the disease had never been known to appear. It was considered that this fact might be due to differences in constitution existing between the specimens of the plant found in various situations, whether arising directly from alterations in the environment, from the occurrence of two or more varieties of the species, or from the presence in some instances of a parasitic organism, either in or on the plant. If any parasitic organism was present it did not give rise to any noticeable macroscopic changes in the plant, nor did it interfere with the vigorous growth of the latter.

The bulk of the evidence suggested strongly that the conditions under which the animals lived were chiefly to be held responsible, and that, whereas in some cases the animals on an unaffected farm had no opportunity of eating *matricaria* (in spite of its presence elsewhere on the farm), in most instances the important point was that there was no inducement or compulsion for them to do so.

A very considerable amount of the plant was found to be growing on land attached to the Allerton Laboratory, although no spontaneous case of the disease had ever been observed there. The land is in two entirely distinct portions, separated by a private property and a public road, and the laboratory, stables, and experimental pens stand on the smaller division, which also includes the three small paddocks utilised for experimental cattle in the incubation stage (*see p. 292*). This division was repeatedly searched, but no *matricaria* was found in it, and it is quite certain that on no occasion was any *matricaria* eaten by the experimental cattle, other than the amount furnished to them in the course of the experiment. The larger portion, which is subdivided into many small paddocks, was never grazed by any cattle in *matricaria* experiments, but there were

always many other cattle grazing on it. The only considerable amount of the plant was found in one small camp, to which no laboratory cattle had been allowed access for a long time; here there was a vigorous growth of *matricaria* over a considerable area that in normal years was covered by water and formed a large pond. This camp was used as a source for the supply of the plant given in a number of the feeding tests mentioned in Section IV. (the plant being the type species). *Matricaria* was present in various other small camps of this larger division of the laboratory grounds, but only in very small amount.

I do not believe that during 1918-19 any laboratory animal had access to a sufficient amount of the plant to cause the intoxication, but it is probable that this has not always been the case in past years, during cycles of heavier rainfall, and that the occurrence of cases has been prevented more especially by the relatively small number of cattle carried by an area with an abundance of fairly good grazing.

III.—*MATRICARIA NIGELLÆFOLIA* AND ITS DISTRIBUTION IN THE NATAL MIDLANDS.

Matricaria nigellæfolia D.C. belongs to the family *Compositæ*, tribe *Anthemidiæ*, sub-tribe *Chrysanthemidinæ*.

The flowers have a yellow or yellowish-brown central disc and comparatively very small white rays, which are few in number and often lost at a fairly early stage, so that flowers are often seen with only one or two, or even no rays. The leaves are green and much divided. The plant, whether in flower or not, has a bitter taste, and a very strong, rather agreeable and characteristic odour. In the Lions River area the plant has an average height of from 6 to 8 inches, although in unfavourable situations its height is considerably less, and on the bank of the river some plants attain a height of more than 1 foot. The *matricaria* found around Pietermaritzburg is a much larger and coarser plant, and this was identified by Mr Mogg as the type species, *Matricaria nigellæfolia* D.C. He identified the small form from Lions River as the variety *B tenuior* D.C. Both forms of the plant are found only in certain situations, and their distribution is obviously dependent on that of water.

The plant does not actually grow in water, and submersion soon causes the appearance of obvious degenerative changes. On the other hand, it never flourishes in dry soil, and, although on occasions a few stunted and unhealthy-looking plants were found in soil that was very dry, they occurred in situations that would undoubtedly be very damp during years of normal or heavy rainfall.

The plant appears to thrive best in two particular situations:—

(a) In mud in the process of drying up, after the receding of water from a previously submerged area; ditches and drainage channels subject to occasional flooding are evidently very favourable situations.

(b) On ploughed land, where the humidity is sufficient. The plant was sometimes found in great abundance on ploughed land, although it was only scantily represented in the undisturbed vegetation surrounding the ploughed area.

It appears that the plant is an early and energetic colonist of bare places, where the ground is sufficiently damp, and it is of interest to note here that two species of *matricaria* indigenous to Great Britain (*Matricaria inodora* or mayweed, and *Matricaria chamomilla*, white or German chamomile), although they have not the same requirements with respect to moisture as *Matricaria nigellæfolia*, are also colonists of bare places, and are recognised weeds of arable land.

There is much to suggest that the seed is spread by the agency of water, but it is recognised that the occurrence of the plant on the banks of rivers and streams, and on frequently flooded ground, does not prove this to be so, as these places may only represent the situations in which the seeds, dispersed by other means, encounter the particular conditions necessary for germination and growth.

In connection with the dispersal of fruits by rivers and ocean currents, Small (3) remarks that no case of such dispersal in the *Compositæ* is quoted, and he refers later to "the meagre list of water-dispersed *Compositæ*." He is considering here, however, the dispersal of seed to great distances, and, until there is experimental evidence bearing on the point, there seems *a priori* to be no reason to exclude the possibility that water plays an important rôle in the local dispersal of *Matricaria nigellæfolia*.

Dispersal by wind probably occurs, at least to some extent, and it may play an important part. There is no evidence bearing on the question of dispersal by animals as far as this species is concerned, but the observations on the fate of ingested seeds (quoted by Brenchley (4)) which have been made by Hansen with *Matricaria chamomilla* and by Petersen with *Matricaria inodora* suggest that this possibility cannot be ignored.

The plant has no commonly recognised name amongst the Europeans in Natal as far as I could ascertain. The natives in different districts term it "msolo" and "mhlonzan," and it appears to be very well known to them and to be used very extensively for medicinal purposes.

IV.—FURTHER INVESTIGATION OF MATRICARIA INTOXICATION.

(A)—*Experiments with Cattle.*

The experiments to be described were all conducted at the Allerton Laboratory, and the precautions that were taken to avoid errors arising from the choice of naturally-affected animals, or the feeding of harmful agents along with the supplementary rations, have already been mentioned.

Each experimental animal was placed in a separate pen, containing a wooden box or trough for the reception of foodstuffs. The animals were watered with buckets, the water in all cases being obtained from the same source as that used for all the other animals at the laboratory.

In all cases animals were starved for a period of from eighteen to twenty-four hours before beginning the test, and some animals had to be starved for longer periods and on several occasions. The

usual procedure was only to give supplementary rations of ordinary foodstuffs after the matricaria ration, or a considerable proportion of it, had been consumed.

Weighed amounts of matricaria were given to the various animals, and after a suitable interval the amounts which remained uneaten were also weighed separately and recorded. In some instances the animals displayed such reluctance to eat the plant, in spite of hunger, that it was necessary to cut it up and mix it with other food materials.

At the conclusion of the experimental feeding each animal was turned out to graze, and for this purpose I utilised three very small paddocks which were immediately adjacent to the laboratory, and in which no matricaria was found after a number of very searching examinations. Moreover, these paddocks were utilised from time to time for other cattle, and no cases of the disease occurred in any cattle other than those subjected to experimental matricaria feeding.

In the first instance a series of feeding tests on twelve cattle was arranged; in every case a positive result was obtained, and the main fact disclosed by the field experiments, that "pushing disease" is an intoxication produced by the ingestion of *Matricaria nigellæfolia*, was thoroughly confirmed.

The more important data relating to these twelve experimental cases are given in Table I., but a number of special points connected with the tests and the observations made during their performance are dealt with more fully in the succeeding section.

1.—*Source, Varieties, and Condition of the Matricaria used.*

Both the type species and the variety *B tenuior* were tested and both reproduced the disease, but it is impossible to offer any definite opinion as to their comparative toxicity. This point could not be determined without conducting a larger number of tests specially arranged for that purpose, but the facts on the whole suggest that the type species probably contained less of the toxic substance or substances. The variety was obtained from St. Ives, freshly-cut material being sent daily to the laboratory by train; it was very often fed to animals about twenty-four hours after having been cut, but at times there was a further interval of two and even three days. When not fed immediately, the plant was removed from the bags and spread out on a cement floor, in order to prevent fermentation and the growth of moulds. The type species was procurable in the laboratory grounds, and was fed when quite fresh.

2.—*Readiness with which the Plant was Eaten.*

The freshly-cut plant was nearly always taken more readily than matricaria that had been cut a day or several days previously; in all experimental cases a preliminary period of about eighteen or twenty-four hours' starvation was observed, and is to be understood where not specifically mentioned.

The amounts consumed within twenty-four hours (after the preliminary starvation) by nine animals that were given 10 lbs. of fresh, or almost fresh, matricaria were: 10 lbs. in two cases, $8\frac{1}{2}$ lbs. in one case, 6 lbs. in two cases, 3 lbs. in one case, and none at all in three cases. In one instance, under similar conditions, another animal was

TABLE I.

Number of Animals.	Description.	Material used in Test.		Details of Special Feeding.			Period to Appearance of Symptoms (in days).		Chief Symptoms. (Italics indicate symptom particularly well shown.)	Termination.	Period from Onset of Symptoms to Death (in days).
		Source.	State.	Total Amount consumed (in lbs.).	Total Period of Feeding (in days).	Number of Days on which consumed.	From Beginning of Feeding.	From End of Feeding.			
A.—EXPERIMENTS WITH NORMAL ANIMALS.											
235	Ox	Allerton	Fresh	157	10	10	23	13	Tame, salivation, head carried low, staggering gait, <i>violent pushing</i> , finally <i>tonic convulsions</i> if touched.	Killed in very violent stage	8
123	Cow	St. Ives	Kept 1-3 days	100	20	17	27	7	Salivation, lachrymation, lateral swaying, <i>violent pushing</i> , grinding of teeth, etc.	Killed when comatose	7
140	Cow	"	"	80½	21	15	38	17	Tame (originally vicious), <i>difficulty in drinking</i> , very <i>violent pushing</i> , grinding of teeth.	"	8
253	Ox	"	"	53	9	9	32	23	Restless, swaying, crossing of legs, knocking of fore fetlocks, later on knees, <i>loud grinding of teeth</i> .	"	9
264	Heifer	"	"	40½	9	9	32	23	Staggering, very little pushing, grinding of teeth, well-marked <i>knocking of fore fetlocks</i> , later on knees.	"	7
246	Ox	"	"	21½	5	5	47	42	Salivation, staggering gait, <i>knocking of fore fetlocks and knees</i> .	"	17
48*	Cow	Allerton	Fresh	20	½	1	—	—	Remained healthy.	—	—
153	Bull	{ St. Ives { Allerton	Autoclaved	75 } 103 28 }	26	21	26	0	Salivation, lachrymation, grinding teeth, <i>pushing</i> .	{ Killed when { comatose }	3
196	Ox	{ St. Ives { Allerton	"	40 } 100 60 }	25	20	27	2	Grinding of teeth, swaying, <i>violent pushing</i> , <i>tonic spasms</i> .	"	9
261	Heifer	St. Ives	Hay	42	20	17	20	0	Salivation, head kept low, <i>violent pushing</i> , etc.	"	4
193	Cow	{ St. Ives { Allerton	"	12 } 53 41 }	22	18	24	2	{ <i>Shaking and quivering</i> of whole body, swaying, salivation, head low, grinding of teeth. }	"	5
B.—EXPERIMENTS WITH ANIMALS THAT HAD RECOVERED FROM A PREVIOUS ATTACK.											
202	Heifer	{ St. Ives { Allerton	Kept 1-3 days Fresh	123½ } 143½ 15 }	28	24	23	1	{ <i>Quivering ears</i> , grinding teeth, <i>knocking of fore fetlocks</i> , well-marked inco-ordination.	{ Killed when { comatose }	6
203	Heifer	{ St. Ives { Allerton	Kept 1-3 days	142½ } 142½ }	28	24	28	0	<i>Quivering ears</i> , grinding teeth, staggering, fore feet lifted high, balance uncertain—but <i>sensible</i> .	Died	7

* This case is inserted here for comparison, but did not form one of the first series of tests. The animal was fed with matricaria in good condition, however, at an earlier date than that of the negative experiments mentioned on p. 301.

offered 20 lbs. of the plant on the first day, and consumed the whole quantity very readily, but this seemed to be an exceptional case.

The periods of partial starvation required to induce the above-mentioned nine animals to consume the first 10 lbs. of the plant ranged from less than one day to a week, the average period being three days. The periods required to compel the consumption of the second 10 lbs. in seven of the same animals varied from about twelve hours to two days, with an average of one and a third days; for the third ten lbs. the average period in five of the same animals was about one day, with variations from about eighteen hours to two days.

The observations made on the experimental cattle may be summarised thus:—

(a) Some degree of compulsion was always required, but the amount necessary to induce the commencement of matricaria feeding varied greatly in different cases.

(b) In all cases animals were induced later to consume the plant more readily, and in some instances they were quite easily persuaded to eat comparatively large quantities (up to 29 lbs. per diem), whereas in other cases the increased consumption could only be maintained by the repeated application of even severe methods of compulsion; there were also cases of intermediate character in this respect.

(c) In none of these cases did it appear than an animal would eventually select the plant under conditions permitting free choice of food material, and in most cases it was clear that the matricaria was still regarded with some distaste, although accepted.

These observations agreed well with those made in the field, where it was seen clearly that the tethered animals in every case avoided matricaria when placed for the first time on an area containing it, and ate it only when the grass and other attractive herbage was becoming really scarce; it also appeared that the plant was rather more readily eaten when such an animal was afterwards transferred to further matricaria areas. Nothing was ever observed which could be interpreted as evidence of the formation of a matricaria habit.

In this connection one interesting observation was made during the course of the St. Ives tethering experiments (III. and III.a), the subject of the observation being Animal E. On the eighteenth day after its introduction to the matricaria zone, and eighteen days before the first symptoms of the intoxication appeared, this animal, which was then hungry, devoured matricaria just as readily and ravenously as it consumed freshly-pulled green grass. It was then found, however, that the animal would readily consume certain other plants that were much more distasteful to normal cattle than the matricaria. The conduct of this animal could not be explained as a mere manifestation of excessive hunger, for the same plants were repeatedly refused by other cattle of which the diet had been much more restricted than that of Animal E. It seems that in this instance there was no matricaria habit, as was at first thought to be the case, but that the heifer had largely lost the power to discriminate. This would indicate the rather interesting possibility that the consumption of matricaria (or of some toxicologically

similar plant) might lead to the eating of some other, and perhaps more rapidly acting, poisonous plant that would otherwise be avoided, and it is at least possible that such an action might be induced by an amount of *matricaria* which in itself would not prove fatal. This possibility acquires added interest in view of the recent discovery of the combination of factors responsible for the occurrence in cattle of *Lamziekte* (5), and some obscure cases of poisoning may perhaps be explained along these lines.

3.—*The Period of Latency.*

In the feeding experiments with the fresh plant, as shown in Table I., there was a period of latency, comparable to the incubation period of a microbic disease, which showed the following limits:—

(a) From twenty-three to forty-seven days after the commencement of the *matricaria* feeding, and (b) from seven to forty-two days after its suspension.

These figures agree well with Mr Raw's experience at St. Ives, that cases of the disease usually ceased to develop about four weeks, and exceptionally as long as six weeks, after the cattle were removed from the vlei. In certain cases the onset of the disease was so insidious that it was hardly possible to fix definitely the time of the appearance of the earliest symptoms. Of course the lower limit of (b) has no particular significance. With respect to the lower limit of (a), the minimum period within which the intoxication was induced by the feeding of fresh *matricaria*, it may be noted that in one animal fed on *matricaria* hay the symptoms appeared on the twentieth day.

4.—*Immediate Effects of the Ingestion of Matricaria.*

The feeding tests afforded opportunities of observing something that had not been seen in the field, and of which no reports had been received, viz., the immediate effects of the ingestion of the plant.

In rather more than half of the experimental cases no such effects were noted, but in the other cases the animals, at some time during the period of special feeding, displayed signs of digestive disturbance, and even of moderate abdominal pain. These effects were seen, in different cases, as early as the second day and as late as the eighth day of the test, and they were never really severe; they were never noticeable for a longer period than about twenty-four or forty-eight hours at the most, and in no case did an animal appear to suffer in this way on more than one occasion.

In all cases the animals lost condition during the special feeding, but it was difficult to estimate the proportion of this loss which could be attributed directly to the periods of starvation that had to be imposed. After the cessation of the special feeding a number of the animals improved considerably, but in other cases the animals continued to lose condition slowly until visible symptoms of the disease developed; after this the loss was rapid.

5.—*Symptoms and Course of Intoxication.*

With one exception, all the manifestations of the natural disease were reproduced in the experimental cattle by feeding them with

Matricaria nigellæfolia. The single exception was the peculiar nodding of the head that was seen only in a very few of the natural cases, but which was reported to be quite commonly shown in some outbreaks.

With this exception, and making due allowance for the comparatively small number of experimental cases, it can be said that the account already given of the symptoms observed in natural cases of "pushing disease" serves equally well to describe those seen in most of the experimental cases of *matricaria* intoxication. It was possible to follow the experimental cases more thoroughly and constantly, however, and many additional observations were made.

Attention was soon attracted to a peculiar symptom that had not been particularly well-marked in any of the naturally-contracted cases which had come under observation; this was an affection of the fore limbs which led to knuckling over at the fetlock joints, and even at the knees. This symptom was often noticed to occur in the later stages of ordinary acute cases, but it constituted one of the most striking clinical features of the cases set up by the ingestion of relatively small amounts of *matricaria*, and it was very noticeable during the course of the intoxication induced by feeding *matricaria* to animals that previously had recovered from a naturally-contracted (and comparatively mild) attack of "staggers." The first stage of this condition was shown by the tendency to stumble, so frequently observed in cases of all types, and in most cases nothing further of this nature was seen up to the time when the animal went down. In the particular cases mentioned, however, the tendency soon became much intensified, and the animals when driven were very liable to stumble, almost to fall, and then to recover the balance but remain standing with one or both fetlocks knuckled over completely, so that the anterior aspect of the extremity, from the fetlock to the toe, was in contact with the ground.

The condition was practically always first observed to affect only one (and on all occasions, in that case, the same) leg, although sooner or later both fore limbs were more or less equally involved. In many cases the tendency towards knuckling-over was first observed, or was seen most easily, when the animal was rising after having been down for some hours, and for some time exercise had a beneficial effect; when the animal had been driven for some minutes the knuckling-over and stumbling would often disappear completely for several hours. As the condition advanced it became increasingly difficult for the animal to rise from the fetlocks to the feet, and still later it exhibited increasing difficulty in rising from the knees to the fetlocks. During this period, however, it retained the power to move quite freely the upper portion of the limb, and it often seemed for a long time to be unaffected otherwise, and moved about on the knees eating quite well.

It is of interest to note that Hutcheon (6) recorded in Cape Colony a somewhat similar condition in connection with "krimp-ziekte," an intoxication following the ingestion of "klimop" (an *asclepiad*), and he stated that it was due to a gradual contraction of the flexors of the fetlock joint.

In matricaria intoxication there was no evidence of flexor contraction, and it was always very easy to extend the flexed joints by manipulation. The animal was unable to maintain them firmly extended, but they remained loosely extended as long as the animal's weight was supported more or less completely by other means. The condition appeared obviously to be one of paresis that was at first in most cases quite transitory, and that eventually increased in some cases to one of more or less complete paralysis, affecting particularly (and perhaps exclusively) the extensors of the carpal and metacarpo-phalangeal joints; it recalls the "wrist-drop" characteristic of a proportion of the cases of chronic lead poisoning in man.

In no case have I observed any special evidence of paresis or paralysis of the hind limbs.

With respect to the tendency to push the head against an obstacle, the experimental cases exhibited practically all the variations that have been recorded in natural outbreaks. The tendency to perform this act was very much slighter, however, in the cases set up by the ingestion of small quantities of matricaria; and in the cases induced in recovered animals, and in one of those due to the ingestion of matricaria hay, the pushing symptom was manifested only for a short time and on few occasions.

Under natural conditions, without the very close and almost constant observation to which these animals were subjected, the very few and brief bouts of pushing might very easily have escaped observation.

It was attempted to ascertain whether the act of pushing was deliberate or only accidental, and to what extent consciousness was retained. If deliberate, it might conceivably arise from efforts to maintain equilibrium, and at times animals are undoubtedly able to remain on their feet, with the weight thrown forward against a wall, when they would be incapable of maintaining their balance away from such a support. On the other hand, they frequently evince signs of a marked tendency to thrust with the head at a time when there is no evidence whatever of any difficulty in maintaining equilibrium, and the object against which the head is thrust is often quite unsuitable for such a purpose.

Observation showed that in less severe cases, and in the earlier stages of most cases, an animal actually seeks an object against which the head may be thrust, and that it derives much satisfaction from the performance of this act. This may be seen, moreover, at a time when the animal appears hardly to be affected in any other respect, and while it is still fully conscious of every sound or movement in its vicinity. It is perhaps possible that the animal suffers from headache, and that a certain amount of relief is obtained by local pressure.

It by no means follows that the action is always due to the same causes, or that it is always consciously and deliberately performed; in fully developed acute cases there generally appears to be serious disturbance of consciousness, and the impairment of vision may have rendered the attainment of any particular object quite accidental. In its later and more violent forms it is very possible that the action is due to stimulation to general muscular

activity while co-ordination is still effected more or less normally, but in the absence of the control of the highest cerebral centres. The effect of various forms of artificial stimulation is perhaps of some significance in this connection.

It is of interest to note that, as has been shown by Graham Brown, Forbes, and Sherrington: "When the intensities of the two opposing influences on the same centre are nearly equally matched, a rhythmic discharge results" (Bayliss, *Principles of General Physiology*, p. 498). Having regard to the fact that in matricaria intoxication the higher centres appear to be chiefly affected, and that there is disturbance of the normal mechanisms of inhibition (as evidenced by the exaggerated and diffuse responses to simple stimuli), it is not improbable that some centres are subjected to the simultaneous action of antagonistic stimuli which normally would not be of sufficient intensity to reach the centre at all.

It is perhaps possible that the forcible, but apparently purposeless or involuntary, forward movement seen in many acute cases and the violent pushing (often accompanied by a stepping movement of the legs) may have an origin similar to that of the stepping reflex observed in the above-mentioned experiments. The rhythmic nodding movement of the head may also arise in a similar manner.

In bovines the reflexes, with the exception of the pupil and eyelid, cannot very easily be studied, and it is rather difficult (in my experience) to obtain results that are accurate and really comparable, but such tests as were found to be practicable were applied on various occasions. Diminution or absence of response to stimulation in general was seen only in the final stage of most fatal cases. If an animal was tested when actually exhibiting nervous symptoms it was generally found to be very sensitive to tactile and painful stimuli, and perhaps abnormally sensitive to auditory stimuli, but it appeared to be relatively insensitive to visual impressions.

It was often impossible to obtain a definite and appropriate response to a given stimulus; thus an animal in the act of pushing (unless only mildly affected) would respond to all stimuli which had any effect at all by pushing more violently. Similarly, the various kinds of involuntary movements were increased and intensified by the different stimuli applied, and the appropriate responses were apt in many cases to be absent or masked; when present, they were usually exaggerated in degree.

When the reflexes were tested during quiescent periods they appeared usually to be normal, at least at first; on repetition of the stimulus there was in severe cases a tendency for the responses to become exaggerated and diffuse, and for further stimuli to provoke a renewed display of the manifestations of the active phases of the condition.

In one type of case the reflex excitability continued to increase up to the time when it was necessary to destroy the animal on account of its injuries. In such cases this irritability persisted for quite an unusual length of time after the cord had been completely severed in pithing, and the reflex movements excited by attempts to cut the skin were not only abnormally slow in disappearing, but were also very noticeably more violent than those

usually seen. In the majority of cases, however, the reflex excitability finally diminished until only very feeble or no movements could be elicited.

When an animal with very contracted pupils was placed in darkness the pupils were seen to expand very fully; re-exposure to light caused very rapid and excessive contraction to occur, and it seems that the myosis usually observed is an exaggeration of the usual pupillary reflex.

In the experimental subjects the weather was seen to exercise the same influence as that described in connection with naturally-contracted cases. It was not possible to determine the nature of the action on the animals, or whether it was particularly a light or a heat effect; the recorded temperatures of the animals lent no support to the suggestion that the effect might be due to disturbance of the heat-regulating mechanism.

It is probable that any considerable interference with, or stimulation of, the animals may exercise an unfavourable influence, as is the case in tetanus and in strychnine poisoning, and it is possible that the harmful effect of hot summer weather is due to the strong and prolonged stimulation of the retina of an animal which is abnormally sensitive to most or all stimuli.

As in natural cases, the urine was sometimes found to contain a reducing substance. Unfortunately I was able at that time to perform only such tests as Fehling's and Nylander's, and it was not practicable to make daily observations; my records in this respect are therefore very incomplete.

It will be noted that in the feeding experiments no animal recovered after having exhibited definite symptoms of the intoxication, and the course of the intoxication was undoubtedly more acute in the experimental cases than in the majority of those naturally contracted.

In two cases the periods of visible illness were only three and four days respectively, and such acute cases appear to be very rare under natural conditions. In most of the cases the duration of the disease was from five to nine days, and such periods are quite commonly noted in the field, but the average period in natural cases is probably from twelve to fourteen days.

The experimental animals may in some cases have been killed rather earlier than the majority of naturally-affected animals in a similar condition, although I consider that to be questionable. The frequent handling to which the animals were subjected may have tended to hasten the end, but, on the other hand, the close watch kept on the animals must have ensured very early diagnosis.

6.—*Naked-eye Lesions.*

The lesions found *post-mortem* in the twelve experimental cases agreed very closely with those found in natural cases of "pushing disease." The same changes were apparent in the liver and myocardium, and generally (but to a less extent) in the kidneys also; pulmonary emphysema was observed in five cases, and ulcers occurred in the abomasum in three cases.

No abnormal appearances could be detected in connection with the brain, cord, meninges, or cerebro-spinal liquid.

7.—*Microscopic Lesions.*

A considerable amount of material was collected from a number of cases, both natural and experimental, but it has not yet been possible to examine more than a very small portion of it. Nothing can be said at present about the lesions in the nervous system.

Sections of liver, myocardium, and kidney, taken from a few cases (both natural and experimental), have been examined, and in some instances they present signs of fatty change. The lesion is of the type that was formerly (especially in connection with the liver) known as fatty degeneration, as distinguished from fatty infiltration.

In some of the cases examined no signs of fatty change have been detected, and in no case could the degeneration be described as advanced.

The connective tissue of the liver is not increased in amount, nor have any signs of proliferation of connective tissue cells been detected.

8.—*Minimum Lethal Dose.*

The result of the test made on seven animals with fresh (or almost fresh) *matricaria* would suggest that, at least for animals of the size and class of those used, the minimum quantity that will give rise to the intoxication is rather more than 20 lbs., but this result is not at all in accord with the observations made in the field, and more particularly those made on tethered animals.

In a number of the naturally-acquired cases that have come under observation the subjects may possibly, or even probably, have eaten considerably larger quantities of the plant than 20 or 30 lbs., but in some cases that would appear to have been impossible. It was quite impossible in the case of some of the tethered animals that contracted the disease. Thus No. 240, the animal which was kept on area D3 for twenty days, and which showed symptoms of the disease twenty-two days later, could hardly have eaten more than 5 or 6 lbs. of the plant. Allowance has to be made for the growth of the plant during the period of twenty days, but I do not think that at any period (during the duration of the investigation) the area D3 carried as much as 4 lbs. of *matricaria* at one time. Similarly, No. 271, tethered for eighteen days on D5, could not have had access to more than about 6 lbs. of *matricaria* during that period. Moreover, in both of these cases the latent period was considerably shorter than in that of No. 246, the animal fed experimentally on 21½ lbs., and the symptoms of the intoxication conformed more to the common type seen experimentally after feeding much larger quantities of the plant.

It seemed scarcely justifiable to reconcile these apparently incompatible observations by assuming that the St. Ives plant used in the Allerton experiments had lost, during the day or days which elapsed between its collection and consumption, a considerable proportion of the active principle or principles originally present. The feeding tests with *matricaria* hay indicated that the loss in toxicity, after very much more thorough desiccation and longer preservation, was probably not great.

It was also difficult to explain the negative result of the experiment in which Cow No. 43 was fed with 20 lbs. of *matricaria*

by assuming that this animal happened to be particularly resistant to the intoxication, or that the material used in the test (the type species) contained much less of the active principle, for the result of the test with No. 43 agreed fairly well with those obtained with Nos. 264 and 246. Moreover, an individual resistance of any magnitude appeared to be quite uncommon; and, although the type species was believed to be less toxic than the variety found at St. Ives, the available evidence suggested that the difference was relatively small.

A possible explanation of the discrepancy was sought in connection with the number of fractions into which the total quantity consumed had been divided, or in the length of the period during which the *matricaria* feeding had continued. It was considered to be unlikely that such large amounts are eaten daily under natural conditions as in the experimental cases; it is far more probable that in ordinary circumstances animals commence by eating very small amounts of the plant, gradually increasing the daily intake, and that in most cases they continue to consume some of the plant every day until the intoxication definitely appears. In the experimental cases the loss of condition that was apparent before the appearance of any characteristic symptoms suggested that in most cases the consumption of *Matricaria* had been forced to an unnatural degree.

It was therefore resolved to institute a further series of feeding tests based on considerations of rate and duration of consumption; the subjects were all yearling heifers or oxen, and the material used was the type species freshly collected at Allerton. The intention was to feed a given total amount to each of a group of four animals, of which one was to consume the total quantity in one day, another to receive half of the total amount on each of two successive days, and the others to receive respectively 1 lb. and $\frac{1}{2}$ lb. daily, for the required number of days.

The experiment could not be carried out exactly according to plan, but the modifications were unimportant.

The following tests were performed:—

<i>Animal</i>	<i>Total Quantity Consumed.</i>	<i>Details of Daily Consumption.</i>
1	20 lbs.	20 lbs. in one day.
2	20 "	10 lbs. daily on two successive days.
3	20 "	1 lb. daily for twenty days.
4	20 "	$\frac{1}{2}$ lb. daily for forty days.
5	10 "	$8\frac{1}{2}$ lbs. and $1\frac{1}{2}$ lbs. on two successive days.
6	10 "	6 lbs. and 4 lbs. on two successive days.
7	10 "	1 lb. daily for ten days.
8	10 "	$\frac{1}{2}$ lb. daily for twenty days.
9	5 "	5 lbs. in one feed.
10	5 "	$3\frac{1}{2}$ lbs. and $1\frac{1}{2}$ lbs. on two successive days.
11	5 "	1 lb. daily for five days.
12	5 "	$\frac{1}{2}$ lb. daily for ten days.
13	3 "	3 lbs. in one feed.
14	3 "	$2\frac{1}{4}$ lbs. and $\frac{3}{4}$ lb. on two successive days.
15	3 "	1 lb. daily for three days.
16	3 "	$\frac{1}{2}$ lb. daily for six days.
17	1 "	1 lb. in one feed.

No positive results were obtained. It would appear that the failure to obtain cases may partly have been due to the fact that the material used belonged to the type species, and the latter may have been poorer in active principle, as compared with the St. Ives variety, than was realised. Moreover, the plant was gathered when in the post-flowering stage; and, although certain natural outbreaks appear to prove that the plant in this stage may cause the intoxication, it is not at all improbable that larger quantities of it may be required to do so. Owing to heavy rains and extensive floods, however, my sources of supply were all more or less completely submerged, and a considerable portion of the *matricaria* used in these later tests had undergone obvious changes which may well have been quite sufficient to account for the negative results. Similar tests should be repeated under more favourable conditions, and the St. Ives variety of *matricaria* should be used, but it was, of course, impossible to perform any further feeding experiments during the same season.

The data relating to the first (positive) series of feeding tests have been analysed as closely as possible, with the object of extracting further information bearing on the question of the influence of the rate or duration of consumption. It is recognised that no definite conclusions can justifiably be based on the results of the feeding (with fresh plant) of the six normal bovines, for there were several factors that were variable, and each animal was, in a sense, the subject of a separate experiment, so that the individual factor was not eliminated or balanced. Nevertheless, the study of these results yields indications that are of some interest, and at least afford a basis for further experimentation.

If one plots a curve, taking as ordinates the number of days elapsing from commencement of experimental feeding to the onset of definite symptoms, and as abscissæ the total quantities consumed, the result is an intelligible but irregular curve. It expresses roughly the fact that increased total consumption is accompanied by a shortening of the latent period, and that after an early and very rapid descent the curve becomes almost flat, the apex being in the region of the point representing a consumption of 40 lbs. of *matricaria*. The curve is irregular, however, and, in particular, Cow 140 appears to have shown quite an excessively long latent period.

Curves have been plotted in which the periods to the onset of symptoms have been reckoned from the days on which the various animals had consumed 10 and 20 lbs. respectively of the plant; the resulting curves are somewhat more regular than the one mentioned above, but the case of Cow 140 is still considerably out of line. Very similar curves have been obtained by reckoning the periods from the dates of the consumption of the fifth and ninth *matricaria* rations, and here again the case of Cow 140 fails to fall into line.

The records of Cow 140 show that this animal was particularly unwilling to eat *matricaria*, and the amounts consumed daily during the first seven days of the experiment were:—3 lbs., nil, nil, 2½ lbs., nil, 5 lbs. and nil. After that an amount of 5 lbs. of the plant was taken daily for six consecutive days, and during the following five

days the daily consumption varied from 3 to 9 lbs. It is quite possible that this animal was endowed with more than average resistance, but the symptoms and course of the intoxication were of the acute type. It certainly seems that the intermittent character of the matricaria feeding during the first seven days may most probably have accounted for the delay in the onset of the symptoms.

A further curve has been obtained by reckoning the periods to the onset of noticeable symptoms from the time of the consumption of the fourth consecutive daily ration, and this curve is very much more regular, the case of Cow 140 approximating much more closely to the general curve.

The constant occurrence of a latent period, even after the consumption of an amount of matricaria more than seven times as great as that actually shown to be capable of causing a fatal intoxication, shows clearly that the process under investigation is not a simple matter of the accumulation within the body of some toxic constituent of the plant, although some accumulation may occur, and may be essential.

It is perhaps probable that repeated injury to certain cells is the essence of this condition, and it is not unlikely that, in the earlier stages, any more than usually prolonged interval between the successive doses may afford an opportunity for resolution to occur in the affected cells, although at a later stage such intervals may very probably have little effect, on account of the inability of the severely injured cells to utilise them. It must be admitted that this is at present merely a matter of speculation, but it is hoped to conduct further experiments designed to test the effect of observing various intervals between the successive fractions, in addition to repeating those which were intended to show the result of varying the number (and conversely the size) of the fractions.

9.—*The Effect of the Ingestion of the Plant when Dried.*

The material used in this experiment was dried thoroughly by repeated exposure in a thin layer to the direct rays of the sun (during the summer), and it was at least as thoroughly dried as any that might be included in hay prepared under ordinary conditions. It produced a fatal intoxication in both of the experimental subjects submitted to the test; in both cases the period of development was short (in one instance only twenty days) and the course was decidedly acute.

The data suggest that the hay made from the St. Ives material (variety) was distinctly more toxic than that derived from the Allerton plant (type species). No 193 showed more extensive and pronounced signs of tremor than were observed in any other case, experimental or naturally-contracted; the animal literally shook from head to foot under the influence of rapid but irregularly distributed muscular contractions that seemed to affect, at one time or another, practically every region.

It is obvious from the figures given that, weight for weight, the hay is very much more toxic than the fresh plant, but it is not possible to state at all definitely whether any of the active principle was lost during the drying process. It was not practicable to weigh the total amount of matricaria utilised before drying it, and the

results of observations on the drying of small test amounts showed some considerable variation, but it appears to be probable that the loss in active principle during drying (under the conditions mentioned) is not at all large.

10.—*The Effect of Sterilisation of the Plant by Moist Heat.*

The required amounts of the fresh plant were first weighed, and then autoclaved at 115° C. for fifteen or twenty minutes. In both of the subjects of this experiment the result was positive, and the symptoms exhibited were quite characteristic, although not identical in the two cases; in one instance the course was exceptionally short. The total quantity consumed was approximately 100 lbs. in both cases, and it may be noted that the periods elapsing before the onset of definite symptoms agreed very closely with that observed in the case of No. 123, which received 100 lbs. of fresh and unheated matricaria. It therefore appears that autoclaving under the stated conditions has little or no effect on the active principle of the plant.

This experiment proved that the disease cannot be due to infection of the animal with a living organism attached to, or contained in, the plant, and also that the toxic material is thermostable.

11.—*The Ingestion of Matricaria by Animals that had Recovered from a Naturally-contracted Attack of "Pushing Disease."*

The animals utilised were two of those that had contracted the disease under natural conditions at Balgowan (*see* Field Experiment II.). All the Balgowan animals which recovered after having exhibited some of the symptoms of the disease were kept on the clean area at Lidgetton for two weeks, and were then sent to the Allerton Laboratory and confined there to a small paddock that was free from matricaria. It is of interest to note that none of them displayed any of the after-effects which have been recorded on various farms, under natural conditions. When examined in December 1919, immediately before the institution of this experiment, and more than three months after their recovery, the animals were all in good condition and very active; they showed no trace of any tendency to become confused or to stumble when driven.

Of the two animals chosen for the test, No. 202 had actually "pushed," and No. 203, when driven from Balgowan to Lidgetton (in August), had blundered into obstacles and had only been brought to its destination with great difficulty. In both cases a fatal intoxication was produced.

It had been suggested that the apparent protection conferred in certain cases by a previous attack of the disease might be due to an acquired distaste (or increased distaste) for the plant; but, although cattle are commonly believed to learn by experience to avoid such rapidly-acting plants as "tulps" (*Morea* and *Homeria* spp.), it was difficult to understand how a similar feeling could arise in connection with a substance that produced its effects after an interval of several weeks. In the two experimental cases the animals accepted the matricaria ration more readily than any other cattle tested. The amount consumed by them was comparatively large, and it was given in a larger number of fractions, and over a longer period, than in any other experimental case.

Clinically the cases were interesting because the symptoms shown differed very considerably from those exhibited by other animals which had received similar, or even much smaller, amounts of *matricaria*. The actual duration of visible illness was quite short, but the symptoms to some extent resembled rather those seen after the ingestion of small amounts of the plant; thus the pushing tendency was almost entirely absent, and in both cases the only sign of this was seen at a late stage, when the animal was down.

In one case paresis (and finally paralysis) of the extensors of the fore extremities was a very noticeable feature; in the other case it appeared only at the last, and the case was characterised by inco-ordination of movement and difficulty in maintaining the balance.

What was really striking in this second case (much less so in the first one) was the obvious fact that the highest cerebral centres were not involved. The animal showed perfect recognition and understanding of its surroundings, and attempted to act normally; for instance, on seeing a distant bucket or hearing the rattle of a bucket handle it hastened to attempt to assuage its constant thirst, and it succeeded in arriving at the desired point in spite of staggering and repeated deviations from the straight course.

It was intended to perform further but less severe tests on other animals of the same group, and also on one animal which had recently recovered from a particularly bad attack of the disease, but supplies of the plant became unobtainable for the rest of that season on account of floods.

(B.)—EXPERIMENTS WITH ANIMALS OTHER THAN BOVINES
(see TABLE II.).

Six horses, three sheep, two goats, and two pigs were fed with *Matricaria nigellæfolia*. In no case was there seen to be produced any condition at all resembling the "pushing disease" of cattle.

The results obtained with rabbits and guinea-pigs were inconclusive, but it appears to be fairly well established that these animals are comparatively insusceptible to the action of the toxic substance, when ingested along with the plant.

The ease with which a fatal intoxication was induced in bovines affords an interesting contrast to the failure to produce any definite results at all in the other species. It is not easy to quote examples of poisoning substances to the action of which only one species of domesticated animal is very susceptible, all the other common species being almost (if not quite) resistant, and the case is particularly interesting when it is the bovine species that displays the exceptional lack of resistance.

On the whole the ox is distinguished among the domesticated animals by its relative insusceptibility towards poisons, and Lander (7), after referring to "the usually high degree of resistance of the ox and goat," points out that it is no doubt on account of their more indiscriminate feeding habits that bovines are the commonest victims of accidental poisoning.

It may be noted that the osteophagia induced in cattle feeding on vegetation deficient in phosphorus, as shown by Theiler and his assistants in the investigations on Lamziekte (5), is not noticed in

TABLE II.

Animals.			Material.		Details of Experimental Feeding.				Remarks.
Kind.	Number.	Description.	Source.	State.	Total Amount consumed (in lbs.)	Daily Ration.	Total Period (in days).	Number of Days on which consumed.	
Horses—	17	Mare	St. Ives	Kept 1-3 days	23½	2-5-10 lbs.	40	34	During experiment conjunctiva occasionally ecchymosed. Later given hard work. No ill-effects. { During experiment conjunctiva occasionally ecchymosed. but general condition improved. No ill-effects. No noticeable effects. } " Petechiae on conjunctiva, very weak, died five days after test ended. <i>Post-mortem</i> —Emaciation, gastro enteritis. No noticeable effects. { No effect other than loss of condition attributed to periods of partial starvation. Fed together. No visible effects. Fed together. No visible effects. No visible effects other than some loss of condition (partial starvation?). No visible effects. Died thirteenth day—apparently malnutrition. Died sixty-second day—apparently malnutrition. On ninth day head swaying, etc., and died. <i>Post-mortem</i> .—Large abscess in liver, one in stomach wall. Peritonitis. Died eleven days after cessation of feeding. Malnutrition? No definite lesions found. Died fifteenth day—apparently malnutrition. Died twenty-ninth day—apparently malnutrition. No effects other than slight loss of weight. Died thirteenth day—apparently malnutrition. No effects seen other than some loss of weight. Died sixteenth day. Congestion of liver and kidneys. Acute peritonitis. No effects seen.
	198	Gelding	{ St. Ives { Allerton	Fresh	206½ } 229½ 23 } 8	2-5-8 lbs.	50	42	
	8	"	{ St. Ives { Allerton	Kept 1-3 days Fresh	18 } 25 7 }	½ lb.	55	50	
	13	"	"	"	130	5-8 lbs.	55	50	
	172	"	"	"	130	"	20	17	
Sheep—	214	"	"	"	130	"	20	17	During experiment conjunctiva occasionally ecchymosed. Later given hard work. No ill-effects. { During experiment conjunctiva occasionally ecchymosed. but general condition improved. No ill-effects. No noticeable effects. } " Petechiae on conjunctiva, very weak, died five days after test ended. <i>Post-mortem</i> —Emaciation, gastro enteritis. No noticeable effects. { No effect other than loss of condition attributed to periods of partial starvation. Fed together. No visible effects. Fed together. No visible effects. No visible effects other than some loss of condition (partial starvation?). No visible effects. Died thirteenth day—apparently malnutrition. Died sixty-second day—apparently malnutrition. On ninth day head swaying, etc., and died. <i>Post-mortem</i> .—Large abscess in liver, one in stomach wall. Peritonitis. Died eleven days after cessation of feeding. Malnutrition? No definite lesions found. Died fifteenth day—apparently malnutrition. Died twenty-ninth day—apparently malnutrition. No effects other than slight loss of weight. Died thirteenth day—apparently malnutrition. No effects seen other than some loss of weight. Died sixteenth day. Congestion of liver and kidneys. Acute peritonitis. No effects seen.
	104 { 334 { 337	Merino "hamel" " " " " " " Crossbred "hamel"	{ St. Ives { Allerton { Allerton	Kept 1-3 days Fresh "	24½ } 27½ 8 } 22	½-2 lbs. 2 lbs.	50 13	29 11	
Goats—	{ 230 { 236	Angora cross "hamel"	{ Allerton { Allerton	Fresh	18½	1-2 lbs.	13	10	During experiment conjunctiva occasionally ecchymosed. Later given hard work. No ill-effects. { During experiment conjunctiva occasionally ecchymosed. but general condition improved. No ill-effects. No noticeable effects. } " Petechiae on conjunctiva, very weak, died five days after test ended. <i>Post-mortem</i> —Emaciation, gastro enteritis. No noticeable effects. { No effect other than loss of condition attributed to periods of partial starvation. Fed together. No visible effects. Fed together. No visible effects. No visible effects other than some loss of condition (partial starvation?). No visible effects. Died thirteenth day—apparently malnutrition. Died sixty-second day—apparently malnutrition. On ninth day head swaying, etc., and died. <i>Post-mortem</i> .—Large abscess in liver, one in stomach wall. Peritonitis. Died eleven days after cessation of feeding. Malnutrition? No definite lesions found. Died fifteenth day—apparently malnutrition. Died twenty-ninth day—apparently malnutrition. No effects other than slight loss of weight. Died thirteenth day—apparently malnutrition. No effects seen other than some loss of weight. Died sixteenth day. Congestion of liver and kidneys. Acute peritonitis. No effects seen.
Pigs—	12 11	Large black "	St. Ives Allerton	Kept 1-3 days Fresh	40½ 48½	½-2½ lbs. 2-4 lbs.	41 19	33 16	
Rabbits—	I.	—	St. Ives	Kept 1-3 days	4½	—	13	13	During experiment conjunctiva occasionally ecchymosed. Later given hard work. No ill-effects. { During experiment conjunctiva occasionally ecchymosed. but general condition improved. No ill-effects. No noticeable effects. } " Petechiae on conjunctiva, very weak, died five days after test ended. <i>Post-mortem</i> —Emaciation, gastro enteritis. No noticeable effects. { No effect other than loss of condition attributed to periods of partial starvation. Fed together. No visible effects. Fed together. No visible effects. No visible effects other than some loss of condition (partial starvation?). No visible effects. Died thirteenth day—apparently malnutrition. Died sixty-second day—apparently malnutrition. On ninth day head swaying, etc., and died. <i>Post-mortem</i> .—Large abscess in liver, one in stomach wall. Peritonitis. Died eleven days after cessation of feeding. Malnutrition? No definite lesions found. Died fifteenth day—apparently malnutrition. Died twenty-ninth day—apparently malnutrition. No effects other than slight loss of weight. Died thirteenth day—apparently malnutrition. No effects seen other than some loss of weight. Died sixteenth day. Congestion of liver and kidneys. Acute peritonitis. No effects seen.
	II.	—	{ St. Ives { Allerton	" Fresh	16 } 10½ 3½ }	—	62	58	
	III.	—	"	"	1	2 oz.	8	8	
	IV.	—	"	"	5½	2-4 oz.	29	27	
Guinea-pigs—	I.	—	St. Ives	Kept 1-3 days	5½	—	15	15	During experiment conjunctiva occasionally ecchymosed. Later given hard work. No ill-effects. { During experiment conjunctiva occasionally ecchymosed. but general condition improved. No ill-effects. No noticeable effects. } " Petechiae on conjunctiva, very weak, died five days after test ended. <i>Post-mortem</i> —Emaciation, gastro enteritis. No noticeable effects. { No effect other than loss of condition attributed to periods of partial starvation. Fed together. No visible effects. Fed together. No visible effects. No visible effects other than some loss of condition (partial starvation?). No visible effects. Died thirteenth day—apparently malnutrition. Died sixty-second day—apparently malnutrition. On ninth day head swaying, etc., and died. <i>Post-mortem</i> .—Large abscess in liver, one in stomach wall. Peritonitis. Died eleven days after cessation of feeding. Malnutrition? No definite lesions found. Died fifteenth day—apparently malnutrition. Died twenty-ninth day—apparently malnutrition. No effects other than slight loss of weight. Died thirteenth day—apparently malnutrition. No effects seen other than some loss of weight. Died sixteenth day. Congestion of liver and kidneys. Acute peritonitis. No effects seen.
	II.	—	"	"	8½	—	29	29	
	{ III. { IV.	—	{ St. Ives { Allerton	" Fresh	2½ } 6½ 4 }	4 oz.	30	29	
	V.	—	"	"	4½	—	12	12	
	VI.	—	"	"	14½	—	30	30	
	VII.	—	"	"	2	2 oz.	16	16	
	VIII.	—	"	"	4½	2-4 oz.	30	30	

horses, sheep, and goats grazing over the same pasture. It may be that the bovine species is also peculiarly liable to the development of pica under the influence of conditions other than phosphorus deficiency, and that pica may often account for the ingestion of poisonous substances by cattle.

It can hardly be doubted, however, that *Matricaria nigellæfolia* is very unattractive to most bovines, and that it is at least as readily eaten by horses and goats, and probably by many sheep also. Whether the resisting species may owe their protection to a more rapid excretion can only be determined when the active principle can be isolated from the plant and identified (either as such or in changed form) in the urine, etc. In any case it is quite probable, of course, that the other domesticated animals would prove susceptible to the action of the active principle in large doses, but that under natural conditions large doses cannot be obtained within a short period.

(C.)—DETERMINATION OF THE ACTIVE PRINCIPLE.

A few preliminary experiments in this direction have been made, with only a small amount of material, in the Institute of Physiology at University College, London. It was decided to treat the material according to the scheme recommended by Lander (7) for the isolation of various groups of poisonous substances when present in the ingesta or organs of a poisoned animal.

In this way three different fractions were obtained :—

(a) The acid distillate, from which was obtained a volatile oil—a light yellowish clear liquid with a very strong and pleasant odour, recalling somewhat that of lemon. Soon after its separation the oil began to deposit small particles of a solid substance. The alcoholic solution was optically inactive.

(b) The alkaline distillate.

(c) The acid-alcohol extract obtained from the material remaining after distillation.

It is recognised that it will be necessary to repeat this extraction on unheated material before drawing any conclusions as to the absence of poisonous glucosides, non-volatile alkaloids, etc., although the active principle was shown to be thermostable.

Preliminary tests were performed on rabbits with these three fractions, but no positive results were obtained by administering (b) and (c), either subcutaneously or *per os*. Symptoms of illness, and even death, could naturally be obtained by administering the volatile oil, but the results of such experiments did not permit one to form any opinion as to the possible connection of the oil with the causation of the bovine intoxication.

Further and much more extensive work with a large quantity of material is obviously necessary, but that the active principle (which causes the intoxication) is the volatile oil is at least an interesting possibility, deserving further investigation.

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TICK PARALYSIS.

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ALONG the whole of the eastern coast of Australia a form of paralysis, accompanied by other symptoms, most common in the domesticated animals but occasionally reported in human beings, is well known; popular as well as professional opinion is unanimous in ascribing it to the bite of a tick, known as the "scrub tick." There is, however, more than one genus of tick and several species inhabiting the scrubs or thickly wooded parts of eastern Australia, and the name scrub tick is applied popularly to any of them and, as a rule, indifferently.

Among the so-called scrub ticks are those which most stock men differentiate under the name of "bottle tick," on account of the large size which the fully engorged female attains. The bottle tick appears to be either an *Amblyomma* or *Hyalomma*. In this connection Mr L. Harrison, B.Sc., Lecturer in Zoology at the University of Sydney, informs me that he has examined numerous ticks from dogs in the neighbourhood of Sydney, and they have all been *Ixodes holocyclus*.

In Queensland and a small part of northern New South Wales the cattle tick, *Margaropus annulatus*, is more or less prevalent, but popular opinion does not include this among the scrub ticks. No scientific determination of the ticks removed from human beings or animals affected with tick paralysis in Australia appears hitherto to have been made, the nearest being such remarks as "it was almost certain," or "it was probably" a particular species, viz., *Ixodes holocyclus*. With regard to the experimental proof as to which, if any, of the so-called scrub ticks in this country is the cause of the undoubted cases of paralysis in human beings and animals, and so often fatal in the young of the latter, I have been unable to find any published record of experiments, whether negative or positive. I have been informed that such experiments have been attempted at various times, but as the results have not been published the conclusion to be arrived at is that they were unsuccessful.

Tick paralysis is most commonly seen at that period of the year when ticks are most prevalent in the coastal scrubs, viz., spring and summer. In the more northern parts of eastern Australia however,