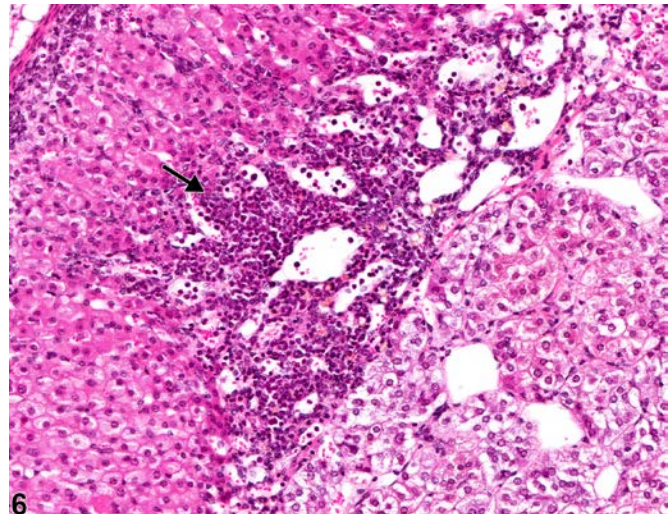
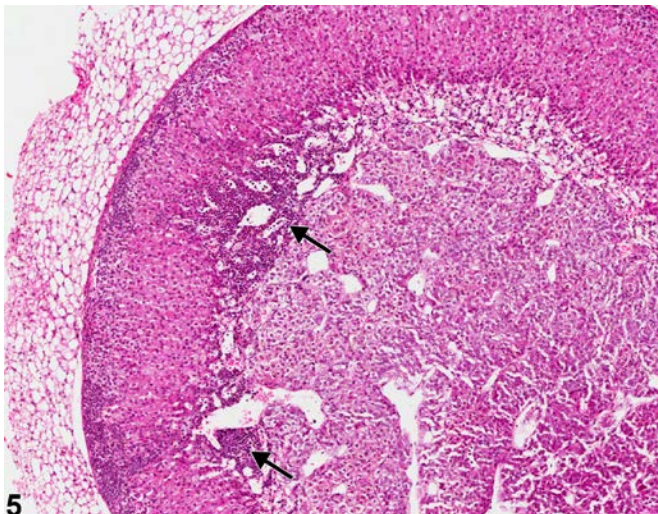
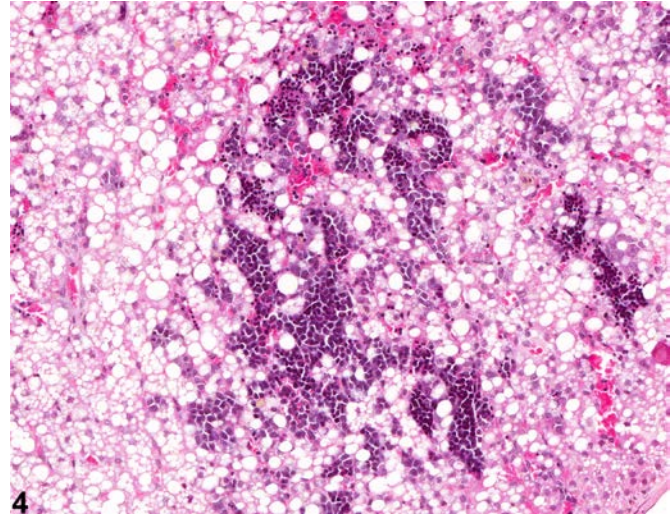
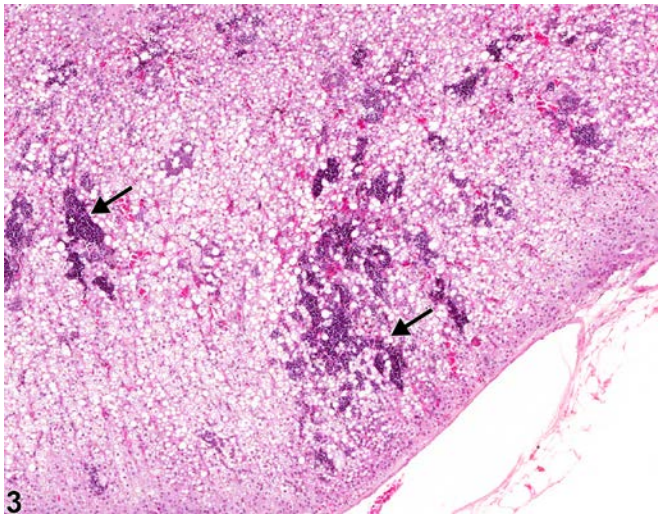
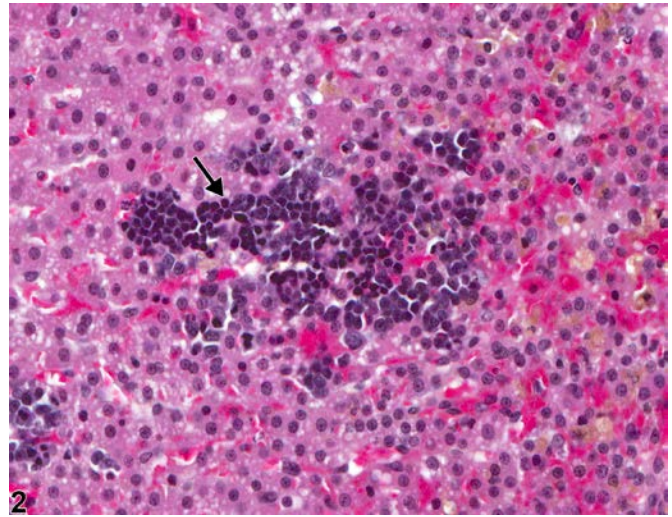
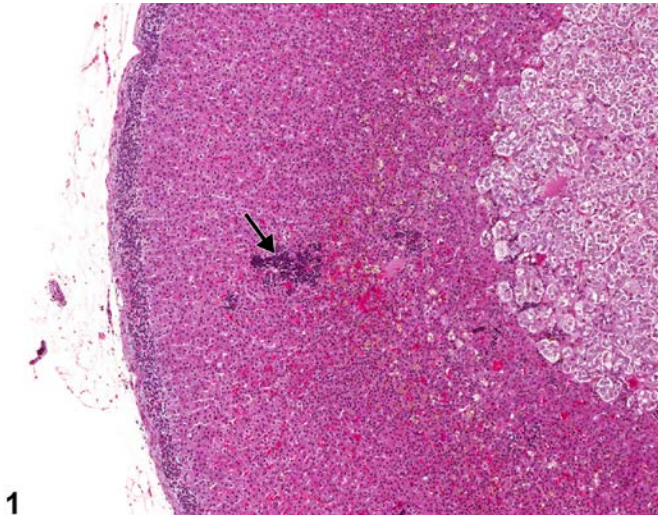




NTP Nonneoplastic Lesion Atlas

Adrenal Gland – Extramedullary Hematopoiesis





NTP Nonneoplastic Lesion Atlas

Adrenal Gland – Extramedullary Hematopoiesis

Figure Legend: **Figure 1** Adrenal gland, Cortex - Extramedullary hematopoiesis in a female F344/N rat from a chronic study. There is a focus of hematopoietic cells (arrow) in the cortex (zona fasciculata). **Figure 2** Adrenal gland, Cortex - Extramedullary hematopoiesis in a female F344/N rat from a chronic study (higher magnification of Figure 1). There is a focus of immature hematopoietic cells (arrow) in the sinusoids of the cortex (zona fasciculata). **Figure 3** Adrenal gland, Cortex - Extramedullary hematopoiesis in a male F344/N rat from a chronic study. There are multiple foci of hematopoietic cells (arrows) in the adrenal zona fasciculata. **Figure 4** Adrenal gland, Cortex - Extramedullary hematopoiesis in a male F344/N rat from a chronic study (higher magnification of Figure 3). There is a focus of immature hematopoietic cells (arrow) within the sinusoids of the zona fasciculata. **Figure 5** Adrenal gland, Cortex - Extramedullary hematopoiesis in a female B6C3F1/N mouse from a chronic study. There are several foci of hematopoietic cells (arrows) at the corticomedullary junction. **Figure 6** Adrenal gland, Cortex - Extramedullary hematopoiesis in a female B6C3F1/N mouse from a chronic study (higher magnification of Figure 5). A focus of immature hematopoietic cells (arrow) is present at the corticomedullary junction.

Comment: Extramedullary hematopoiesis (EMH) can occur in various tissues, including the adrenal cortex and medulla. EMH is not commonly seen in the adrenal gland, so if it is present, it will likely also be present in other organs, most likely the spleen and liver (see Spleen - Extramedullary Hematopoiesis and Liver - Extramedullary Hematopoiesis). EMH is typically composed of mixed myelopoietic and erythropoietic cells but may be primarily (rarely exclusively) composed of one or the other lineage. Extramedullary myelopoiesis is usually secondary to various inflammatory or immune responses and is a reaction to the need for additional white blood cells. Extramedullary erythropoiesis is frequently a response to certain types of anemia (e.g., hemolytic anemia or blood loss) and some situations leading to hypoxia (e.g., respiratory disease). Low-grade EMH in the adrenal gland of rats and especially mice can also occur without any clear inciting cause.

Adrenal EMH consists of variably sized, noncompressive clusters of immature hematopoietic cells and/or megakaryocytes scattered throughout the cortex and/or medulla (Figure 1, Figure 2, Figure 3, Figure 4, Figure 5, and Figure 6). Myelopoietic cells are typically larger than erythropoietic cells and have more cytoplasm, whereas erythropoietic cells typically are much darker. Adrenal EMH must be



NTP Nonneoplastic Lesion Atlas

Adrenal Gland – Extramedullary Hematopoiesis

distinguished from inflammation (mature leukocytes, often associated with tissue necrosis or degeneration) and from systemic lymphoid or hematopoietic neoplastic infiltrates (poorly differentiated, often anaplastic cells usually in extensive accumulations that distort or obliterate normal architecture).

Recommendation: Adrenal extramedullary hematopoiesis (EMH) should be diagnosed and assigned a severity grade only if there are treatment-related increases in incidence and/or severity. When it is diagnosed, a site modifier (i.e., cortex or medulla) should be included in the diagnosis to indicate the location of the lesion. If EMH is present in both the cortex and medulla, the site modifier may be omitted and the location described in the pathology narrative. If EMH is seen in both adrenal glands, the modifier “bilateral” should be added to the diagnosis (lesions are assumed to be unilateral unless otherwise indicated). If the lesion is composed primarily or exclusively of a particular cell lineage (e.g., myelopoietic or erythropoietic), this should be indicated in the pathology narrative.

References:

Frith CH, Botts S, Jokinen MP, Eighmy JJ, Hailey JR, Morgan SJ, Chandra M. 2000. Non-proliferative lesions of the endocrine system in rats, E-1. In: Guides for Toxicologic Pathology. STP/ARP/AFIP, Washington, DC.

Full Text: <https://www.toxpath.org/ssdnc/EndocrineNonprolifRat.pdf>

Hamlin MH, Banas DA. 1990. Adrenal gland. In: Pathology of the Fischer Rat: Reference and Atlas (Boorman GA, Eustis SL, Elwell MR, Montgomery CA, MacKenzie WF, eds). Academic Press, San Diego, 501-518.

Abstract: <http://www.ncbi.nlm.nih.gov/nlmcatalog/9002563>

Johns JL, Christopher MM. 2012. Extramedullary hematopoiesis: A new look at underlying stem cell niche, theories of development, and occurrence in animals. *Vet Pathol* 49:508-523.

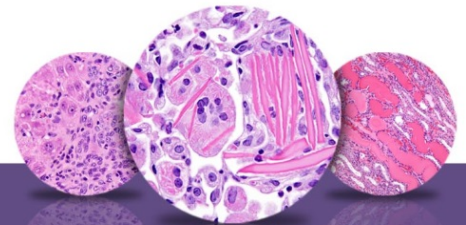
Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/22262354>

McInnes EF. 2011. Wistar and Sprague Dawley rats. In: Background Lesions in Laboratory Animals: A Color Atlas (McInnes EF, ed). Saunders Elsevier, Amsterdam, 16-36.

Abstract: <http://www.sciencedirect.com/science/book/9780702035197>

National Toxicology Program. 1993. NTP TR-402. Toxicology and Carcinogenesis Studies of Furan (CAS No. 110-00-9) in F344 Rats and B6C3F1 Mice (Gavage Studies). NTP, Research Triangle Park, NC.

Abstract: <http://ntp.niehs.nih.gov/go/12255>



NTP Nonneoplastic Lesion Atlas

Adrenal Gland – Extramedullary Hematopoiesis

References:

National Toxicology Program. 1993. NTP TR-434. Toxicology and Carcinogenesis Studies of 1,3-Butadiene (CAS No. 106-99-0) in B6C3F1 Mice (Inhalation Studies). NTP, Research Triangle Park, NC. Abstract: <http://ntp.niehs.nih.gov/go/6012>

National Toxicology Program. 1997. NTP TR-463. Toxicology and Carcinogenesis Studies of D&C Yellow No. 11 (CAS No. 8003-22-3) in F344/N Rats (Feed Studies). NTP, Research Triangle Park, NC. Abstract: <http://ntp.niehs.nih.gov/go/6070>

Nyska A, Maronpot RR. 1999. Adrenal gland. In: Pathology of the Mouse: Reference and Atlas (Maronpot RR, Boorman GA, Gaul BW, eds). Cache River Press, Vienna, IL, 509-536. Abstract: <http://www.cacheriverpress.com/books/pathmouse.htm>

Taylor I. 2011. Mouse. In: Background Lesions in Laboratory Animals: A Color Atlas (McInnes EF, ed). Saunders Elsevier, Amsterdam, 45-72. Abstract: <http://www.sciencedirect.com/science/book/9780702035197>

Authors:

Mark J. Hoenerhoff, DVM, PhD, DACVP
Associate Professor
Veterinary Pathologist, In Vivo Animal Core
Unit for Laboratory Animal Medicine
University of Michigan
Ann Arbor, MI

Georgette D. Hill, DVM, PhD
Toxicologic Pathologist/Assistant Pathology Program Manager
Comparative Molecular Pathology Division
Integrated Laboratory Systems, Inc.
Research Triangle Park, NC

Margarita M. Gruebbel, DVM, PhD, DACVP
Senior Pathologist
Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC