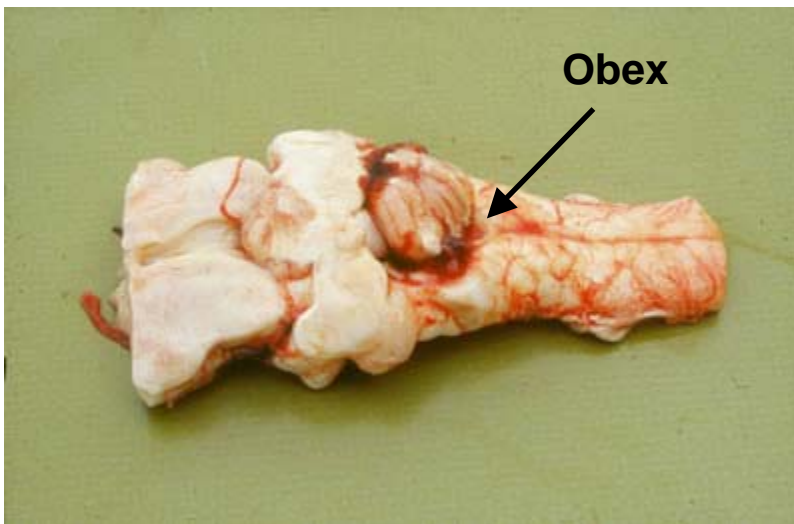


Neuropathology: Confirmatory diagnosis of transmissible spongiform encephalopathies (TSEs) in cattle and sheep

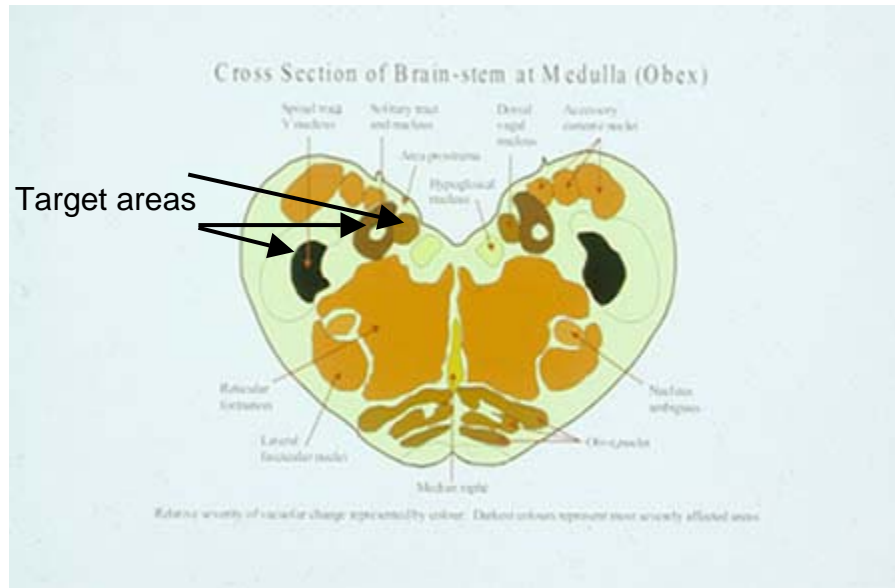
INTRODUCTION

This gives guidelines for the routine statutory diagnosis of transmissible spongiform encephalopathies (TSE) based on histological and immunohistochemical (IHC) examinations of the brainstem at the level of the obex.

The gross identification of the target region at the obex



Cross Section of Brain-stem at Medulla (Obex)



MATERIALS

Equipment

Obex section(s) stained with haematoxylin eosin (HE).

Obex section(s) stained immunohistochemically for TSE-specific protease resistant protein (PrP).

Light microscope with low, medium and high power objectives.

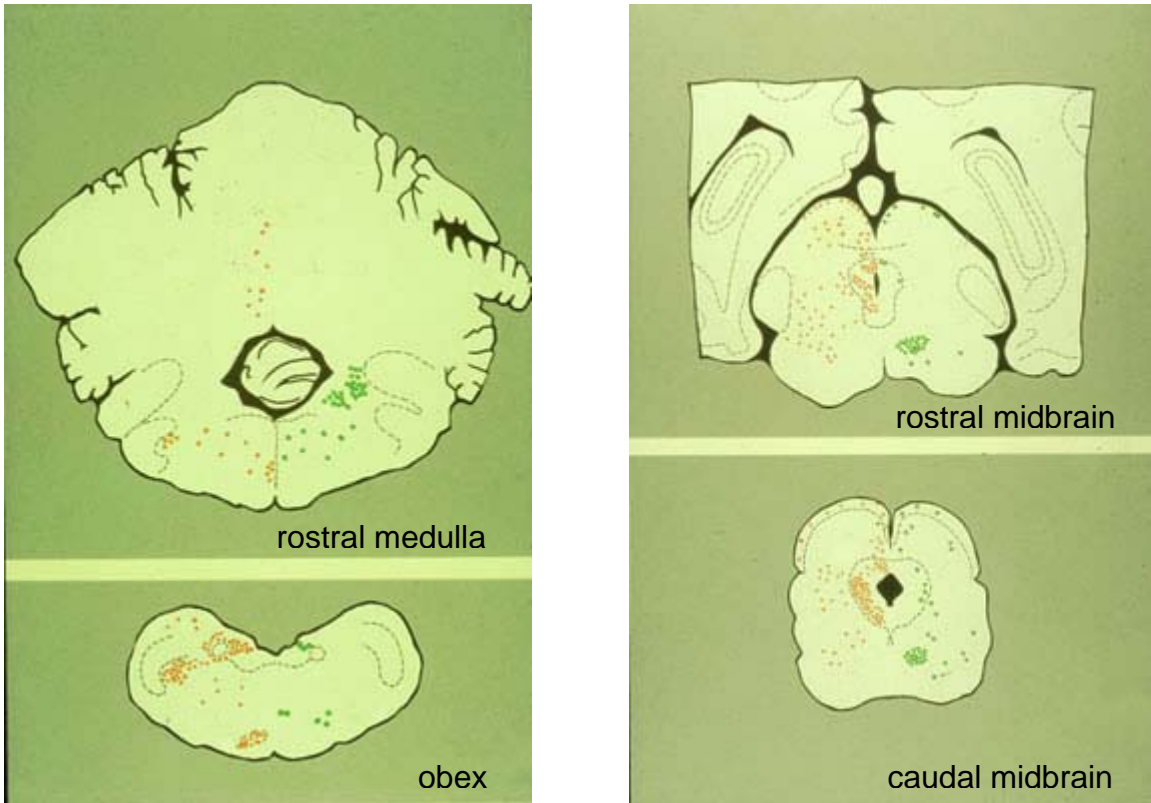
PROCEDURE/METHOD

1. Check that the identification on each labelled slide corresponds with that recorded on the accompanying paperwork.
2. Examine each section (and the relevant controls, where appropriate) methodically using standard histopathological practices. The major target sites at the level of the obex include the solitary tract nucleus, the dorsal nucleus of the vagus nerve, the spinal tract nucleus of the trigeminal nerve and the olivary nuclei.
3. The following guidelines will aid interpretation:

Positive (histopathology):

The presence of characteristic vacuolation (spongiform change) affecting the neuropil with an anatomically precise and usually bilaterally symmetrical distribution. Vacuolation in a single target site is sufficient for histopathological

confirmation. Usual target sites in bovine are the solitary tract nucleus and the nucleus of the trigeminal tract, and in ovine the dorsal nucleus of the vagus (or unusually, the olivary nuclei). A positive bovine case should usually show more than three neuropil vacuoles per target site. (Wells and others 1989). It is not possible to be this precise for ovine suspects due to the occurrence of incidental neuronal vacuolation in some sheep (Zlotnik & Rennie 1957).



neuropil vacuolation - bovine

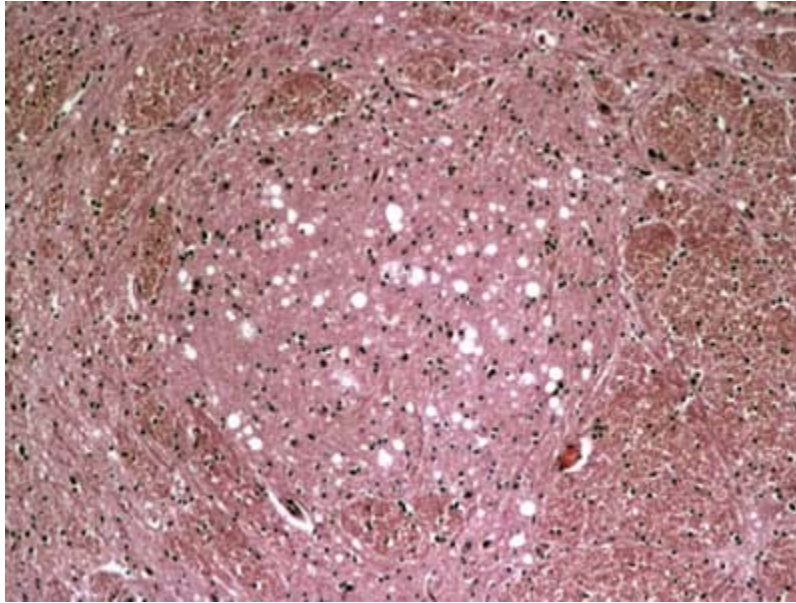
(in red)

neuronal vacuolation- bovine

(in green)

All are bilaterally symmetrical lesions.

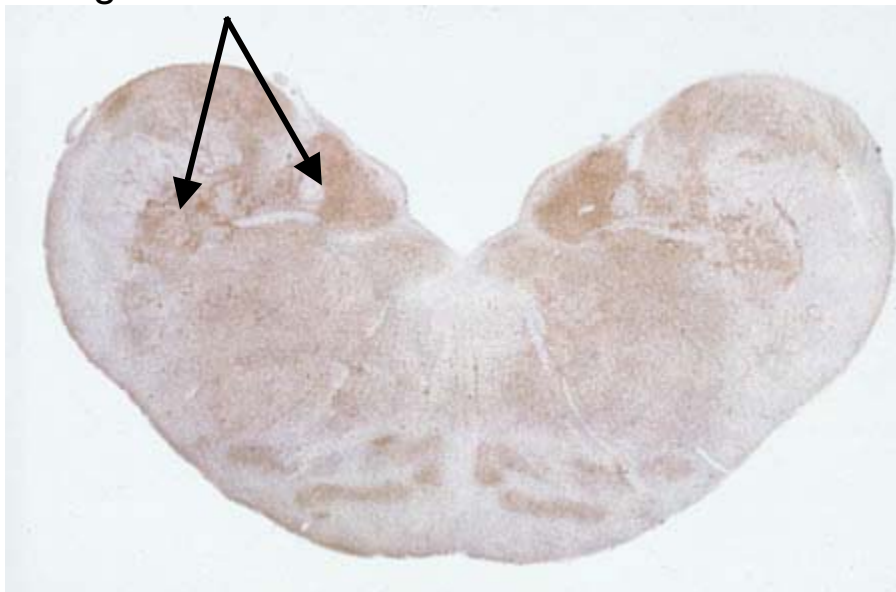
BSE positive - neuropil vacuolation in the nucleus of the solitary tract (Bovine brainstem at the level of the obex)



Positive (immunohistochemistry):

PrP distribution with similar distribution to above. This is always found co-localised with disease-specific vacuolation (see above) and may also be observed in the absence of spongiform changes.

Target areas



Inconclusive (histopathology):

Insufficient vacuolation of neuropil for unequivocal confirmation by above criteria.

Inconclusive (immunohistochemistry):

Presence of equivocal immunostaining confined to the TSE neuropil target areas.

Unsuitable (histopathology):

Inadequate submission due to either poor (or no) representation of target sites, or the presence of severe confounding autolytic (or other artefactual) changes.

Lesions indicative of an alternative neuropathological diagnosis which prevent assessment of TSE target sites for the presence or absence of specific spongiform change.

Unsuitable (immunohistochemistry):

Absence of appropriate target sites. Technical failures. Failure of positive run control.

Negative (histopathology):

Absence of characteristic neuropil vacuolation in sections where the target areas can be confidently identified and assessed.

Lesions indicative of an alternative neuropathological diagnosis which still allow adequate assessment of target areas.

Negative (immunohistochemistry):

Absence of immunostaining in target areas. Must be able to identify target sites. Appropriate positive control.

REFERENCES

Wells GAH *et al* (1989). BSE: Diagnostic significance of vacuolar change in selected nuclei of the medulla oblongata. *Veterinary Record* **125**, 521-4.

Zlotnik, I. and Rennie, J.C. (1957). The occurrence of vacuolated neurones and vascular lesions in the medullas of apparently healthy sheep. *Journal of Comparative Pathology* **67**, 30-36.