Abstract
Spontaneous vestibular syndrome in mice, characterized clinically by head tilt, circling or rolling, can be attributed to otitis media, arteritis or central nervous system lesions. Post-mortem examination on seven non-inbred Swiss mice (one Hsd:ND4 and six Hsd:ICR(CD-1)) was performed to investigate the cause of vestibular signs. The mice were euthanized with carbon dioxide and heads were decalcified with Formical™ for 24 hours, sectioned and submitted for histology. Immediately after postmortem examination, the thoracic cavity was opened and the heart was removed. The heart was perfused with saline followed by 4% paraformaldehyde (PFA) and the brainstem was dissected out and fixed in 4% PFA for 24 hours. The brainstem was sectioned and submitted for histology. Immediately after postmortem examination, the thoracic cavity was opened and the heart was removed. The heart was perfused with saline followed by 4% paraformaldehyde (PFA) and the brainstem was dissected out and fixed in 4% PFA for 24 hours. The brainstem was sectioned and submitted for histology.

Introduction
The vestibular system provides sensory input about body position and movement. Sensory receptors are located in the inner ear and consist of hair cells that detect movement and head position. Circular motion is detected by cells in the crista ampullaris of the semicircular canals, while linear motion and head position are detected by hair cells associated with calcium carbonate crystals called otoconia in the utricle and saccule. Afferent projections from the hair cells synapse on neurons in the vestibular nuclei of the brainstem or the uvula or nodulus of the cerebellum. Lesions in any of these components can cause vestibular syndrome, which in mice is characterized by head tilt, rolling, spinning and inability to eat, drink and groom normally. Otitis media, arteritis and CNS lesions have been reported to cause vestibular syndrome in mice.

Objective
To investigate the cause of vestibular syndrome in seven Swiss mice with no evidence of otitis, CNS neoplasia or vasculitis.

Methods
Post-mortem examinations were performed on seven non-inbred Swiss mice (one Hsd:ND4 and six Hsd:ICR(CD-1)) with acute vestibular signs. The mice were euthanized with carbon dioxide and heads were decalcified with Formical™ for 24 hours, sectioned and submitted for histology. Immediately after postmortem examination, the thoracic cavity was opened and the heart was removed. The heart was perfused with saline followed by 4% paraformaldehyde (PFA) and the brainstem was dissected out and fixed in 4% PFA for 24 hours. The brainstem was sectioned and submitted for histology. Immediately after postmortem examination, the thoracic cavity was opened and the heart was removed. The heart was perfused with saline followed by 4% paraformaldehyde (PFA) and the brainstem was dissected out and fixed in 4% PFA for 24 hours. The brainstem was sectioned and submitted for histology.

Results
Figure 1. Some causes of vestibular syndrome in mice. A. Carotid arteritis. B. Otitis media. C. CNS tumor (astrocytoma).

Table 1. Seven non-inbred Swiss mice submitted for necropsy because of vestibular signs had unilateral brainstem necrosis. All mice were from Harlan (Frederick, MD).

<table>
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Figure 2. Intracardiac injection of yellow latex in a control mouse shows the course of the vertebral artery through the transverse foramina (open arrow) of the cervical vertebrae then joining the contralateral artery to form the basilar artery. The first major branch of the basilar artery is the caudal cerebellar artery.

Figure 3. A putative thrombus in a branch (arrow) of the vertebral artery (arrow head) at the level of C1. There is moderate hemorrhage around the vessel.

Figure 4. Postmortem intracardiac injection of ink highlights the vertebral artery. A and B. At the level of C2, both vertebral arteries contain ink. C and D. At the level of C1, there is a filling defect in the right vertebral artery. E and F. At the level of the caudal medulla, ink is visible in only the left vertebral artery as it merges with the right to form the basilar artery. There is a discrete area of malacia in the dorsolateral medulla on the right side.

Discussion
Vestibular syndrome, characterized by head tilt, spinning and rolling, has been previously reported in mice with otitis media/innera, carotid arteritis and CNS tumors affecting the vestibular nuclei or cerebellum. The mice discussed here had lesions consistent with unilateral brainstem infarction involving the vestibular nuclei. The infarction is most likely secondary to occlusion or rupture of the vertebral artery or one of its branches. Unilateral brainstem infarction represents another potential cause of vestibular phenotype in mice and shares features with Wallenberg’s Lateral Medullary Syndrome, the most common brainstem stroke in humans.

Conclusions
1. Vestibular syndrome in seven Swiss mice was associated with unilateral brainstem lesions consistent with infarcts. 2. Brainstem lesions are similar to those reported with Wallenberg’s Lateral Medullary Syndrome in humans.

References

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