Moredun Institute
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SCRAPIE

(A Review)

by

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Scrapie is a progressive disease of sheep characterised by nervous symptoms and by a diffuse or focal degeneration of the grey matter of the subcortical centers along the neuroaxis of the central nervous system. The disease as far as we are aware is invariably fatal.

The clinical symptoms in the sheep consist of incoordination of gait, trembling and severe itch which causes persistent rubing of parts of the body against various fixed objects. In many cases one or more of the above symptoms may be either, diminished or grossly exaggerated, (Fig. 1 and 2).

Apart from an obvious increase in the amount of the cerebro-spinal fluid, all other pathological changes are microscopical and require for their identification histogical methods of examination. Lesions are most prominent in the brain stem, especially in the medulla but are also present in all other parts of the brain, such as the midbrain, thalamus, hypothalamus, paraterminal body and the cerebellum The spinal cord is also affected in a proportion of naturel cases, but no lesions are found as a rule in the cerebral haemispheres, cortex, hippocampus and amygdala (Zlotnik, 1957, 1958 1, 2 1960 and Zlotnik and Katiyar, 1961).

The bulk of pathological changes is present in the neurones and in the the perineural brain substance, but the astrocytes and other glial elements may be also affected. The typical scrapie lesions consist thus of widespread degeneration of neurones and status spongiosus of the perineural brain substance. All forms of neurone degeneration may be found in scrapie, ranging from chromatolysis, pyknosis, sclerosis, necrosis and simple and multiple vacoulation (Fig, 3, 4, 5, 6, 7, 8). However the vacules play a special

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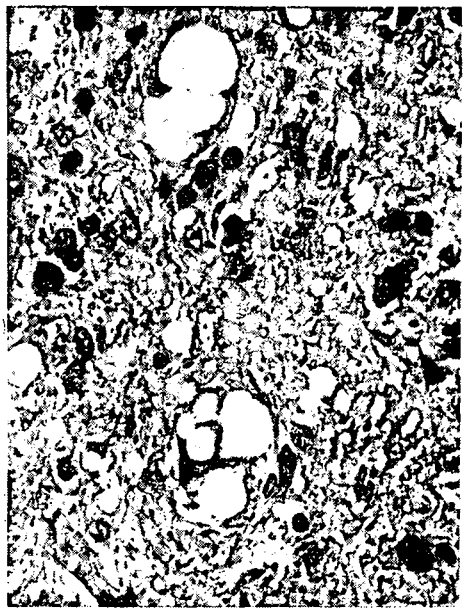

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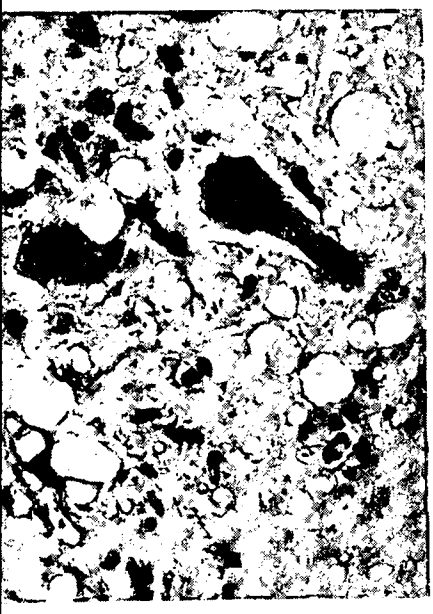

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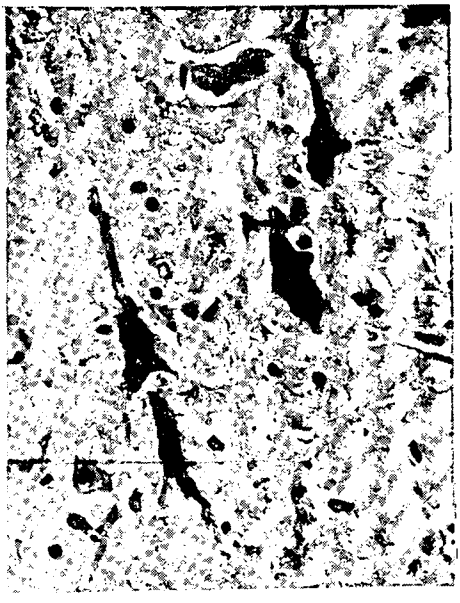

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part in scrapie in view of the fact that the of are invariabley present in increasing numbers in all clinical cases of scrapie, and are therefor considered to be typical, characteristic and diagnostic for the disease. As already mentioned neuronal vacuoles may be of various types and shapes; the vacuoles may form simple cavities in otherwise healthy cytoplasm or may consist of multiple cavitations in degenerated cells. Somestimes the vacuoles are seen to contain round eosinophilic bodies or are completely filed with necrotic debris. The status spongiosus which is very common in Suffolk Sheep, gives rise to empty spaces between the neurones or may cause progressive damage leading to detruction of large areas of the brain substance. The latter change appears as an obvious network with occasional sclerotic neurones and glial cells. All the lesions in scrapie are as a rule symmetrical, producing change on both sides of the neuroaxis.

The aetiology of scrapie is somewhat obscure and various theories have been advenced which can be divided broadly into those supporting a familial or genetical character of scrapie and those suggesting an infectious agent to be the cause of the disease. Experimentel evidence and results of transmission experimental work point very clearly to an infective agent as the cause of scrapie, and not to a lethal recessive gene, in spite of the familial tendences of natural scrapie (Parry 1957 and 1960, and Stamp, 1959).

The causative agent of scrapie has not yet been defined and although some of its properties are not entirely consistent with a virus, nevertheless they point strongly to a hitherto unknown type of a biologically active agent. Cell free fitrates of brain and other organs (spleen, pituitary, adrenal gland and liver) when inoculated into heathly sheep will give rise to scrapie after an incubation period of 4–12 months. Nearly all routes of inoculation are succesful (intracerebral, intraocular, intramuscular) and the disease reproduced as a result of subinoculation is very similar if not identical with naturel scrapie, both in respect of clinical symptoms, and pathological brain lesions. A point of interest is that not all inoculated sheep will go down with the disease, but only a proportion, which varies from 10 to 80 per cent, with an avarege at 33 %. Not only will untreated filtrates of brain give rise to clinical scrapie, but also boiled and those subjected to the action of 3.5 per cent phenol and formol. The scrapie agent appears to be very small as it is capable of passing through dialysing membranes, (Stamp et all, 1959, Pattison and Sansom, 1964).

Apart from sheep scrapie has now been transmitted from sheep to goats and from both sheep and goats to mice. Finally mouse passaged scrapie has been further transmitted to hamsters and rats and also both into sheep and goats. In the goat scrapie has been reproduced not only by actual inoculations of brain homogenates, but also by prolonged contact with clinically affected sheep. Two clinical entities or syndromes can be recognized in the goat which will reproduce the same syndrome by further subinoculation; the drowsy or lethargic and the itchy or scratching syndrome. The brain lessions in scrapie affected goats are, similar in the two syndromes and resemble those seen in the brain of sheep affected by scrapie, however the lesions of the goat are by far more severe and tend to spread further out to the anterior parts of the brain such as the thalamus, hypothalamus and paraterminal body. As far as the goat is concerned intracerebral inoculation produce scrapie in 100 % of cases, (Chandler, 1961, 1962, 1963, Chandler and Fisher, 1963, Hadlow, 1961, Pattison et al, 1959, Pattison and Millson, 1960, Zlotnik, 1961, 1962, 1963. and Zlotnik and Rennie, 1962, 1963).

The transmission of scrapie to mice inflicted a very severe blow to the supporters of the hereditary concept of scrapie. All breds of mice are susceptible to the disease and both the scratching and drowsy goat syndromes have been transmitted to mice as well as scrapie from Suffolk and Southdowns sheep. As in the sheep, mice can be infected by many routes including feeding with organs of scrapie affected sheep. The take in mice is similar to that of the goat where all inoculated mice develop scrapie. The incubation period in the mouse on first pasage varies from 7 months in the case of the drowsty goat strain to 15 months in natural scrapie of suffolk sheep. In both Southdowns and scratching goat scrapie the incubation period in the mouse averaged 12 months. A very drastic shortening of the incubation period is noted in mouse to mouse passages, where in all forms of scrapie the incubation period is reduced to 4–5 months in the third and subsequent passages.

Three cilinical syndromes have been described in scrapie affected mice; the hyperexcitable, the lethargic and the fat from, but no correlation could be found between the clinical symptoms and the type of inocolum used. The Pathological changes in mice on first transmission are similar to these of sheep and goats and are confined to subcortical centres of the brain. In subsequent muose to mouse passages all parts of the brain including the cerebral cortex and hippocampus are invariably affected.

The brain lessions consist of neuronal vacuolation and spongy degeneration, however in mice affected with the drowsy got strain there is only severe status spongiosus without neuronal vacuolation of subcortical brain centres.

Mouse adapted and passaged scrapie has been transmitted to hamsters and rats and while the clinical picture in these animals was that of a drowsy and incoordinated hamster or rat, the pathological changes resembled those of mice, where lesions can be found throughout the whole brain .

As pointed out previously mouse passged scrapie of both scratching goat and Suffolk sheep origin has been transmitted back to goats and to Cheviot sheep. The incubation period varied from 8 -12 months and while the pathological changes in the subcortical centres of the brain were the same as in sheep or goat scrapie, lesions were found also in some areas the cortex, hippocampus and the amygdaloid nucleus. The spread of lesions in these animals to the cortex shows that passaging through mice produced a biological change in the scrapie agent (Zlotnik and Rennie, 1964).

Özet *

SCRAPIE **

SCRAPIE koyunlarda sinirsel semptomlarla karakterize edilen progressiv bir hastalıktır ve santral sinir sisteminin subkortikal boz madde merkezlerinde neuroaxis'ler boyunca diffuz veya fokal olarak dejenerasyona sebep olur. Bugünkü bilgilerimize göre hastalık her zaman ölüm ile neticelenir.

Cerebro-spinal mayiin belirli bir şekilde artmış olmasından başka, diğer bütün patolojik değişiklikler mikroskopik olup identifikasyonları histolojik araştırma metotlarına ihtiyaç gösterir. Lezionlar CAUDEX CEREBRİ'de en belirlidir. Bunlar özellikle medulla'da ve ayni zamanda mesencephalon, thalamus, hypothalamus, paraterminal corpus ve cerebellum gibi diğer bölgelerde de mevcuttur.

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Tipik scrapie lezionları neuronların geniş sahalarda dejenerasyonu ve perineural beyin maddesinin status spongiosus'undan ibarettir.

Scrapie'nin bütün klinik olaylarında her zaman ve artan bir sayıda mevcut olmaları bakımından cytoplasmic vakuoller özel bir rol oynarlar. Bunlar hastalık için tipik, karakteristik ve diagnostik olarak kabul edilirler.

Scrapie'de bütün lezionlar kaide olarak simetriktirler ve neuroaxis'in her iki yanında benzeri değişiklikler meydana gelir.

Experimentel deliller ve transmission tecrübeleri hastalığın ailevi temayülüne rağmen letal recessive bir gen ile alâkası olmayıp enfeksiyöz bir etken olduğunu açıkça göstermektedir.

Beyin ve diğer organların (dalak, hypophyse, adren ve karaciğer) hücresiz filtratları sıhhatli koyunlara inokule edildiği zaman 4 veya 12 aylık bir inkubasyon devresinden sonra scrapie meydana getirilebilmiştir. Sadece, muameleye tabi tutulmamış beyin filtratları değil, ayni zamanda kaynatılmış ve % 3.5 phenol ve formol ile muamele edilmiş filtratlar da klinik bir scrapie meydana getirmeğe muktedirdir.

Koyundan başka son zamanlarda scrapie koyundan keçiye ve her ikisinden de farelere nakledilebilmiştir. Bundan başka farelerde pasajı yapılan scrapie hamsterlere ve sıçanlara ve oradan da tekrar koyun ve keçilere nakledilebilmiştir.

Keçilerde iki syndrome tefrik edilir ve bu syndrome'lar ileri subinokulasyonlarda tekrar meydana çıkar. Bunlar *uyuşuk veya lethargic* ve *kaşıntı* ile seyreden hastalık syndromlarıdır. Scrapie'li keçilerdeki beyin lezionları her iki syndrome'da da birbirinin benzeridir ve koyundaki beyin lezionlarını andırır. Mamafih, keçideki lezionlar daha şiddetli ve thalamus, hypothalamus ve paraterminal corpus gibi beynin ön taraflarına kadar uzanmaktadır. Keçide intracerebral inokulasyon ile hastalığı % 100 meydana getirmek mümkündür.

Her türlü fare ırkları hastalık etkenine karşı hassastır.

Scrapie'li farelerde 3 türlü klinik syndrom tarif edilmiştir; HYPEREXİTATİON, LETHARGIC ve YAĞLAMA şekilleri. Beyin lezionları neuronal vakuolizasyon ve süngerimsi dejenerasyondan ibarettir.

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Legends to Illustrations

1. Naturel scrapie in Suffolk sheep and experimental scrapie in goats.
2. Experimental scrapie in Cheviot sheep.
3. Simple vacuolation of neurones in the medulla of sheep. , X 600
4. Multiple vaculation of neurones in the reticular formation of sheep. X 600.
5. Severe vaculation of neurones in the medulla of sheep. X600.
6. Status spongiosus in the medulla of goats. X 600.
7. Chromatolysis in the neurones in the medulla of sheep. X 600.
8. Pyknosis of neurones in the hippocampus of goats. X 44.

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