

duced pain of the tooth pulp, by the method and discipline of Harris and Blockus. Rigorous elimination of bias was exercised. The treatments were: A. d-amphetamine, 5 mg; amobarbital, 32 mg; acetylsalicylic acid, 162 mg; acetophenetidin, 162 mg; B. acetylsalicylic acid, 162 mg; acetophenetidin, 162 mg; C. placebo; D. no medication, *i.e.*, a dry-run. The threshold of experimentally induced pain was elevated more significantly during the 2½ hours after the amphetamine mixture than

after the other 3 treatments.

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Demyelination in Lambs from Ewes which Feed on Seaweeds. (20402)

P. A. PÁLSSON AND H. GRÍMSSON. (Introduced by B. Sigurdsson)

From the Institute for Experimental Pathology, University of Iceland, Keldur, Reykjavik.

A nervous disorder in newborn and young lambs has been known to occur since the middle of the last century on many farms in Iceland *i.e.* farms near the coast where the sheep graze on seaweeds during the winter. Ewes are most prone to give birth to affected lambs when they eat much seaweed during the last half of the gestation period.

Many of the farmers along the coast graze their sheep on seaweeds in order to save hay. The daily intake of seaweeds per animal may become quite high (6 to 10 kg). Sheep seem to prefer certain species of seaweed such as *Rhodymenia palmata* and *Alaria esculenta* but where these species are scarce they consume other species too. The disease is rare on farms off the coast. Its incidence varies considerably from year to year on the same farm. On many farms the *mortality* may vary annually from 1% to 50% of the lambs born on the farm, but occasionally the losses may be as high as 80% to 90%. On some farms the disorder occurs every year, on other farms, even in the same area, the disorder seems to occur for one or 2 years after the herd has been free from the disorder for a number of years. Ewes which have given birth to affected lambs one year may produce either affected or healthy lambs the following year. This disorder is not so widespread now as it was 20-30 years ago, probably because the ewes are now fed much more hay during the

gestation period, and on many farms the ewes are kept away from the seaside altogether during the last half of pregnancy. When the hay crop is poor for one year large losses among the lambs still occur. Older ewes seem to be more prone to give birth to affected lambs than young ewes, but ewes at any age may give birth to affected lambs.

The symptoms are usually essentially similar, but vary considerably in severity. The most prominent and common symptom is incoordination of movement, in many cases the lambs are unable to rise and stand, but lie helpless, some may be able to rise, but walk with much difficulty and collapse almost immediately, others walk with a staggering gait. Mild cases show only weakness of the hind quarters, especially when hustled. Many lambs are blind. The body temperature is normal. Most cases are fatal, but those lambs which do not show symptoms until some weeks after birth, often survive and if bred later, they may give birth to healthy lambs.

The macroscopic pathological lesions seem to be confined to the nervous system, particularly the cerebrum. In approximately one-half of the cases which we have examined, macroscopic lesions were present. In the most typical cases the convolutions of the cerebrum were flattened and poorly defined, on palpation fluctuation could easily be felt on the hemispheres and the cerebral cortex was in



FIG. 1. Brain from a lamb which showed symptoms of ataxia (left). For comparison a brain from a normal lamb.

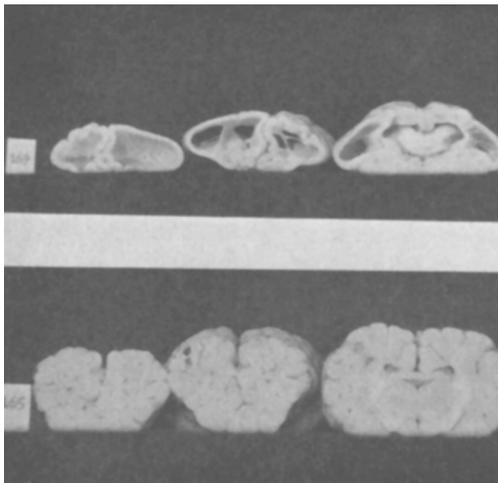


FIG. 2. Same brains as in Fig. 1. Series of coronal sections showing marked bilateral cavitation. Some dilatation of the lateral ventricles.

these cases extremely thin, (Fig. 1). When sliced into coronal sections a bilateral degeneration of the cerebral white matter was observed. The white matter had been almost completely liquified, and destroyed, leaving a cavity in which a network of a gelatinous substance was seen (Fig. 2). These cavities seemed to extend from the occipital pole and could in extreme cases be followed to the frontal pole. Around the cavitations the grey matter seemed to be fairly normal. In a few cases the lateral ventricles were somewhat distended. No hemorrhages were observed. The midbrain, cerebellum and the brain stem showed no macroscopic lesions and the meninges were normal. In the milder or delayed

cases macroscopic lesions were usually absent. By comparing microscopic sections from affected lambs stained for myelin (Weigert-Pal) with corresponding sections from normal lambs stained in the same way, demyelination was found to be the characteristic lesion. In cases where macroscopic lesions had been prominent there seemed to be an almost total absence of myelin in the hemispheres. In other cases the destruction of cerebral myelin was less marked and in many cases only small foci of demyelination were observed. Focal or diffuse infiltration by inflammatory cells were not observed and hemorrhages were not seen.

As this condition resembles in many respects "swayback" as described by Innes and Shearer(1) an investigation was carried out in order to determine the copper content in blood, organs, samples of seaweeds and sheep foodstuffs. This work is still in progress but some of the preliminary results are as follows:

Seaweeds. The average copper content of oven dried *Rhodymenia palmata* taken in February, March and April was found to be 22 p.p.m., *Alaria esculenta* and *Alaria pylaii* 9.5 p.p.m. Other species of seaweed which the sheep consume contain a varying amount of copper from 3 to 28 p.p.m. It may be concluded that the condition is not caused by too low an intake of copper.

Blood from ewes. The average value for blood copper of ewes from an affected area is less than 0.2 mg Cu per litre. The average blood copper content in ewes from a non-affected area is higher than 1.0 mg Cu per litre.

Livers from lambs. The average copper content of oven dried livers from affected lambs is below 7 p.p.m. which is 20 to 30 times lower than the average copper content of oven dried livers of lambs from non-affected areas.

In order to test the effect of feeding a supplement of copper on the incidence of the disease in lambs a field experiment was carried out during the years 1949-1952. Altogether a group of 1399 ewes on affected farms were given a supplement of copper sulfate, 0.3 g every 10th day during the last 3-4 months of the gestation period. On the same farms 566 ewes were kept as controls.

The ewes which were given the supplement gave birth to 1484 living lambs and of these 35 or 2.3%, showed clinical symptoms of ataxia. The 566 control ewes gave birth to 612 living lambs and of these 101 or 16.3% showed clinical symptoms of the nervous disorder. Stillborn lambs are not included in the figures because of the practical difficulties in bringing the lambs to the laboratory quickly enough for post mortem examination.

In view of the above results, we think that the nervous disorder found in Icelandic lambs born by ewes fed on seaweed during pregnancy is similar to "swayback" or enzoötic ataxia in lambs as described in other countries(1,2).

Summary. 1. A brief description is given of a nervous disorder in lambs born by ewes which

feed on seaweeds during pregnancy. Pathologically the disease is characterized by a demyelination confined to the cerebrum. The copper intake in affected areas does not seem to be low, but the ewes in these areas show low values for blood copper, *i.e.* less than 0.2 mg Cu/litre. The copper content of livers from affected lambs is very low. 2. A field experiment showed that the disorder can be largely prevented by giving a supplement of copper to the pregnant ewes.

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Growth Characteristics of the Krebs Ascites Tumor. (20403)

HARVEY M. PATT, MARGARET E. BLACKFORD, AND JEAN L. DRALLMEIER.

From the Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill.

Ascites tumors, which consist essentially of a suspension of neoplastic cells growing in the peritoneal cavity, have been the subject of numerous investigations since the classical observations of Lowenthal and Jahn(1). The suitability of ascites tumors for study of the chemistry and physiology of growth has been emphasized by Klein(2-4), Lettré(5) and others. A number of tumors have been shown to have the capacity for growth as ascites tumors and certain of their chemical and biological characteristics have been described (3,4,7,8). Takes may occur after intraperitoneal injection of a single neoplastic cell (6,9). It is known from earlier work with the Ehrlich ascites tumor of mice that the survival time and body weight increase bear some relationship to the extent of tumor growth. Under certain controlled conditions, survival time is dependent on the number of tumor cells inoculated and the weight increase reflects ascites development(2,4,5,10). While such indices are useful in a general way, a more direct and quantitative measure of the growth characteristics is desirable. This has been attempted in the present experiments by

estimating the volume of ascites by dye dilution and the concentration of tumor cells at intervals after intraperitoneal inoculation of the Krebs-2 carcinoma in mice. These studies are preliminary to an investigation of the radiosensitivity of the ascites tumor and related phenomena.

Methods. The ascites tumor* employed in these experiments was derived originally from the Krebs-2 solid carcinoma. The Krebs ascites tumor is closely related cytologically and chemically to the Ehrlich ascites tumor (11). Female CF-1 mice 10 to 12 weeks of age were injected intraperitoneally with 0.2 ml of freshly obtained ascitic fluid diluted with Tyrodes solution to give the desired tumor cell concentration. Animals were sacrificed by cervical fracture at intervals after tumor inoculation. Evans blue dye, usually 1.5 ml of a 0.05% solution, was injected *i.p.* immediately after sacrifice, care being taken to inject the entire volume directly into the peritoneal cavity. The dye solution was prepared in cell free ascitic fluid obtained by

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