Epidermoid and dermoid cysts are embryologic defects believed to be the result of inclusion of epithelial remnants of ectoderm at the time of closure of the neural tube. Spinal cysts in humans may have a traumatic origin from iatrogenic penetration of skin fragments due to repeated lumbar punctures. Both epidermoid and dermoid cysts have been produced experimentally in the brain and spinal cord of young rats in a similar fashion. Epidermoid and dermoid cysts are both lined by stratified squamous epithelium but can be distinguished by the presence of adnexal structures such as hair follicles, sebaceous glands, or sweat glands only in the dermoid cysts.

In humans, there are definite differences in the clinical and anatomic incidence of these two types of cysts, often grouped together as pearly tumors. Epidermoid cysts, also called cholesteatomas, are more frequent than dermoid cysts especially in the cranial cavity, and dermoid cysts are more common in the spinal canal where most occur in the lumbosacral region. Symptoms generally arise in the second or third decade for dermoid cysts and the fifth decade for epidermoid cysts and are related to slowly progressive neurologic dysfunction. Grossly, epidermoid cysts are well defined with a shiny, irregular nodular surface. They are filled with waxy or flaky material and may contain cholesterol crystals or focal calcification. Microscopically, the wall is composed of stratified squamous epithelium with variable degrees of keratinization. This epithelium rests on an outer layer of connective tissue, which may be vascularized. Chronic-active inflammation may be associated with the epithelium.

In dogs, there have been six reported cases of intracranial epidermoid cysts and a single report of an intraspinal epidermoid cyst. Intracranial cysts were associated with hemiparesis or cerebellar-vestibular dysfunction in three dogs ranging in age from 2 to 8 years and were incidental findings in a 3-month-old male English Setter examined because of signs related to canine distemper virus infection and in a 17-month-old female Beagle euthanatized at termination of a chronic toxicity study. No clinical information was given for an affected 11-month-old female mixed-breed dog. In all six dogs, the intracranial cysts occurred in the cerebellopontine angle and/or fourth ventricle. The intraspinal cyst occurred in a 2-year-old female Rottweiler with clinical signs related to thoracolumbar pain and proprioceptive deficits of the pelvic limbs. In all cases, the lesions were observed grossly at necropsy or during postfixation trimming as cysts containing white caseous material and ranging in size from 3 mm to 2.5 cm. Microscopically, all cysts were lined by stratified squamous epithelium of variable thickness and contained keratinaceous debris, desquamated epithelial cells, and occasional inflammatory cells. The intraspinal cyst appeared to be arising from the leptomeninges.

The incidence of epidermoid cysts in the central nervous system of rodents used in experimental neuropathologic studies has been reported, but only sporadic cases have been
reported from toxicologic studies. An epidermal cyst containing structures resembling hair shafts and glands that was reported in the cerebellum of a 2-year-old F344 rat may be more consistent with the diagnosis of dermoid cyst as described in humans.

A relatively high incidence of epidermoid cysts was reported in the spinal cords of rats being scored for experimental allergic encephalomyelitis. In that study, the spinal cord had been divided into four or five segments and embedded longitudinally in its entirety. Three transverse sections of brain stem and cerebellum were also examined. No clinical signs were associated with the presence of cysts, and they were not detected macroscopically. Epidermoid cysts were found only in the spinal cord and were observed in 2.5% (47/1,909) of CD F rats, 1.3% (25/1,901) of inbred Lewis rats, and 1.3% (5/375) of random bred HH Wistar rats examined. They occurred in both males and females and were solitary except in one female CD F rat. No cysts were seen

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**Fig. 1.** Brain; control female Crl:CD mouse from an 18-month oncogenicity study. Irregularly shaped epidermoid cyst is located on the midline ventral to the corpus colossum. HE. Bar = 0.5 mm.

**Fig. 2.** Brain; control female Crl:CD mouse from an 18-month oncogenicity study. Squamous epithelium lining the epidermoid cyst varies in thickness, and inner layers contain keratohyalin granules. A mixed inflammatory cell infiltrate is associated with some areas of the cyst. HE. Bar = 50 μm.
in the cervical spinal cord or brain, although the forebrain was not studied thoroughly. Cysts were round to oval, 0.3–0.7 mm in diameter, and located in the leptomeninges usually associated with a nerve root. Indentation of the underlying cord resulted in slight compression, but there were no other associated changes. Stratified squamous epithelium that varied in thickness from two to 10 layers of cells lined the walls, and the lumina were filled with desquamated keratin. Similar spinal cord cysts were reported in various inbred strains of mice used in experiments on the pathogenesis of lactate dehydrogenase-elevating virus. Three to six serial sections of perfused spinal cord taken at two levels were examined. Cysts involving the lumbar or sacral region were observed in 3.7% (2/54) of C57BR/cdJ and 6.3% (5/79) of C57BL/6J mice.

Fig. 3. Lumbar spinal cord; control male Crl:CD® rat from a two-generation reproduction study. Ovoid epidermoid cyst is located just under the pia in close association with a nerve root. The underlying cord is indented and slightly compressed. HE. Bar = 0.4 mm.

Fig. 4. Lumbar spinal cord; control male Crl:CD® rat from a two-generation reproduction study. The epidermoid cyst is lined by a thin layer of flattened squamous epithelium with concentric layers of desquamated keratin in the lumen. HE. Bar = 70 μm.
examined. None were observed in C58/J, AKR/J, or C57L/J mice.

The present report describes the incidence of central nervous system cysts in animals from routine toxicity studies where three levels of brain and multiple levels of spinal cord, including the thoracolumbar or lumbar regions, were examined as part of the experimental protocol. The combined incidence of epidermoid cysts from two chronic/oncogenicity studies in Crl:CD examined was 0.3% (2/748) in the spinal cord and 0.1% (1/750) in the brain. This lesion was observed in the lumbar spinal cord of one male and one female each from the high dose groups of one study; none were observed in the sections of brain examined. In the other study, a cyst was found in the brain of one control female (Figs. 1, 2); none were observed in the spinal cord. In a two-generation reproduction study in Crl:CD rats, an epidermoid cyst was observed in the lumbar spinal cord of one control male; overall incidence in the study was 1/198 (0.5%) (Figs. 3, 4). None were observed in the brain. Six additional cases of epidermoid cysts were observed as single occurrences in routine toxicity studies; five in the spinal cord of mice and one in the brain of a rat. No additional information was available regarding the strain and sex involved or the number of animals examined in these studies.

No clinical signs were observed in affected animals, and no abnormalities were detected grossly at the time of necropsy or postfixation trimming. In the spinal cord, cysts were peripherally located often beneath the pia. In the brain both cases were midline, one dorsal to the third ventricle and one ventral to the genu corpus callosum. Microscopically, the cysts were lined by stratified squamous epithelium with no evidence of adnexal structures. The lumen of the cysts contained keratinaceous debris, and occasionally a few chronic or chronic-active inflammatory cells were associated with the wall. A variety of terms including keratin cyst, squamous cyst, keratinaceous cyst, and inclusion cyst have been used to describe this lesion, which is consistent morphologically with the diagnosis of epidermoid cyst as described in humans and dogs.

Experimental studies in which multiple sections of spinal cord were examined demonstrate that epidermoid cysts are more common in rodents than is reflected by data from routine toxicity tests. The present and previous reports suggest that epidermoid cysts are more common in mice than in rats and that the spinal cord is more frequently affected than is the brain. Unlike humans and dogs, no clinical signs have been associated with the presence of central nervous system cysts in rodents nor have they been observed grossly. Epidermoid cysts are observed in toxicity studies only by fortuitous sectioning when examination of the brain and lumbar spinal cord are required by the experimental protocol.

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References

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