A STUDY OF "SWAYBACK" - A DEMYELINATION DISEASE OF LAMBS WITH AFFINITIES TO SCHILDER'S DISEASE, (ENCEPHALITIS PERIAXIALIS DIFFUSA) IN MAN

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by

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XI. APPENDIX: Papers on other pathological subjects additional to those incorporated in the thesis and published since the date of proceeding to the last degree.

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1. "Blood tumours" or Haemangioendotheliomata in the Fowl. (With F. Blakemore). (1931). 2nd. Rept. Inst.Anim.Path. Camb. Univ.

No.

2.	The Comparative Pathology of Tumours.	(1932).	Proc.Roy.Soc.Med.
3.	The Chemical Identification of Vitamin C. (With L.J. Harris and I. Mills).	(1932).	Lancet.
4.	The Pathogenesis of Avitaminosis A. (With L.J. Harris & S. Griffith).	(1932).	Lancet.
5.	Beitrag zur Wirkung des Cyanids auf die Schilddrüsen der Ratte.	(1933).	Endokrinologie.
6.	Über Nebennierenveränderungen bei experimentellen Skorbut.	(1934).	"
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8.	The Pathological Diagnosis of Swine Fever.	(1935).	Veterinary Record.
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10.	The effect of P. deficient diets on metabolism blood bones of sheep by J. Stewart, with addendum. The Anatomical Changes in the bones and their relationship to Rickets.	(1936).	4th. Rept. Inst. Anim. Path. Camb. Univ.
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12.	The lesions produced in Rabbits by single and repeated doses of BCG.	(1937).	Proc.Roy.Soc.Med.
13.	The Pathogenesis of Tuberculosis in Domesticated Animals according to the Nieberle School.	(1937).	Veterinary Record.
14.	The Assimilation of the Stenboch Diet in Normal and Vitamin D deficient rats with and without Caecum. (With I. Nicolaysen).	(1937).	Biochemical Journal.

15. Studies in Debatable Tumours. I. Lymphoepthelioma. (With Col. W.F. Harvey and Dr. Edith K. Dawson, Roy. Coll. Physicians Lab., Edin.) (1937). Edinburgh Medical Journal.

16. II. Lymphosarcoma. (1937). " "

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20. VI. Meningioma. (1939). " "

21. VII. Granulosa Cell Tumour of Ovary. (1939). " "

22. VIII. Melanoma. (1939). " "

23. Permanent Stomach Fistulae in Ruminants (With A.T. Phillipson). (1939). Quart. J. Physiology.

24. Studies in Animal Pathology. I. The Pathology and Pathogenesis of Tuberculosis in Domesticated Animals compared with Man. (~~With E.G. White~~). (1939). Veterinary Journal

25. Neoplastic Diseases of the Testicle in Animals. (1940).

26. Hereditary Cerebellar Aplasia in Calves (With Dorothy S. Russell). (1940). J. Path. & Bact.

27 Diseases of the Nervous System Common to Man and Animals (1940) Proc Roy. Soc Med

28 Thrombo-angiitis obliterans in a Horse (with J. W. Whittick) (1940) J Path. Bact

29 Multiple malignant tumours in a dog with Portal obstruction without ascites (with J W. Whittick) (1940) J Comp Path

1. INTRODUCTION.

While much is known about the comparative anatomy and histology of the nervous system of the lower animals, the same cannot be said regarding neuropathology; indeed it might be said that veterinarians have hardly yet entered the new field which modern neuropathological technique has opened for investigations. Whether animals are insusceptible to many of the nervous disorders which afflict man is therefore as yet unknown. There are, however, many disease entities in man which either do not occur in animals or have not been described. A few of the diseases which would come into this category include, for example, various congenital and hereditary ataxias, while it would seem that the gliomata and the vascular disorders are extremely rare. The history of the identification of viruses with encephalitis has shown that animal studies have contributed considerably towards a fuller understanding of the aetiological agent and the associated disease. There is thus no reason to disbelieve that the comparative pathology of nervous diseases will be for a long time to come a profitable field of research, and of value, both from the animal and medical aspect. The identification ~~in animals~~ of a hitherto unknown type of nervous disease in animals, which in man has defied all attempts to

explain its aetiology, may therefore be of importance apart from its direct veterinary interest.

As a sequel to the identification of virus infection with certain types of encephalitis, it has been possible to classify encephalitis into comparable groups based upon the fundamental nature of the morbid process. Along these lines Greenfield (1933) suggested that a classification might be as follows:-

(1) "Incidental" encephalitis in which the brain lesions, septicaemic in nature, are essentially the same as lesions in other parts of the body, e.g. typhus in man and perhaps swine fever encephalitis in animals.

(2) "Polioclastic" encephalitis due to a neurotropic virus, the path of infection in some of which is certainly by the nerve axons, e.g. poliomyelitis, rabies, Borna disease in horses and louping-ill in sheep. The lesions due to these neurotropic viruses are more marked in the grey than in the white matter in contrast to the localisation of those in the following group.

(3) "Myelinoclastic" encephalitis. It is a type of disease related to this third group with which this work is concerned.

The demyelination diseases in man have in recent years been greatly extended in their scope, (e.g. see Brain and Strauss (1934), Wertham and Wertham (1934), Ferraro (1937) and Hadfield and Garrod (1938). Diseases which are now embraced in this category includes acute disseminated encephalomyelitis occurring as a primary spontaneous disease or as a post-infective complication of measles, small-pox, chicken-pox, and influenza or as post-vaccinial encephalitis; another group, perhaps more idiopathic than the above, includes disseminated sclerosis, neuroptico-myelitis of Devic, Schilder's disease (encephalitis periaxialis diffusa) and the various progressive infantile or juvenile (sometimes familial) forms of diffuse sclerosis which have been described by so many different authors with varied nomenclature, or are simply known by reference to the author (e.g. Krabbe and Pelizaeus-Merzbacher's disease). To this formidable list must still be added the encephalitis following anti-rabic treatment (see review of Stuart and Krikorian, 1930), sulphar-sphenamine encephalitis (e.g. see Russell, 1937), lead encephalopathy, (e.g. see Ferraro and Hernandez, 1932, Blackmore, 1937), CO encephalopathy (see Hsu and Chang, 1938) and a variety of non-systematised demyelination associated with certain nutritional disorders, e.g. with pernicious anaemia and pellagra.

The list is long and appears to complicate so many disassociated conditions that a common solution would appear to

be impossible. It is therefore important to realise that in the pathology there is a certain amount of identification. The essential lesion in all is the demyelination, whether it occurs as scattered foci in disseminated sclerosis, as perivascular areas in post-vaccinial encephalitis or as massive diffuse, sometimes symmetrical, areas in Schilder's disease. This lesion of demyelination is in contrast to that occurring in any of the neurotropic virus infections in which an inflammatory reaction is outstanding, in which there is a greater tendency for the process to affect the grey matter, and with which intracellular inclusion bodies are so often associated. Ferraro (1937) has attempted to unify the demyelination diseases on purely anatomico-pathological grounds, and has classified them into sporadic and familial forms in either of which the lesions may have a patchy or diffuse distribution, and in any of which the disease may run an acute or chronic course. He considers that in diffuse sclerosis the histo-pathological changes are fundamentally the same in all, irrespective of the name given. Any pathological or clinical differences which do occur from case to case, according to this author, can be reconciled with the age of the patient at the onset of the disease, the localisation of the lesions, the initial intensity and subsequent tempo of the process and the constitutional make-up of the patient at the time when the causative factor began to work. The aetiology of these

demyelinating maladies being unknown, it is obviously, however, almost impossible to assess the relationship of one to the other. It is for all that highly probable that the reaction of the brain to pathogenic agents is limited and that different causal agents can produce a similar, if not identical, anatomical change. The demyelination problem might therefore be several, and not fundamentally one, as has been suggested by some workers.

So far all attempts to establish the aetiology of the demyelination diseases have failed; no specific organism or virus has been identified with any of them, and experimental transmission has never been achieved. The claims of Levaditi et al (1930) that all demyelination diseases are due to a neurotropic virus, Steiner (1920) regarding the incrimination of a spirochaete in disseminated sclerosis, or of Gye (1921) regarding the transmission of an "infective agent" in the same disease into rabbits by injection of cerebro-spinal fluid, have never been substantiated. There appears to be no authentic instance in which a known virus or infective agent, acting directly on the nervous system, has produced demyelination of the type found, e.g. in disseminated sclerosis, Schilder's disease etc., and when well recognised neurotropic viruses do attack the brain and cord, demyelination is not found, Rivers (1932), Hurst (1936) and Ferraro (1937).

Many other theories of causation have been periodically

suggested without any particular one ever receiving much general support. "Toxins" were claimed to be a possible cause of disseminated sclerosis by Dawson (1916); a "toxaemia" for the same disease by Hallevorden and Spatz (1933); Glanzman (1927) and others have suggested that acute disseminated encephalomyelitis might rest on some allergic basis, an idea perhaps supported by some recent experimental work of Alexander and Campbell (1937); Putnam and his co-workers (1930-37) have suggested that the process of multiple sclerosis might rest on a cerebral vascular basis; in the case of post-infective encephalitis (e.g. after influenza, measles etc.) and post-vaccinial encephalitis, there have been strong contentions that the diseases were caused by the primary virus infections or that they were caused by an "unknown virus" empowered in some way by the exanthematous diseases to attack the nervous system (see Brain and Strauss, 1934); an old idea that disseminated sclerosis was caused by lead intoxication was revived by Cone, Russell and Harwood (1934); Brickner et al (1930-36) and Crandall and Cherry (1931-32) and others have demonstrated the presence of myelin splitting ferments in oxalated blood plasma of patients with multiple sclerosis; Collier and Greenfield (1924) suggested that Schilder's disease might be due to a primary affection of the oligodendroglia, which cells are now regarded as influencing the nutrition of the myelin sheaths; this theory was later supported by another

observation of Greenfield (1933a) of a type of progressive cerebral sclerosis in infants which was associated with a primary degeneration of the oligodendroglia and also by the fact that in Schilder's disease oligodendroglia disappear from demyelinated areas, although they were often present in the margins. The above theories are many, and although distinct advances can be claimed, there have been no real undisputed solutions put forward regarding the cause of any of the demyelination diseases.

Experimentally, tetanus toxin has been claimed to produce demyelination by Claude (1897) and Putnam, McKenna and Morrison (1931), cyanide by Ferraro (1933) and Rubino (1935), Co poisoning by Meyer (1928), saponin by Weil (1930) and Cornil, Poursines and Giraud-Costa (1938), while Rivers, Sprunt and Berry (1933) and Rivers and Schwenkter (1935) have claimed to produce demyelinations in monkeys by injections of emulsions of heterologous brain substance over a prolonged period. Few of these experimental methods have been sufficiently followed up; the approach to the problems has, of necessity, thus been restricted to studies of the static pathological pictures of the human diseases, usually end stages, seen at autopsy.

The above is a synopsis of the problems as they affect man, and we may now turn to a consideration of analagous

spontaneous conditions in animals; it is apparent that the identification of any spontaneous demyelinating disease of animals, particularly if it occurred with any frequency, might be of paramount importance. The animal worker is in a position to kill the animals and study the disease in all its phases and field experimentation may be tried out on a scale often denied to the medical worker.

A disease resembling Schilder's encephalitis has been described in monkeys by Perdrau (1930), Levaditi et al (1930 & 1933) Schob (1931), Scherer (1932), Davison (1934) and Hurst (1937); apart from the isolated claim of Levaditi, in none of these cases were transmission experiments successful when attempted. The aetiology thus rests on the same obscure basis as that of the human diseases.

A type of encephalo-myelitis in dogs (usually referred to as "post distemper" encephalitis) was described by Perdrau and Pugh (1930) in which demyelination, of a type commonly found in subacute disseminated sclerosis of man, was found in 4 out of 14 cases. Many veterinary authorities still believe that this encephalitis is a true post-distemper virus complication, although no connection was established by Perdrau between the encephalitis and the distemper virus. From an examination of nearly 50 cases and from some preliminary transmission experiments, my own work, Innes (1939) on the same subject, confirms much of Perdrau and

Pugh's findings. Distemper virus cannot be identified from the brain or spleen of such cases nor can a true encephalomyelitis be set up by intra-cerebral inoculations of the virus. The aetiology, therefore, rests on the same uncertain basis as the post-infective or post-exanthematous demyelination diseases of man.

An "anti-rabic encephalitis" also occurs in dogs, Mocsy (1937) which, as in man, demands an explanation of its relationship to the rabies virus.

Finally, there is this disease in lambs referred to as "Swayback" which has attracted attention only recently. "Swayback" is regarded as being the nearest and only analogy in domestic animal pathology to the more idiopathic demyelination diseases of man, and in particular to Schilder's encephalitis. The problems of its aetiology must be regarded therefore as having a bearing on those of the human maladies.

II. HISTORY AND GEOGRAPHICAL DISTRIBUTION OF "SWAYBACK".

"Swayback", "Swingleback", "Swingback", "Jinkback", "Jingleback", "Bentback", "Evil", "Warfa" (Derbyshire), "Belland" (Derbyshire), and "Bride" or "Cefn-Gwan" (Wales) are the names which have been given, probably by shepherds in different localities, to this disease of young lambs; some of them presumably on account of the outstanding symptom, namely the inco-ordination. While records of this disease have only appeared in the literature recently, there is plausible evidence available that it has been known in England for generations, e.g. in Derbyshire certainly over 100 years.

It may appear peculiar that "Swayback" should have evaded description by early veterinary writers as most of the diseases of sheep were well enough known to the older veterinarians. The enzootic nature of the disease may have been partly responsible for this, as even to-day, sheep farmers in areas which are relatively near to Swayback districts often do not know of the disease, while some of the earlier clinical descriptions of lamb paralysis may well apply to those of "Swayback", e.g. Steel (1890). The classical writings of the Ettrick shepherd, Hogg (1807), contains no description of any condition which might be comparable with "Swayback".

Swayback appears similar to a disease of lambs in Peru investigated by Gaiger (1917) and called "Renguerra" - a word of Spanish origin referring to an "injured back", (or with a Creole origin meaning to wobble or sway). This disease was (and still is) well-known to the sheep farmers there and considered responsible for annual losses of several thousands of lambs. Symptoms of paralysis were observed in lambs between two and six weeks old. Most of the lambs died but some of the more slightly affected cases survived. Gaiger must have then been aware of a similar disease in Britain as he stated that "Renguerra" bore some resemblance to "Swingback", but because little was known at that time about the various nervous disorders in sheep, (viz. louping-ill, scrapie and Swayback), it was uncertain how far this similarity existed. He also mentioned that "Renguerra" compared closely with descriptions of a nervous disorder in lambs called "pataleta", which occurred in Argentine and Patagonia. There have been, apparently, severe periodic outbreaks of "Renguerra" from 1911 onwards extending over two or three lambing seasons, followed by a period of relative freedom - a feature not unlike that met with in England. The pathology of "Renguerra" was not investigated and the aetiology not determined.

Magnusson (1920) recorded a disease in Sweden which appears similar to "Swayback". Young lambs between a week and a month old were affected with a limb paralysis; although

macroscopic lesions were said to be absent from the nervous system, the pathology was also not determined. Attempts to identify either a causal organism or virus, or indeed any other aetiological factor, failed. He also referred to the clinical resemblance between the Swedish disease and louping-ill, Swing-back and Scrapie in Britain. No further communications have appeared from Swedish veterinarians concerning the disease.

The first record of the disease in Britain was by Lyle Stewart (1932), although from certain official files of the Ministry of Agriculture, the late Sir Stewart Stockman was evidently well aware of its existence and serious nature in several parts of the country. Bacteriological examinations were made of two cases with negative results. A pathological examination of the brain was not made, but this author described degeneration in the ventro-lateral columns of the spinal cord. It was concluded, however, that this represented a degeneration of the ascending tracts, a conclusion which was subsequently shown to be incorrect. The aetiology was again not determined.

A disease of young lambs was described by Bennetts (1932) in Australia and called enzootic ataxia. He observed degeneration in the cord and also came to the conclusion that it was of an ascending type. No mention was made then regarding any examination of the brain, and the pathology was left as

obscure. Brief communications were subsequently made by Dunning (1933) from South Africa*, and Krishnapa (1936) from India, suggesting that clinically at least, a condition like "Swayback" existed in these countries.

In spite of the absence of accurate pathological data the descriptive similarity of the history, symptoms and age incidence of affected lambs, might indicate that a disease comparable to "Swayback" has been known to occur in South America (Peru, Patagonia and Argentine), Sweden, India, South Africa, Australia and New Zealand.** As a result of personal enquiry it appears that the disease is unknown, or has not yet been observed, in the central European countries.

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* Dr. Du Toit, Onderstepoort, has informed me that the disease, if it occurs in S. Africa at all, is certainly not widely known.

** Personal communication by Mr. C.S.M. Hopkirk, New Zealand.

III. OCCURRENCE, INCIDENCE AND FIELD ASPECTS OF THE DISEASE IN BRITAIN.

The attention of other workers in Cambridge was first attracted to the subject in 1926 by reports of sporadic outbreaks of a form of paralysis in newly-born or young lambs from apparently healthy ewes in various parts of the country. All attempts to isolate a causal organism or to transmit the disease to healthy animals failed, the pathology was not investigated and no further serious work was done until 1935. Since then investigations have been made both in the field and laboratory, and much new information obtained which has caused the problem to be viewed in an entirely new light.

The disease appears to have a wide geographical distribution throughout England, Wales and Scotland. Outbreaks have either been personally investigated (or cases received from outbreaks) in Derbyshire, Buckinghamshire, Northamptonshire, Worcestershire, Leicestershire, Bedfordshire, Gloucestershire, Wiltshire, Yorkshire, Herefordshire, Suffolk, Lincolnshire, Rutlandshire, Warwickshire, Somerset, and in several counties in Wales - Glamorgan, Breconshire, Denbighshire, Merioneth, Montgomery, N. Cardigan. These data have been substantiated by Roberts (1938) in his extensive survey of the incidence of

sheep diseases in Britain and who also recorded the occurrence of "Swayback" in Scotland in the Island of Cathay, Caithness and the South-West and Border counties.

The incidence varies from year to year on the same farm and in the same districts; it seldom, if ever, occurs only on any one farm in a district, i.e. there is always an area involved. While the disease has a wide distribution throughout the country with an irregular annual incidence, there are districts in which it occurs with disastrous periodicity; the disease might be regarded as an enzootic in these areas. The incidence in other parts of the country may be very low, the farmer losing only one or two lambs annually; according to Roberts (1938) this is a common experience in Scotland. In the more severely affected areas the mortality may vary annually from 1-50 per cent. of the lambs born, while exceptionally bad losses may be even 90 per cent., and large numbers of outbreaks have been encountered since 1935 with such a severe mortality.

On some farms outbreaks have occurred each lambing season for many years, while on others it was observed for the first time in 1935 when these investigations were begun. Further enquiries have revealed comparable instances of the disease occurring on farms after many years freedom. On the other hand, the disease has disappeared from certain areas in which it was

prevalent in 1935, e.g. on certain farms in Leicestershire. Many farmers believe that the prevalence has increased recently; it is impossible to confirm or refute this belief as until 1935 almost no attention was given to the problem.

Another belief that the progeny of the Border Leicester was more susceptible than other breeds was disproved by personal observations. "Swayback" has been seen in lambs of all the well-known breeds, - Suffolk, Masham, Wensleydale Cross, Southdown, Welsh Mountain, Blackface, Kerry, Exmoor, Swaledale, Gritstone, Woodland, Baumshire, and in many of these breeds crossed with Oxford, Suffolk, Hampshire and Border Leicester rams.

Ewes of any age may give birth to affected lambs, but there was a suggestion that the older ewes were more prone. For example, the records of the disease on one farm in 1934 indicated that the majority of cases were lambs from ewes which had three to four previous gestations in that area. In 52 recorded cases that year only two were from first-lamb ewes. This suggestion is confirmed by some farmers and refuted by others in different parts of the country, but further personal experience indicates that in a large number of cases, old ewes, or ewes which have been in an affected area more than one year, are more prone to give birth to Swayback lambs. Cases have, however, been observed in lambs from ewes which have been kept on an "affected" farm for a

period of only six months.

Ewes which have given birth to "Swayback" lambs one year may produce either affected or healthy lambs the following season. Either sex, single lambs, both of twins and all three of triplets are prone with no proclivity for any of these. Rarely only one of twin lambs was observed to be affected at birth, but in such cases the other twin often showed symptoms later, (see cinematograph). When only one of twin lambs is visibly affected at birth we do not know whether the other lamb remains permanently free from symptoms.

My own experience has shown that most of the cases have been affected at birth, but some do not show symptoms (or are not observed) until they are a few weeks old, at the latest about six weeks. (In Derbyshire it is said that some cases are not affected until they are two months old, and then get gradually worse. It was impossible to obtain and examine any of these cases, and it is therefore impossible to be sure that they are true "Swayback"). Earlier unrecorded experiences suggested that the disease was more often of this latter type and that in recent years there had been a greater incidence of newly-born lambs affected; again, however, this may be largely a matter of hearsay. In any one outbreak both forms are usually encountered.

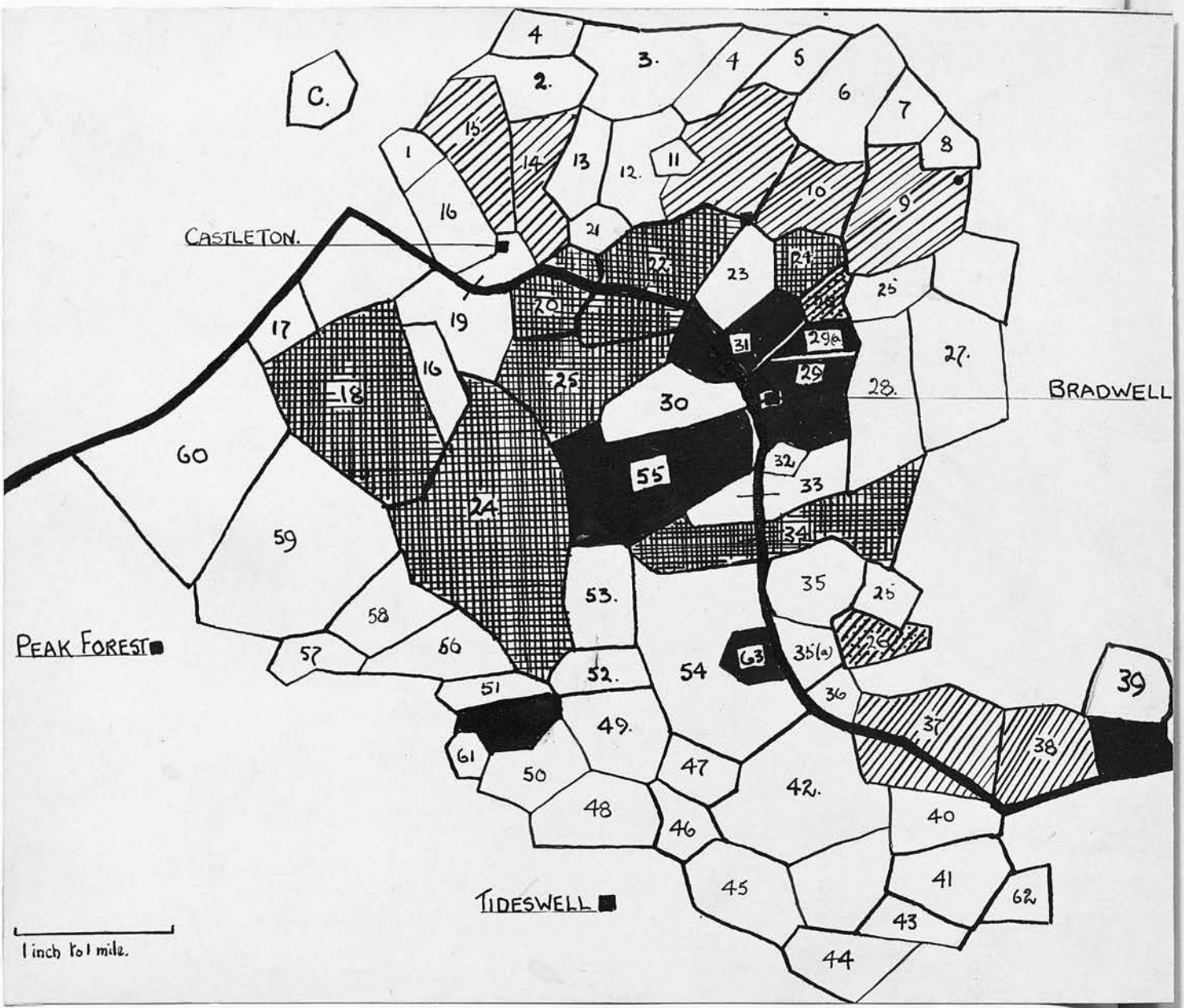

Fig.1.

Diagram of an area in Derbyshire covering 63 farms in which the disease has been particularly prevalent. "Affected" farms closely adjoin "non-affected" farms. There has been some suggestion that the disease occurs more commonly on lime-stone regions; the thick black line is a rough indication of the division of this area into limestone and grit-stone formations; the disease occurs in both sides of this line.

Swayback farms Non-swayback farms

Farms on which sheep breeding was given up because of losses due to Swayback.

Farms in which the ewes are sent away to other areas during pregnancy.

IV. FIELD INVESTIGATIONS IN AN ENZOOTIC AREA IN NORTH DERBYSHIRE.

In the spring of 1938 it was decided to conduct some field investigations in this area and for this purpose a laboratory was temporarily established near Bakewell where some time was spent both before and during the lambing season. While much of the information concerning the disease in other parts of Britain, and given in the previous section, was amply confirmed by observations here, many other new features were elucidated in Derbyshire.

Swayback ("Warfa", "Belland" or "Evil" as it is known in this district) has been known to farmers there for generations, certainly over a hundred years. Almost all flock-owners were unanimous in the opinion that it has occurred in waves or spells - occurring each lambing season as a severe pest for a number of years, with other seasons of relative freedom. During the period of field work there a total of 80 farms were visited to make a survey of the incidence of the disease; this covered an area of about 38 square miles with the village of Bradwell in the centre. Although most of the farms in this area were affected annually with the disease, there were others situated in the centre of the region in which it did not occur.

33	41	8	1	7
17	32	3	1	2
45	53	8	3	5
26	36	8	2	6
40	43	3	3	-
-	-	-	-	-
12	20	1	1	-
12	15	3	1	2
7	8	3	2	1
41	64	36	31	5
72	123	21	14	7
32	41	11	11	-
100	145	15	4	11
15	27	9	6	3
54	76	16	12	4
52	60	7	1	6
18	18	1	1	-
24	31	5	4	1
50	61	19	5	14
42	42	16	2	14
21	27	7	2	5
53	52	7	4	3
40	52	14	4	10
12	12	4	3	1
28	30	7	2	5
20	30	1	1	-
24	41	17	3	14
42	68	13	5	8
31	54	14	2	12
2	2	2	2	2
40	50	14	8	6

TABLE II.

18 NON-SWAYBACK FARMS.

Farm No.	No.of Ewes.	Lambs Born 1938.	Mortality all causes; no Swayback.
3	104	105	5
6	75	76	2
7	50	56	4
8	21	25	1
14	20	37	4
18	60	61	1
22	20	32	5
36	17	28	3
37	34	59	6
38	18	31	3
41	40	57	7
43	19	32	-
43a	20	30	-
47	14	16	-
49	43	59	6
50	34	-	-
56	30	34	4
73	15	25	1

TABLE III.

TABLE OF TOTAL EWE AND LAMB POPULATION ETC.

	Total Ewe Population.	Total No.of lambs born 1938.	Fertility Lambs per ewe.	Total Lamb Mortality.	Total Swayback Mortality.	Total Mortality from all other causes.	Percentage loss from Swayback of total losses.
1938 62 "SWAYBACK" FARMS.	2214	3029	1.36	646 21% (3-81% on different farms)	311 10% (1-72%)	335 11% (0-41%)	48% (9-100%)
1938 18 NON-"SWAYBACK" FARMS.	634	763	1.20	52 7% (0-15% on different farms)	-	52	-

ESTIMATED "SWAYBACK" MORTALITY IN THE SAME AREA - 1937.

32 "SWAYBACK" FARMS.	1250	1557	1.2	?	248 (15.3%)	-	-

TABLE I.

62 SWAYBACK FARMS.

Farm No.	No.of Ewes.	Lambs Born 1938.	Lamb Losses.	No. of Swayback Cases.	Losses from all other Causes.
1	22	42	10	10	-
2	12	11	1	1	-
4	90	112	12	2	10
5	50	55	5	3	2
9	21	34	14	6	8
10	34	45	4	1	3
11	25	41	10	6	4
12	10	16	11	8	3
13	20	36	9	9	-
15	36	33	18	18	-
15a	119	151	57	5	52
16	27	45	7	4	3
19	25	40	5	5	-
20	90	146	6	3	3
21	19	34	2	2	-
23	50	80	20	12	8
24	12	16	1	1	-
25	20	26	5	2	3
26	36	49	6	2	4
27	86	96	10	6	4
28	28	36	5	1	4
30	16	22	18	16	2
32	16	25	19	19	-
33	100	116	16	8	8
34	50	63	11	1	10
35	19	31	7	4	3
35a	14	22	7	5	2
39	50	80	35	2	33
40	19	36	9	6	3
42	53	72	4	1	3
44	40	64	9	1	8
45	33	41	8	1	7
46	17	32	3	1	2
48	45	53	8	3	5
51	26	36	8	2	6
53	40	43	3	3	-
54	-	-	-	-	-
54a	12	20	1	1	-
54b	12	15	3	1	2
55	7	8	3	2	1
57	41	64	36	31	5
58	72	123	21	14	7
59	32	41	11	11	-
60	100	145	15	4	11
61	15	27	9	6	3
62	54	76	16	12	4
64	52	60	7	1	6
65	18	18	1	1	-
66	24	31	5	4	1
67	50	61	19	5	14
68	42	42	16	2	14
69	21	27	7	2	5
70	53	52	7	4	3
71	40	52	14	4	10
72	12	12	4	3	1
74	28	30	7	2	5
75	20	30	1	1	-
76	24	41	17	3	14
78	42	68	13	5	8
79	31	54	14	2	12
80	2	2	2	2	2
77	40	50	14	8	6

TABLE II.

18 NON-SWAYBACK FARMS.

Farm No.	No.of Ewes.	Lambs Born 1938.	Mortality all causes; no Swayback.
3	104	105	5
6	75	76	2
7	50	56	4
8	21	25	1
14	20	37	4
18	60	61	1
22	20	32	5
36	17	28	3
37	34	59	6
38	18	31	3
41	40	57	7
43	19	32	-
43a	20	30	-
47	14	16	-
49	43	59	6
50	34	-	-
56	30	34	4
73	15	25	1

TABLE III.

TABLE OF TOTAL EWE AND LAMB POPULATION ETC.

	Total Ewe Population.	Total No.of lambs born 1938.	Fertility Lambs per ewe.	Total Lamb Mortality.	Total Swayback Mortality.	Total Mortality from all other causes.	Percentage loss from Swayback of total losses.
1938 62 "SWAYBACK" FARMS.	2214	3029	1.36	646 21% (3-81% on different farms)	311 10% (1-72%)	335 11% (0-41%)	48% (9-100%)
1938 18 NON-"SWAYBACK" FARMS.	654	765	1.20	52 7% (0-15% on different farms)	-	52	-

Figure 1 is a semi-diagramatic representation of the farms in this area in which the distribution of the disease is shown.

The losses in this district from Swayback have been so severe in the past that many farmers have been compelled to give up sheep breeding and indeed many of the farms have been actually vacated. The mortality due to Swayback in 1938 was obtained by data from the farmers and compared with the ewe population. These data are given in Tables I and II. The number of cases of Swayback in this small area alone in 1938 was 311, i.e. about 10 per cent. of all lambs born, and as far as could be ascertained this compared with a 15 per cent. mortality in the same area in 1937 from a smaller selection of farms, (Table III). The incidence on the different farms varied from 1-72 per cent., but information received indicated that in bad years the mortality might approach 100 per cent. The variation in different farms of the same district in any one year is common fidning in many parts of Britain. These figures given above are unassailable evidence that Swayback is probably the most serious disease affecting young sheep in such districts of England.

A fact discovered during this field investigation which, until it is definitely excluded, may still have some causal connection with the disease, (at least in this district), concerns the presence of old abandoned lead workings. The whole of this area is irregularly traversed by what are known locally as

Fig.2.

Lead rake on farm 28. The old lead dump can be seen to be covered with grass and formed part of a ridge which stretched irregularly across many farms in the neighbourhood; animals are not prevented from grazing on these rakes.

Fig.3.

"Belland". This is a photograph of the soil under the grass on these lead rakes and shows the faint whitish deposit on the grass roots to which the term "Belland" is given by the farmers.

"lead rakes" - remains of old lead mines. These "rakes" (Fig.2.) have, in course of time, been overgrown with grass to which grazing animals have free access. Some of the farmers believe that this "bellanded" land is the cause of "Swayback", and indeed refer to it as "Belland".* Instance of "Belland" or lead poisoning in other animals are quoted by the farmer in support of this belief (mainly in horses and poultry). Most of these cases of lead poisoning are sporadic, probably subacute, but while the animals may show a form of posterior paralysis, the pathology has never been investigated. It is necessary to mention that the disease does occur on farms in this area (and in many other parts of England) where there are no known lead outcrops. In England there is no domestic animal apart from the sheep which is kept in the field throughout winter during a pregnancy period, often with no supplementary food to herbage. Many farmers in this area do not feed hay or concentrates during pregnancy; others give them only 3 or 4 weeks before lambing. Therefore, no other domestic animal is exposed, during a winter pregnancy, to identical nutritional and/or environmental conditions as are ewes; it would appear unlikely, therefore, that "Swayback" could occur in any other species. (In Peru the disease "Renguerra" has been reported to occur in kids, llamas, alpacas and vicunas, Mitchell, (1937) - all ruminants in wild life.

The incidence of the disease in this Derbyshire area

* (See footnote on p.21.)

is said to vary from year to year depending on the amount of winter and spring herbage consumed by the ewes. If large amounts of hay and concentrates have to be fed to the pregnant ewes on account of a severe winter, the incidence of the disease in the lambs is said to be reduced. The disease is also said to be prevented by transferring the ewes to "unaffected" areas (mainly to Cheshire and Yorkshire) during pregnancy, (from about November until lambing time), and many of the farmers in this area indeed do practise this method of "prophylaxis". This experience is also quoted by farmers in other areas and by Bennetts (1932) in connection with the Australian disease.

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* "Belland", with its variation "Belliam", are terms used in Derbyshire, Yorkshire and Shropshire to indicate the fine dust of lead ore. As this substance is highly poisonous, the terms have subsequently meant lead poisoning. In a discussion of lead poisoning in animals, (Gardner, 1924), mentioned a farm in Yorkshire apparently notorious for cases in horses, cattle and poultry, in which many of the lambs were "born with rickety backs"!

V. SIGNS AND SYMPTOMS.

(The symptoms of the condition are fully illustrated together with many other features in ~~an accompanying~~ coloured cine film which can be demonstrated).

Whether the animal is affected when born or not until later, the symptoms are essentially the same, varying only in degree of severity. All cases show inco-ordination of movement; some are totally unable to stand or walk and lie helpless; some may rise with difficulty to collapse almost immediately; others may walk with a very straddled staggering gait, while mild cases show only a slight weakness of the hind quarters, particularly when hustled or made to turn quickly. Although this ataxia is always definite, and often severe, there is no flaccidity; on the contrary spasticity may be marked. Fits are not observed. The flexor reflexes and knee jerk are brisk, but not exaggerated; tremors are inconstant and the head-and-neck righting reflexes appear to be unaffected. While the corneal and pupillary reflexes are normal, many of the more severely affected cases are blind. The disease is non-febrile; remissions do not occur.

The most severe cases are those which show flagrant symptoms at birth; the longer the period which elapses from birth until the onset of symptoms results in a more mild type of disease. The mildest cases, usually first observed some weeks after birth, may only show slight unsteadiness when walking, and this inco-

ordination may never progress. Such animals may survive, and when bred from later may give birth to healthy lambs.

Some of the worst cases were artificially fed and kept under observation, but the symptoms progressed and death occurred in a few days to a few weeks from broncho-pneumonia or some other infection, or simply from marasmus. Under natural conditions the survival period is, in all probability, much shorter owing to neglect, exposure, and/or malnutrition, and the mortality of these severe cases must be about 100 per cent. Because of this, these acute cases are usually killed by the farmer as soon as they are observed.

The essential manifestations of the disease are thus a spastic diplegic paralysis particularly of the hind limbs, sometimes blindness, a progressive (non-febrile) course with a generally fatal termination except for the mild cases mentioned.

VI. PATHOLOGY.

1. MATERIAL AND METHODS.

A total of 167 cases have been autopsied during the last five years; these included cases which were sent to the Institute alive for observation, and many others examined during the field investigations. In addition the head or brain alone from many other cases was also examined. These cases were obtained from many different outbreaks all over the country and embraced some from the same flock or even the same ewes in successive years. Some of the live cases were killed for immediate autopsy while others were kept under observation until death. It was thus possible to examine lambs of ages varying from birth to many weeks old. All cases were autopsied in the rigid routine manner, and in many of the cases a bacteriological examination of the blood, visceral organs, and central nervous system was carried out using a wide variety of cultural methods. From certain animals small portions of the central nervous system were taken under sterile precautions for subsequent inoculation into healthy lambs. The viscera from a number of cases, and the nervous system from nearly 50 cases was examined either in part or whole. The following staining methods were employed for histological examination of the nervous system:-

After neutral formalin-saline fixation: haemotoxylin and eosin, van Gieson, Loyez's for myelin sheaths, Wilder's silver impregnation for reticulum and Nissl-Orange G for nerve cells on paraffin sections; Scharlach R for fat, Penfield's combined method for oligodendroglia and microglia, Bielschowsky's method for axis cylinders and Holzer's glia stain on frozen sections; Weigert-Pal and Marchi-Busch on celloidin sections.

After formol ammonium bromide fixation and frozen sections: various Hortega methods for astrocytes, oligodendroglia and microglia, and occasionally Cajal's gold sublimate method.

Pieces of spinal cord were always taken from at least two different levels - cervial enlargement and late thoracic - and also sometimes from other levels. In many cases whole coronal sections through the frontal and occipital lobes were stained by general survey methods - Weigert-Pal and Marchi-Busch. The visceral organs were stained by the usual routine methods.

As a control, sections from various regions of the brain and spinal cord of two foetuses (15 and 17 weeks approximately), a normal one-day-old lamb, and a three-weeks-old lamb were

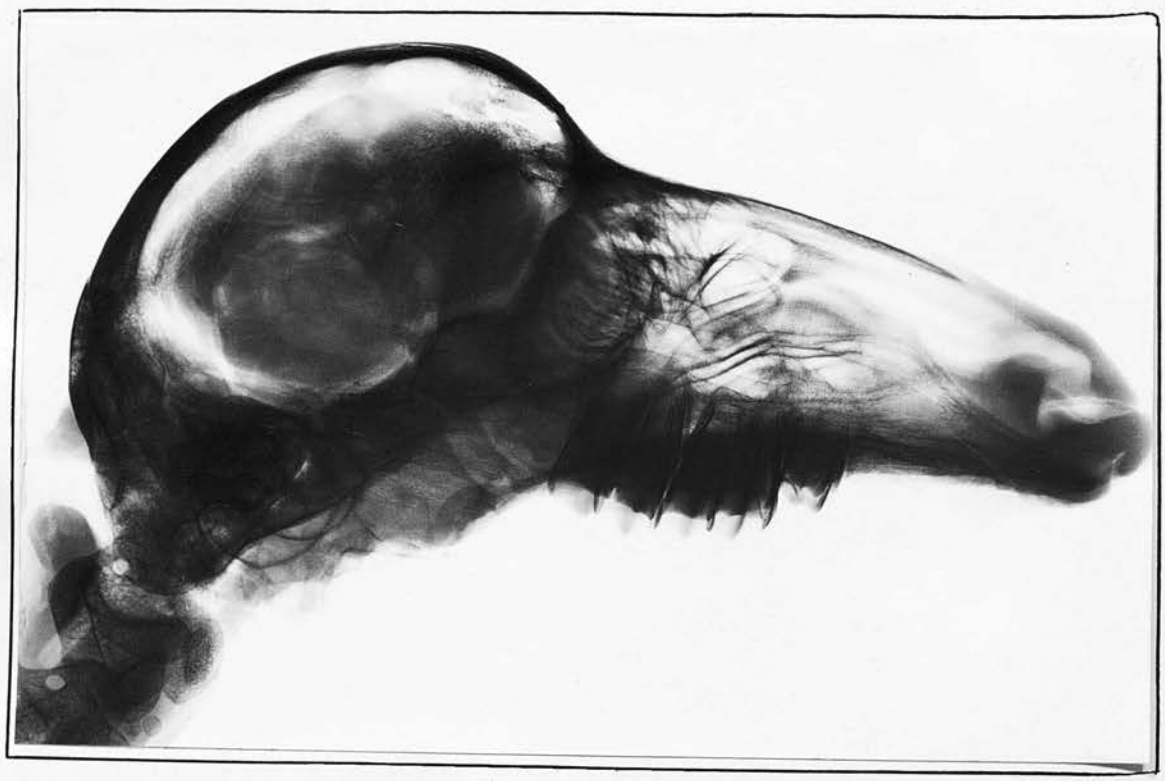


Fig.4.

"Swayback". X-ray of detached lamb's head showing the dilatation of the subarachnoid space and retraction of the brain from the cranium seen in many cases.

Photo by courtesy of Prof. H.A. Harris, School of Anatomy, Cambridge.

also prepared by many of the above methods. Considerable help was also obtained by a study of preparations of the nervous system of sheep at different stages of foetal development obtained through the courtesy of Mr. G. Romanes, School of Anatomy, Cambridge.

2. ANATOMICAL FINDINGS.

(a) Visceral organs.

No significant lesions were found in the visceral organs of any case - the changes were confined to the nervous system. Muscular atrophy was never observed.

In those cases which died from some secondary complication, broncho-pneumonia, pleurisy, and occasionally a purulent meningitis, appeared to be the commonest causes of death.

(b) Nervous system.

Gross changes were present in the brain in 101 out of 167 cases examined. The different macroscopic appearances seen in these cases indicated that any large series such as this gave a good representation of the gross genesis of the lesions.

The most severe or acute type of change seen may be described as follows. The bones of the cranium were thin and easily cut, but with the sutures united. On opening the calvarium a large quantity of clear cerebro-spinal fluid flowed out from dilated subarachnoid spaces. There was thus an obvious retraction or "atrophy" of the brain from the skull, a fact substantiated by

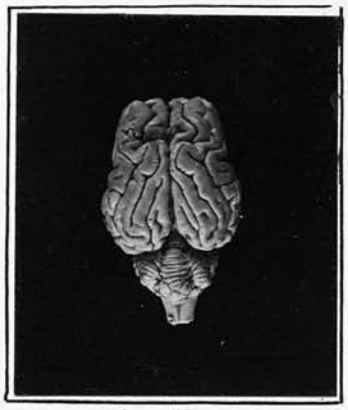


Fig.5.
Brain, normal lamb, superior aspect; for comparison with brains from Swayback cases in Fig.6. About 1/3 natural size.

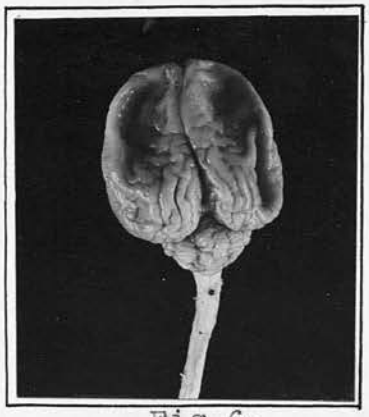


Fig.6.
"Swayback"; dorsal aspect of brain showing the collapsed appearance of the cerebral hemispheres after removal from the skull; the convolutions are blurred. About ½ natural size.

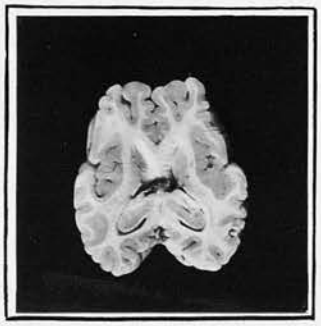


Fig.7.
Brain, normal lamb, horizontal section; for comparison with "Swayback" brains (Fig.8); frontal poles at top of photo. About ½ natural size.

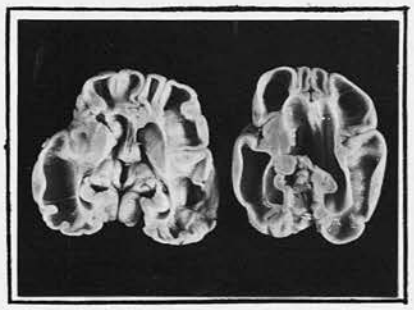


Fig.8.
"Swayback"; horizontal sections of cerebrum of two cases of Swayback showing gross destruction of white matter with extensive cavitation extending from frontal to occipital poles (bottom); the grey matter remains only as a thin shell around the cavities; slight dilatation of the lateral ventricle. Left photo - P.M. Lamb No.184/39; 1 day old; died. Right photo - P.M. Lamb No.30/38. One of twins; both affected at birth; both killed when 1 day old. Other animal showed similar lesions. About ½ natural size.

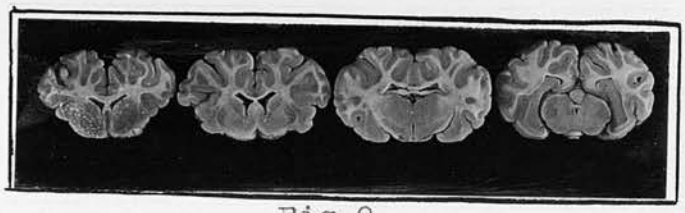


Fig.9.
Brain, normal; 2 day old lamb; series of coronal sections, frontal to occipital poles left to right; for comparison with Swayback brains in Figs.10-13. About 1/3 natural size.

Fig.10.
"Swayback"; series of coronal sections as in Fig.9; extensive symmetrical destruction of cerebral white matter with marked cavitation, wasting of corpus cellosum and relative preservation of the grey matter. P.M. Lamb No.15/38. 5 days old. About 1/3 natural size.

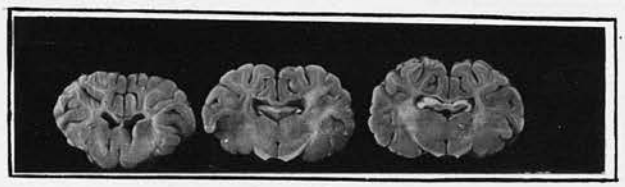


Fig.11.
"Swayback"; coronal sections of brain; one of twins both affected at birth; both able to walk but with straddled gait; killed when 5 days old; there are no lesions to be seen macroscopically; foci of cerebral degeneration, cord degeneration and lesions in the red nucleus would be demonstrated histologically in such a case. About 1/3 natural size.

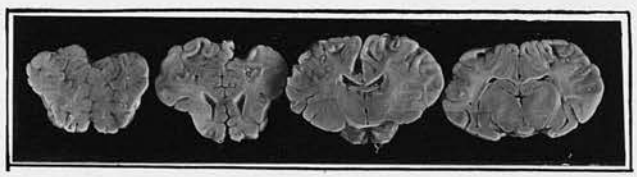


Fig.12. About 1/3 natural size.
"Swayback"; compare with other cases; diffuse symmetrical gelatinous degeneration of the cerebral white matter extending from pole to pole; demarcation between the grey and white matter is extremely blurred; no cavitation; this lesion is reminiscent of that seen in some cases of Schilder's encephalitis in children. P.M. Lamb No.17/38. One of twins; both severely affected at birth; the other lamb died within a few hours of birth and showed gross lesions similar to those illustrated in Fig.13; this case was killed when 6 days old.

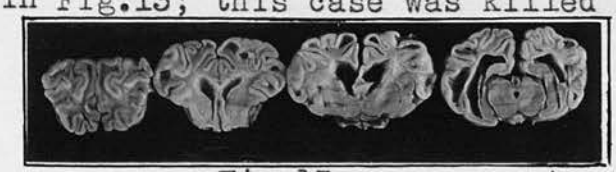


Fig.13. About 1/3 natural size.
"Swayback"; might be regarded as a stage between that illustrated in Figs.12 & 10. Diffuse bilateral degeneration of cerebral white matter, rather gelatinous in type in the frontal poles with more liquefaction and cavitation in occipital region. Lamb No.16/38. 2 days old.

X-ray examination of a detached head (Fig. 4). The brain as a whole looked like a water-logged organ. The convolutions of the cerebrum appeared poorly developed or were ballooned out by fluid within, so that the sulci were shallow and poorly defined. Fluctuation could be felt in the brain, and it was clear that the cerebral cortex consisted only of a thin shell of substance. The latter was sodden, felt flabby, and without care laceration caused collapse of the cerebral hemispheres, and gave the appearance of deflated balloons, (Figs. 5.6). No lesions were ever observed in the meninges (except in two cases which showed a secondary purulent basal meningitis) and there were no marked vascular changes in any part of the brain. Lesions were not found in the cerebellum, hypophysis, mid-brain, brain-stem, chorioid plexuses of fourth ventricle, spinal cord throughout its length, posterior root ganglia and peripheral nerves - the latter in many cases being dissected to their termination. After fixation the brains were cut either into horizontal or coronal sections to disclose a diffuse symmetrical degeneration of the cerebral white matter. The latter was replaced by a loosely-woven, greyish, gelatinous substance or had been completely liquefied, as was evident by the presence of gross cavitation, (Figs.7-13). The transition between the gelatinous degeneration and liquefaction was often evident at different levels of the hemispheres. In the most severe cases the porencephalic-like cavitation extended from the occipital to the frontal poles (Figs.8.10). The central white

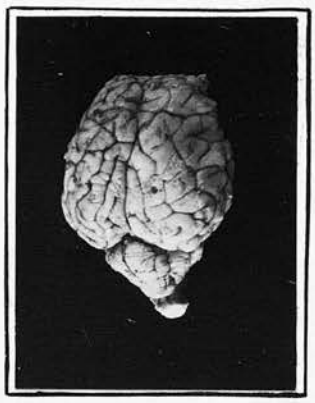


Fig.14.

"Swayback"; dorsal aspect of brain; one of the only two cases which showed lesions unilateral in extent; the convolutions on the right side appear wide and with rather indeterminate sulci; this side felt soft and flabby; on horizontal section the white matter showed diffuse gelatinous degeneration.
P.M. Lamb No.110/39. One of twins both affected at birth; the other animal died when 2 days old and showed only small foci of degeneration in the cerebrum; this animal was killed when 14 days old; the symptoms observed at birth had progressed. About $\frac{1}{2}$ natural size.

matter was thus restricted in most cases of this series to a grossly degenerated centrum ovale, to a wasted corpus callosum and septum pellucidum and to the internal capsules. A cavum septi pellucidi was frequently noticed. The cerebral grey matter was relatively well-preserved but formed only a thin shell around the degenerated white matter or the cavities (Figs. 8.10). There was a slight to moderate internal hydrocephalus of the lateral ventricles in many of these severe cases (Fig. 8); the ventricular walls were smooth, but communications with the cavities had been often affected by small perforations. The aqueduct was rarely dilated and the fourth ventricle never so. The basal ganglia, the thalamus, mid-brain, pons, cerebellum, medulla and spinal cord (at all levels) were normal, even in these severe cases. Gross cerebral changes, as described above, were observed in still-born lambs (5 cases), in lambs killed a few minutes after birth and in animals 4-5 weeks old.

In 29 out of these 101 cases showing gross changes, cerebral lesions were obviously in an earlier stage of development. All gradations were observed in the different cases ranging from small foci of gelatinous softening of the white matter to more diffuse areas involving the entire occipital lobes, and to symmetrical gelatinous degeneration of the whole hemispheres. The brain always felt soft and pulpy; demarcation between the grey and white matter was extremely blurred, but cavity formation was of a minimal

degree or completely absent. Where only the occipital poles appeared to be affected on coronal sectioning, the changes diminished in intensity as the frontal region was approached until a level might be reached which appeared normal (Figs.12.13). Ventricular dilatation was rarely observed in such cases. In only two cases of this series were the lesions of a unilateral nature (Fig.14).

In 66 of the 167 cases no abnormalities were observed to the naked eye in any part of the nervous system. The grey and white matter throughout was clearly demarcated, well preserved and apparently normal in amount and distribution (Fig.11).

3. PATHOLOGICAL HISTOLOGY.

(a) Visceral organs.

No significant lesions were observed in the visceral organs of the animals examined apart from a few cases in which the liver and kidney showed a marked lipoid degeneration. The significance of this lesion was obscure, but owing to its inconstancy, it could not have had any direct connection with the primary nervous disorder.

(b) Nervous system.

Diffuse, focal, extra-adventitial, or perivascular infiltrations ("cuffing") by inflammatory cells was never observed in any part./ (Figs.28.29.32.33) Similar negative findings were obtained in regard to haemorrhages, vascular thrombi, pia-arachnoid changes, pigment

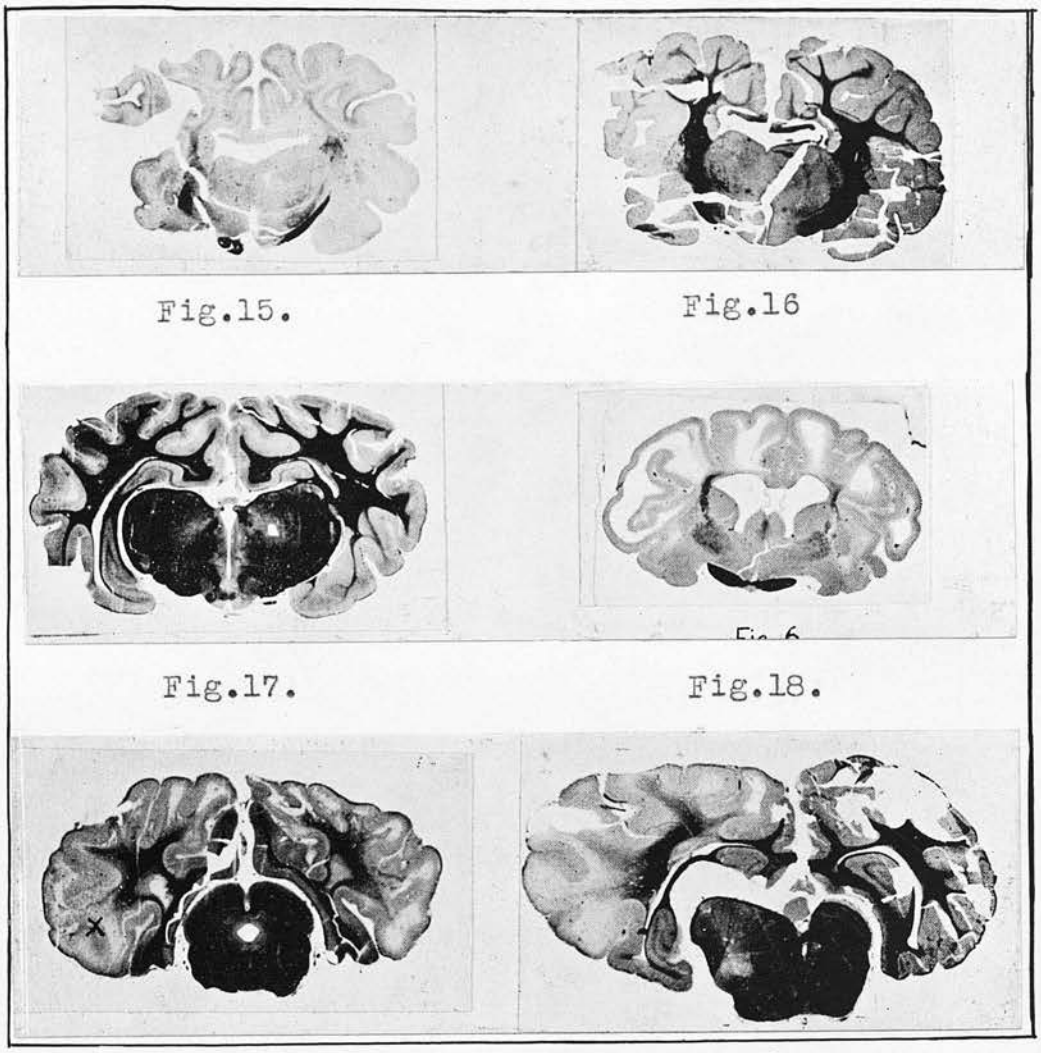


Fig.15. Fig.16

Fig.17. Fig.18.

Fig.19. Fig.20.

Fig.15. Normal foetal lamb, 109 days, (about one month before parturition). Compare the extent of myelination with that of a normal one day and 3 weeks old lamb; there is little evidence of myelination except in the capsules and optic chasma.

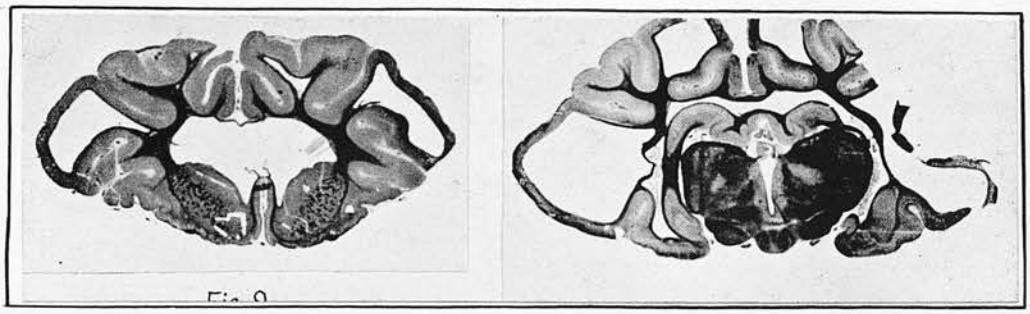
Fig.16. Normal 1 day old lamb. The central white matter is well myelinated and shows that within an interval of one month; the process has been remarkably rapid.

Fig.17. Normal 3 weeks old lamb. (Compare with Fig.15 and 16).

Fig.18. "Swayback"; 2 day old lamb; diffuse bilateral demyelination of hemispheres to the extent of almost total loss of myelin with the exception of the optic chiasma. Sections from the occipital poles showed the same appearance. Lamb 6/35.

Fig.19. "Swayback"; 3 weeks old lamb; no demyelination in the midbrain; diffuse symmetrical demyelination of the hemispheres affecting particularly the subcortical zones; the fibres deep in the centrum ovale are densely stained. Lamb 8/35.

Fig.20. "Swayback"; 2 weeks old lamb; changes are similar to those seen in Fig.19. but are more unilateral in type. Lamb. 16/35.



Figs. 21-22.

"Swayback"; 18 days old lamb; cavity formation and liquefaction extensive; the deeper parts of centrum ovale, the capsules and the mid-brain show no demyelination; lamb 25/35.

deposition and the structure of the choroid plexuses. Occasionally the perivascular spaces of cerebral vessels in the severe types of disease were dilated, no doubt due to distension by the increased fluid present in cavities, ventricles and subarachnoid spaces.

Myelin Sheaths and Axis Cylinders.

All the preparations stained by Weigert-Pal and/or Loyez's method etc. for myelin were compared with corresponding sections from control lambs' brains (foetal, a few days and a few weeks old). (Figs. 15-22).

Demyelination appeared to be the constant, and in all probability, the primary lesion encountered. The most severe type of change was represented by an almost total loss of myelin in the cerebral hemispheres (Fig. 18). The lesion was symmetrical, not sharply defined, and affected all zones of the white matter diffusely, to the summits of the convolutions, the total white matter of the hemispheres was almost unstained except in the coarse fibred optic tracts. All gradations from this complete destruction of cerebral myelin to small symmetrical foci were observed in the series of cases examined (Figs. 8.9. 25 26). Where macroscopic cavitation had been prominent, the white matter was grossly wasted or had completely vanished, and the persisting remnants formed at the most a thin subcortical zone or as an inner

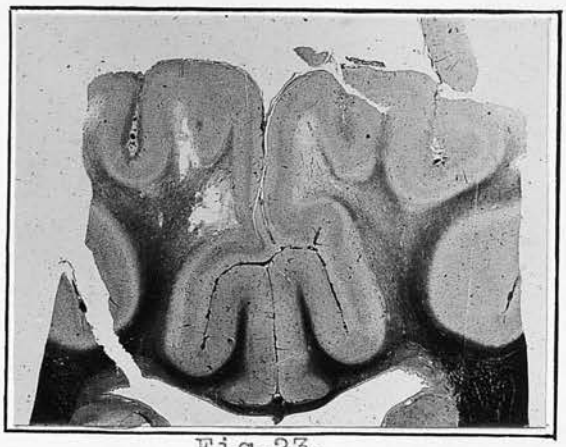


Fig.23.

"Swayback". Coronal section from frontal region about level of superior frontal gyrus (motor area); corpus callosum and ventricle below. Diffuse demyelination affecting the sub-cortical zones to the summits of the convolutions. Lamb 9/35. Weigert-Pal. X 4.

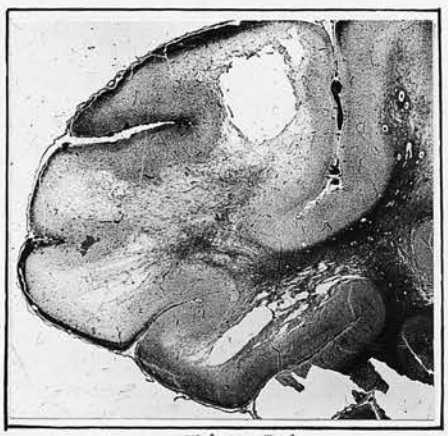


Fig.24.

"Swayback". Occipital pole from same case as Fig.23; beginning of porous cavity formation. Weigert-Pal. X 4.

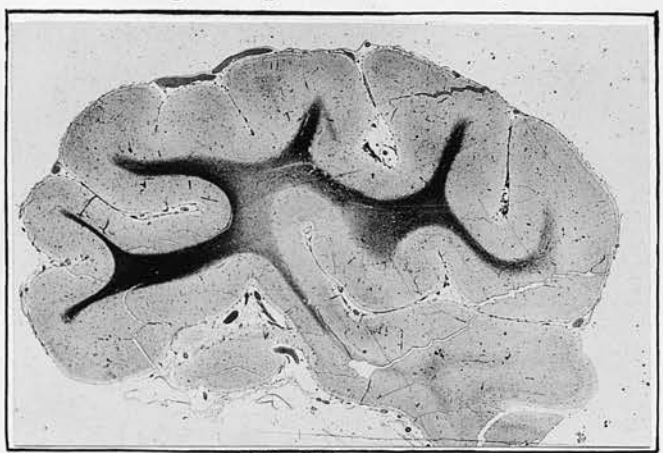


Fig.25.

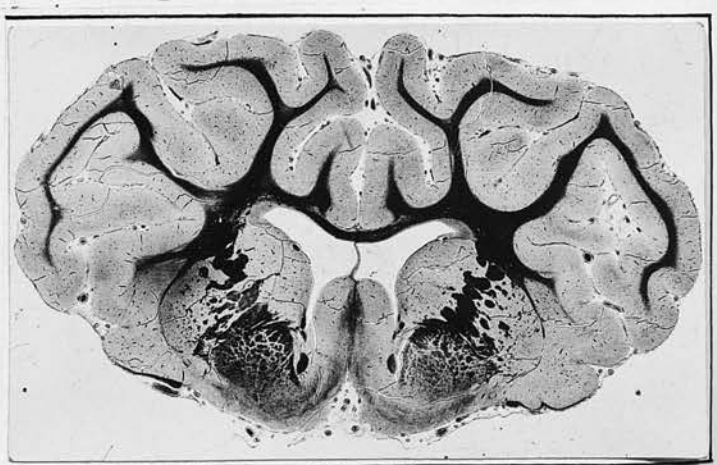


Fig.26.

"Swayback". Occipital pole; early demyelination of centrum ovale with sparing of the arcuate fibres; no naked eye lesions were observed in the brain of this case; these foci were confined to the occipital poles; sections through the frontal poles appear normal. (Fig.25 X 8. Fig.26. X 2. Weigert-Pal.

wall of the cavities. Under high magnification, beading and fragmentation of the sheaths was quite evident where demyelination was in an early stage. In some of the cases in which no naked eye changes had been observed, small foci of demyelination were visible in Weigert-Pal preparations, often confined to the centrum ovale of the occipital lobes (Fig.25). These were not sharply defined and were not restricted to perivascular areas. In other cases of the same type it was often difficult to determine demyelination by the Weigert-Pal or Loyez method; this was perhaps due to the extreme "scattering" of degenerated fibres, as Marchi-Busch preparations showed that degenerated fibres were present.

In the Marchi-Busch preparations of areas adjacent to those which showed unmistakable demyelination by the Weigert-Pal method, accumulations of stainable lipoid were present (Fig.27) Frozen sections of the same areas stained by Scharlach R also gave a faintly pink positive reaction for lipoid. It was, however, surprising to note that these lipoid by-products of myelin destruction (stainable by Herxheimer and Marchi) were never abundant - borne out by the paucity of the amoeboid phagocytic glia in such areas.

In Bielschowsky preparations for axis cylinders it was obvious that these structures had been destroyed as quickly as the myelin sheaths because no stainable structures were seen at all in severely demyelinated areas. The white matter

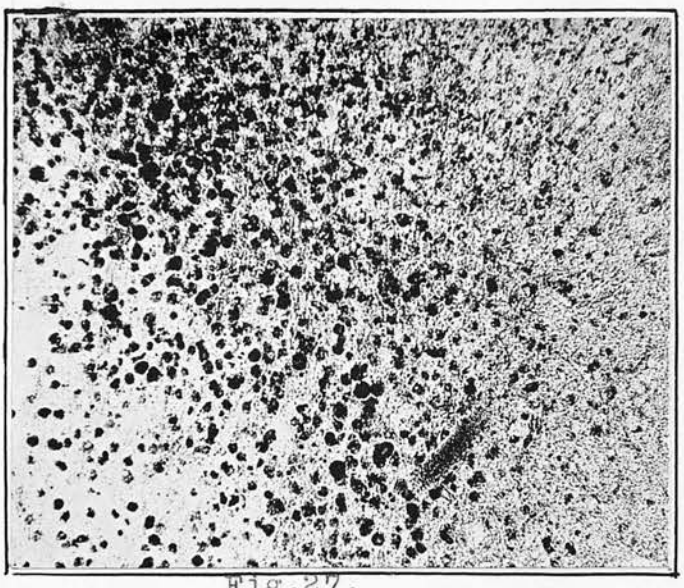


Fig.27.

"Swayback". Sections of demyelinated area in subcortex taken from area (x) in Fig.19. Marchi-Busch method. Granular accumulation of degenerated myelin fibres stained black; many of the fat globules are contained in phagocytic microglial cells. X 100

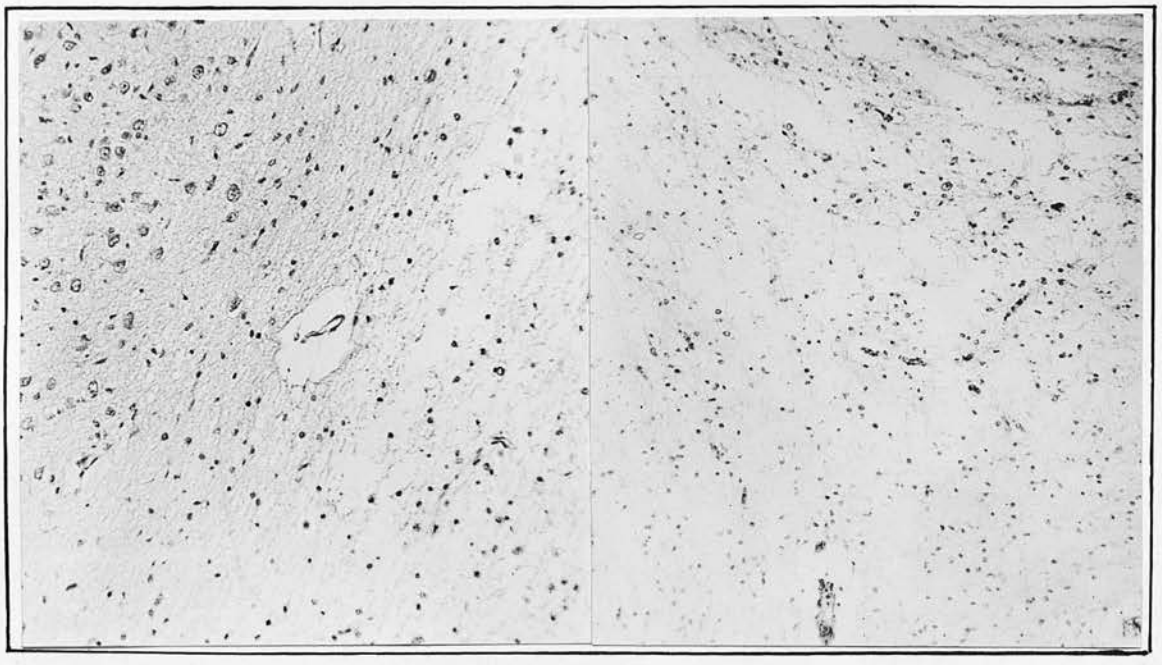


Fig.28.

"Swayback". Section of demyelinated area showing extreme spongy nature of white matter; dilated perivascular spaces; absence of inflammatory cell infiltration; normal grey matter on the left. H.E. X 100.

in toto appeared to be broken up with such rapidity that it was impossible to determine whether or not we were dealing with a primary neurolytic process with secondary affection of the axis cylinders.

Nissl-Orange G and haematoxylin-eosin preparations of different cases showed all gradations of loss of tissue coherence of the white matter from an apparently normal compact appearance, to an extremely spongy state with a few scattered nuclei and finally to complete disappearance with porous areas and cavitation. There were no collections of cells present which are characteristic for known infections. (Figs.28.29).

No gross patches of demyelination were observed in the capsules, mid-brain, cerebellum and mid-brain stem by Weigert-Pal methods.

In Marchi-Busch preparations degenerated fibres could occasionally be traced through the capsules, mid-brain to medulla and cord. Scattering, however, made it extremely difficult to follow these with ease, and it was not until the lower level of the medulla (above the decussation) was reached that grouping of degenerated fibres into definable tract systems was unmistakable. In the upper part of the cord (transverse sections) the degeneration was symmetrical and restricted mainly to (a) the ventral part of the ventro-lateral column of white matter applied close to the

Fig.29.

"Swayback". Section of cerebral cortex outside a cavity, pia mater top left, lumen of cavity bottom right. Relative preservation of nerve cells; absence of any inflammatory cell infiltration; from same case as Fig.21. H.E. X 120.

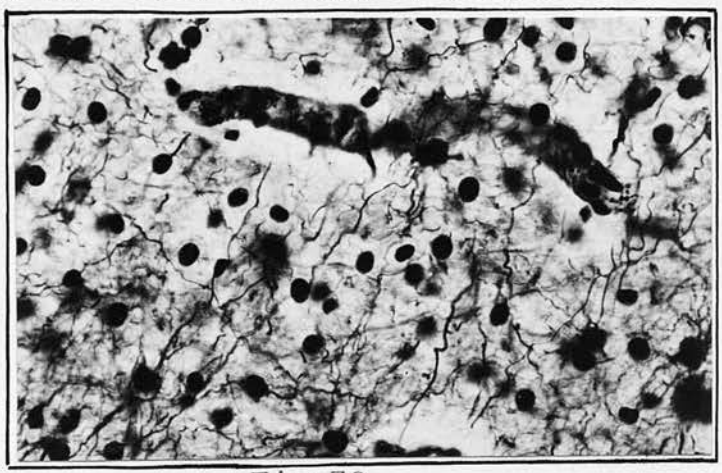


Fig.30.

"Swayback". Demyelinated area; occipital pole; same case as Figs.21,22 and 29 showing early fibrillary gliosis. Hortega's silver carbonate method; frozen section. X 400.

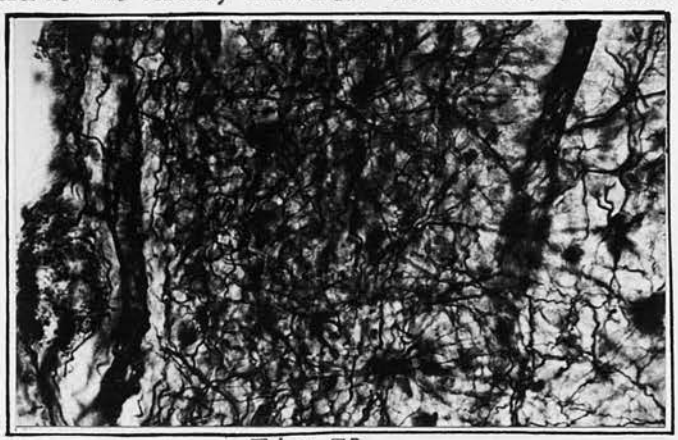


Fig.31.

"Swayback". Section of the subcortex covering a cavity from same case as Fig.29; intense gliosis. Hortega's silver carbonate method; frozen section. X 400.

median fissure and reaching to the surface and (b) the dorsal part of the same column extending from the tip of the dorsal horn of grey matter to the surface below the dorsal root (Fig.34.35). Scattering of degenerated fibres was, however, a constant feature throughout the ventral white columns. Prominent degeneration was never constantly observed in any part of the ascending columns. The degeneration in the ventro-lateral columns was constant and obvious in all Marchi preparations, but by Weigert-Pal it was only visible as a paling of the areas concerned (Fig.36). It was never seen as solid blocks such as might be seen in certain secondary degenerations of the human cord. This feature may have been due to the fact that the degeneration was being observed at a relatively early stage with no sclerosis, and also because the fibre tracts of the sheep normally do not form such group systems as in man. This degeneration was traced to lower levels of the spinal cord without any alteration in anatomical location.

Nerve Cells.

The relative resistance of the nerve cells in all parts of the system was an outstanding feature, and it was clear that, to a large extent, they retained their normal form, arrangement and structure in spite of gross dissolution of white matter (Fig.28./29). Where demyelination in the hemispheres was of a mild degree no distinct cell changes were observed. In those cases

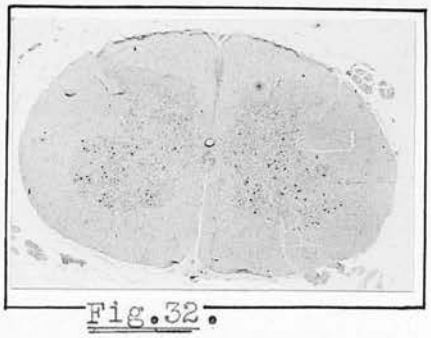


Fig.32.

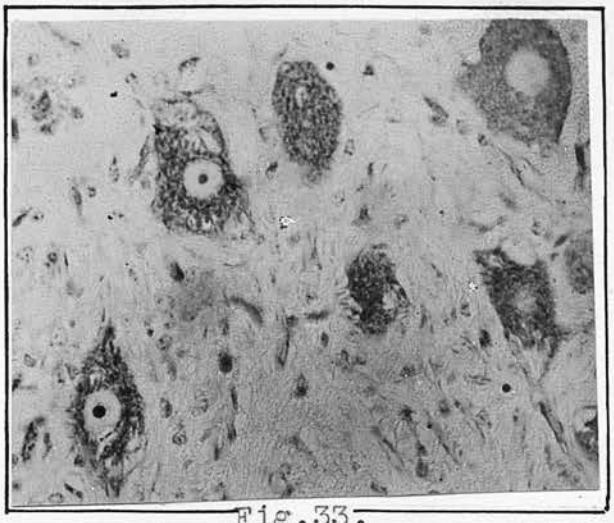


Fig.33.

"Swayback". Spinal cord, low power, showing absence of inflammatory cell infiltrations in the grey or white matter and normal anterior horn cells in Fig.33. Nissl. Fig.32 X 8. Fig.33 X 400.

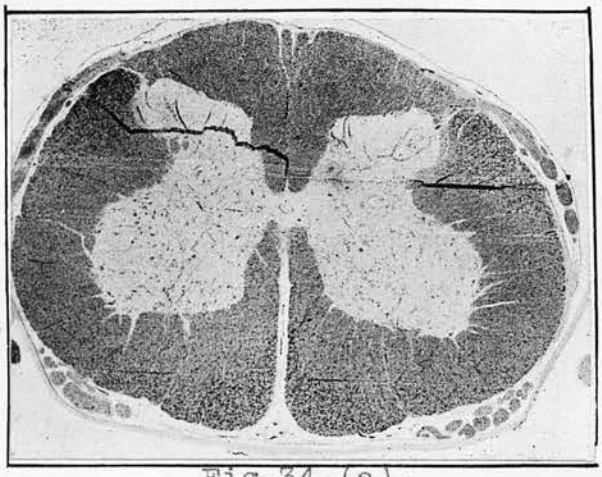


Fig.34.(a).

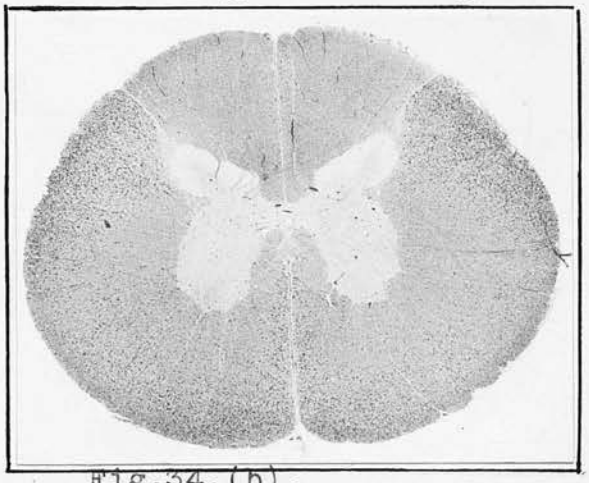


Fig.34.(b).

"Swayback". Spinal cord, lower cervical segments from two cases (a & b); degenerated myelin fibres stained black present in ventral part of ventro-lateral columns near median fissure and dorsal part of same column adjacent to the dorsal horn of grey matter; (a) same case as Figs.19,27 and 28; (b) same case as Figs. 25,26 & 32. Marchi-Busch method. X 8.

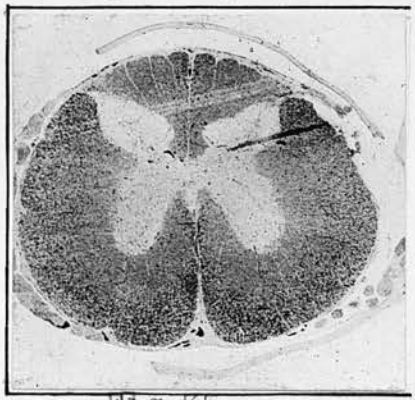


Fig.35.

"Swayback". Spinal cord, lower thoracic segment; same case as Fig.34(a); degenerated fibres present in the same location as in the cervical region. M-B X 8

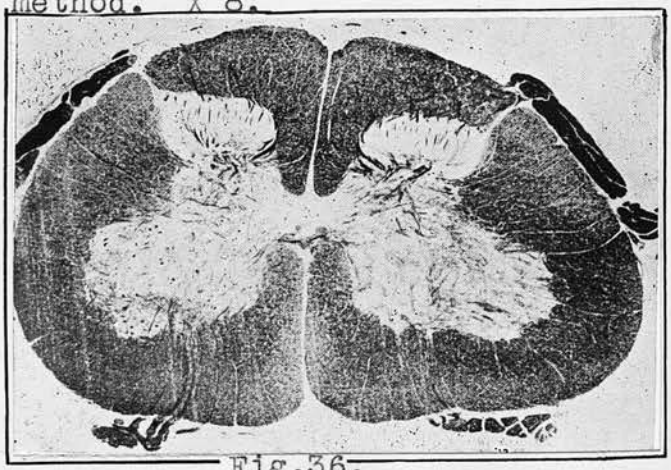


Fig.36.

"Swayback". Spinal cord stained by Weigert-Pal; compare with Fig.34(a); note the paled areas corresp. to those showing degeneration by the Marchi method. X 8.

with gross liquefaction of the white matter, the cerebral cortex showed irregularity in arrangement of the ganglion cells, some of which showed shrinkage and pycnosis, others vacuolation and displacement of the nuclei. Sections of the motor area (superior frontal gyrus) were made from many cases. The pyramidal cells were definable but often shrunken and pycnotic, with a clear perineuronal space around them. Similar but inconstant changes were observed in many other parts of the system, but their significance, if any, is not known. The disorganisation of the nervous system as a whole might have been responsible for many of the changes. For example, small nerve cells were frequently seen deep in the white matter.

In view of the suggestion that the motor tracts of the sheep might (in part) have a subcortical origin, sections of the red nucleus were examined. Unmistakable signs of degeneration were present in the nerve cells of this nucleus in all cases examined. Some showed early chromatolytic changes in the cytoplasm; in others the Nissl granules had completely disappeared with the nucleus shrunken and displaced to the cell margin, the cell having then a clear homogenous appearance. (Figs.37.38.)

Neuronophagia was never observed in any part of the system, and it is important to record that after a careful search inclusion bodies could not be found.

Glia.

No difficulty was encountered in demonstrating by the various specific staining methods the early gliosis in the demyelinated areas. A dense feltwork of fine fibrils ramified in all directions in such zones and in this fibrillary system lay numerous small, darkly stained nuclei (Fig.30.31) The cells concerned in this reaction appeared to be exclusively the fibrous astrocytes. The gliosis was restricted to the areas of degenerated white matter and invaded the deeper layers of the cortex only to a slight degree. Hypertrophy or proliferation of the protoplasmic astrocytes in the grey matter was not observed. In those cases where cavity formation was pronounced, the wall of the cavity consists of a dense meshwork of glia fibrils (Fig. 31).

Owing to the difficulty in successfully impregnating the oligodendroglia by recognised methods, it was uncertain whether these elements are involved in any pathological change. In Nissl preparations, however, of the grossly degenerated areas of white matter there appeared to be a general impoverishment of all cell types apart from the astrocytes, so it was possible that the oligodendroglia may have completely disappeared from these areas (Fig. 28). Similarly, microglial participation was never outstanding either by the formation of rod cells or of the large scavenger cell type. Compound granular corpuscles

containing broken-down myelin was always present in or near demyelinated zones, but never in large numbers (Fig. 27).

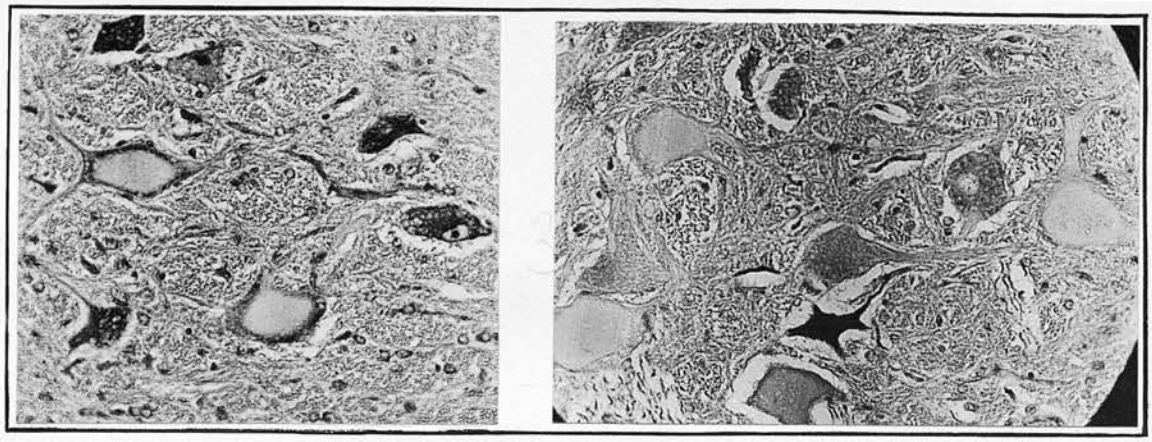
4. PATHOLOGICAL EXAMINATION OF "CHRONIC" OR MILD CASES.

Some lambs may develop symptoms a few weeks after birth, and the disease may not progress then beyond a slight but permanent weakness of the hind legs. These animals will survive, and are often used later for breeding.

It was considered that an examination of the nervous system in such cases might be of value. A sheep, one year old, which had shown such slight non-progressive symptoms after birth, was killed. The animal axhibited only a slight weakness of the hind quarters, particularly when made to turn, otherwise the sheep was in a good healthy condition. (See ciné).

No macroscopic lesions were observed in the viscera nor in any part of the nervous system. A series of sections, stained by Weigert-Pal, were made from the nervous system at regular levels through the cerebrum, mid-brain, pons, medulla and various segments of the spinal cord.

It was expected in such mild cases as this, with a long survival period, that those areas of the white matter which



Figs.37 & 38.

"Swayback". Lesions in the red nucleus from ~~three~~ two separate cases; the large nerve cells show varying degrees of chromatolysis. Nissl Orange-G method. X 400.

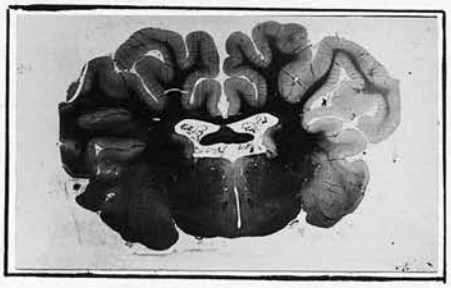


Fig.39.

"Swayback". "Mild case" (27/1937). M. 1 yr. old. Animal affected at birth but with only mild form of inco-ordination which did not progress. No macroscopic changes in the brain and coronal sections, such as this one, stained by W-Pal, revealed no areas of unmistakable demyelination.

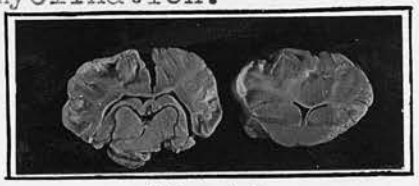


Fig.40.

"Swayback" (Australian disease). Coronal sections of brain through occipital pole (left) and frontal pole (right); demarcation between the grey and white matter extremely blurred; gelatinous type of degeneration without cavitation comparable with many cases seen in this country and demonstrated in Fig.12. (Specimen obtained through the courtesy of Mr. H. Bennetts, W. Australia).

had been demyelinated (presumably sclerosed) would be easily demonstrable by Weigert-Pal technique. This, however, was not the case. The nervous system showed no lesion which was of diagnostic significance, and certainly none recognisable as plaques of demyelination. (Fig.39) Transverse sections of the cord stained by Weigert-Pal to all intents and purposes were normal.

It was concluded that in such mild cases the number of fibres which undergo degeneration in the hemispheres and in the descending motor tracts of the cord must be so small and/or so scattered as to render their recognition by Weigert-Pal technique impossible.

5. PATHOLOGICAL EXAMINATION OF EWES WHICH HAVE GIVEN BIRTH TO SWAYBACK LAMBS.

It was an established observation that ewes, which give birth to Swayback lambs, appear to be healthy and may in subsequent seasons give birth to either healthy or affected lambs. There cannot be, therefore, any serious organic disease in these ewes, in spite of the delivery of diseased progeny. Whether this is more apparent than real may be reconsidered later.

Six ewes which had given birth to Swayback lambs a few days previously were killed and subjected to a post-mortem examination. It is unnecessary to give details of the autopsies

as in each case significant lesions in any part of the body (including the central nervous system) were absent.

6. COMPARISON OF THE AUSTRALIAN DISEASES - (ENZOOTIC ATAXIA) - WITH "SWAYBACK".

The original work by Bennetts (1932) in W. Australia did not include any detailed examination of the brain, and it was uncertain that the disease was identical with "Swayback". Later, in 1937, Bennetts recorded cerebral lesions in Australian cases identical with those described by myself for "Swayback". Dr. E. Weston Hurst of the Medical Research Institute, Adelaide, S. Australia, has also confirmed these findings.*

Through the courtesy of Mr. H. Bennetts, the brains of four cases of the Australian disease, already fixed in formalin, were received for examination. A brief description of these cases is sufficient to show that the Australian disease is identical with "Swayback".

CASE I. (Bennetts, No. W.26.) Born unable to stand; death one day later. The brain was soft and flabby; on section there was a symmetrical gelatinous degeneration of the cerebral white matter extending from pole to pole with early cavitation, particuluarly of the superior convolutions and occipital poles. No lesions were found in other parts of the brain or cord.

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*Personal communication (1937).

CASE II. (Bennetts, No. W.37.) Same history as Case I. On coronal section the lesions were of a minimal grade; small patches of cerebral softening with very early cavitation were present mainly at the summits of the superior convolutions. Superficially the brain of this case looked almost normal.

CASE III. (Bennetts, No. W.47.) This animal was first seen when 12 days old with marked ataxia, and died 5 days later. The brain was sodden and flabby; on cross section there was present an identical appearance to that of many cases seen in this country. No normal white matter was present in any part of the cerebrum; demarcation between the grey and white matter was extremely blurred and cavitation was of a minor grade (Fig.40). The diffuse symmetrical gelatinous nature of the lesion was highly reminiscent of some cases of Schilder's encephalitis seen in children. No lesions in any other part of the brain.

CASE IV. (Bennetts, No. 37.) This subject was weak and unthrifty from birth, the condition developed more slowly and the animal died of pneumonia when one month old. The brain, like many of those seen in England, showed no macroscopic lesions in any part of the white matter.

A few representative sections from these specimens were examined histologically and it was found there were no significant differences in the type, nature or distribution of the lesions as compared with Swayback. Inflammatory changes were absent; demyelination was a constant feature. The cellular lesions in the red nucleus were conspicious and the cord degeneration was identical.

VII. DISCUSSION AND CONCLUSIONS REGARDING THE PATHOLOGY.

1. PATHOLOGICAL SUBSTRATUM OF SWAYBACK.

"Swayback" is a nervous disorder of a type which has not been previously described in domestic animals. The lesions which form the anatomic basis of this disorder are essentially those of cerebral demyelination with consequent destruction of the axis cylinders and later cavitation, and secondary degeneration of the motor paths. The occurrence of ataxia at birth in most cases, and the presence of severe degenerative lesions in the brains of lambs examined within a few minutes of birth as well as in still-born lambs, indicate conclusively that the process is ante-natal in origin. This is not invalidated by the occurrence of cases which do not appear to show symptoms until some time after birth. The symptoms in these might be so slight as to evade notice, and in any case, with minimal damage to the nervous system of the developing lamb late in pregnancy, the symptoms may take some time to develop.

2. DEMYELINATION OR MYELIN APLASIA?

The lesions might be considered to be due to an inhibition or aplasia of myelin and not to an active destruction of formed myelin. The same problem has arisen in connection with infantile cases of diffuse sclerosis in the human being (e.g. see

Bouman, 1934), and Russell and Tallerman, 1937). It must be stressed that in every case of Swayback the brain as a whole is a well-developed full-time organ in respect of size, conformity and development. The idea of a myelin aplasia is thus unacceptable, but even more so because it would not explain the porous areas and the gross cavitation, nor the myelin destruction deminstrated by positive staining reactions (Marchi or Scharlach R methods). An active degeneration is also indicated by the changes in the cells of the red nucleus, in the cells of the motor cortex and in the myelin sheaths of the descending motor paths.

It is improbable that the "destruction" of the cerebral white matter can be regarded other than that of an idiopathic disintegration of a substance which had been formed in utero. It is, however, feasible that with the occurrence of demyelination, normal myelination would be inhibited.

3. GENESIS OF THE LESION.

As the condition is primarily that of an ante-natal demyelination, the state of myelination at the time the causative factor begins to operate, must be an influential factor on the subsequent course of the disease. It is therefore unlikely that the pathogenesis will be fully understood until more is known about myelination in the lamb. Simply because the disease is ante-natal in origin the initial stages of the process cannot be

studied, and it seems improbable that this will be done until it can be produced experimentally. Any reasonable consideration of the pathogenesis is thus greatly hindered.

It might be suggested, however, that in "Swayback" the demyelination occurs at a relatively late stage of gestation. If this were not so, a greater degree of brain deformity than that seen would almost certainly be effected. The disintegration of white matter must have proceeded occasionally with a singular rapidity, as in some cases seen soon after birth, there remained little or no intact cerebral myelin.

The severity and extent of the lesions were not related to the age of the lamb. Some cases between the ages of 5-12 weeks showed no macroscopic changes in the brain; on the other hand gross cerebral damage was seen in still-born lambs and others only a few minutes to four weeks old. While the disease might be thus regarded as a progressive disorder in which cavitation was the end stage of a degenerative process, this was not a constant feature. It is probable that as well as an acute progressive type there is also a more chronic non-progressive mild type of the disease, some of the latter cases indeed surviving. The occurrence of these mild cases might indicate that there is an optimal time during gestation for the causative agent to operate and that it does so with varied intensity. The damage done in the mild

cases is slight or the cause operates too late in relation to normal myelination to be fully pathogenic, while the cause is obviously not continuous beyond the ante-natal period. In support of this statement it might be mentioned, that it is a common practice to suckle other healthy lambs on ewes which have lost their own lamb or lambs from Swayback; these foster lambs never exhibit any signs of the disease, in later life.

4. LIQUEFACTION AND CAVITATION IN THE CEREBRAL LESIONS.

In "Swayback" cavitation was always present when degeneration of the cerebral white matter was intense. This "porencephalic-like" process has its analogy in human pathology but it must not be identified with true porencephaly due to defective development.

It is recognised that the immature brain of infants reacts to dissolution of tissue by liquefaction and cavity formation, while in the case of the human adult brain, glial organisation predominates. The brain of the lamb must be regarded as even more "immature" than the "childs" brain, and at the foetal age when these lambs are affected, glial development and reactivity to a "foreign agent", or trauma, must be of a low grade. The process appears to be so acute in many cases that there may not be time for a proper glial functioning. Hence, cavitation might appear to be the only possible reaction to active destruction of white matter in lambs of this age.

The cavitation seen in Swayback has also been recorded in Schilder's disease, and diffuse sclerosis in man (e.g. see Bouman, 1934, Russell and Tallerman, 1937 and others); and cannot be regarded as an extraordinary feature.

5. THE VENTRICULAR DILATATION IN "SWAYBACK".

The internal hydrocephalus of the lateral ventricles which was observed in many cases of "Swayback" has also its parallel in human pathology. The same phenomenon seems to occur in man consequent to any degree of cerebral atrophy, (Brain,(1933), Wertham, (1934), Bouman (1934), Collier and Greenfield (1924), when it has been regarded as a compensatory process for the cerebral atrophy and not due to increased ventricular pressure. In "Swayback" there was also no sign that it was due to any mechanical obstruction, present, for example, in the interventricular foramen, the aqueduct or outlets in the fourth ventricle.

6. THE NATURE AND ORIGIN OF THE PROCESS - INFLAMMATORY OR DEGENERATIVE?

The nature of demyelinating diseases in man has been discussed so many times, with so much disagreement, that it is fruitless to reopen the question regarding "Swayback", (see Bouman, (1934), Globus and Strauss (1928) and Dawson (1916). In all papers dealing with this aspect the contentions for and against an inflammatory nature have depended on the criteria used to distinguish inflammation from frank degeneration, and the views as to

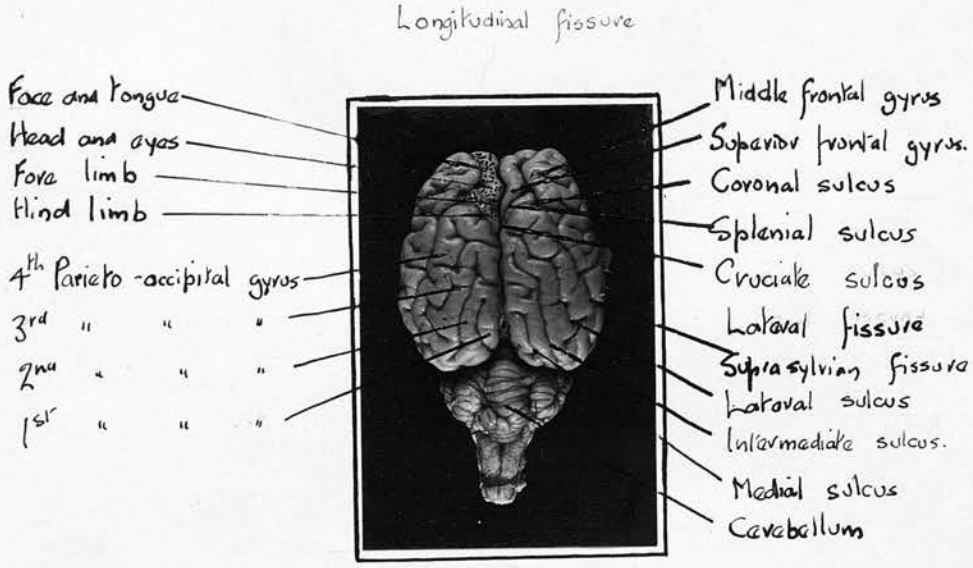

Fig.41.
Dorsal aspect of sheep brain. The situation of the motor area in the superior frontal gyrus (after King).

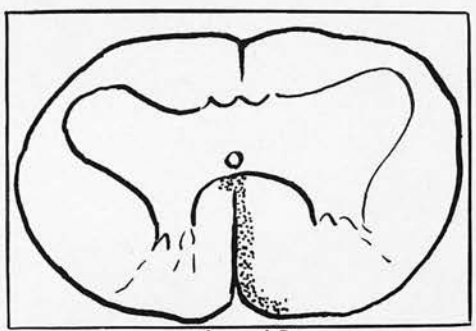

Fig.42.
Spinal cord, upper cervical Region. Diagram (after King) showing the localisation of the degenerated fibre tracts following a hemisection lesion in the motor area; these represent the pyramidal tracts which disappear in the cervical region.

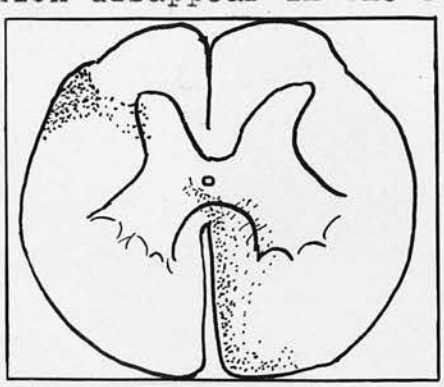

Fig.43.
Spinal cord, C6. Diagram (after King) showing the localisation of the degenerated fibre tracts subsequent to a hemisection lesion in the lower part of the medulla; these correspond to those seen in Swayback and probably represent motor tracts arising at a level in the mid-brain.

what constitutes true inflammation are nowhere so conflicting as when the term is used in connection with the nervous system. It must be emphasised that in "Swayback" (a) there never occurs any infiltrations of "inflammatory" cell elements, (b) a search for inclusion bodies has been negative and, (c) the process has an extraordinary affinity for the white matter. These changes are distinct from those found in known infections of the nervous system. "Swayback" is thus regarded as being allied to a true degeneration and not to an inflammatory process, and perhaps is aptly summed up in the term which has been used by Globus and Strauss (1928) to denote the true anatomical condition in Schilder's disease, viz. progressive degenerative subcortical encephalopathy.

7. MOTOR PATHS OF THE SHEEP AND THE DEGENERATION IN THE SPINAL CORD.

The motor paths of the sheep have been studied by a few workers. King (1911) confirmed a view that the motor area of the sheep was restricted to the superior frontal gyrus (Fig. 41) This was ascertained both by stimulation experiments and by histological study, the latter method showing that the Betz cells were confined to this area, (see also Bagley, 1922). King showed that the sheep, like many lower animals, possessed a comparatively small pyramidal tract. From hemisection experiments it was found that descending fasciculi degenerated as a result of a lesion in the motor area, but that most of the fibres decussated in the

lower part of the medulla and in the first cervical segment, after which they became scattered and could not be followed further (Fig. 42). As a result of a hemisection lesion in the lower part of the pons and medulla, two other well developed descending paths were demonstrated (Fig. 43) (a) one in the dorsal part of the ventro-lateral columns of the cord extending to the sacral region, and probably corresponding to the rubro-spinal tract of the cat, and (b) a smaller ventral tract in the neighbourhood of the ventral fissure. King concluded that the distinct development of these two tracts might indicate that the principal direct motor paths in the sheep (and perhaps other lower animals) are subcortical in origin, and that they might arise from cells in the mid-brain, pons, medulla or even all three regions.

Spinal cord degeneration in "Swayback" was first described by Lyle Stewart (1932) in this country and by Bennetts (1932) in the case of the Australian disease. Both of these workers inferred, however, by analogy with human tracts, that this represented an ascending degeneration; such direct inference cannot be made. In location and extent, the tracts described by them, and those seen constantly in all our own cases of "Swayback", were identical with those described by King, and in any case, little doubt can remain that they are indeed motor in origin and function as the symptoms are indicative of an upper motor neurone lesion.

The destruction of the cerebral white matter must be regarded as being responsible for pyramidal tract degeneration, but we know that these tracts fade out in the upper part of the cord. If the conclusions of King regarding the origin of the motor tracts of the sheep are correct, then the degenerated tracts in "Swayback" seen in the upper segments of the spinal cord represent combined pyramidal and rubro-spinal tracts, while in the lower segments of the cord, only the latter.

The suggestion of King that the motor tracts might originate in the mid-brain might have some corollary in this condition of "Swayback". In all cases of "Swayback" examined, acute chromatolytic changes were found in the nerve cells of the red nucleus (Fig.37.3). In any one field taken at random through the nucleus it was common to find six or more cells which had undergone such a change.

The degeneration in the spinal cord, and its relationship to the general pathlogical picture is, therefore, not yet fully understood. The chromatolytic changes in the cells of the red nucleus may be simply retrograde axonal reaction, yet it is hard to disbelieve that the cord degeneration is not in some way connected with the gross cerebral lesions, or in other words, is a true secondary descending degeneration. It is possible, of course, that whatever the causal agent may be, it might have an independent

action on the motor ganglion cells as well as the cerebral myelin.

8. RELATIONSHIP OF SWAYBACK TO SCHILDER'S ENCEPHALITIS IN MAN.*

The disease was first described ny Schilder (1912) and designated as encephalitis periaxialis diffusa, and since then by numerous other workers, many of whom have suggested a different nomenclature. Globus and Strauss (1928), for example, suggest that the name progressive degenerative subcortical encephalopathy would more correctly indicate the pathological nature of the disease. As it is uncertain how far a distinction can be drawn on anatomical grounds between Schilder's disease and other forms of cerebral sclerosis, as seen at autopsy, there has been a tendency for many authorities to regard the disease only as an anatomical entity. In this case the syndrome might include diseases which are anatomically related but aetiologically independent.

The disease usually occurs in children and young subjects, and is generally non-pyrexial throughout its course. Remissions sometimes occur, but it is invariably fatal in a few months to a few years. The most important clinical symptoms which are said to be unrepresented in any other disease as a triad, are progressive blindness of the cerebral type, progressive spastic paralysis and mental deterioration. Unsteadiness, loss of sense of position and deafness may also occur. Although the majority of cases appear to arise sporadically, a familial

* See Collier & Greenfield (1924), Stewart, Greenfield & Blandy, (1927), Brain (1933), Brain & Strauss (1934), and Bouman (1934); Specimens of Schilder's disease were obtained for study from Dr. A. Meyer, Maudsley Mental Hospital, London.

incidence is being increasingly recognised (Symonds, 1928; Macnamara and Dickson, 1933; Meyer, 1936).

The outstanding pathological feature is the massive cerebral demyelination, commonly starting in the occipital poles and spreading anteriorly through the white matter. In advanced cases the corpus callosum, the frontal and temporal poles may be affected. Thus, according to the stage at which the disease is seen, it may affect a part of a lobe, a whole lobe or a whole hemisphere, and in the majority of cases both sides of the brain may be involved. The white matter of the capsules, crura and pons may also be implicated but the sparing of the subarcuate fibres is often a feature. This degeneration often stops at a short distance from the cortex and the border line may thus extend over a wide territory parallel with the cortex. Frequently other parts of the nervous system may show small foci of demyelination and secondary degeneration may be found in the spinal cord. As a result of the widespread degeneration in the cerebrum, the white matter is converted into a greyish yellow to brown, soft translucent gelatinous substance, or sometimes of a hyaline nature. Subsequent to the demyelination or coincident with it, the axis cylinders are destroyed. In the degenerated areas there is a proliferation of the fibrillary astrocytes with the production of a felt work of glia fibrils, and this gliosis may extend beyond demyelinated areas into the grey matter. A diffuse infiltration

of phagocytes and compound granular corpuscles containing fat globules derived from the broken-down myelin usually occurs in the degenerated white matter. Infiltrations of these cells and of mesodermal cells into the perivascular spaces may be absent, mild, moderate or severe. The presence of the so-called "prelipoid" substances derived from myelin disintegration has been noted by many workers.

This brief description of the disease in man indicates that Swayback has many comparable pathological and clinical features. These would include (a) the diffuse bilateral demyelination of the cerebrum, often also beginning in/or being confined to, the occipital poles; (b) the absence of demyelination in parts of the brain below the cerebral level: (c) the relative preservation of the cortical grey matter; (d) the blindness in some cases: (e) the spastic paralysis and inco-ordination; (f) the progressive course and fatal termination in many cases and (g) the present obscure aetiology from which viruses might be definitely excluded.

Too strict an analogy between neuropathological conditions in man and lower animals must not, however, be expected, mainly owing to the relative "immaturity" of the brain of the latter. The disease process in "Swayback" also begins at so early an age that this immaturity might be considered even more pronounced.

As there is a tendency now to regard Schilder's disease only as an anatomical entity, there can be no doubt that "Swayback" is a disease comparable at least to the Schilder's type. Until more is known about the aetiology of "Swayback" and the demyelination diseases in man, it would be unwise, however, to elaborate further.

9. SYMPTOMS IN RELATION TO THE LESIONS.

The combination of spastic paralysis and inco-ordination which occurs in "Swayback" and is indicative of an upper motor nurone lesion, can thus be explained by the cerebral lesions; the blindness seen in some cases, by those in the occipital lobes.

VIII. AETIOLOGY.

1. BACTERIOLOGICAL AND EXPERIMENTAL TRANSMISSION WORK.

A thorough examination of various organs, blood, brain, and cerebro-spinal fluid, was made of many cases using a wide variety of cultural methods. The cultures of all either remained sterile or showed growths of contaminating bacteria only; no specific organism was isolated. These findings were in full accordance with those obtained in previous years (from 1926 onwards) by other workers in the Institute. Attempts were also made to transmit the disease to healthy lambs. Emulsions of visceral organs or blood, or parts of the nervous system from "Swayback" cases were inoculated into healthy lambs (20 experiments) by many routes; all inoculated lambs remained healthy. The view that "Swayback" was not infectious or contagious in nature was supported by the fact that affected lambs, or their ewes, do not appear to transmit the disease under natural conditions. In an affected area the ewes are usually together throughout pregnancy, while "Swayback" lambs are often in contact with young healthy lambs for some time without any indication of transmission of the disease. There is also the fact that the type of lesion in "Swayback" was unlike that which occurs in known transmissible infections of the nervous system. Finally, it is improbable that ewes could carry an infective agent for years which would be pathogenic only for the developing lambs of consecutive or even

more puzzling, intermittent pregnancies.

With just reason, therefore, it was concluded that neither bacteria nor viruses were concerned in the aetiology. This conclusion is similar to that of Lyle Stewart (1932) in England, Bennetts (1932) in Australia, Gaiger (1917) in Peru and Magnusson (1920) in Sweden, providing that the conditions described by Gaiger and Magnusson were "Swayback".

No serious attention can be given to the claims of Mitchell (1937) who stated that "Renguerra" was due to a virus and that transmission was possible. He apparently was unaware that louping-ill and Swayback are two separate diseases as he used the names as synonyms, and no pathological data are given to indicate which of these two he had investigated.

These negative findings are of importance as they are parallel to those of many workers who have tried repeatedly, without success, to identify either bacteria or viruses with analagous demyelination diseases in man (e.g. disseminated sclerosis, Schilder's disease, post-infective and post-vaccinial encephalitis) in monkeys,(e.g. the Schilder's-like disease) and in dogs (post-distemper encephalitis).

2. BREEDING AND HEREDITARY INFLUENCES.

There is no evidence to indicate that the disease is either hereditary or familial in nature. Lambs of most breeds may be affected, and the inter-crossing of ewes and rams of various breeds in consecutive years, does not influence the incidence of

"Swayback" in the progeny. As an illustration that breeding does not necessarily play a part in the aetiology of the condition, the following history of its occurrence on a particular farm may be of interest since it is typical of a number of outbreaks. The farmer had been in possession of the farm for three years (1933-35); in 1933, 150 Wensleydale Cross ewes were mated with Oxford rams, and in that year the disease did not occur, but in the following year 76 lambs from the same parents were affected; in 1935 the original ewes were mated with Suffolk and Hampshire rams, and 55 cases occurred in the progeny of both types of ram. Many other similar histories indicate that the disease is not confined to the progeny of a particular breed of ewe or ram and that variations in crossing have no influence on the prevalence of the disease.

It is difficult to believe that the disease is a malformation of development partly because of its high incidence and wide occurrence, but more particularly because this concept would not explain the singularly rapid degenerative process in the brain.

3. BIOCHEMICAL ASPECTS.

Deficiencies of any of the recognised vitamins and lack of the more common minerals might seem on superficial examination to be eliminated.

The sheep is able to synthesise vitamins C, D in the presence of sunlight, and some of the B factors in its own body, and as a result they probably suffer no ill-effect from their absence in the food. In many cases of "Swayback", estimations of vitamin A in the livers were made by Dr. T. Moore, Nutritional Laboratory, Cambridge; abundant reserves were always found.

*As a routine measure, chemical analyses were made of the blood of a number of cases and of their ewes on a farm in which "Swayback" had been prevalent for some years. The serum calcium, inorganic phosphorous and magnesium were estimated. Most of the values were within the range of normality, but in a few "Swayback" lambs and their mothers a lower serum P was present. Thus, figures such as 7.8 mg, 8.8 mg, 8.1 mg, 8.5 mg, compared with the normal figures of 12-13 mg. for the lambs and 3.0 mg. compared with 4-5 mg. (per 100 cc. serum) for the ewes were obtained. The significance of this finding is unknown.

Composition of the Grass from Affected and Control Areas.

Grass was collected for chemical analysis free from gross contamination with soil and roots from farms in Derbyshire and Gloucestershire where the disease was prevalent, from farms

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*These analyses were made by Dr. J. Stewart now of the Animal Diseases Research Association, Moredun Institute, Edinburgh.

TABLE IV.

Composition of Grasses from "affected" and "non-affected" areas (on 100% dry matter).

Area & Farm No.	Tot. Ash	Sol. Ash	CaO	P_2O_5	Ether extract	Crude protein	Fibre	Cu	Fe.	Pb.
AFFECTED FARMS.										
Derbyshire Farm 1.	12.02	3.79	0.83	0.64	3.68	17.37	24.31	0.0024	-	0.008
" " 2.	13.10	6.89	2.39	0.38	2.92	10.75	27.72	0.0015	0.0398	0.0009
" " 3.	9.84	3.62	1.04	0.54	3.21	12.44	28.63	0.0014	0.1326	0.0078
" " 4.	13.80	3.93	0.63	0.47	2.60	12.75	27.01	0.0014	0.1669	0.0082
" " 5.	14.43	6.95	1.36	0.67	2.54	13.06	28.43	-	0.1286	0.0052
" " 6.	14.36	5.93	0.93	0.56	3.43	12.37	23.35	0.0027	-	0.0396
Gloucester shire Farm 1.	9.95	4.32	0.72	0.68	3.59	15.94	25.92	0.0017	0.0880	-
" " 2.	9.99	3.42	0.52	0.56	2.63	12.81	25.81	0.0019	0.1047	0.0119
Leicester shire Farm 1.	10.36	3.47	0.50	0.43	3.85	12.13	26.19	0.0019	-	0.0023
CONTROL FARMS.										
Cambs. Farm 1.	11.80	4.89	0.79	0.91	4.96	14.06	24.13	0.0012	0.0492	0.0001
" " 2.	10.12	6.33	0.85	0.66	6.32	22.19	17.85	0.0014	0.0423	0.0001
" " 3.	-	-	-	-	-	-	-	0.0018	0.0467	0.0001
Derbyshire Farm 1.	10.16	6.53	0.85	0.78	5.49	15.31	17.65	-	0.0693	-
" " 2.	10.71	4.68	1.30	0.54	4.24	15.38	25.23	0.0015	0.1342	0.0068
" " 3.	8.54	2.54	0.30	0.49	3.33	13.31	27.42	0.0019	0.1299	0.0085
Leicester shire Farm 1.	23.33	4.91	2.24	0.74	2.49	16.50	20.27	0.0024	-	-

adjacent to these where the disease was unknown, and from farms in Cambridgeshire far removed from affected areas. No special precautions were observed in collecting the samples as a more accurate assessment of the intake of the various constituents could thus be obtained. This chemical work was carried out by my colleague, Dr. G.D. Shearer, to whom I am indebted for the results set out in Table IV.

With the exception of the Cu, Fe and Pb content of the grass, it will be seen that while the chemical composition of the grass from affected farms compares unfavourably in most instances with that of good pasture, especially with regard to the P_2O_5 content, no gross deficiency of any constituent is evident, and that of the control farms in Derbyshire is similar to that of affected farms.

In connection with the Cu, Fe and Pb content of these pastures, the most striking feature is the remarkable constancy of the amount of Cu. Of the thirteen samples analysed from widely separated areas, the range is between 1.2-2.7 mgs. per cent. with no difference between "Swayback" and "Control" areas. The Pb content, however, shows a wide range of values. Grass from "Swayback".farms in Derbyshire shows, except in one instance, a Pb content of over 5 mgs. per cent., and in one case has the very high value of 39.6 mg. per cent. A high Pb content of grass

is also shown in samples from one "Swayback" farm in Gloucester. While grass from control farms in Derbyshire near "Swayback" areas also show similar figures to these, that from control farms away from "Swayback" areas contains very small amounts of Pb. The significance of the Cu and Pb figures will be discussed later.

The amount of Fe in the grass from both "Swayback" and control farms in Derbyshire, and also from Swayback farms in Gloucester, is much higher than is usually found in grass. The significance of these figures is difficult to assess.

4. LEAD POISONING IN RELATION TO SWAYBACK.

Lead has for many years been known to produce changes in the nervous system. In chronic lead poisoning of children one of the most dreaded complications is lead encephalopathy. In adults, on the other hand, while cerebral disturbances may occur, the common lesion is a peripheral neuritis affecting the motor nerves. Innumerable reports on the pathology of the nervous lesions have been made, e.g. see Aub et al (1925), Ferraro (1932), Blackmore (1937) and Baker (1936). Extreme cerebral ordema may be present and demyelination has been recorded. Putnam (1883) recorded cases of diffuse lesions of the spinal cord and brain with spasticity of the legs in which he found lead in the urine, and as a result suggested the metal as the cause. An association of lead with multiple sclerosis has been suggested since then, e.g. by Eichorst (1913) and by Cone, Russel and Harwood (1934).

It is therefore of interest that a connection between lead and "Swayback" has been suggested from entirely different sources (see below) and as yet cannot be dismissed as a possible causal factor.

It was concluded in 1935 that if the disease was caused by some "toxic" substance it must be carried by the pregnant ewe (and over a period of years) to exert a pathogenic effect only on the developing lamb. It was thus essential that this "toxic agent" could pass freely through the placenta in order to affect the brain of the lamb.

These conclusions were similar to Bennetts (1934 and 1935) in Australia who thought that the causal agent might be excreted through the milk,* and suggested the possibility of a plant or mineral poison and that lead might be the "poison" involved. Analyses of the milk from "affected" ewes showed the presence of traces of lead, although traces were found in the milk of normal ewes. "Deleading" experiments were made by administering ammonium chloride licks to pregnant ewes with an apparent reduction in the incidence of "Swayback" in their progeny. In the absence of other proof the association of lead was uncertain.

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* It is unlikely that there is any pathogenic "toxic or deficiency factor" in the milk as healthy lambs can be fostered to "Swayback" ewes with no ill-effect.

During the lambing season of 1936 a similar experiment was carried out by myself with the help of a sheep farmer in Buckinghamshire. This farm had suffered severe losses from Swayback for a number of years. Ammonium chloride was given to pregnant ewes mixed in their food in amounts representing a dose to each ewe of 20 g. per day; 200 ewes were used with an equal number of control animals and the treatment was carried over the last two months of pregnancy. There was little or no difference between the incidence of Swayback in the progeny of experimental and control groups (about 5 per cent.) The incidence of the disease in many "untreated" farms in this locality was much lower in 1936 than in previous years; the results were therefore inconclusive in every way.

It has already been mentioned on page 20 how in the affected area in Derbyshire there are several facts which might also suggest a causal connection of lead with "Swayback", and the reasons for the common belief there regarding the disease as a form of plumbism.

The condition "Renguerra" in Peru, which may be similar to "Swayback", has also been associated with lead by Tabusso (see Gaiger, 1917 and Mitchell, 1937).

These various suggestions indicated that lead could not be cursorily dismissed as of no moment in the aetiology, and work was necessary along this line. Chemical analyses were therefore made by Dr. G.D. Shearer of the pastures from farms in this and other "Swayback" areas and also of various body tissues of "Swayback" lambs and their mothers.

The analyses of the grass from affected and Swayback

areas will be found in Table IV where the extremely high amount of Pb will be at once evident. Analyses were made of the livers from cases of "Swayback" and from two ewes which had given birth to "Swayback" lambs. The results are given in Table ; the large amount of Pb in the livers of "Swayback" lambs supports the view that Pb is transported through the placenta. Lead analyses were also made of the brains of 15 cases of "Swayback"; values were obtained ranging from a trace to 5.5 mg. per 100 g. dried brain compared with the figures of nil to 0.7 in 4 control brains.

Conclusions regarding the association of lead with Swayback.

It is necessary to emphasise certain conclusions of Aub et al (1925). - There appears to be only a quantitative difference between the so-called "normal lead" of tissues with that found in cases of poisoning. It is therefore essential to determine how much lead is likely to be absorbed by individuals living a normal life at a given time and place. As far as the pathology is concerned there are few diagnostic lesions apart from the blue line in the gums and the anaemia with stippling of the red cells; many other anatomical changes have been described, e.g. in the nervous system, but they are not constantly found in every case. There is also some difference in reaction to the metal between children and adults.

As far as lead poisoning in animals is concerned these facts must be considered and should be investigated along these lines because we know little about the animal aspect, especially when it is a matter of deciding whether lead is involved in a condition ("Swayback") unlike that which has not been described in plumbism.

It is known that young animals with lead poisoning show a form of posterior paralysis, not unlike "Swayback", but this parallel symptomology makes it difficult to determine whether Pb is involved in "Swayback". The occurrence of the disease in districts of Derbyshire, Yorkshire and the Mendips, where there is much lead, has perhaps focussed too much attention on the metal. Much of the work has been done in Derbyshire and it would be essential to carry out similar investigations in other "Swayback" areas, as the disease occurs in parts of England which cannot be compared with Derbyshire as far as the lead content of the soil is concerned, and there may actually occur a lead encephalopathy ("Swayback-like") in lambs to be distinguished from "Swayback".

There was no constant lesion either in the ewes or affected lambs which could be regarded as similar to those known in plumbism. The lead line in the gums was occasionally seen in ewes in Derbyshire; an anaemia with punctate basophilia of the

red cells, although present in a number of ewes and lambs, was not a constant feature, and X-ray examination of the bones of one case showed nothing similar to the "lead lines" in human lead poisoning. The cerebral lesions in "Swayback" are of no diagnostic help as there are no data regarding the state of the nervous system in animals, particularly young lambs, suffering from lead poisoning. In spite of this, however, the quantities of lead present in the tissues of "Swayback" lambs (from Derbyshire and other areas) Table V and of the ewes must be highly abnormal, so that the ewes must ingest, while grazing, relatively large amounts of lead over a prolonged period, although in what form or with what significance is unknown.

If lead is connected causally with "Swayback" it must be absorbed insidiously by the ewes so that they do not suffer from outspoken plumbism, as is known can happen in the human being. In that light, feeding experiments might not be successful in proving or disproving any possible causal connection. An initial experiment was, however, carried out with two sheep, (one pregnant) for this purpose. The dose of lead acetate given, small though it appeared, (0.5 g. per diem.), was sufficient to cause death from lead poisoning in 45 days. Chemical analyses were made to determine the distribution of the metal in various tissues of these animals. The results are shown in Table V. One important fact emerged from these analyses namely that in the pregnant

sheep, like in the rat (Bauman, 1933) and in women (Boyd, 1934) the metal can pass through the placenta to the foetus. - In Japan congenital plumbism has been described owing to the pregnant mother having used cosmestic powders containing lead (see Boyd, 1938).

TABLE V.

Distribution of Lead in Organs of Sheep dosed with Lead Acetate.

Total weight in mgs. of Pb in each organ.

	Sheep I	Sheep II.
Spleen	0.63	1.32
Liver	17.06	10.46
Kidneys (both)	10.98	24.28
Brain	0.32	1.17
Foetus	-	0.96

The facts indicate that until we know more about the exact aetiology of "Swayback" lead cannot be ignored as a possible causal factor. It need not be, and in fact cannot be, direct plumbism, but we do not know, for example, how lead might affect the assimilation of other substances. As Minot (1938) has stated, there can be no doubt that the continual absorption of lead in

quantities, which might still be regarded as relatively small, results in "poisoning". The urgent need at the moment, therefore, is to establish a more exact set of criteria which would enable us to recognise the early aetiological connection between lead and injuries to the animal organism.

5. EXPERIMENTAL DEMYELINATION.

When these experiments were initiated in 1935 there was almost no tangible evidence left to show how the problem could be successfully attacked, and it was clearly realised that new observations or outlook were necessary if any further advances were to be made. The usual approaches to a study of disease causation had been unproductive of any positive result (see previous sections), and it was felt that some experimental method would be essential as a basis for further research.

For various reasons it was decided that the work of Rivers, Sprunt and Berry (1933) and Rivers and Schwenkter (1935) offered the most hopeful line for experimental work. By repeated intramuscular injections of heterologous (rabbit) brain emulsions into monkeys, Rivers recorded the production of ataxia, facial paralysis, and blindness; a diffuse demyelinating encephalomyelitis was observed after autopsy. Although, as Rivers freely acknowledged at the time, the methods adopted might seem to be far removed from anything which could occur under natural conditions, the

results, nevertheless, indicated a means to study the actual mechanism of the demyelination process. They also lent some support to the suggestion that certain of the demyelinating disorders might be linked causally with some sensitisation process. Speculation would, however, have been more interesting if either brain antigen or antibrain antibodies had ever been demonstrated in the blood of patients suffering from demyelinating maladies.

A series of experiments parallel to those of Rivers were carried out with sheep.

Aqueous brain emulsion of the brains of three rabbits taken out under strict sterile precautions was freshly made before each inoculation. The emulsions were prepared according to River's method. Sterility cultures were always put up from each batch of emulsion.

Eleven ewes, two months pregnant, were subsequently given 10 ccs. of this emulsion intramuscularly three times per week up to parturition. A week after parturition these injections were again continued until nearly the end of the next pregnancy period. Each of these ewes, therefore, received 120 (or more) injections within a period of one year. In the same way the lambs born from the first lambing were similarly injected with emulsions beginning when they were about one week old and continuing until the end of the experiment with the ewes, i.e. about 80 injections over nine months.

In no case was any form of paralysis or any nervous disorder observed in the ewes or the lambs. Healthy lambs were also born from the experimental ewes in their second pregnancy.

Although these experiments prove to be negative, they are not without interest from another aspect of the demyelination

problem. It has already been mentioned that an "antirabic encephalitis" occurs in man and dogs for which a satisfactory answer has never been obtained. Stuart and Krikorian (1933) have recently reviewed the problem and also suggested that the cause is some toxic product of the breakdown of nervous tissue contained in the rabies vaccine. Along the same line Hurst (1932) investigated the effects of injection of normal brain tissue into rabbits and observed toxic manifestations leading to wasting paralysis and death in a few instances. He concluded, however, that there was insufficient evidence to warrant the view that paralytic accidents of antirabic treatment are directly due to the foreign nervous substances injected. The results of these sheep experiments strongly support this view of Hursts and it is clear that the sheep can withstand enormous quantities of foreign brain emulsions over a prolonged period without any ill-effect whatsoever.

6. ANAEMIA AND COPPER DEFICIENCY AS A CAUSE OF SWAYBACK.

Bennetts and Chapman (1937) gave a fresh stimulus to investigations along this line when they contended that the disease in Australia was due to a copper deficiency. Their observations are summarised as follows:- Pregnant ewes pastured on "affected land" developed a macrocytic hyperchromic anaemia and as a result their lambs were affected with "Swayback". The copper content of the blood, liver and milk of these anaemic pregnant ewes was much below normal. The feeding of copper to the ewes caused a marked response in the blood picture with a reticulocyte crisis, and the anaemia was thus prevented or cured; as a result the progeny were not affected with "Swayback". This anaemia of pregnancy was considered as similar to pernicious anaemia of man although it did not respond to liver therapy in the few cases tried. Copper sulphate was claimed to arrest the progress of the disease in the lamb although the initial ataxia was not improved. (In England many mild cases do not progress and may survive without any therapeutic treatment). A few analyses showed that there was no copper deficiency present in the grass compared with that from affected farms, and it was contended that either the copper content of affected pastures varied throughout the year or that there was always an adequate amount present, but that some unknown factor interferred with its proper assimilation. These findings required further confirmation, but in any case, the pathogenesis requires a fuller explanation. The results of prophylactic copper treat-

ment carried out on a small scale by Bennetts in Australia were, however, remarkable.

A relation between copper and erythropoiesis has been long contended, but that such a trace element might be vitally connected with myelin formation was a new observation, and suggested another approach to problems of certain nervous disorders. Similarly, the occurrence of a macrocytic hyperchromic anaemia had not previously been established in animals, and if an association of an anaemia of this type with a demyelination disorder ("Swayback") was confirmed, the problem again offered attractive possibilities from the comparative aspect.

(a) The Physiological Role of Copper in the Animal Organism.

While there is evidence to show that copper is essential for normal erythropoiesis, the exact role of the metal is not fully understood, and many of the reports in the literature are highly conflicting. Much information is to be obtained in the papers of Hart, Steenbock, Waddell and Elvejhem (1928 and 1929), McHargue, Heally and Hill (1928), Morison and Nash (1930), Beard and Myers (1931), Cunningham (1931), Parsons (1932), Mackay (1933), Stein and Lewis (1933), Sachs, Levine and Fabian (1935), Tompsett and Anderson (1935) and Elvejhem and Hart (1936). The whole position was reviewed by Elvejhem (1935). The work of these investigators in general seems to indicate that in the presence of

iron, copper stimulates the regeneration of haemoglobin in animals made anaemic by a milk diet. In addition, copper alone appears to catalyse the formation of red cells, as animals receiving copper without iron show a rise in the erythrocyte count, although a low haemoglobin persists. In experimental milk anaemia there is a specific deficiency of copper which must be corrected, before the utilisation of iron, for the production of haemoglobin and before the formation of erythrocytes. In the case of spontaneous anaemias of man, the position is not so clear and can be summed up in the words of Janet Vaughan (1936) who stated "that copper probably plays some part in haematopoiesis possibly by assisting in the conversion of inorganic iron into haemoglobin, thus speeding on the process of red cell maturation. At present we can recognise no anaemia due specifically to lack of copper and no anaemia cured by treatment with copper only". In the case of domestic animals there have been suggestions that copper might be responsible for certain diseased conditions. For example, Neal, Becker and Shealy (1931) observed a recurring nutritional anaemia in cattle in Florida due to a deficiency of Fe and Cu in the vegetation which could be cured by supplements of Fe and Cu but not by Fe alone. Thomson and Wheller (1932) produced a nutritional anaemia in lambs by a diet of cow's milk. Only a slight response was obtained by feeding $FeCl_3$ free from Cu, but when both $FeCl_3$ and $CuSO_4$ was given, a rapid return of the haemoglobin to normal levels was obtained. Similarly, Sjollema (1933 and 1938) recorded that in certain

districts of Holland the vegetation was deficient in Cu; "lecksucht", a disease of cattle, in which anaemia was a feature, was prevalent in these areas and this condition was cured by copper sulphate treatment. The immediate effect of copper treatment was, however, an apparent increased food consumption, the rise in the haemoglobin level occurring later, and Sjollema suggested that the action of the copper was primarily on appetite and not on blood formation.

Investigations were necessary along the lines indicated by the above works; this involved much haematological and chemical work which is now dealt with separately.

(b) Haematological Work.

The purpose of this aspect of work was to examine the blood of a large number of pregnant ewes in farms in the Derbyshire area where "Swayback" was prevalent. The suggestion of Bennetts (1937) that a macrocytic hyperchromic anaemia occurred in ewes which gave birth to "Swayback" lambs, could be investigated in this way. Some of this work was done in 1938, repeated and extended during the gestation period in 1938-39. The results are discussed together.

About one month before lambing, blood examinations were made of many pregnant ewes on different farms in this area. The same ewes were examined again after lambing and to determine whether healthy or "Swayback" lambs had been born. Blood

examinations of many "Swayback" lambs and their mothers were also made in the same district. Although several haematological studies of sheep blood have been made by previous workers (e.g. see Fraser, 1929), blood examinations were made of a number of normal ewes and lambs in different parts of the country as controls. This was necessary to obtain data which was not available in the literature and in order to correlate the blood picture with the Cu blood values.

Haematological examinations were thus made of the following groups of animals, (1) Normal pregnant ewes in non-affected areas, e.g. in Cambridgeshire and Leicestershire; (2) Normal pregnant ewes from a farm in Derbyshire near a "Swayback" area but on which "Swayback" did not occur; (3) Pregnant ewes from "Swayback" farms which subsequently gave birth to normal lambs; (4) Pregnant ewes from "Swayback" farms which gave birth to "Swayback" lambs; (5) Normal lambs and young sheep in "non-affected and affected" areas; (6) "Swayback" lambs.

Technique.

All blood examinations were carried out on venous blood obtained either from an ear vein or direct from the jugular. Haemoglobin estimations were made with a Hellige haemoglobinometer standardised against O_2 capacity measurements; red and white cell counts were made in the usual routine manner; smears were stained by the May-Grunwald Giemsa method for examination of the red cells and differential leucocyte counts. In many cases observations were also made on the sedimentation rate, reticulocyte count, percentage volume of packed cells, colour index and Price-Jones curves. There was no information available regarding red cell diameters of domestic animals. A red cell diameter distribution

curve for a normal ewe was therefore prepared.

After the work had been in progress for some time it was obvious that much of the haematological data was irrevelant as there were no significant deviations from normal standards. In the following chapters, therefore, only those data are given which may have some bearing on the aetiology of "Swayback" as suggested by Bennetts and Chapman (1937).

Normal Standards of Sheep Blood.

From our own examinations the following have been accepted as normal values, (Table VI).

Table VI.

Erythrocyte count (millions per c.mm)	6-11
Haemoglobin per cent	60-80
Packed cells (c.c. per 100 cc. of blood)	26-38
Colour Index	0.5-1
Mean corpuscular volume (cubic microns)	34-50
Mean corpuscular haemoglobin (micrograms)	12-20
Diameter of erythrocytes (microns)	3-6
Reticulocytes (per cent)	0-0.1
Leucocytes (thousands per c.mm)	5-14

Before discussing the haematological findings in "Swayback", certain facts concerning sheep haematology must be emphasised. A large series of examinations such as have been made in man has not been done on the normal sheep. The above standards are, therefore, very arbitray as deviations were found to occur in apparently normal animals within even wider limits than those given, with the exception perhaps of the red cell diameters. In

TABLE VII. D. Normal Lambs.

Non-affected Area (Cambs).

Ewe No.	Hb %	RBC x 10^6	Cell Vol.	Cu Mg.%
1	64	9.0	32.4	0.061
2	67	7.5	-	0.075
3	65	10.9	-	0.379
4	67	12.2	34.2	0.057
5	65	12.2	36.4	0.18
6	70	13.7	32.3	0.200
7	70	10.7	-	0.232
8	74	16.2	36.6	0.232
Av.	68	11.6	34.4	0.173

Affected Area (Derby).

Ewe No.	Hb %	RBC x 10^6	Cell Vol.	Cu Mg.%
1	75	7.2	-	-
2	85	7.9	-	-
3	85	8.5	-	-
4	74	7.9	-	-
Av.	79	7.9	-	-

TABLE VII.C.

C. Control Ewes (1 yr. old). (Cambs.)

Ewe No.	Hb %	RBC 6 x 10^{6}	Cell Vol.%	Cu Mg%
1	71	11.54	0.31	0.153
2	69	8.31	0.41	0.138
3	85	10.13	0.42	0.180
4	75	12.34	0.30	0.148
5	88	12.02	0.32	0.143
6	77	11.25	0.34	0.151
7	88	10.13	0.43	0.128
8	83	11.98	0.35	0.153
9	75	12.00	0.31	0.133
10	85	9.89	0.43	0.130
11	84	12.73	0.33	0.143
12	77	9.68	0.40	0.161
13	77	10.88	0.35	0.155
14	80	11.74	0.34	0.139
15	86	12.39	0.35	0.157
16	92	13.32	0.34	0.164
17	84	11.51	0.36	0.123
18	80	10.45	0.38	0.137
19	80	12.18	0.32	0.145
20	85	12.69	0.34	0.134
21	77	10.36	0.37	0.157
22	72	10.93	0.33	0.147
23	88	11.76	0.37	0.133
Av.	81	11.31	0.36	0.146

TABLE VII.B.

Control Ewes on Swayback Farms, Derbyshire, giving birth to Normal lambs (1938).

Ewe No.	Hb %	RBC 6 x 10^{6}
1	60	6.0
2	70	5.0
3	65	
4	62	
5	73	4.0
6	60	3.0
7	50	2.0
8	58	6.0
9	50	3.0
10	62	
11	55	6.6
12	50	3.1
13	47	5.2
14	62	3.0
15	47	3.0
16	60	3.0
17	50	3.0
18	56	4.0
19	58	5.9
20	75	

Ewe No.	Hb %	RBC 6 x 10^{6}
21	50	4.5
22	66	5.3
23	58	4.5
24	56	4.0
25	55	4.2
26	54	3.0
27	57	4.2
28	58	3.0
29	50	3.0
30	42	4.8
31	60	4.0
32	60	4.0
33	65	5.0
34	75	5.0
35	65	5.2
36	70	5.4
37	67	5.0
38	66	5.2
39	69	5.0

Ewe No.	Hb %	RBC 6 x 10^{6}	Cell Vol.	Cu Mg.%
40	50	4.2	27.8	0.040
41	50	4.5		0.040
42	55	4.8	33.2	0.036
43	55	4.7	31.7	0.037
44	60	4.9	26.7	0.034
45	53	3.5	26.1	0.039
46	53	3.7	26.5	0.041
47	44	3.8		0.054
48	53	5.9	28.2	0.050
49	69	7.7	44.9	0.049
50	56	4.6		0.045
51	70	5.6	33.9	0.054
53	57	5.6	29.7	0.061
54	65	5.8		0.044
55	54	4.9		
56	49	4.7		
57	61	5.0		
58	60	5.2		
59	64	5.2		
60	46	4.9		
61	53	5.8		
62	64	5.2		
63	60	4.8		
66	51	3.0	39.7	0.037
67	70	4.0	32.6	0.034
68	70	5.5		0.045
69	62	5.3	30.9	0.048
70	85	9.4	35.2	0.047
Av.	58	4.8	31.9	0.045

TABLE VII.

Haematological findings and Cu analyses of blood (i) Of Ewes from Swayback and non-Swayback areas giving birth to normal and Swayback lambs. (ii) Of Normal and Swayback lambs.

1938 work.

TABLE VII.A.

Normal Pregnant Ewes from Non-affected Areas.

CAMBRIDGE

Ewe No.	Hb %	RBC $x10^6$	Cell Vol.	Cu Mg.%
1	83	9.0	30.5	0.136
2	75	8.7	30.5	0.124
3	73	8.2	33.7	0.128
4	77	8.3	37.4	0.115
5	80	8.2	-	0.130
6	70	8.0	29.8	0.125
7	74	9.1	34.4	0.111
8	71	9.6	38.9	0.128
9	72	9.6	37.5	0.138
10	76	8.1	38.8	0.125
11	67	8.7	31.5	-
12	70	8.4	33.8	0.133
13	62	6.8	33.4	0.160
14	60	7.6	29.6	0.281
15	60	6.6	27.9	0.130
16	64	9.3	33.9	0.089
17	70	8.6	38.0	0.054
18	72	10.0	-	0.055
Av.	71	85	33.7	0.127

LEICESTER

Ewe No.	Hb %	RBC $x10^6$	Cell Vol.	Cu Mg.%
1	75	6.6	36.0	0.050
2	76	6.0	33.3	0.127
3	70	6.4	33.6	0.093
4	75	5.4	38.3	0.051
5	71	6.0	32.6	0.047
Av.	73	6.1	34.8	0.074

Non-Swayback Area (Derby)

Ewe No.	Hb %	RBC $x10^6$	Cell Vol.	Cu Mg.%
1	65	5.9	29.1	0.082
2	65	6.6	30.7	0.092
3	65	5.2	37.8	0.086
4	65	5.9	28.1	0.122
Av.	65	5.9	31.4	0.095

our relatively small series it is evident that the age of sheep is responsible for extraordinary variations (see also Fraser 1929). For example, in new-born and young lambs there occurs normally an exaggerated physiological polycythaemia and the red cells may number 13.0 - 16.0 millions per c.mm. (Table VII D & E). With advancing age the red cells appear to decrease in number although in a number of normal one-year-old non-pregnant ewes the red cell counts were still much higher than in the many older pregnant and non-pregnant ewes which were examined, (Table VII. C.). Apart from this age variation the haemoglobin and red cells might be affected by locality, e.g. compare our findings in ewes in Cambridgeshire, Leicestershire and Derbyshire, (Tables VII A. & B.) Recent work by Barcroft, Kennedy and Mason (1939) has also shown that during pregnancy in the sheep there is a rise in blood volume with a decrease in the haematocrit reading. There are thus many factors to be considered when assessing the significance of haematological findings in sheep, while an opinion on the blood of any one sheep without knowing more of the influence of age, locality and of pregnancy becomes virtually impossible.

Examination of Pregnant Swayback Ewes.

The relevant haematological data in the ewes are given in Tables (VIIb & VIII,). The uniformly lower level in the haemaglobin and red cells of pregnant ewes in a "Swayback" area in Derbyshire (Table VIIb. & VIII) compared with

TABLE VIII.

Haematological and Chemical findings in Swayback Lambs and their Mothers. (Cu and Pb content of the grass from the farms are also given.

A. Derbyshire (1938).

	Lamb.						Mother of lambs.						Grass.	
Case No	Hb %	RBC$_6$ x 10	Cell Vol.	Cu in blood Mgs.%	Cu in liver Mgs.%	Pb in liver	Hb %	RBC$_6$ x 10	Cell Vol.	Cu in blood Mgs.%	Cu in liver Mgs.%	Pb in liver	Cu Mg%	Pb Mg
1	74	8.4	43.5	0.065	0.78	0.56	58	8.3	29.7	0.050	-	-	-	5.
2	75	8.0	40.5	0.049	0.79	0.336	47	6.4	22.2	0.059	-	-	1.82	25.
3	66	8.8	35.5	0.056	0.46	0.398	40	5.0	21.2	0.037	-	-	-	-
4	82	8.9	27.4	0.062	1.36	-	-	-	-	-	-	-	2.4	8.
5	-	-	-	-	1.11	1.57	-	-	-	-	-	-	1.82	25.
6	63	6.9	29.6	0.042	0.52	2.51	34	5.1	18.5	0.039	0.68	0.33	-	-
Twins (7	74	7.3	32.2	0.039	1.12	1.29	65	5.8	-	-	1.75	0.44	1.82	25.
Twins (8	75	6.6	33.7	0.050	0.89	-	-	-	-	-	-	-	-	-
9	69	6.9	14.9	0.039	1.10	1.08	62	7.7	28.8	0.058	-	-	1.70	4.
10	77	9.2	-	-	0.95	0.27	43	6.0	25.6	0.039	-	-	1.73	5.
11	60	10.0	29.0	0.072	0.85	1.63	60	8.6	24.9	0.084	-	-	2.17	6.
12	48	7.7	-	-	-	-	54	7.5	26.0	0.070	-	-	2.17	6.
13	61	9.0	26.8	0.064	0.89	0.39	41	6.2	22.8	0.060	-	-	1.82	25.
14	59	7.8	27.8	0.070	0.95	-	48	6.2	24.2	0.078	-	-	1.82	25.
15	68	9.3	38.3	0.066	1.55	0.25	43	6.5	21.8	0.068	-	-	1.82	25.
16	79	8.6	33.8	0.050	1.14	0.60	40	6.1	17.9	0.056	-	-	1.82	25.
17	69	7.0	30.3	0.044	-	-	56	5.8	26.6	0.060	-	-	1.70	4.
Twins (18	94	10.9	47.0	0.084	-	-	56	6.4	-	0.048	-	-	1.67	4.
Twins (19	72	8.0	22.2	0.061	-	-	-	-	-	-	-	-	-	
20	-	-	-	0.065	-	0.26	-	-	-	-	-	-	1.82	25.
21	92	11.0	46.0	0.048	-	-	-	-	-	-	-	-	-	
22	70	8.8	-	-	-	-	-	-	-	-	-	-	-	
23	90	9.9	44.5	0.060	-	-	-	-	-	-	-	-	-	
24	60	7.8	-	-	-	-	-	-	-	-	-	-	-	
25	62	7.9	39.0	0.049	-	-	-	-	-	-	-	-	-	
26	62	6.9	-	0.024	-	-	70	7.3	27.4	0.062	-	-	-	
27	68	7.5	38.4	0.047	-	-	-	-	-	-	-	-	-	
Av.	71	8.4	34.0	0.055	-	-	51	6.6	24.1	0.058	-	-	-	

B. Gloucestershire.

64	7.4	33.7	0.103	-	-	1.9	11.
72	12.9	36.5	0.077	-	-		
72	7.6	29.2	0.084	-	-		
76	11.9	36.0	0.080	-	-		
42	6.7	25.2	0.069	-	-		
72	7.2	35.6	0.047	-	-	1.7	-
66	6.6	29.9	0.046	-	-		
68	6.5	29.5	0.048	-	-		
66	8.1	31.9	0.074				

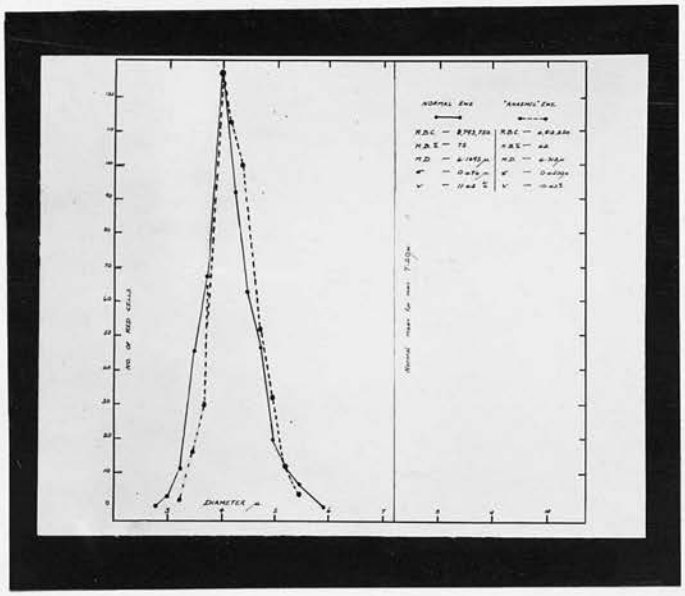

Fig.44.

Red cell diameter distribution curve for normal pregnant ewe compared with one for an "anaemic" ewe in Derbyshire.

control ewes in Cambridgeshire (Table VIIa) might indicate the occurrence of a specific anaemia. There is, however, no correlation between this anaemia in the ewe and the occurrence of "Swayback" in the progeny. Ewes in this area giving birth to healthy lambs may show a similar low haemoglobin and red cell count to those giving birth to "Swayback" lambs (compare Tables VII & VIII). Further, many ewes both in Derbyshire and another area in Gloucestershire, which gave birth to "Swayback" lambs, showed a blood picture which must be regarded as within the normal limits (Table VIII). (These findings were obtained in the work of 1938 and confirmed in 1939). It must be repeated that these latter ewes never seem to show any sign of ill-health and it is thus difficult to consider that there exists in these ewes an anaemia of a type which would be expected to produce grave symptoms.

Any attempt to substantiate an anaemia of pregnant ewes in Derbyshire is beset with difficulties which have already been mentioned. In some of these ewes there may be a greater reduction of red cells than haemoglobin thus giving a high colour index, but this is not constant and a determination of red cell diameter curves (Price Jones) of many of these cases showed no significant differences to those obtained in a series of normal ewes (Fig. 44). Blood films from some of these ewes showed a marked degree of anisocytosis, poikilocytosis and punctate basophilia, but this again was not constant, and in many animals

with a low haemoglobin and red cells, the latter appeared normal.

There was thus no evidence to show that macrocytic hyperchromic anaemia occurs in the mothers of "Swayback" lambs. Macrocytosis is undoubtedly absent and there is no indication that the anaemia is even hyperchromic. A gastric analysis was made on one anaemic ewe; there was no evidence of achylia which was additional proof regarding the dissimilarity with pernicious anaemia in man. Barcroft's observation of a raised blood volume and decreased haematocrit during pregnancy might indicate that the "anaemia" could be explained partly on this physiological basis, and that the lowered haemoglobin and red cells might not indicate the existence of anaemia at all.

In spite of being unable to confirm the observations of Bennetts regarding the type of anaemia, an experiment was carried out in 1939 to determine if the anaemic blood picture would respond to copper or iron treatment. Six "anaemic" ewes in a Swayback area were given daily doses of copper sulphate and another six similar doses or iron chloride for 16 days. Haemoglobin estimations, red cell and reticulocyte counts were made every second day. No beneficial effects were observed on any of the blood constituents.

The cause of this anaemic condition in the ewes thus remains obscure although it is clear that it plays no part in the pathogenesis of Swayback. It must be remembered that a macrocytic

hyperchromic anaemia of pregnancy occurs in women which is not pernicious anaemia.

Examination of Swayback Lambs.

In different cases there is no uniformity either in the haemoglobin or red cell counts (Table VIII). Many of the very severe cases showed values within the normal range, while other cases showed a reduction in both haemoglobin and red cells. In this connection it must be stated that if the acute cases live for any length of time they undoubtedly suffer from malnutrition; some of them require to be artificially fed while others have great difficulty in obtaining enough milk from the ewes.

(c) The Copper Content of Blood and Tissues of Swayback Lambs and their Mothers.

(Analytical work carried out by Dr. G.D. Shearer). (See Tables XII, VIII & IX.)

For this purpose blood was taken from most of the sheep, form normal and Swayback areas used for haematological work in 1938, and are tabulated in the same tables (VII and VIII).

The average figure of 0.127 mg/100 ml. whole blood obtained from normal control pregnant ewes (about one month before lambing) in Cambridge (Table VIIa) compares favourably with that of 0.172 mg. given by Tompsett (1934) for normal sheep. Both

TABLE IX.

(1938 work).

Copper Content of the Blood and Liver of Ewes and Lambs and Pastures.

(Mg. per 100 cc. whole blood; 100 g. dry liver and 100 g. dried grass).

BLOOD. BENNETTS FINDINGS.

Control Ewes (Cambs)	Control Ewes (Derby-shire)	Control Ewes (Leics)	"Non-Swayback Ewes" in Sway-back area.	"Swayback Ewes" (Derby-shire)	"Swayback Ewes" (Glos.)	Normal Ewes Australia	Ewes with Swayback lambs Australia.
0.125 (0.084-0.281)	.0951 (.0816-0.122)	.074 (0.047-0.127)	.045 (.034-.061)	.058 (.037-.084)	.069 (.046-.103)	0.075 (.064-.087)	0.006 (0.004-0.01

BLOOD.

Control Lambs (Cambs)	Swayback Lambs	Ewes (1 yr. old)
0.175 (0.061-0.379)	0.055 (0.039-0.085)	0.146 (0.123-0.180

LIVERS. BENNETTS FINDINGS.

Normal Lambs (Dunlop-Young)	Normal Ewes.	Swayback Lambs (Derby)	Derby Ewes with Sway-back Lambs.	Control Ewes	Ewes with Swayback Lambs, (Australia)
13.2	32.3 (21.2-49.7)	0.859 (0.46-1.56)	1.22 (0.68-1.75)	24.3 (12.0-36.0)	0.076 (0.03-0.08)

PASTURES.

Non-Swayback Area. (Cambs)	Non-Swayback Area. (Derby).	Non-Swayback Areas. (Various)	Swayback Area (Derbyshire)	Another Swayback Area.
1.19	1.7	2.38	2.00	1.8

figures are, however, much higher than that of 0.075 mg. given by Bennetts and Chapman (1937). The latter value is, however, similar to our figures obtained from ewes on control farms in Derbyshire which were adjacent to "Swayback areas" (Table VIIa). Pregnant ewes from "Swayback" farms, giving birth to normal lambs in Derbyshire, showed an average of 0.045 mgs. per cent. of Cu in the blood (Table VIIb) which is much lower than that of 0.095 mgs. per cent. from ewes on adjacent farms (Table VIIa) on which the disease is unknown, but this figure was similar to that obtained for ewes from the same area which gave birth to Swayback lambs, (aver: 0.055, Table VIIIa).

Young lambs showed a much higher concentration of Cu in the blood than mature sheep (Table VIId), a finding in accordance with work done in other species; for example, in the case of the rat, Cunningham (1931), and human being, Morison and Nash (1930).

Cu analyses of the blood and liver from cases of "Swayback" and from their mothers were made, and the results are given in Table VIIIa& b.

It will be seen from Tables VIId and VIIIa that the Cu content of the blood of "Swayback lambs" is much lower than that of normal lambs although the average figure is higher than that given for the blood of "Swayback" lambs by Bennetts and Chapman (1937); the Cu content of the mother's blood is likewise low, and

although not constant, there seems to be a relationship between the blood Cu of the lamb and its mother.

The Cu in the livers of these "Swayback" lambs (Table VIIIa) is of the same order of magnitude as that given by Bennetts and Chapman, but is much lower than the normal figure of 14.2 mg/100 g. dry liver given by Young (1937).

Cu analyses of the livers from two ewes which had given birth to "Swayback" lambs also showed a low figure compared with normal values given by Cunningham (1931).

7. LARGE SCALE FIELD EXPERIMENT TO DETERMINE THE PROPHYLACTIC VALUE OF COPPER. *

The results which have been given in previous sections lent considerable support to some of the conclusions of Bennetts and Chapman (1937), and it was decided that the next logical step would be to conduct a large scale experiment to test out the prophylactic value of copper.

Plan and Purpose of the Experiment.

The investigation was made on Bradwell Moor which is the geographical centre of a large area in North Derbyshire where

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* The field experiment was organised and conducted with the help of Dr. G. Dunlop, Agricultural Institute, Derby and Mr. H.E. Wells, Assistant Agricultural Organiser, North Derbyshire.

the incidence of Swayback has been high for many years. The farmers within this area were invited to co-operate in the work and a committee was formed to take over the administrative and financial side of the investigations. Forty-four farmers agreed to contribute 10-15 per cent. of their breeding stock and 253 ewes were thus obtained for experimental purposes. These were ewes which had either produced "Swayback" progeny in previous years or had been grazing within the affected area for at least a year. Three hundred acres of good but "affected" land on the moor were placed at our disposal and the boundary stone walls were made sheep proof to divide the area into four separate but contiguous enclosures. A fifth enclosure, about a mile away from the main area, was taken over to act as an additional control area.

A field laboratory was fitted up in a hut located on an adjoining moor; spells of work were carried out there for a period of 3-4 weeks in November, 1938, January 1939, and during the whole of the lambing season.

Early in November 1938 the 253 ewes were branded and numbered with ear tags for identification purposes. Mating had begun early in November but the rams remained with the ewes on the experimental ground for some time. The experimental flock was then divided into the following groups, care being taken that each farmer's contribution of ewes was randomised over these

groups as far as possible:-

GROUP.		TREATMENT.
1. Control group.	50 ewes.	No licks; kept away from main area.
2. Control group.	47 ewes.	Pure salt licks only. No Cu.
3. Experimental.	101 ewes.	Licks containing 0.3% Cu.
4. Experimental.	55 ewes.	Licks containing 1% Cu.

From December 9th., 1938, group 2 and all the other animals in the experimental groups (3 and 4) before being drafted on to the copper licks, received licks containing only the copper free salt for 14 days. The above amounts of copper (1% and 0.3%), as $CuSO_4$, were mixed with purified NaCl and made up into 5 lb. licks, one lick being allotted to 20 ewes. Subsequently a number of ewes from the experimental groups 3 and 4 were drafted on to the copper lick treatment (0.3 and 1% Cu) on 23.12.38, 11.1.39, 1.2.39 and 23.2.39 or roughly for 13, 10, 7 and 4 weeks respectively before lambing. These groups are all given with the results in Table ~~XIX~~ X.

The treated groups (3 and 4) and control group 2 were moved around the contiguous enclosures in sequence every three weeks to ensure that all the ewes had access to the same herbage throughout the experiment. The appropriate mineral licks for each group were sheltered from weathering in covered hay racks and these were moved around the enclosures with the ewes. The ewes in control group 1 were kept in the isolated field until just before lambing.

On the 20th December, 1938, a heavy snowstorm occurred and the experimental ground, which lay at an altitude of 1,000-1,300 feet, remained covered until mid-January. The herbage was also covered with snow for periods in February and again in March. Supplementary feeding was thus essential; the rations and amounts fed in lb. per ewe were as follows:-

	Dec.	Jan.	Feb.	March.	April.	Totals.
Hay	9	40	40	28	26	243
Concentrates	2	4.8	10	14.5	16.3	47.6
Sugar beet pulp	-	-	-	0.8	6	6.8

The hay was obtained from two badly "affected" farms; the concentrates consisted of kibbled oats, wheat bran, flaked maize and ground nut flake. These were chosen after copper analyses had been made of bulk samples of different food stuffs; the copper content of the above concentrates was 7.1, 12.3, 0.8 and 18.6 (p.p.m.) respectively. The Cu content of the mixed rations used during the experiment varied from 6.5 to 10.5 (p.p.m.)

Autopsies were made on all ewes which died during the course of the experiment. During the lambing period all lambing dates were recorded daily and each batch of lambs examined soon after birth. Some of the lambs severely affected with "Swayback" were killed while others died. All lambs which died or were killed were subjected to a post-mortem examination, particular attention being paid to the nervous system for diagnostic

purposes. In those cases which showed macroscopic lesions, further examination was obviously unnecessary. In the case of the other dead lambs in which no gross lesions were present in the brain, portions of the brain and/or spinal cord were fixed in formalin for subsequent histological work; included in this series were all still-born lambs and near-full-time aborted lambs. As some lambs were found dead without having been seen alive this latter procedure was necessary to establish either a positive or negative diagnosis of "Swayback". The difficulties which attend the clinical diagnosis of the mild cases of "Swayback" are great, as the slight staggering posterior weakness seen in such cases might be simulated by a number of different conditions. For the purposes of our records, all such animals were regarded as cases of Swayback; a few were killed and the cord or brain examined histologically to establish a diagnosis. Some of the cases did not show lesions of Swayback. I did not include in this category lambs which showed slight symptoms a month to six weeks after being returned to their respective owners, as the lambs must then be regarded as being in a different environment which varied from farm to farm.

Haematological and chemical examinations of the blood of the ewes were carried out, (1) at the end of November, 1938, soon after the ewes arrived on the experimental ground and before any treatment was commenced; (2) in the middle of January, 1939,

i.e. about the middle period of gestation, and (3) after lambing - usually within 4-7 days or as soon after that as possible. The samples of blood were taken from the jugular vein in all cases for the haematological work and /or Cu and Pb analyses. In this way it was hoped to get further data regarding possible anaemic manifestations in ewes which gave birth to "Swayback" lambs compared with suitable control animals which had received copper treatment or no treatment at all. This was also done to correlate the blood picture with Cu and Pb content. The chemical work was done to obtain data regarding the Cu and Pb content of the blood of (1) control ewes, (2) of ewes given Cu treatment and (3) of the mothers of "Swayback" lambs throughout pregnancy. During the lambing period the blood of many affected and control lambs was also examined haematologically and Cu and Pb analyses made of the blood and body tissues. Subsequent to lambing, a number of control ewes and ewes which had given birth to "Swayback" lambs were killed and autopsied, and tissues taken for chemical analyses.

Results.

Lambing began on the 13th of March; for the first 14 days bad weather was experienced and there were many still-born lambs and deaths shortly after birth. As lambing progressed, however, the mortality rate decreased and after mid-April almost all normal lambs were successfully reared.

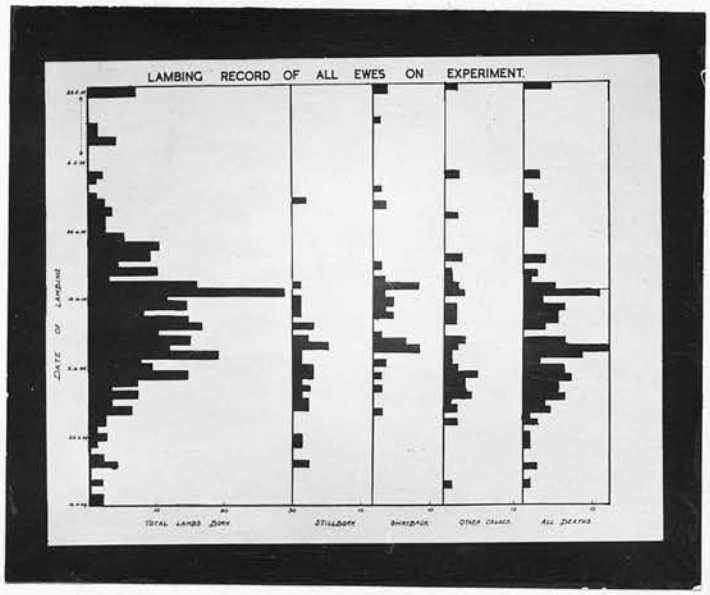

Fig.45.

Graph showing numbers of lambs born, cases of Swayback and deaths from all other causes against the date of lambing.

The results of feeding copper to ewes in the form of licks in different percentages and at various times during pregnancy, are summarised in tabular form (Table X). These require little comment or discussion.

Fig. 45. gives a graphic analysis of the numbers of lambs born, cases of Swayback, and deaths from all other causes against the date of lambing. This is given simply to show that there is no correlation between the occurrence of Swayback or the other mortality with any particular time of the lambing period. It has, for example, been suggested by some farmers that Swayback occurs more frequently in the animals born at the beginning of the lambing season.

There might be two ways in which the results of this experiment could be analysed - the percentage of "Swayback" lambs to the percentage of lambs born or the percentage of ewes which gave birth to affected progeny (single, twins or triplets) to the total ewes on experiment. As the disease is primarily one of intra-uterine origin, and as it was the ewes which were treated to prevent the disease. the most logical way might be the latter. The results, however, show remarkable little difference whichever way is adopted.

In Table X are given the various data regarding numbers of ewes on experiment, lambs born, deaths and cases of

TABLE XXXXX.

Summary showing results of Cu treatment.

Group.	No. of ewes at begin. Nov. 1938.	No. ewes died	No. ewes barren	No. ewes discarded	Actual No. ewes on expmt	No. lambs born	Tot. lamb deaths	No. Sway-back cases	% of Sway-back cases	No. of ewes with Sway-back lambs	% of ewes with Sway-back lambs
1. Control; no treatment.	50	3	3	4	40	63	40	24[x]	37	16	40
2. Control; salt lick only.	47	1	4	2	40	60	28	12[x]	20	10	25
3. Experimental group which rec. 1% cu lick treatment from:											
23.12.38.	21	4	2	0	15	27	7	0	0	0	0
11. 1.39.	11	0	1	0	10	16	4	0	0	0	0
1. 2.39.	12	1	0	0	11	17	5	1	6	1	9
23. 2.39.	11	0	1	0	10	17	4	1	6	1	10
Totals:	55	5	4	0	46	77	20	2	2	2	2
4. Group 0.3% Cu treatment from:											
23.12.39.	40	7	0	1	32	50	20	0	0	0	0
11. 1.39.	20	3	2	0	15	20	3	1	5	1	7
1. 2.39.	20	1	1	2	16	25	7	4	16	3	18
23.2.39.	21	1	1	1	18	28	13	8[x]	28	6	33
Totals:	101	12	4	4	81	123	43	13	10	10	12

a total
x includes/4 cases of Swayback which were not killed.

Swayback in the various groups. It will be seen that the incidence of "Swayback" is highest in the control group of (1) ewes which had been wintered away from the main experimental area; there were 24 cases of "Swayback" out of 63 lambs born from 40 ewes, while there were 12 out of 60 lambs born from 40 ewes in the other control group (2). Compared with these figures the total absence of cases of Swayback in the groups which received Cu licks from the 23.12.38. until lambing (77 lambs from 47 ewes) is striking, and convincing proof of the efficacy of copper in the prevention of the disease. It is also shown that in the various experimental groups the incidence increases accordingly as copper lick treatment was delayed; so that in the group which received 0.3% Cu licks only for a short time before lambing (from 23.2.39) there is little difference in the incidence compared with the control group. There is, however, a higher incidence of the disease in the group which received 0.3% Cu licks compared with those which received 1% Cu licks at any of the given dates. The number of ewes on the various sub-groups appear to be too few to permit of any conclusions being drawn regarding the critical period in gestation for Cu treatment.

TABLE XI.

Group.	% Lamb crop.	Tot. % of lamb dths.	% of lambs with Sway-back	% of deaths from other causes.	% of ewes giving birth to Swayback lambs.
1. Control	157.5	63.5	37.1	28.6	40.0
2. Control	150.0	46.7	25.0	28.3	30.0
3. Experi-mental 0.3% Cu lick	151.9	34.9	10.6	25.2	12.3
4. Experi-mental 1% Cu lick	167.3	25.8	2.5	23.4	4.4

Lambing records expressed in percentages: Swayback cases including few animals showing slight symptoms only and not killed.

Expressed in the form of percentages the differences between the control and experimental groups are even more striking. These are given in Table XI in which the percentages of total deaths, cases of Swayback and deaths from all other causes related to percentage of lamb crop are given. This table shows that the great increase in mortality of lambs in the control groups compared with the experimental groups is almost entirely due to Swayback; in other words, that the death rate from all causes apart from Swayback is remarkably steady in all groups.

TABLE XII.A.

Group 1. (Control - Away from Experimental Area).

Nov. 1938					Jan. 1939			Apl. 1939			Lambing Record				
Ewe No.	Age	Hb %	RBC	Cu.	Hb %	RBC	Cu	Hb %	RBC	Cu	No born	Still-born	No. died ork.	Sway-back	
1	MA	70	-	0.029	66	-	0.067	56	-	0.082	1	0	1	1	SWAYBACK
2	MA	60	9.3	0.022	64	8.7	0.060	65	-	0.060	2	1	1	1	
3	MA	67	10.0	0.029	67	9.2	0.061	64	8.8	0.066	2	0	2	2	
4	A	61	8.0	0.063	83	8.9	0.033	69	7.9	0.061	2	0	1	1	
5	MA	70	7.8	0.052	83	7.8	0.018	76	8.0	0.075	2	0	2	2	
6	MA	67	-	0.025	79	-	0.068	73	-	0.055	1	1	0	1	
7	A	70	-	0.012	79	-	0.054	61	-	0.049	2	0	2	2	
8	MA	67	-	0.049	61	-	0.076	50	6.8	0.079	1	0	1	1	
9	Y	68	-	0.029	71	-	0.063	64	5.9	0.069	2	0	2	2	
10	A	-	-	-	-	-	0.053	60	-	0.048	1	0	1	1	
11	MA	65	7.9	0.022	79	8.1	0.031	67	7.4	0.041	2	0	2	2	
12	Y	72	-	0.066	68	-	0.042	70	-	0.091	2	1	1	2	
13	A	68	-	0.059	70	-	0.066	74	-	0.097	1	0	1	1	
14	A	54	-	0.012	65	-	0.075	66	-	0.071	1	0	1	1	
15	A	62	-	0.016	72	-	0.069	70	-	0.047	2	0	2	2	
16	MA	60	7.4	0.009	73	8.5	0.083	60	6.9	0.073	2	0	2	2	
Av.		60	8.4	0.033	72	8.5	0.057	66	7.3	0.068	-	-	-	24	
17	A	64	-	0.018	77	-	0.050	64	-	0.088	2	2	0	0	NON-SWAYBACK
18	A	70	-	0.016	77	-	0.065	79	-	0.106	2	0	2	0	
19	Y	84	-	0.030	80	-	0.068	76	-	-	2	2	0	0	
20	A	79	10.1	0.018	89	10.1	0.032	84	9.5	0.103	1	0	0	0	
21	MA	64	-	0.029	73	-	0.069	77	-	0.074	1	1	0	0	
22	A	67	10.4	0.032	73	10.3	0.018	66	8.9	0.051	2	1	0	0	
23	A	75	-	0.021	-	-	0.060	75	-	0.077	2	0	0	0	
24	MA	66	-	0.013	55	-	0.076	60	-	0.104	2	0	0	0	
25	MA	76	-	-	71	-	0.054	67	-	0.045	1	0	0	0	
26	VA	62	7.9	0.031	62	8.1	0.050	68	8.9	0.054	2	0	0	0	
27	A	75	-	0.040	75	-	0.053	70	-	0.069	1	0	1	0	
28	MA	64	8.7	0.018	73	9.9	0.061	60	7.0	0.048	2	2	0	0	
29	MA	74	-	0.033	73	-	0.099	-	-	-	2	0	0	0	
30	A	67	8.6	0.016	83	7.8	0.059	-	-	-	2	0	1	0	
31	MA	75	-	0.029	76	-	0.091	64	-	0.088	2	0	1	0	
32	A	74	-	0.025	73	-	0.059	69	7.2	0.088	2	0	1	0	
33	MA	75	-	0.017	84	-	0.070	76	-	0.071	2	0	0	0	
34	Y	67	-	0.032	87	-	0.070	79	-	0.052	1	0	0	0	
35	Y	76	-	0.017	87	-	0.054	71	-	0.053	1	0	0	0	
36	MA	63	-	0.043	79	-	0.076	70	-	0.085	1	0	0	0	
37	A	68	-	0.026	60	-	0.083	65	-	0.074	1	0	0	0	
38	MA	74	-	0.097	78	-	0.071	68	-	0.047	1	0	0	0	
39	Y	71	-	0.064	68	-	0.084	67	-	0.074	1	0	0	0	
40	Y	74	7.5	0.020	76	7.2	0.055	77	-	0.011	1	1	0	0	
Tot. & Av.	-	71	8.8	0.043 0.030	74	8.9	0.064	70	8.3	0.070	63	12	29	24	

TABLE XII.B.

Group 2 (Control - Salt Lick Treatment).

		November			Jan.			Feb.			Lambing Record.				
Ewe No	Age	Hb %	RBC	Cu	Hb %	RBC	Cu	Hb %	RBC	Cu	No born	Still-born	Died or K	Sway-back	
1	MA	77	-	0.014	70	-	0.034	72	-	0.045	1	0	0	1	SWAYBACK
2	A	71	-	0.055	77	-	0.028	61	6.7	0.060	2	0	2	2	
3	A	72	-	0.025	67	-	0.013	65	-	0.040	1	1	0	1	
4	MA	68	-	0.029	64	-	0.026	59	7.2	0.096	1	0	1	1	
5	A	63	-	0.020	63	-	0.034	66	6.7	0.047	1	0	1	1	
6	A	75	-	0.029	79	-	0.016	70	-	0.106	2	0	1	1	
7	A	81	-	0.021	77	-	0.030	68	-	0.098	2	0	1	1	
8	Y	70	9.3	0.013	71	8.6	0.015	66	6.9	0.086	1	0	1	1	
9	A	62	-	0.008	58	-	0.011	60	-	0.100	2	1	1	2	
10	MA	71	-	0.022	70	-	0.025	76	-	0.059	2	1	1	1	
Av.		71	-	0.024	70	-	0.023	66	6.8	0.074				12	
11	A	74	10.4	0.030	80	10.8	0.041	78	-	0.090	1	0	0	0	NON-SWAYBACK
12	A	67	-	0.010	72	-	0.055	64	-	0.050	2	0	0	0	
13	MA	80	-	0.015	70	-	0.014	71	-	0.092	1	0	0	0	
14	MA	73	-	0.043	69	-	0.026	60	-	0.079	1	1	0	0	
15	MA	71	8.4	0.064	66	9.9	0.075	67	9.8	0.073	1	0	0	0	
16	MA	64	7.8	0.040	69	8.2	0.021	69	8.4	0.066	2	0	0	0	
17	A	73	-	0.016	72	-	0.015	73	-	0.061	2	0	0	0	
18	MA	65	-	0.045	71	-	0.031	68	-	0.073	1	0	0	0	
19	A	76	8.2	-	69	8.0	0.024	66	6.8	0.019	1	1	0	0	
20	A	64	-	0.027	75	-	0.020	52	5.4	-	2	0	2	0	
21	MA	78	-	0.011	72	-	0.024	53	-	0.055	2	2	0	0	
22	A	61	-	0.016	61	-	0.073	63	-	0.061	1	0	0	0	
23	Y	78	-	0.009	86	-	0.032	84	-	0.088	1	0	0	0	
24	A	63	-	0.056	65	-	0.015	-	-	-	2	0	1	0	
25	Y	76	-	0.079	71	-	0.101	62	-	-	2	2	0	0	
26	MA	78	-	0.013	71	-	0.045	70	-	0.048	2	0	0	0	
27	Y	79	6.9	0.019	65	7.4	0.013	75	-	0.085	2	0	1	0	
28	A	81	-	0.038	71	-	0.011	76	-	0.064	2	0	0	0	
29	A	64	-	0.068	-	-	-	68	6.3	0.059	1	0	1	0	
30	A	78	9.9	0.055	74	9.6	0.075	76	-	0.109	1	0	0	0	
31	Y	78	-	0.018	69	-	0.037	71	-	0.088	1	1	0	0	
32	A	57	-	0.033	65	-	0.014	64	-	0.068	1	0	0	0	
33	VA	74	-	0.019	74	-	0.015	60	5.5	0.095	3	2	1	0	
34	A	70	-	-	-	-	0.030	60	-	0.075	1	0	0	0	
35	A	62	-	0.049	-	-	0.058	70	-	0.077	1	0	0	0	
36	A	60	5.5	0.007	66	8.4	0.020	64	7.2	0.062	2	1	0	0	
37	A	64	-	0.021	79	-	0.032	69	-	0.053	2	0	0	0	
38	A	62	7.8	0.058	66	8.1	0.051	68	-	0.047	1	0	0	0	
39	MA	60	8.9	0.022	66	10.1	0.017	64	8.7	0.051	2	0	0	0	
40	A	73	-	0.018	69	-	0.011	71	-	0.061	1	1	0	0	
Av.		69	8.2	0.032	70	8.9	0.034	67	7.3	0.068	61	14	15	12	

TABLE XII.C.

Group 3 (Experiment 1% Cu lick treatment).

November					Jan.			Apl.			Lambing Record				
Ewe No.	Age	Hb %	RBC	Cu	Hb %	RBC	Cu	Hb %	RBC	Cu	No. born	Still-born	Died or K	Sway-back	
1	MA	78	-	0.025	85	-	0.047	81	-	0.084	2	0	0	0	
2	MA	83	-	0.013	87	-	0.089	80	-	0.105	2	0	0	0	
3	A	60	-	0.024	79	-	0.020	81	-	0.100	2	0	0	0	
4	A	68	-	0.041	71	-	0.055	64	-	-	2	1	0	0	
5	MA	54	-	0.053	56	-	0.051	59	-	0.111	2	0	1	0	
6	Y	66	-	0.043	73	-	0.053	-	-	-	1	1	0	0	
7	MA	57	-	0.036	75	-	0.051	65	-	0.096	1	0	0	0	
8	A	80	-	0.016	72	-	0.060	-	-	-	2	2	0	0	
9	A	62	-	0.035	-	-	0.040	66	-	0.110	2	1	0	0	
10	MA	61	-	0.028	74	-	0.059	71	-	0.084	2	1	0	0	
11	A	66	-	-	-	-	0.050	-	-	0.175	2	0	0	0	
12	MA	62	-	0.013	68	-	0.060	74	-	0.104	2	0	0	0	
13	MA	71	-	0.057	77	-	0.096	80	-	0.111	2	0	0	0	
14	MA	69	-	0.073	59	-	0.095	55	-	0.091	1	0	0	0	
15	MA	69	-	0.052	75	-	-	79	-	0.106	2	0	0	0	
Av.		67	-	0.033	73	-	0.059	71	-	0.106	27	6	1	0	
16	Y	73	-	0.014	69	-	0.038	-	-	0.142	1	0	0	0	
17	MA	64	-	0.015	77	-	0.024	78	-	0.059	2	0	0	0	
18	A	70	-	0.079	65	-	0.048	79	-	0.121	1	0	0	0	
19	A	65	-	0.047	64	-	0.074	68	-	0.106	2	0	1	0	
20	MA	62	-	0.040	71	-	0.038	63	-	0.089	2	0	0	0	
21	A	66	-	0.034	71	-	0.034	61	-	-	2	0	2	0	
22	A	58	-	0.042	75	-	0.040	66	-	0.096	1	0	0	0	
23	VA	67	-	0.029	88	-	0.059	76	-	0.107	2	0	0	0	
24	A	63	-	0.041	69	-	0.053	61	-	0.088	1	0	0	0	
25	MA	66	-	0.028	71	-	0.037	59	-	0.072	2	1	0	0	
Av.		65	-	0.037	72	-	0.045	69	-	0.098	16	1	3	0	

Cu from 23.12.38.

Cu from 11.1.39.

TABLE XII.C. (contin.)

Group 3. (Experimental - 1% Cu lick).

November					Jan.			Apl.			Lambing Record.				
Ewe No.	Age.	Hb %	RBC	Cu	Hb %	RBC	Cu	Hb %	RBC	Cu	No born	Still-born	Died or K.	Sway-back	
26	MA	64	-	0.048	-	-	-	70	-	0.158	2	0	1	0	Cu from 1.2.39.
27	Y	85	-	0.021	-	-	-	85	-	0.063	2	2	0	0	
28	MA	79	-	0.024	-	-	-	84	-	0.135	2	0	0	0	
29	MA	75	-	0.041	-	-	-	70	-	0.152	2	0	1	0	
30	Y	74	-	0.080	-	-	-	73	-	0.100	1	0	0	0	
31	A	59	-	0.057	-	-	-	61	-	0.061	1	0	0	0	
32	A	72	-	0.010	-	-	-	70	-	0.059	2	0	1	1	
33	MA	81	-	0.065	-	-	-	80	-	0.063	1	0	0	0	
34	A	56	-	0.007	-	-	-	64	-	0.076	1	0	0	0	
35	A	60	-	0.029	-	-	-	77	-	0.104	1	0	0	0	
36	A	65	-	0.015	-	-	-	60	-	0.029	2	0	0	0	
Av.		70	-	0.036	-	-	-	72	-	0.094	17	2	3	1	
37	MA	90	-	0.030	-	-	-	80	-	0.135	1	0	0	0	Cu from 23.2.39.
38	A	63	-	0.012	-	-	-	66	-	0.080	2	0	0	0	
39	A	71	-	0.092	-	-	-	59	-	0.088	2	0	2	0	
40	MA	74	-	0.019	-	-	-	-	-	0.145	2	0	0	0	
41	MA	66	-	0.087	-	-	-	-	-	-	2	0	0	0	
42	Y	73	-	0.023	-	-	-	-	-	0.101	2	0	0	0	
43	Y	70	-	0.014	-	-	-	-	-	-	1	0	0	0	
44	A	67	-	0.032	-	-	-	59	-	0.102	2	0	1	0	
45	A	60	-	0.008	-	-	-	66	-	0.095	1	0	0	0	
46	A	72	-	0.027	-	-	-	64	-	0.092	2	1	0	1	
Av.		70	-	0.034	-	-	-	66	-	0.105	17	1	3	1	

TABLE XII.D.

Group 4 (Experimental 0.3% Cu Lick).

November					Jan.			Feb.			Lambing Record.			
Ewe No.	Age	Hb %	RBC	Cu	Hb %	RBC	Cu	Hb %	RBC	Cu	No. born	Still-born	Died or K	Sway-back
1	A	63	-	0.017	69	-	0.034	64	-	0.080	1	0	0	0
2	MA	68	-	0.018	72	-	0.036	69	-	0.078	2	0	0	0
3	MA	68	7.4	0.010	71	9.8	0.057	68	8.8	0.072	2	1	1	0
4	A	61	-	0.014	73	-	0.055	66	-	0.127	2	0	0	0
5	MA	74	-	-	71	-	0.081	70	-	0.069	1	0	0	0
6	MA	66	-	0.024	64	-	0.038	64	-	0.042	2	0	2	0
7	MA	65	-	0.044	74	-	0.024	76	-	0.058	2	0	1	0
8	Y	68	-	0.043	73	-	0.093	64	-	0.082	2	0	1	0
9	A	62	6.8	0.019	68	7.7	-	68	-	0.058	1	0	0	0
10	A	73	-	0.018	74	-	0.021	67	-	0.116	2	0	0	0
11	A	74	-	0.049	80	-	0.028	76	-	0.094	1	0	0	0
12	MA	60	-	0.022	64	-	0.024	65	-	0.079	2	0	2	0
13	A	70	-	0.038	73	-	0.056	55	-	0.070	1	0	1	0
14	MA	62	-	0.017	71	-	0.030	68	6.9	0.047	1	0	0	0
15	Y	72	-	0.050	75	-	0.077	70	-	0.099	2	1	1	0
16	MA	71	-	-	80	-	0.076	72	-	0.056	1	0	0	0
17	A	71	-	-	73	-	0.038	70	-	0.092	2	0	0	0
18	A	68	-	0.034	74	-	0.029	60	-	0.096	2	0	2	0
19	Y	49	5.7	0.024	55	5.7	0.046	44	3.9	-	2	0	0	0
20	MA	66	-	0.050	82	-	0.049	79	-	0.095	2	0	0	0
21	MA	68	-	0.020	70	-	0.067	58	-	0.051	2	0	2	0
22	A	70	-	0.054	67	-	0.035	71	-	0.054	2	0	0	0
23	A	66	-	0.052	78	-	0.064	71	-	0.109	3	1	1	0
24	MA	66	-	0.023	73	-	0.079	68	-	0.107	1	0	0	0
25	MA	81	-	0.011	80	-	0.085	64	-	0.089	1	0	0	0
26	Y	85	-	-	71	-	0.028	63	-	0.073	1	0	0	0
27	A	70	-	0.018	77	-	0.081	64	-	0.073	1	0	0	0
28	A	74	-	0.052	83	-	0.045	71	-	0.064	1	0	0	0
29	Y	70	-	0.079	76	-	0.063	69	-	0.125	1	0	0	0
30	MA	71	-	0.052	69	-	0.033	70	-	0.115	1	1	0	0
31	A	63	8.1	0.014	61	8.2	0.056	50	5.5	0.061	2	0	1	0
32	A	62	6.6	0.053	61	5.6	0.048	64	7.0	0.077	1	0	1	0
Av.	-	68	6.9	0.038	72	7.4	0.050	66	6.4	0.080	50	4	16	0

0.3% Cu from 23.12.38.

TABLE XII.D. (Contin).

November					Jan.			Apl.			Lambing Record.				
Ewe No.	Age	Hb %	RBC	Cu	Hb %	RBC	Cu	Hb %	RBC	Cu	No. born	Still-born	Died or K	Sway-back	
33	Y	61	-	0.029	71	-	0.026	44	-	0.123	1	0	0	0	
34	A	70	-	0.059	70	-	0.047	60	-	0.077	1	0	0	0	
35	Y	91	-	0.099	92	-	0.045	73	-	-	1	0	1	0	
36	Y	80	-	0.021	78	-	0.020	74	-	0.074	1	0	0	0	
37	A	72	-	0.030	73	-	0.038	67	-	-	2	0	0	0	
38	-	-	-	-	72	-	-	68	-	-	1	0	0	0	
39	A	65	-	0.016	69	-	0.042	60	-	0.053	1	0	0	0	
40	MA	73	-	0.010	76	-	0.034	78	-	0.045	2	0	0	0	
41	MA	64	-	0.040	-	-	0.053	66	-	0.060	2	0	1	0	
42	A	69	-	-	72	-	-	66	-	-	1	0	0	0	
43	A	74	-	0.073	74	-	0.057	61	-	0.067	1	0	0	0	
44	MA	70	-	0.029	76	-	0.023	67	-	0.157	2	0	0	0	
45	MA	82	-	0.046	80	-	0.039	79	-	0.176	2	0	0	0	
46	-	-	-	-	77	-	0.041	71	-	0.077	1	0	1	1	
47	A	66	-	0.051	71	-	0.066	68	-	0.079	1	0	0	0	
Av.		71	-	0.032	75	-	0.040	67	-	0.099	20	0	3	1	
48	MA	75	-	0.041	-	-	-	62	-	0.011	1	0	0	0	
49	MA	70	-	0.015	-	-	-	61	-	0.078	1	0	0	0	
50	A	65	-	0.023	-	-	-	65	-	0.088	2	0	0	0	
51	A	72	-	0.027	-	-	-	66	-	0.059	2	0	0	0	
52	A	74	-	0.067	-	-	-	71	-	0.070	2	0	0	0	
53	A	71	-	0.051	-	-	-	-	-	-	1	1	0	0	
54	MA	64	-	0.074	-	-	-	62	-	0.083	2	0	0	0	
55	MA	86	-	0.020	-	-	-	80	-	0.075	1	0	0	1	
56	MA	62	-	0.026	-	-	-	66	-	0.075	1	0	0	0	
57	MA	65	-	0.013	-	-	-	60	-	0.091	2	0	2	2	
58	A	66	-	0.052	-	-	-	68	-	0.065	2	0	1	1	
59	MA	74	-	0.073	-	-	-	62	-	0.063	2	0	0	0	
60	MA	68	-	0.053	-	-	-	70	-	0.115	2	0	2	0	
61	A	72	-	0.014	-	-	-	67	-	0.060	1	0	0	0	
62	MA	-	-	-	-	-	-	66	-	0.054	1	0	0	0	
63	-	76	-	-	-	-	-	65	-	0.092	2	0	1	0	
Av.		70	-	0.039	-	-	-	66	-	0.079	25	1	6	4	
64	A	68	-	0.015	-	-	-	61	-	0.105	1	0	0	0	
65	A	70	-	0.014	-	-	-	56	-	0.079	2	0	0	0	
66	MA	74	-	0.014	-	-	-	70	-	0.092	2	1	0	1	
67	A	64	-	0.079	-	-	-	64	-	0.118	2	0	0	0	
68	MA	73	-	0.040	-	-	-	70	-	0.088	2	0	2	2	
69	A	61	-	0.016	-	-	-	64	-	0.088	2	1	1	0	
70	A	70	-	0.032	-	-	-	66	-	0.075	2	1	1	0	
71	A	58	-	0.048	-	-	-	62	-	0.049	1	0	0	0	
72	MA	60	-	0.049	-	-	-	75	-	0.052	1	1	0	1	
73	A	59	-	0.043	-	-	-	65	-	0.117	2	1	0	1	
74	MA	67	-	0.037	-	-	-	61	-	0.079	1	0	1	1	
75	Y	65	-	0.063	-	-	-	70	-	0.068	1	0	1	0	
76	A	56	-	0.039	-	-	-	57	-	0.067	2	1	0	0	
77	A	64	-	0.018	-	-	-	70	-	0.060	1	0	0	0	
78	Y	80	-	0.060	-	-	-	75	-	0.068	2	0	0	0	
79	A	81	-	0.032	-	-	-	78	-	0.071	2	1	1	2	
80	A	72	-	0.043	-	-	-	66	-	0.095	1	0	0	0	
81	MA	72	-	0.055	-	-	-	73	-	0.115	1	0	0	0	
Av.		66	-	0.038	-	-	-	69	-	0.081	73	8	15	8	

0.3% Cu from 11.1.39.

0.3% Cu from 1.2.39.

0.3% Cu from 23.2.39.

TABLE XIII.

Averages of Different Groups.

Group	Nov.			Jan.			Apl.		
	Hb	RBC	Cu	Hb	RBC	Cu	Hb	RBC	Cu
Group 1 Control-No treatment excluding Swayback ewes.	71	8.9	0.030	75	8.9	0.067	70	8.3	0.070
Group 2 Control-Cu free salt lick treatment excluding Swayback	69	8.2	0.032	71	8.9	0.034	67	7.2	0.068
Group 3 Experimental 1% Cu lick treatment from: 23.12.38.	67	-	0.034	73	-	0.059	71	-	0.106
11. 1.39.	65	-	0.037	72	-	0.044	69	-	0.098
1. 2.39.	70	-	0.036	-	-	-	72	-	0.095
23. 2.39.	70	-	0.034	-	-	-	68	-	0.104
Group 4 Experimental 0.3% Cu lick treatment from: 23.12.38.	68	-	0.032	72	-	0.050	66	-	0.080
11. 1.39.	72	-	0.038	75	-	0.040	66	-	0.099
1. 2.39.	70	-	0.039	-	-	-	65	-	0.079
23.2 .39.	68	-	0.038	-	-	-	69	-	0.081
Total Swayback cases (47) from all groups.	68	8.6	0.028	72	8.5	0.033	66	7.0	0.074
Total Non-Swayback treated & controls	69	8.5	0.035	72	8.8	0.048	67	7.7	0.088

Haematological Work.

The main data regarding the blood examination of the ewes in the different groups are given in Tables XII A-D and XIII. The work substantially confirmed the results obtained during the lambing season of 1938 and need not be discussed in detail. It must be emphasised again that there is more than ample evidence to show that ewes which give birth to Swayback lambs do not suffer from a specific anaemia; many indeed show a normal blood picture. It is also apparent that the feeding of Cu supplements over a prolonged period to pregnant sheep has no significant effect on the blood, even in those which have a relatively low haemoglobin (see Tables XII C and D).

Chemical Work.

The blood copper content of all the ewes on this experiment are given in the same tables, while the averages of the different groups are given in Table XIII. The results may be summarised as follows:-

(a) During pregnancy there is a uniform rise in the blood Cu which appears to be a normal physiological event as it is seen in all groups irrespective of the treatment given, (Tables XII A-D).

(b) This rise in the blood Cu is, however, more marked in those ewes which received Cu licks compared with untreated animals. (Table XIII).

(c) In those ewes which gave birth to Swayback lambs the rise is less when compared with the treated or untreated controls.

(d) The Cu content of the blood of these "affected" ewes is constantly lower than control animals in the same group (Table XII A and B), and differences of the same magnitude are seen when the average blood Cu of all "Swayback" ewes is compared with that for all other ewes which gave birth to normal lambs. (Table XIII).

(e) The blood Cu of "Swayback" ewes, while lower than comparable control animals, is not of the same magnitude obtained during the work of 1938, (see Table IX).

8. GENERAL CONCLUSIONS REGARDING THE AETIOLOGY.

The results of the field experiment show that the administration of copper in the form of salt licks to pregnant ewes has a remarkable beneficial effect in preventing the disease in the progeny. Together with the chemical results this might suggest that Swayback was another example of a disease due to a trace element deficiency, i.e. to copper, but proof of this is in reality entirely lacking.

There can be no question that the disease is one due to a copper deficiency per se as the analyses of many samples of pasture from affected areas showed no difference in the Cu content compared with suitable control samples. Similarly, while the blood Cu values of ewes which give birth to Swayback lambs are on the whole lower than control animals, there are many ewes which show low values during

pregnancy which give birth to normal lambs. The blood copper content is not, therefore, the primary factor which controls the occurrence of the disease in the progeny. On the other hand there does not seem to be much doubt that copper is in some way intimately linked with the disease because a depletion of Cu reserves of the mother takes place before the birth of an affected lamb; this is reflected in the reduction of the Cu stores of the newly-born Swayback lamb compared with a normal animalx.

On the assumption that the Cu reserves in Swayback lambs and their mothers are below normal, the following circumstances might account for the "Cu deficiency" even although normal amounts appear to be available in the pastures:-

(a) The Cu is present in the grass in such a form that the ewes cannot absorb it - a circumstance which might account for the facts that the disease can be prevented either by feeding extra copper in the diet, or by transferring the pregnant ewes to "unaffected" areas during the latter part of pregnancy.

(b) There is some other unknown factor present in the grass which inhibits the absorption of the Cu.

(c) There exists in these ewes some dysfunction of the alimentary tract which inhibits or limits the absorption of Cu.

There are speculations which are worthy of consideration although there still remains to be explained the exact mode how the

of how the Cu deficiency exerts its pathogenic effect.

What can be stated with a reasonable degree of certainty is as follows. It takes considerable time for the "Cu deficiency" in the ewe to manifest itself; this is apparent from the more frequent occurrence of the disease in lambs of older ewes. The amounts of available Cu in the pastures of affected areas is normal so that the "deficiency" can only then be one of non-utilisation of the trace element. This non-utilisation is not necessarily followed by a lowering of the blood values but appears, at least initially, to cause a depletion of the Cu stores in the pregnant ewe. The subsequent course of events is not so clear. The "deficiency" has no pathogenic effect on the mother and in the developing lamb is restricted to an action on the developing myelin. This might indicate that the latter is more sensitive than that of the adult brain or that there is some intrinsic cerebral factor bound up with copper, the complex of which causes demyelination. The absence of lesions in the body of the mother or elsewhere in the lamb is strong evidence that this factor is not extra-cerebral. Evidence has already been given which indicates that the process begins late in gestation; this is supported by the fact that only one case occurred out of 17 lambs from ewes which were given copper treatment for the last four weeks of gestation. This period corresponds with that when cerebral myelination is beginning to occur with any degree of activity (15-16 weeks).

There is no indication at present that a similar explanation can be offered for any of the demyelination diseases of man although the question of any of these being due to a trace element has never been investigated.

It can be concluded that a prophylactic measure has been discovered against Swayback, but until more is known about the relation of copper to myelin metabolism, there can be little hope of a complete understanding of the pathogenesis of the disease. In some ways there is thus an analogy with the introduction of liver therapy for pernicious anaemia in man which, as Boyd says, "has greatly widened the circle of light, but the margin of that circle still fades forever as we move; step by step the fountain of mischief has been pushed back ..... but the problem remains".

IX. SUMMARY.

1. When this investigation was begun in 1935, relatively little was known about the Swayback other than it was a form of lamb "paralysis". These studies established the pathological nature of the disease for the first time and as a result caused it to be viewed in an entirely new light, and thus placed it on sounder basis for further important work.

2. Swayback is a nervous disorder of new-born and young lambs of different breeds occurring in many parts of England, Scotland and Wales. The same disease occurs in Australia and New Zealand and probably corresponds to conditions which have occurred in South America, Sweden, South Africa and India. The incidence in Britain varies annually and may be as high as 90 per cent. of the lambs born on any one affected farm. In some areas (e.g. Derbyshire) the disease is enzootic.

3. The symptoms are those of a spastic paralysis of the limbs with resultant inco-ordination and occasionally blindness; the disease is progressive in most cases with a fatal termination.

4. The pathology is characterised by a diffuse symmetrical demyelination of the cerebrum varying in extent in different cases from small foci in the centrum ovale to gross demyelination of the whole hemispheres. Liquefaction and cavitation is a common

end stage of the lesion. Secondary degeneration of the motor tracts in the cord is always present. The disease is a degenerative disorder bearing some resemblance to Schilder's disease in man and is of ante-natal origin.

5. Bacteria and/or viruses are not concerned in the aetiology; "Swayback" is analagous in this respect to the demyelinating disorders in man, monkey and the dog.

6. The causal agent causes no obvious disturbance in the health of the ewe but exerts a pathogenic effect on the foetus or young lamb. In the latter this agent has a specific affinity for the cerebral myelin and/or for the mechanism or cells responsible for the laying down of myelin which it destroys with singular rapidity.

7. The suggestion that a disturbance of copper metabolism in the pregnant ewes was concerned in this way with the aetioloty was subsequently investigated. Chemical analyses of the blood and body tissues of "Swayback" lambs and their mothers show lower Cu values compared with suitable controls. The remarkable prophylactic value of Cu is clearly proved as a result of a large scale field experiment carried out in Derbyshire. The exact role which the trace element plays in the aetiology is not, however, understood as it is apparent from the Cu analyses of the pastures that

the disease is not a Cu deficiency *per se*. Until more is known about function of copper and its relation to myelin metabolism, the pathogenesis may not be easily explained. A specific anaemic complication in the mother is not part of the syndrome and Sway-back is not thus a blood-brain complex parallel with pernicious anaemia and subacute combined degeneration in man.

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