vaginal plugs, showed that the early fœtal pattern was seen from the twelfth to the fourteenth or fifteenth day of inter-uterine life, but that from the sixteenth day onward the adult pattern was generally obtained. The early fœtal pattern differs from the adult in a diminution of the relative amounts of the fastest moving band and a predominance of the third rather than the second component. The slowest-moving band was well marked in the early fœtal samples but was also present, though irregularly, in later life : the significance of this slowest band needs to be investigated further.

It can thus be seen that, in *CBA* mice. early fœtal blood may be distinguished from later fœtal, newborn or adult blood by the relative distribution of the different hæmoglobins.

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PATHOLOGY

Brain Glycogen- and Copper-Levels in Normal Sheep and Sheep affected with Scrapie

Little is known about the biochemical changes responsible for the characteristic symptoms of scrapie. We intend to examine systematically the brain and other tissues for evidence of biochemical derangements. A communication describing the lack of alteration of the serum proteins has already been published[1].

Attempts to relate disease conditions in domestic animals to those in man can be most informative. While scrapie has been likened to kuru, a disease affecting tribesmen in a localized area of New Guinea[2], we have considered, in view of the familial nature of scrapie[3], that scrapie may be related to two familial conditions in man, one a glycogen storage disease (Castaigne-Lhermitte) and the other associated with an excess of copper in certain organs (Wilson's disease)[4].

In Casteigne-Lhermitte's disease, a familial cardiomuscular variant of Von Gierke's hepato-renal glycogen storage disease, histological examination of the nervous system reveals the accumulation of glycogen within the nerve cells, varying from small droplets to confluent masses. The latter may actually displace the nucleus. This raises the question as to whether these could be confused with the neuronal vacuoles characteristic of scrapie. In individuals with the glycogen storage disease there is a motor disability characterized by muscular hypotonia. Death usually follows from bulbar paralysis or respiratory infection. Somewhat similar nervous symptoms may occur in scrapie.

Wilson's disease is a familial disease characterized by progressive rigidity, a coarse tremor of the limbs and a spastic condition of the face, mouth and pharynx with some degree of dementia in the final stages. A few cases develop in the first decade, but the onset is most common in the second decade. The disease is associated with the finding of a great excess of copper in the liver, corpus striatum, and the cornea. This is due to the failure of the serum globulins to bind copper as it is absorbed from the intestine. While there are differences in symptomatology between this disease and scrapie, the importance of copper in sheep neuropathology[5] suggested the necessity for basic information on copper-levels in sheep affected by scrapie and normal sheep.

Six sheep in which symptoms of scrapie had been experimentally induced were killed, the brains frozen within 60 min. and kept frozen until analysed. Nine normal brains from a packing house and similarly treated were used as controls.

For glycogen, 1 gm. of the frozen brain was weighed into alcoholic potassium hydroxide and hydrolysed by Kerr's method[6]. The glycogen was separated by centrifugation, taken up in trichloroacetic acid solution and analysed by the anthrone procedure described by Kahan[7].

For copper, 15 gm. of sheep brain were ashed overnight in platinum at 600° C. The residue was repeatedly digested with nitric acid, dried and returned to the muffle at 600° C. for 1 hr. until white and then made up to volume with dilute hydrochloric acid. The final determination was carried out on a suitable aliquot by Forster's method[8].

Brain glycogen values of the six sheep affected by scrapie ranged from 0·86 to 1·04 mgm./gm. of dry matter while the range for nine normal brains was 0·57–1·18. The early onset of scrapie, differences in symptomatology and the fact that brain tissue from affected sheep does not show elevated glycogen-levels indicate that scrapie is not similar to Castaigne-Lhermitte's disease.

Brain copper values of affected sheep ranged from 12·2 to 16·7 parts per million of dry matter while the range for normal brains was 13·0–35·0. The values for scrapie sheep thus fall within the lower part of the normal range. This indicates that a defect in copper metabolism is unlikely to occur in the pathogenesis of scrapie and that there is little chance of a relationship to Wilson's disease.

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