THE PATHOLOGY OF FACIAL ECZEMA

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IT IS UNFORTUNATE that the condition known as facial eczema should be so named for it gives no clue to the primary or essential character of the disease. Moreover, facial lesions develop in only a small percentage of affected animals. Facial eczema can be defined as an acute obliterative cholangitis to which all other changes are secondary.

The purpose of this paper is to describe the morbid anatomy and histopathology of the liver damage in natural cases of the disease in sheep, to refer briefly to the disease in other species and to show that certain clinical and biochemical abnormalities are dependent on the specific liver lesions.

Morbid Anatomy

For descriptive purposes it is convenient to consider four types of liver damage, namely mild, moderate, severe, and chronic, but it must be appreciated that the differences are mainly in degree. Mild and moderate facial eczema damage is seen most often in the livers of lambs killed at the freezing works a short time after they have eaten toxic grass. In the majority of such livers the damage occurs around the border of the left lobe.

Mild Facial Eczema: The lesions are seen as well defined areas, lighter in colour than normal and usually commencing at the liver border. They are slightly below the level of the adjacent parenchyma and have a distinct finely mottled arborescent appearance. Similar isolated patches may be seen on either surface and in any part of the liver. When sectioned, the appearance within the liver is similar to that on the surface, but the lesions are found to be roughly cone or wedge shaped, and to extend further into the parenchyma than is obvious on the exterior. When the sections are continued into the apparently normal parenchyma it is seen that a few of the medium sized bile ducts, like those within the lesion, have thickened white oedematous walls. At some point distal to the lesion an occluded duct or ducts may be found. It has been shown by McFarlane *et al.* (1959) that the occlusion may extend along a duct for a distance over 3 cm.

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Moderate Facial Eczema: In this case the only difference from the mild type is that a much greater part of the liver is abnormal. However, even when there is less than 10 per cent. of the liver which appears normal there is often no clinical or other gross post mortem abnormality.

Severe Facial Eczema: When the liver suffers severe damage there are usually marked clinical signs such as photosensitivity and icterus. The liver damage is often generalized but may be much more marked in the left lobe. In these cases the liver is green or yellow-green throughout and the whole surface and sections show the fine mottling. The gall bladder is usually distended with bile and the extra-hepatic ducts are thick and prominent and contain inspissated bile which may occlude them. The liver is larger than normal, is very firm and the borders are thick and rounded. It is very tough to cut and when sectioned many thickened bile ducts, often plugged with inspissated bile, are seen.

Chronic Facial Eczema: This term is reserved for the liver in which all active change has ceased. The appearance of the liver varies greatly depending on the extent and site of previous bile duct damage and occlusion. However, the type most frequently seen is the liver which, on the diaphragmatic surface, is composed of a thin layer of dense, white, very fibrous tissue and shows on the visceral surface one or more large bulbous masses of regenerated liver. Many such livers are found in healthy sheep.

Histopathology

This has been described previously by Cunningham *et al.* (1942) and later in more detail by McFarlane *et al.* (1959). Only brief reference will therefore be made to the more prominent features.

The earliest and essential lesion is degeneration of the epithelium of medium sized bile ducts, usually accompanied by periductal oedema and infiltration by a variety of leucocytes. If the damage at any one site is sufficiently severe the lumen of the duct becomes occluded as the result of fibrous tissue proliferation. An inevitable sequel to bile duct occlusion is rapid proliferation of bile ductules proximal to the occlusion. As a result of the proliferation of bile ducts and fibrous tissue in the portal areas, the liver cells are gradually replaced around the periphery of the lobules. Eventually the area is composed of mature contracted fibrous tissue with small bile ducts scattered throughout. There is no evidence of any specific effect on the parenchymal cells. In

severe facial eczema, when the whole liver is green and enlarged, many obliterated ducts can be found, but in addition to the duct proliferation and fibrosis there may be much bile staining of liver cells and numerous bile infarcts. Many of the larger ducts are also filled with bile plugs and desquamated epithelial cells.

The Toxin Hypothesis

Attempts to transmit facial eczema were conducted at Wallaceville some fifty years ago and from these Gilruth (1905) concluded that the disease was due to "dietetic errors". Similar attempts to transmit facial eczema from diseased to healthy sheep were later reported by Reid (1911) and by Cunningham *et al.* (1942). The regular failure to infect normal animals led these workers to the conclusion that facial eczema was dietetic in origin. This was upheld by the reproduction of liver damage in sheep fed pasture cut from areas where facial eczema had occurred.

The toxin hypothesis was also supported by the nature of the liver damage which showed no evidence that the lesions were caused by an infectious agent.

Development of Photosensitivity and Icterus

If bile ducts become occluded, substances which are normally carried away in the bile will gain entry to the blood stream. The two most important of these substances from the clinical pathology viewpoint are bilirubin and phylloerythrin. The amount of bilirubin which appears in the blood varies greatly but abnormal amounts can be detected before clinical jaundice is apparent. Phyllocrythrin, which is a normal breakdown product of chlorophyll, has been shown to be the agent responsible for the development of photosensitivity. When this substance, as the result of bile duct occlusion, accumulates in the blood in sufficient quantity, unpigmented areas of the skin which are exposed to sunlight develop the lesions which have led to the name of the disease. In sheep the parts affected are mainly the face and ears, but in cattle the udders and white skin surface are affected. The skin damage begins with an accumulation of fluid under the skin, giving the part a puffy appearance. Yellow serum-like fluid then exudes through the skin on to the surface where it dries and forms eventually a hard dry scabrous covering. Necrosis of the skin occurs at the same time. Often the tips of the ears or sometimes even the whole ear sloughs away. If the animal survives the scab finally falls off, to expose normal healed skin.

Comparative Pathology

The bovine is the only other species in which facial eczema is known to occur naturally but it can be produced in both guinea pigs and rabbits by feeding toxic grass. The liver damage in all these species is comparative to that in the sheep, but there are some slight differences. In the guinea pig there is more bile ductule proliferation and less fibrosis than in the sheep, whilst the reaction in the rabbit liver tends to be of a more acute type, for here there is marked periductal oedema which is proportional to the size of the duct. Thus the oedema is most pronounced in the extra-hepatic biliary system. The guinea pig liver may also show large areas of non-inflammatory liver cell necrosis (Evans *et al.*, 1957).

Discussion

There are a number of other photosensitivity diseases which clinically can be confused with facial eczema, but which can be differentiated on pathological grounds. Photosensitization caused by *Panicum* spp. is apparently, to some extent at least, an exception. No detailed report of the liver damage has been published but according to Filmer (1949) the changes resemble those seen in early facial eczema.

Much work remains yet to be done on the pathology of this disease, particularly with respect to the development of the lesions. All the evidence gathered so far with the techniques used indicates that the biliary epithelial cell is the primary site of action of the toxin. No specific damage has been found in the liver cells, but even though there may be no histological signs of damage their function and biochemical activities could well be altered.

Summary

Facial eczema is essentially an acute cholangitis which leads to obliteration of a variable number of intra-hepatic bile ducts. The sequel to obliteration is proliferation of portal bile ducts proximal to the lesion, portal fibrosis and gradual replacement of the liver cells as the portal lesion becomes more extensive. When large areas of the liver are affected in this manner, compensatory liver cell regeneration takes place in undamaged parts of the liver.

Literature Cited

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DISCUSSION

D. MCFARLANE: The discipline of pathology has through the years contributed significantly to our progress in facial eczema research.

The first major contribution was the recognition that facial eczema is primarily a disease of the liver, a point which, if it had been recognized at the beginning, would have led to the selection of a much more suitable name for the disease.

The second major contribution of pathology was to recognize that the essential feature of the disease is severe bile duct damage leading to duct obliteration. Gross liver damage, photosensitization and jaundice are secondary.

The third major contribution was the recognition of the guinea pig as a suitable test animal, so making laboratory scale grass extraction possible.

Pathology has much to contribute to an understanding of this and related diseases. Among points worthy of consideration and investigation are:

(1) The known wide between-sheep differences on a similar intake of toxic grass.

(2) The between-species difference in liver damage.

(3) A detailed description of the development of liver damage in sheep given controlled dosage and killed at intervals.