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Review of approaches to the recording of background lesions in toxicologic pathology studies in rats

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ABSTRACT

Pathological evaluation of lesions caused directly by xenobiotic treatment must always take into account the recognition of background (incidental) findings. Background lesions can be congenital or hereditary, histological variations, changes related to trauma or normal aging and physiologic or hormonal changes. This review focuses on the importance and correct approach to recording of background changes and includes discussion on sources of variability in background changes, the correct use of terminology, the concept of thresholds, historical control data, diagnostic drift, blind reading of slides, scoring and artifacts. The review is illustrated with background lesions in Sprague Dawley and Wistar rats.

Contents

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1. Introduction

Background (incidental) lesions have been described as an array of individual variations within an accepted reference range (Shackelford et al., 2002) and more specifically defined as findings that are usually thought of as a change in tissue morphology outside of the range of normal variation for a particular species or strain (Long and Hardisty, 2012). For the purposes of this paper we have also included background changes which may be recorded but are within the accepted reference range for a particular animal species. Background changes can be congenital or hereditary, normal variations of findings that are unique to the histology of an animal species, related to trauma or normal aging, and physiologic or hormonal changes (McInnes, 2012a). Selected background lesions in rats have been included in Table 1.

2. What are background lesions?

2.1. Congenital lesions

Congenital lesions are present at birth and probably represent abnormalities in normal embryogenesis or organogenesis and migration of these organs and/or substructures in the foetus. Squamous cysts, often containing keratin, are common congenital background lesions in the stomach, particularly in the region of the limiting ridge and antral mucosa and in the central nervous system midline. Minor developmental anomalies can include cysts in various tissues or ectopic tissue. In the rat eye, retinal rosettes are often noted as a congenital background change although can also be an artifact of tissue handling (Fig. 1).

Table 1
Selected background lesions noted in laboratory rats (Wistar and Sprague Dawley).

Organ system	Background lesion	Category	Reference	Age distribution	Frequency
Lymphoid	Mast cells are in the mandibular lymph nodes	Physiological	(McInnes, 2012a)	Young and old	Common
	Pigmented macrophages in the sinuses of lymph nodes (ceroid or lipofuscin material)	Aging	(Stefanski et al., 1990)	Old	Common
	Thymic cysts or epithelial remnants in the rat thymus, epithelial tubules or nests, remnants of the thymopharyngeal duct or dilatations of thymic tubular structures	Congenital	(Stefanski et al., 1990)	Young and old	Common
	Germinal centres and lymphoid follicles in the bone marrow of normal rats	Physiological	(Frith et al., 2000b)	Young and old	Rare
Gastrointestinal tract	Adipocytes in the interstitium and tinctorial changes in salivary glands	Physiological	(Detilleux et al., 1995)	Young an old	Common
	Tension lipidosis in the median cleft area of liver characterized by generalised hepatocyte vacuolation	Traumatic	(Stalker and Hayes, 2007)	Young an old	Common
	Ectopic hepatocyte islands in the pancreas, particularly situated around the islets	Congenital	(Detilleux et al., 1995)	Young an old	Rare
Cardiovascular system	Cartilaginous foci at the base of the aorta Sprague Dawley rats	Histological	(Ruben et al., 2000)	Young and old (in older rats the cartilaginous foci may mineralize)	Common
Central nervous system and eye	The nucleus circularis is a focus of neurones in the neonatal rat	Histological	(Hatton, 1976)	Neonatal	Rare
	Lenticular degeneration and cataracts in older rats	Aging	(Taradach and Greaves, 1984)	Old	Common
Respiratory	Perivascular lymphocytes, inflammatory cells alveolar macrophages and epithelial hyperplasia	Infectious	(Albers et al., 2009; Livingston et al., 2011)	Young	Common
	Small foci of neuroendocrine cells in the lung	Congenital	(Haworth et al., 2007)	Old	Rare
	Eosinophilic inclusions (globules and droplets) in the nasal epithelium of rats	Aging	(Renne et al., 2009)	Old	Common
	Mineralised concretions or corpora amylacea in nasal epithelia lining the nasal turbinates	Congenital	(Monticello et al., 1990)	Young and old	Common
Musculoskeletal system	Staphylococcal infections causing ulcerative tarsal dermatitis (also known as tarsal granulomas) seen in male rats	Aging	(Percy and Barthold, 2007)	Old	Common
	Degenerative joint disease of the femur-tibial joint (knee) of aging rats	Aging	(Long et al., 1996)	Old	Common
Urinary system	Nephropathy	Aging	(Montgomery and Seely, 1990)	Old	Common