Illustrated Atlas of Rat Liver Histopathology

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INTRODUCTION AND BACKGROUND INFORMATION

Iconix's extensive experience in investigating the gene expression correlates of pharmacological and toxicological effects of drugs, toxicants, biological molecules and other chemicals has led us to the conclusion that gene expression events are extremely sensitive and precise indicators of pathological responses. We have therefore undertaken to develop a correspondingly sensitive and precise review of histopathology readings from Iconix's microarray data-generating experiments of sufficient detail for use in mining gene expression data for patterns characteristic and predictive of specific liver effects. This Atlas of liver histopathology was built through an expert veterinary pathologist review by EPL of liver sections from greater than 4000 male Sprague Dawley rats from repeat dose toxicity studies conducted by Iconix Pharmaceuticals using more than 350 compounds. We believe that the number and variety of chemicals we have studied, most of which were dosed at a maximum tolerated dose for 5 days or longer, means that we are likely to have observed the majority of non-neoplastic liver lesions possible following short to medium-term drug exposure to male rats.

The Atlas includes a list of all liver findings observed, a narrative description of the specific observations leading to the diagnoses and digital photomicrographic images from each type of diagnosis and severity of lesion. Due to the fact gene expression changes are very sensitive and changes characteristic of injury may occur before the appearance of any histomorphologic alterations, these livers were read without the imposition of subjective thresholds. Every cluster of cells was recorded, as accurately as possible, as to its location and cell type. When such subtle alterations within a tissue are recorded, it can make the data more accurate but possibly less consistent. This study was approached with the goal of both maximum accuracy and consistency, and every effort was made to maintain the highest level of both.

One result of recording every alteration observed during this project is that very few livers were recorded as "normal" (i.e. having no observed alterations in the morphology of the liver). Some of the observations made therefore, such as minimal to mild periportal glycogen accumulation, may not generally be considered pathological but were recorded since this study was not meant solely to evaluate pathologic outcomes, but to try to correlate changes in the morphology of the liver with changes in the gene expression profile. For instance, although periportal glycogen would be considered normal, even expected in unfasted animals, it does not preclude that the expression profile of an animal that has not been fasted may be demonstrably different from one that has been fasted and does not show glycogen accumulation. Periportal glycogen, along with other such common, background findings was therefore recorded when present even to a minimal degree.

This Atlas is currently being used by veterinary pathologists involved in assessing the pathological effects of drugs, toxicants and other chemicals in Iconix studies. We present it with the hope and expectation that the precise and comprehensive nature of the Atlas, along with the narrative descriptions and photomicrographs will assist other researchers using gene expression analysis and other such sensitive and exacting techniques in obtaining the same level of sensitivity, precision and reproducibility in histopathological evaluations that we require of our own studies.

DICTIONARY OF DIAGNOSES

These livers were read without thresholds. Every cluster of cell was recorded, as accurately as possible, as to its location and type of cell. Each lesion was categorized depending on its distribution (centrilobular, periportal, diffuse, non-zonal) and its severity (grade 1 – minimal; grade 2 – mild; grade 3 – moderate; grade 4 – severe). The modifiers focal and multifocal were not used; severity grades were used to indicate the extent of a lesion. Therefore, a higher severity grade could indicate a larger focal lesion or multiple smaller lesions.

A description of the terms used in this project follows.

Normal –Some livers that had lesions recorded may have been within normal limits as far as pathology is concerned, but due to the purpose of this study, any change that was observed was recorded. Some changes that were recorded that might be considered within normal limits include minimal periportal lymphocytes and minimal to mild periportal glycogen. The liver was recorded as normal when no alterations were observed. Figure 1.

Autolysis – Autolysis was recorded in a few animals in order to distinguish the changes observed from necrosis. In livers that were autolytic, there was individualization of hepatocytes and serum leakage between cords of hepatocytes. Figure 2.

Bile duct dilatation – Bile duct dilatation was not recorded in many animals. With minimal bile duct dilatation, small ducts were slightly distended, and the lumens were devoid of contents. There was a very fine ring of fibrous connective tissue encircling the ducts. With mild dilatation, there was a focal area of dilated ducts, which were lined by basophilic epithelium and contained basophilic material consistent with mucus in the lumens. Figures 3 and 4.

Bile duct hyperplasia – Bile duct hyperplasia was characterized by increased profiles of bile ducts in the portal region, from a barely noticeable increase in some of the triads with minimal bile duct hyperplasia, to multiple extra profiles in most or all of the triads with mild bile duct hyperplasia. With moderate hyperplasia, there were multiple extra profiles of bile ducts in the portal areas, and bile ducts were visible extending further out into the hepatic lobule. Also, the cells that lined the bile ducts were often hypertrophic and hyperplastic. Mild to moderate bile duct hyperplasia was often associated with inflammatory cell infiltrates, edema or even periportal fibrosis. Figures 5-7.

Bile duct necrosis, oncocytic – This lesion was characterized by bile ducts lined by irregular epithelium, with missing epithelial cells, remaining epithelial cells being slightly attenuated, and some cells showing evidence of degeneration and necrosis, such as shrunken, dark nuclei, and eosinophilic cytoplasm. Figure 8.

Capsule, inflammatory cell infiltrate, mixed cell – A mixture of inflammatory cell types (lymphocytes, plasma cells, macrophages, and neutrophils) present on the surface of the liver was diagnosed as capsule, inflammatory cell infiltrate, mixed cell. These cells might extend a short distance into the underlying hepatocytes. Figures 9-11.

Capsule, mesothelial cell, hyperplasia – Typically, the mesothelial cells lining the capsule of the liver were not obvious. When mesothelial cell hyperplasia was present, there were increased numbers of these cells. The cells were rounded and contained lightly basophilic

cytoplasm and would occasionally form tags that protruded off the surface of the liver. Figures 12 and 13.

Capsule, thrombus – One animal was recorded as having a capsular thrombus. There was a fibrin thrombus within a small vessel in the capsule of this animal. Figure 14.

Centrilobular, fibrosis – Centrilobular fibrosis consisted of collagen fibers deposited around the central vein. It was only recorded as a minimal lesion. Figure 15.

Centrilobular, inflammatory cell infiltrate, lymphoid – This lesion was characterized by clusters of lymphocytes (and possibly plasma cells) around or adjacent to the central vein. A minimal lesion might consist of just one small cluster of a few cells; mild lesions would consist of a single large cluster, or several small clusters of cells. Figures 16 and 17.

Centrilobular, inflammatory cell infiltrate, mixed cell – This lesion consisted of clusters of inflammatory cells around or adjacent to the central vein. Most commonly, there was a mixture of lymphoid cells (lymphocytes and plasma cells) with macrophages, however, neutrophils could also be seen. A minimal lesion might consist of just one small cluster of a few cells; mild lesions might consist of a single large cluster or several small clusters of cells; moderate lesions might be diagnosed when multiple large clusters of cells were present or there were many small clusters of cells. Figures 18-20.

Clear cell focus – Clear cell foci were clusters of cells that had clear or vacuolated, cytoplasm, consistent with glycogen accumulation. Minimal clear cell foci were small, usually much smaller than the size of a hepatic lobule, and sometimes consisting of as few as a dozen cells. Mild clear cell foci were larger, but still smaller than the size of a hepatic lobule. Within the clear cell foci, there might be hepatocytes with eosinophilic cytoplasm mixed in, but if the predominance of cells had clear or vacuolated cytoplasm, the diagnosis of clear cell focus was used. Figures 21 and 22.

Hepatocyte, centrilobular, atrophy – Centrilobular hepatocellular atrophy was characterized by small hepatocytes around the central vein. There was a decreased cytoplasm:nuclear ratio, and hepatic sinusoids were prominent. Figure 23.

Hepatocyte, centrilobular, cytoplasm, eosinophilia – Eosinophilia of the hepatocellular cytoplasm referred to an increase in the usual eosinophilia of the hepatocyte. In addition, the cytoplasm typically was granular. Minimal increases in the eosinophilia of hepatocytes consisted of a barely discernable increase in the granularity and eosinophilia of the cells. Mild eosinophilia consisted either of a greater degree of granularity and eosinophilia or a more widespread change. Centrilobular hepatocellular eosinophilia was confined to the centrilobular portions of the hepatic lobule and was typically associated with centrilobular hypertrophy of hepatocytes. Figures 24 and 25.

Hepatocyte, centrilobular, degeneration – Centrilobular degeneration was characterized by a loss of hepatocytes and degenerate hepatocytes around the central vein. Affected hepatocytes were swollen and vacuolated and often had condensed nuclei. Figures 26 and 27.

Hepatocyte, centrilobular, glycogen accumulation – Hepatocytes with glycogen accumulation had cytoplasm containing spaces with poorly demarcated borders. Nuclei typically remained centrally located. Centrilobular glycogen accumulation was limited to, or

appeared to arise from, the centrilobular area of the hepatic lobule. Minimal glycogen accumulation consisted of a few cells with a small amount of glycogen around some of the central veins in the liver. Mild, moderate and marked glycogen accumulation revealed an increased amount of glycogen within cells, increased numbers of cells involved around the central vein and increased number of hepatic lobules involved. With moderate and severe glycogen accumulation, some hepatocytes were enlarged due to the glycogen accumulation. Figures 28-31.

Hepatocyte, centrilobular, hypertrophy – Hypertrophy of hepatocytes was recorded when the hepatocytes appeared subjectively larger than normal. This was not an objective measurement, but an impression from looking at the number of nuclei per field and the cytoplasm:nucleus ratio. Centrilobular hypertrophy was diagnosed when the lesion appeared restricted to, or arising from, the centrilobular area. A minimal lesion would involve the cells immediately adjacent to the central vein, and the subjective increase in the size of the cells was less than in greater severities. A mild lesion might affect about half of the lobule, from the central vein outwards to the portal areas. Moderate lesions would affect the majority of the lobule, and the cells would be clearly enlarged. A marked grade was not used, as this would be difficult to distinguish from diffuse hypertrophy. Figures 32-34.

Hepatocyte, centrilobular, lipid accumulation, macrovesicular – Hepatocytes with macrovesicular lipid accumulation contained discrete vacuoles. Some cells contained a single large vacuole, which caused peripheral displacement of the nucleus. Other cells contained single or multiple vacuoles of varying size. Centrilobular lipid accumulation was limited to, or appeared to arise from, the centrilobular area of the hepatic lobule. Minimal macrovesicular lipid accumulation consisted of a few cells with small vacuoles around some of the central veins in the liver. Mild, moderate and marked macrovesicular lipid accumulation revealed increased size of the lipid vacuoles, increased numbers of cells involved around the central vein, and increased numbers of hepatic lobules involved. Figures 35-38.

Hepatocyte, centrilobular, lipid accumulation, microvesicular – Hepatocytes with microvesicular lipid accumulation had cytoplasm that had a granular appearance with low magnification, but with higher magnification, small vacuoles could be observed. Centrilobular lipid accumulation was limited to, or appeared to arise from, the centrilobular area of the hepatic lobule. Minimal microvesicular lipid accumulation involved a few cells around some of the central veins in the liver. Mild and moderate microvesicular lipid accumulation involved an increase in the vacuolation of the affected cells, increased numbers of cells involved around the central vein, and increased number of hepatic lobules involved. Figures 39-41.

Hepatocyte, centrilobular, necrosis, apoptotic – Apoptotic necrosis typically involved single cells, and the cells were small, rounded, and eosinophilic. They were often present in vacuoles, phagocytosed by hepatocytes. Apoptotic cells normally lacked nuclear changes seen in oncocytic necrosis, such as pyknosis and karyorrhexis, and in most cases, were not associated with inflammatory cells although occasionally lymphocytes were present around an apoptotic cell. With centrilobular apoptosis, the apoptotic cells were localized around central veins. A single apoptotic cell was enough for a diagnosis of minimal apoptosis. Mild and moderate apoptosis was characterized by an increased number of apoptic cells and more widespread involvement in the liver (i.e., more central veins were involved). Figures 42-44.

Hepatocyte, centrilobular, necrosis, oncocytic – Oncocytic necrosis could involve a single necrotic cell or a large area of hepatocytes. Single cells were often swollen, with eosinophilic cytoplasm and pyknotic nuclei, but they could also be shrunken and basophilic. They were typically surrounded by an inflammatory cell reaction, which was often a mixture of lymphocytes and macrophages, and sometimes neutrophils. Larger areas of necrosis were composed of a coagulum of eosinophilic material; distinct cell borders and features could not be observed. A single necrotic cell would be given a severity grade of minimal; a small focus of necrosis would be graded as mild. Moderate lesions consisted of several areas of necrosis, and severe lesions were very large or widespread. With centrilobular oncocytic necrosis, the necrosis was localized around central veins. Figures 45-48.

Hepatocyte, diffuse, cytoplasm, eosinophilia – Eosinophilia of the hepatocellular cytoplasm referred to an increase in the usual eosinophilia of the hepatocyte. In addition, the cytoplasm typically was granular. Minimal increases in the eosinophilia of hepatocytes consisted of a barely discernable increase in the granularity and eosinophilia of the cells. Mild, moderate, and severe eosinophilia consisted of greater degrees of granularity and eosinophilia. Diffuse hepatocellular eosinophilia involved the entire hepatic lobule and was typically associated with centrilobular hypertrophy of hepatocytes. Figures 49-52.

Hepatocyte, diffuse, hypertrophy – Hypertrophy of hepatocytes was recorded when the hepatocytes appeared subjectively larger than normal. This was not an objective measurement, but an impression from looking at the number of nuclei per field and the cytoplasm:nucleus ratio. Diffuse hypertrophy was diagnosed when the entire lobule of the liver appeared to be affected. A minimal lesion would show only a borderline increase in cell size. Mild, moderate and severe grades would be greater increases in cell sizes. Figures 53-56.

Hepatocyte, midzonal, lipid accumulation, macrovesicular – Hepatocytes with macrovesicular lipid accumulation contained discrete vacuoles. Some cells contained a single large vacuole, which caused peripheral displacement of the nucleus. Other cells contained single or multiple vacuoles of varying size. Midzonal lipid accumulation was limited to the zone between the central vein and the portal triad. Minimal macrovesicular lipid accumulation consisted of a few cells with small vacuoles around some of the central veins in the liver. Mild macrovesicular lipid accumulation was characterized by an increased size of the lipid vacuoles, increased numbers of cells involved in the midzonal area, and increased number of hepatic lobules involved. Figures 57 and 58.

Hepatocyte, midzonal, lipid accumulation, microvesicular – Hepatocytes with microvesicular lipid accumulation had cytoplasm that had a granular appearance with low magnification, but with higher magnification, small vacuoles could be observed. Midzonal lipid accumulation was limited to the zone between the central vein and the portal triad. Figure 59.

Hepatocyte, midzonal, necrosis, apoptotic – Apoptotic necrosis typically involved single cells, and the cells were small, rounded, and eosinophilic. They were often present in vacuoles, phagocytosed by hepatocytes. Apoptotic cells normally lacked nuclear changes seen in oncocytic necrosis, such as pyknosis and karyorrhexis, and in most cases, were not associated with inflammatory cells although occasionally lymphocytes were present around an apoptotic cell. With midzonal apoptosis, the apoptotic cells were localized in the zone between the central vein and the portal triad. A single apoptotic cell was enough for a

diagnosis of minimal apoptosis. Mild apoptosis was characterized by an increased number of apoptotic cells. Figures 60 and 61.

Hepatocyte, midzonal, necrosis, oncocytic – Oncocytic necrosis could involve a single necrotic cell or a large area of hepatocytes. Single cells were often swollen with eosinophilic cytoplasm and pyknotic nuclei, but they could also be shrunken and basophilic. They were typically surrounded by an inflammatory cell reaction which was often a mixture of lymphocytes and macrophages and sometimes neutrophils. Larger areas of necrosis were composed of a coagulum of eosinophilic material; distinct cell borders and features could not be observed. A single necrotic cell would be given a severity grade of minimal. Midzonal oncocytic necrosis was located in the zone between the central vein and the portal triad. Figure 62.

Hepatocyte, nonzonal, degeneration – Nonzonal degeneration was characterized by scattered individual or small clusters of hepatocytes that contained cytoplasm that was swollen or vacuolated or nuclei that were pyknotic. The location of the affected cells, the appearance of the vacuoles, and the associated nuclear changes helped to distinguish this lesion from fat or lipid accumulation. Figures 63 and 64.

Hepatocyte, nonzonal, erythrophagocytosis – This lesion was only recorded in one animal. It consisted of several enlarged hepatocytes that had phagocytosed erythrocytes. Figure 65.

Hepatocyte, nonzonal, glycogen accumulation – Hepatocytes with glycogen accumulation had cytoplasm containing spaces with poorly demarcated borders. Nuclei typically remained centrally located. Nonzonal lipid accumulation lacked a specific zonal pattern. Minimal nonzonal glycogen accumulation consisted of a few cells with a small amount of glycogen in the liver. This lesion would have to be differentiated from clear cell foci, but the cells in nonzonal glycogen were not located in a single discrete focus. Figure 66.

Hepatocyte, nonzonal increased mitoses – This lesion was characterized by a subjective increase in the number of mitotic figures within a section of liver. A specific zonal pattern of the mitotic figures was not observed. Severity grades were based on the subjective number of mitoses present. Figures 67-69.

Hepatocyte, nonzonal, lipid accumulation, macrovesicular – Hepatocytes with macrovesicular lipid accumulation contained discrete vacuoles. Some cells contained a single large vacuole, which caused peripheral displacement of the nucleus. Other cells contained single or multiple vacuoles of varying size. Nonzonal lipid accumulation lacked a specific zonal pattern; some of the cells may have been centrilobular but others appeared to be periportal, or the cells were just scattered throughout the hepatic lobe. Minimal macrovesicular lipid accumulation consisted of a few cells with small vacuoles. Mild and moderate macrovesicular lipid accumulation revealed increased size of the lipid vacuoles and increased numbers of cells involved. Figures 70-73.

Hepatocyte, nonzonal, lipid accumulation, microvesicular – Hepatocytes with microvesicular lipid accumulation had cytoplasm that had a granular appearance with low magnification, but with higher magnification, small vacuoles could be observed. Nonzonal lipid accumulation lacked a specific zonal pattern. Minimal microvesicular lipid accumulation involved a few scattered cells throughout the liver. Figure 74.

Hepatocyte, nonzonal, mineralization – Nonzonal mineralization was typically associated with nonzonal necrosis and consisted of aggregates of deeply basophilic granular material consistent with mineral. Figure 75.

Hepatocyte, nonzonal, multinucleated – This diagnosis was recorded when hepatocytes contained more nuclei (generally >2) than can be seen with the normal variation in the liver. These had to be differentiated from megakaryocytes and multinucleated giant cells due to inflammation. Figure 76.

Hepatocyte, nonzonal, necrosis, apoptotic – Apoptotic necrosis typically involved single cells, and the cells were small, rounded, and eosinophilic. They were often present in vacuoles, phagocytosed by hepatocytes. Apoptotic cells normally lacked nuclear changes seen in oncocytic necrosis, such as pyknosis and karyorrhexis, and in most cases, were not associated with inflammatory cells although occasionally lymphocytes were present around an apoptotic cell. Non-zonal apoptosis lacked a specific zonal pattern. It was sometimes difficult to determine the zonality of the lesion due to the small number of cells involved. A single apoptotic cell was enough for a diagnosis of minimal apoptosis. Mild apoptosis was characterized by an increased number of apoptotic cells. Figures 77 and 78.

Hepatocyte, nonzonal, necrosis, oncocytic – Oncocytic necrosis could involve a single necrotic cell or a large area of hepatocytes. Single cells were often swollen with eosinophilic cytoplasm and pyknotic nuclei, but they could also be shrunken and basophilic. They were typically surrounded by an inflammatory cell reaction which was often a mixture of lymphocytes and macrophages and sometimes neutrophils. Larger areas of necrosis were composed of a coagulum of eosinophilic material; distinct cell borders and features could not be observed. A single necrotic cell would be given a severity grade of minimal; a small focus of necrosis would be graded as mild. Moderate lesions consisted of several areas of necrosis. Non-zonal apoptosis lacked a specific zonal pattern. Figures 79-81.

Hepatocyte, periportal, cytoplasm, eosinophilia – Eosinophilia of the hepatocellular cytoplasm referred to an increase in the usual eosinophilia of the hepatocyte. In addition, the cytoplasm typically was granular. Minimal increases in the eosinophilia of hepatocytes consisted of a barely discernable increase in the granularity and eosinophilia of the cells. Mild and moderate eosinophilia consisted of a greater degree of granularity and eosinophilia and a more widespread change. Periportal hepatocellular eosinophilia was centered on the portal triads and was typically associated with periportal hypertrophy of hepatocytes. Figures 82-84.

Hepatocyte, periportal, glycogen accumulation – Hepatocytes with glycogen accumulation had cytoplasm containing spaces with poorly demarcated borders. Nuclei typically remained centrally located. Periportal glycogen accumulation was limited to, or appeared to arise from, the portal area of the hepatic lobule. Minimal glycogen accumulation consisted of a few cells with a small amount of glycogen. Mild, moderate and marked glycogen accumulation revealed an increased amount of glycogen within cells, increased numbers of cells involved in the portal area, and increased number of hepatic lobules involved. Moderate lesions would affect the majority of the lobule, and the hepatocytes might be enlarged. Severe glycogen accumulation involved almost the entire lobule, so that the lesion was diffuse, with the exception of the centrilobular area, and the hepatocytes were frequently enlarged. Figures 85-88.

Hepatocyte, periportal, hypertrophy – Hypertrophy of hepatocytes was recorded when the hepatocytes appeared subjectively larger than normal. This was not an objective measurement, but an impression from looking at the number of nuclei per field and the cytoplasm:nucleus ratio. Periportal hypertrophy was diagnosed when the lesion appeared restricted to, or arising from, the portal area. A minimal lesion would involve the cells immediately adjacent to the portal triad, and the subjective increase in the size of the cells was less than in greater severities. A mild lesion might affect about half of the lobule, from the portal area outwards to the central vein. Moderate lesions would affect the majority of the lobule, and the cells would be clearly enlarged. A marked grade was not used, as this would be difficult to distinguish from diffuse hypertrophy. Figures 89-91.

Hepatocyte, periportal, lipid accumulation, macrovesicular – Hepatocytes with macrovesicular lipid accumulation contained discrete vacuoles. Some cells contained a single large vacuole which caused peripheral displacement of the nucleus. Other cells contained single or multiple vacuoles of varying size. Periportal lipid accumulation was limited to, or appeared to arise from, the portal area of the hepatic lobule. Minimal macrovesicular lipid accumulation consisted of a few cells with small vacuoles. Mild, moderate and severe macrovesicular lipid accumulation revealed an increased size of the lipid vacuoles, increased numbers of cells involved around the portal triad, and increased numbers of hepatic lobules involved. Figures 92-95.

Hepatocyte, periportal, lipid accumulation, microvesicular – Hepatocytes with microvesicular lipid accumulation had cytoplasm that had a granular appearance with low magnification, but with higher magnification, small vacuoles could be observed. Periportal lipid accumulation was limited to, or appeared to arise from, the portal triad area of the hepatic lobule. Minimal microvesicular lipid accumulation involved a few cells around some of the portal triads in the liver. Figure 96.

Hepatocyte, periportal, necrosis, apoptotic – Apoptotic necrosis typically involved single cells, and the cells were small, rounded, and eosinophilic. They were often present in vacuoles, phagocytosed by hepatocytes. Apoptotic cells normally lacked nuclear changes seen in oncocytic necrosis, such as pyknosis and karyorrhexis, and in most cases, were not associated with inflammatory cells although occasionally lymphocytes were present around an apoptotic cell. With periportal apoptosis, the apoptotic cells were localized around the portal triads. Minimal apoptosis was diagnosed if even a single apoptotic cell was observed. Figure 97.

Hepatocyte, periportal, necrosis, oncocytic – Oncocytic necrosis could involve a single necrotic cell or a large area of hepatocytes. Single cells were often swollen with eosinophilic cytoplasm and pyknotic nuclei, but they could also be shrunken and basophilic. They were typically surrounded by an inflammatory cell reaction, which was often a mixture of lymphocytes and macrophages and sometimes neutrophils. Larger areas of necrosis were composed of a coagulum of eosinophilic material; distinct cell borders and features could not be observed. A single necrotic cell would be given a severity grade of minimal; a small focus of necrosis would be graded as mild. With periportal oncocytic necrosis, the necrosis was localized around portal triads. Figures 98 and 99.

Hepatocyte, subcapsular, mineralization – Subcapsular mineralization was associated with subcapsular necrosis. In animals in which this lesion was recorded, there was a line of

necrosis and mineralization that extended along the liver just under the capsular surface. Figure 100.

Hepatocyte, subcapsular, necrosis, oncocytic – Oncocytic necrosis could involve a single necrotic cell or a large area of hepatocytes. Single cells were often swollen, with eosinophilic cytoplasm and pyknotic nuclei, but they could also be shrunken and basophilic. They were typically surrounded by an inflammatory cell reaction which was often a mixture of lymphocytes and macrophages and sometimes neutrophils. Larger areas of necrosis were composed of a coagulum of eosinophilic material; distinct cell borders and features could not be observed. Subcapsular necrosis was only recorded if the necrosis seemed to follow a pattern under the capsule of the liver. If the necrosis was just a focal area near the surface of the liver, it was recorded as non-zonal oncocytic necrosis. Figures 101-103.

Malignant lymphoma – Malignant lymphoma was characterized by large numbers of lymphocytes within the sinusoids and capillaries of the liver. This had to be distinguished from lymphocytic inflammation and was differentiated based on the large numbers of cells, and the relative uniformity and immaturity of the cells. Figure 104.

Nonzonal, extramedullary hematopoiesis – Extramedullary hematopoiesis was recorded in animals when megakaryocytes could be identified. Due to the difficulty in distinguishing between immature red and white blood cells and lymphocytes, the presence of megakaryocytes was considered evidence of hematopoiesis. Figure 105.

Nonzonal, inflammatory cell infiltrate, granulomatous – This lesion was characterized by inflammation within the hepatic parenchyma that consisted primarily of activated macrophages and multinucleated giant cells. Figure 106.

Nonzonal, inflammatory cell infiltrate, lymphoid – This lesion was characterized by clusters of lymphocytes (and possibly plasma cells) in the hepatic parenchyma. The distribution of these infiltrates lacked a distinct zonal pattern. A minimal lesion might consist of just one small cluster of a few cells; mild lesions would consist of a single large cluster or several small clusters of cells. Figures 107 and 108.

Nonzonal, inflammatory cell infiltrate, mixed cell – This lesion consisted of clusters of inflammatory cells in the hepatic parenchyma. The distribution of these infiltrates lacked a distinct zonal pattern. Most commonly, there was a mixture of lymphoid cells (lymphocytes and plasma cells) with macrophages, however, neutrophils could also be seen. A minimal lesion might consist of just one small cluster of a few cells; mild lesions might consist of a single large cluster or several small clusters of cells; moderate lesions might be diagnosed when multiple large clusters of cells were present or there were many small clusters of cells. Figures 109-111.

Oval cell, hyperplasia – Oval cell hyperplasia was characterized by an increase in the number of oval cells. This lesion was limited in location to the portal areas. Figure 112.

Periportal, edema – Periportal edema was evidenced by spaces around and between elements in the portal triad. It was usually associated with periportal inflammatory cells and bile duct hyperplasia. Figure 113.

Periportal, fibrosis – Periportal fibrosis was evidenced by the deposition of collagen, and the presence of fibroblasts around bile ducts in the portal triads. Periportal fibrosis was

usually associated with periportal inflammatory cells and bile duct hyperplasia. Figures 114 and 115.

Periportal, inflammatory cell infiltrate, lymphoid – This lesion was characterized by clusters of lymphocytes (and possibly plasma cells) around or adjacent to the portal triad. A minimal lesion might consist of just one small cluster of a few cells; mild lesions might consist of a single large cluster or several small clusters of cells; moderate lesions might be diagnosed when multiple large clusters of cells were present or there were many small clusters of cells. Both periportal lymphoid infiltrates and periportal mixed cell infiltrates could be diagnosed in the same animal. Figures 116-118.

Periportal, inflammatory cell infiltrate, mixed cell – This lesion consisted of clusters of inflammatory cells around or adjacent to the portal triad. Most commonly, there was a mixture of lymphoid cells (lymphocytes and plasma cells) with macrophages, however, neutrophils could also be seen. In some cases, neutrophils were the predominant type of cell, however, if the infiltrate was composed exclusively of neutrophils, then the diagnosis of periportral, inflammatory cell infiltrate, neutrophil was used. A minimal lesion might consist of just one small cluster of a few cells; mild lesions might consist of a single large cluster or several small clusters of cells; moderate lesions might be diagnosed when multiple large clusters of cells were present or there were many small clusters of cells. Both periportal lymphoid infiltrates and periportal mixed cell infiltrates could be diagnosed in the same animal. Figures 119-121.

Periportal, inflammatory cell infiltrate, neutrophilic – This lesion was characterized by neutrophils within the portal triad. This lesion was only diagnosed with a minimal severity which would have been diagnosed when even a single portal triad was affected. If the portal infiltrates contained neutrophils and other types of cells such as macrophages or lymphocytes, a diagnosis of periportal, inflammatory cell infiltrate, mixed cell was used. An animal could have both periportal neutrophilic infiltrates and mixed cell infiltrates recorded. Figure 122.

Subcapsular, fibrosis – Subcapsular fibrosis was characterized by collagen deposition just under the capsule of the liver. Figures 123-125.

LEGENDS OF PHOTOGRAPHY

Figure No.	Magnification	Diagnosis
001a	10.0	Normal
001b	20.0	Normal
001c	20.0	Normal
002	20.0	Autolysis
003	20.0	Bile Duct Dilatation +1
004	20.0	Bile Duct Dilatation +2
005	40.0	Bile Duct Hyperplasia +1
006	40.0	Bile Duct Hyperplasia +2
007a	10.0	Bile Duct Hyperplasia +3
007b	40.0	Bile Duct Hyperplasia +3
008	32.0	Bile Duct Necrosis, Oncocytic +1
009a	10.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +1
009b	16.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +1
009c	32.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +1
010a	10.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +2
010b	16.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +2
010c	32.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +2
011a	10.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +3
011b	16.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +3
011c	32.0	Capsule, Inflammatory Cell Infiltrate, Mixed Cell +3
012	40.0	Capsule, Mesothelial Cell, Hyperplasia +1
013a	10.0	Capsule, Mesothelial Cell, Hyperplasia +2
013b	16.0	Capsule, Mesothelial Cell, Hyperplasia +2
013c	32.0	Capsule, Mesothelial Cell, Hyperplasia +2
014	32.0	Capsule, Thrombus +1
015	40.0	Centrilobular Fibrosis +1
016a	20.0	Centrilobular, Inflammatory Cell Infiltrate, Lymphoid +1

Figure No.	Magnification	Diagnosis
016b	40.0	Centrilobular, Inflammatory Cell Infiltrate, Lymphoid +1
017a	20.0	Centrilobular, Inflammatory Cell Infiltrate, Lymphoid +2
017b	40.0	Centrilobular, Inflammatory Cell Infiltrate, Lymphoid +2
018a	20.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +1
018b	40.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +1
019	25.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +2
020a	10.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +3
020b	20.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +3
020c	40.0	Centrilobular, Inflammatory Cell Infiltrate, Mixed Cell +3
021	20.0	Clear Cell Focus +1
022	10.0	Clear Cell Focus +2
023a	10.0	Hepatocyte, Centrilobular, Atrophy +2
023b	20.0	Hepatocyte, Centrilobular, Atrophy +2
024	20.0	Hepatocyte, Centrilobular, Cytoplasm, Eosinophilia +1
025	10.0	Hepatocyte, Centrilobular, Cytoplasm, Eosinophilia +2
026	20.0	Hepatocyte, Centrilobular, Degeneration +1
027	10.0	Hepatocyte, Centrilobular, Degeneration +3
028	40.0	Hepatocyte, Centrilobular, Glycogen Accumulation +1
029	20.0	Hepatocyte, Centrilobular, Glycogen Accumulation +2
030	10.0	Hepatocyte, Centrilobular, Glycogen Accumulation +3
031	10.0	Hepatocyte, Centrilobular, Glycogen Accumulation +4
032	10.0	Hepatocyte, Centrilobular, Hypertrophy +1
033	25.0	Hepatocyte, Centrilobular, Hypertrophy +2
034	10.0	Hepatocyte, Centrilobular, Hypertrophy +3
035	20.0	Hepatocyte, Centrilobular, Lipid Accumulation, Macrovesicular +1
036	10.0	Hepatocyte, Centrilobular, Lipid Accumulation, Macrovesicular +2
037	10.0	Hepatocyte, Centrilobular, Lipid Accumulation, Macrovesicular +3
038	10.0	Hepatocyte, Centrilobular, Lipid Accumulation, Macrovesicular +4

Figure No.	Magnification	Diagnosis
039a	10.0	Hepatocyte, Centrilobular, Lipid Accumulation, Microvesicular +1
039b	20.0	Hepatocyte, Centrilobular, Lipid Accumulation, Microvesicular +1
040a	10.0	Hepatocyte, Centrilobular, Lipid Accumulation, Microvesicular +2
040b	20.0	Hepatocyte, Centrilobular, Lipid Accumulation, Microvesicular +2
041	25.0	Hepatocyte, Centrilobular, Lipid Accumulation, Microvesicular +3
042	40.0	Hepatocyte, Centrilobular, Necrosis, Apoptotic +1
043	40.0	Hepatocyte, Centrilobular, Necrosis, Apoptotic +2
044	40.0	Hepatocyte, Centrilobular, Necrosis, Apoptotic +3
045	40.0	Hepatocyte, Centrilobular, Necrosis, Oncocytic +1
046	40.0	Hepatocyte, Centrilobular, Necrosis, Oncocytic +2
047	20.0	Hepatocyte, Centrilobular, Necrosis, Oncocytic +3
048	10.0	Hepatocyte, Centrilobular, Necrosis, Oncocytic +4
049	20.0	Hepatocyte, Diffuse, Cytoplasm, Eosinophilia +1
050	20.0	Hepatocyte, Diffuse, Cytoplasm, Eosinophilia +2
051	20.0	Hepatocyte, Diffuse, Cytoplasm, Eosinophilia +3
052	40.0	Hepatocyte, Diffuse, Cytoplasm, Eosinophilia +4
053	20.0	Hepatocyte, Diffuse, Hypertrophy +1
054	20.0	Hepatocyte, Diffuse, Hypertrophy +2
055	20.0	Hepatocyte, Diffuse, Hypertrophy +3
056	20.0	Hepatocyte, Diffuse, Hypertrophy +4
057	20.0	Hepatocyte, Midzonal, Lipid Accumulation, Macrovesicular +1
058	10.0	Hepatocyte, Midzonal, Lipid Accumulation, Macrovesicular +2
059	20.0	Hepatocyte, Midzonal, Lipid Accumulation, Microvesicular +3
060	20.0	Hepatocyte, Midzonal, Necrosis, Apoptotic +1
061	20.0	Hepatocyte, Midzonal, Necrosis, Apoptotic +2
062	25.0	Hepatocyte, Midzonal, Necrosis, Oncocytic +1
063	40.0	Hepatocyte, Nonzonal, Degeneration +1
064	40.0	Hepatocyte, Nonzonal, Degeneration +2

Figure No.	Magnification	Diagnosis
065	20.0	Hepatocyte, Nonzonal, Erythrophagocytosis +2
066	20.0	Hepatocyte, Nonzonal, Glycogen Accumulation +1
067	40.0	Hepatocyte, Nonzonal, Increased Mitoses +1
068	40.0	Hepatocyte, Nonzonal, Increased Mitoses +2
069	40.0	Hepatocyte, Nonzonal, Increased Mitoses +3
070	10.0	Hepatocyte, Nonzonal, Lipid Accumulation, Macrovesicular +1
071	10.0	Hepatocyte, Nonzonal, Lipid Accumulation, Macrovesicular +2
072	10.0	Hepatocyte, Nonzonal, Lipid Accumulation, Macrovesicular +3
073	10.0	Hepatocyte, Nonzonal, Lipid Accumulation, Macrovesicular +3
074	40.0	Hepatocyte, Nonzonal, Lipid Accumulation, Macrovesicular +1
075	20.0	Hepatocyte, Nonzonal, Mineralization +2
076	40.0	Hepatocyte, Nonzonal, Multinucleated +1
077	32.0	Hepatocyte, Nonzonal, Necrosis, Apoptotic +1
078	32.0	Hepatocyte, Nonzonal, Necrosis, Apoptotic +2
079	40.0	Hepatocyte, Nonzonal, Necrosis, Oncocytic +1
080	20.0	Hepatocyte, Nonzonal, Necrosis, Oncocytic +2
081	12.5	Hepatocyte, Nonzonal, Necrosis, Oncocytic +3
082	20.0	Hepatocyte, Periportal, Cytoplasm, Eosinophilia +1
083	20.0	Hepatocyte, Periportal, Cytoplasm, Eosinophilia +2
084	20.0	Hepatocyte, Periportal, Cytoplasm, Eosinophilia +3
085	10.0	Hepatocyte, Periportal, Glycogen Accumulation +1
086	10.0	Hepatocyte, Periportal, Glycogen Accumulation +2
087	10.0	Hepatocyte, Periportal, Glycogen Accumulation +3
088	10.0	Hepatocyte, Periportal, Glycogen Accumulation +4
089	10.0	Hepatocyte, Periportal, Hypertrophy +1
090	10.0	Hepatocyte, Periportal, Hypertrophy +2
091	10.0	Hepatocyte, Periportal, Hypertrophy +3
092	20.0	Hepatocyte, Periportal, Lipid Accumulation, Macrovesicular +1

Figure No.	Magnification	Diagnosis
093	20.0	Hepatocyte, Periportal, Lipid Accumulation, Macrovesicular +2
094	20.0	Hepatocyte, Periportal, Lipid Accumulation, Macrovesicular +3
095	20.0	Hepatocyte, Periportal, Lipid Accumulation, Macrovesicular +4
096	40.0	Hepatocyte, Periportal, Lipid Accumulation, Microvesicular +1
097	40.0	Hepatocyte, Periportal, Necrosis, Apoptotic +1
098	20.0	Hepatocyte, Periportal, Necrosis, Oncocytic +1
099	20.0	Hepatocyte, Periportal, Necrosis, Oncocytic +2
100	10.0	Hepatocyte, Subcapsular, Mineralization +3
101	10.0	Hepatocyte, Subcapsular, Necrosis, Oncocytic +1
102	10.0	Hepatocyte, Subcapsular, Necrosis, Oncocytic +2
103	10.0	Hepatocyte, Subcapsular, Necrosis, Oncocytic +3
104	10.0	Malignant Lymphoma
105	20.0	Nonzonal, Extramedullary, Hematopoiesis +1
106	20.0	Nonzonal, Inflammatory Cell Infiltrate, Granulomatous +2
107	20.0	Nonzonal, Inflammatory Cell Infiltrate, Lymphoid +1
108	20.0	Nonzonal, Inflammatory Cell Infiltrate, Lymphoid +2
109	20.0	Nonzonal, Inflammatory Cell Infiltrate, Mixed Cell +1
110	20.0	Nonzonal, Inflammatory Cell Infiltrate, Mixed Cell +2
111	6.4	Nonzonal, Inflammatory Cell Infiltrate, Mixed Cell +3
112	40.0	Oval Cell, Hyperplasia +1
113	20.0	Periportal Edema +2
114	20.0	Periportal, Fibrosis +1
115	20.0	Periportal, Fibrosis +2
116	20.0	Periportal, Inflammatory Cell Infiltrate, Lymphoid +1
117	20.0	Periportal, Inflammatory Cell Infiltrate, Lymphoid +2
118	4.0	Periportal, Inflammatory Cell Infiltrate, Lymphoid +3
119	20.0	Periportal, Inflammatory Cell Infiltrate, Mixed Cell +1
120	20.0	Periportal, Inflammatory Cell Infiltrate, Mixed Cell +3

Figure No.	Magnification	Diagnosis
121a	4.0	Periportal, Inflammatory Cell Infiltrate, Mixed Cell +3
121b	10.0	Periportal, Inflammatory Cell Infiltrate, Mixed Cell +3
122	20.0	Periportal, Inflammatory Cell Infiltrate, Neutrophilic +1
123	10.0	Subcapsular, Fibrosis +1
124	10.0	Subcapsular, Fibrosis +2
125	10.0	Subcapsular, Fibrosis +3

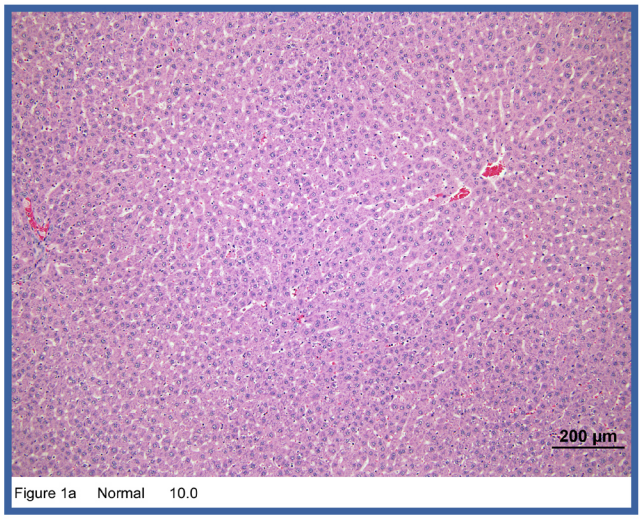

Figure 1a Normal 10.0

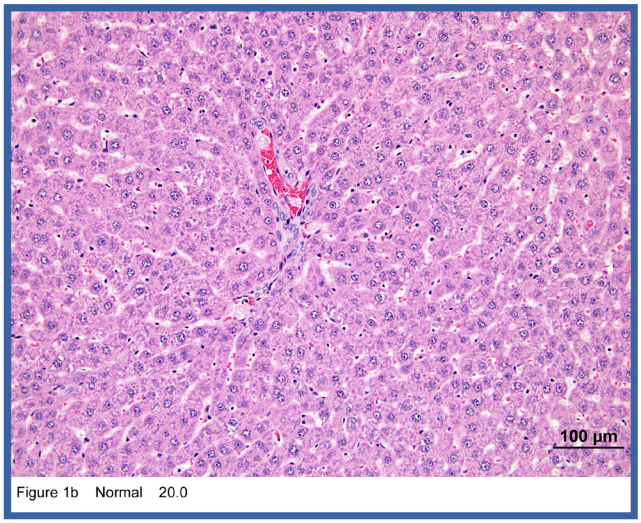

Figure 1b Normal 20.0

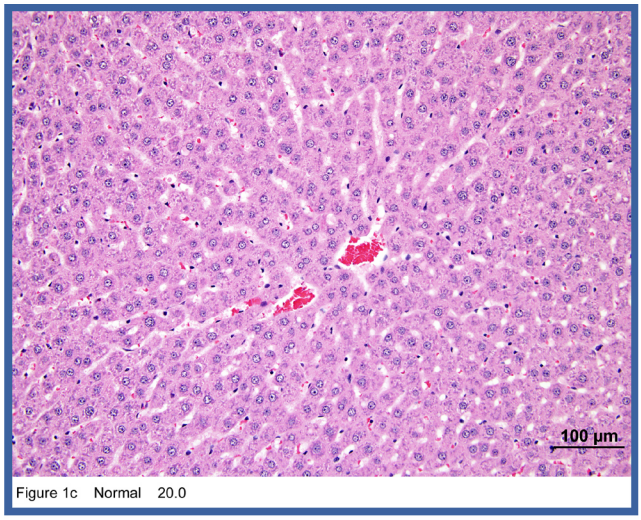

Figure 1c Normal 20.0

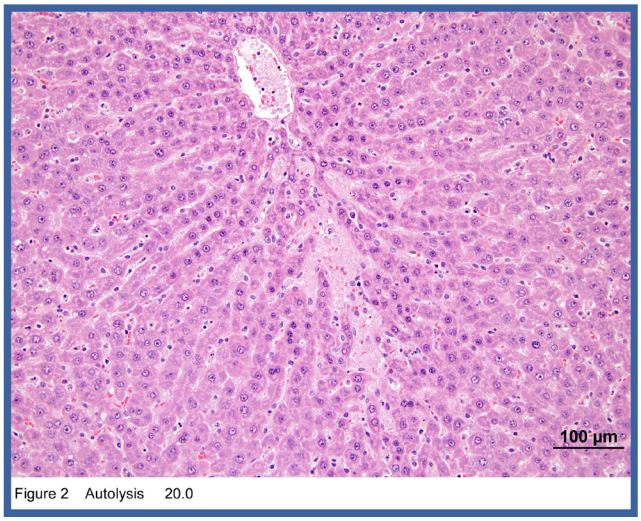

Figure 2 Autolysis 20.0

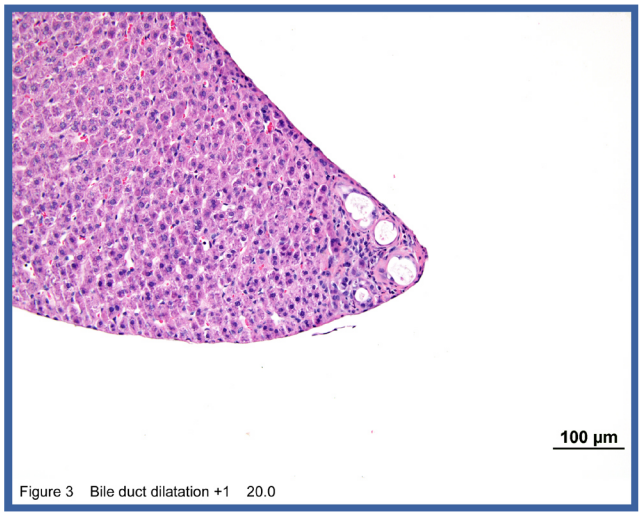

Figure 3 Bile duct dilatation +1 20.0

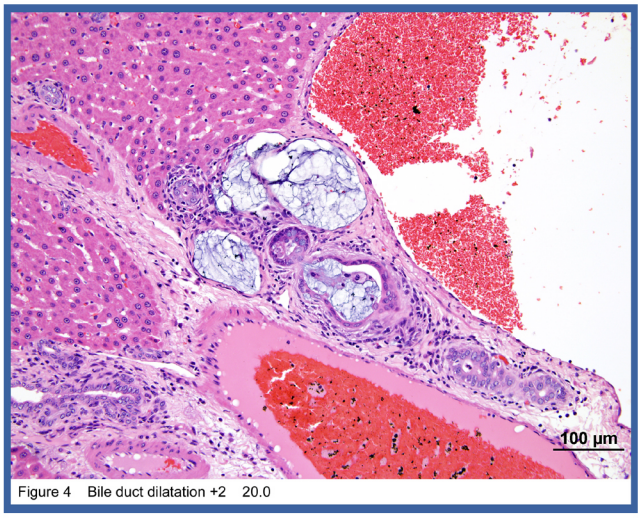

Figure 4 Bile duct dilatation +2 20.0

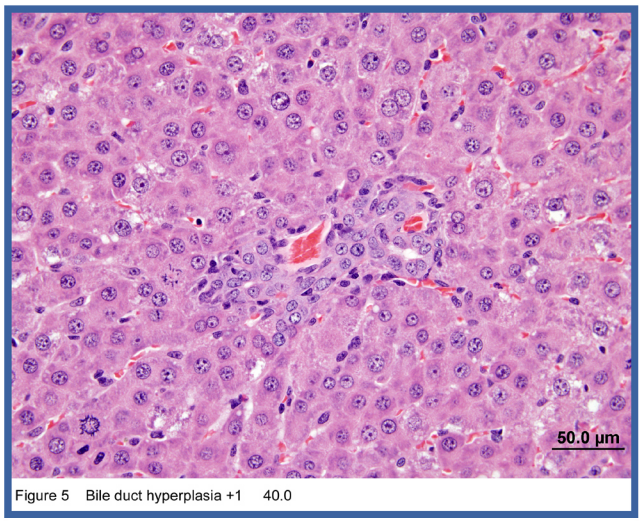

Figure 5 Bile duct hyperplasia +1 40.0

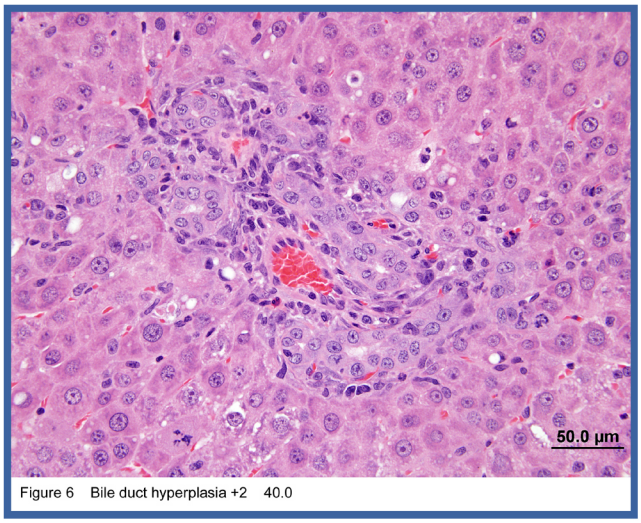

Figure 6 Bile duct hyperplasia +2 40.0

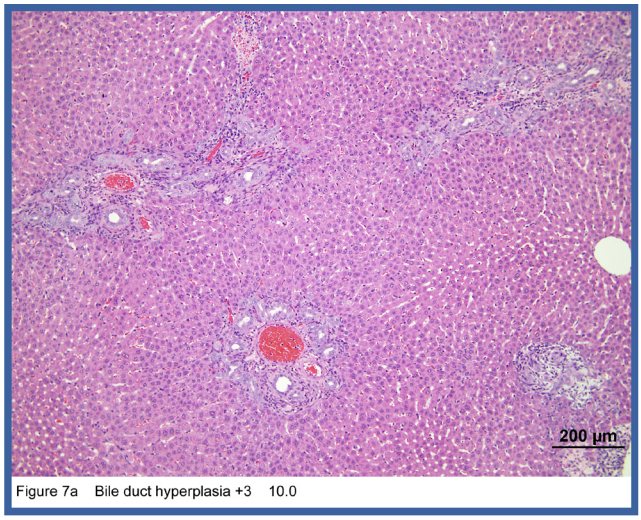

Figure 7a Bile duct hyperplasia +3 10.0

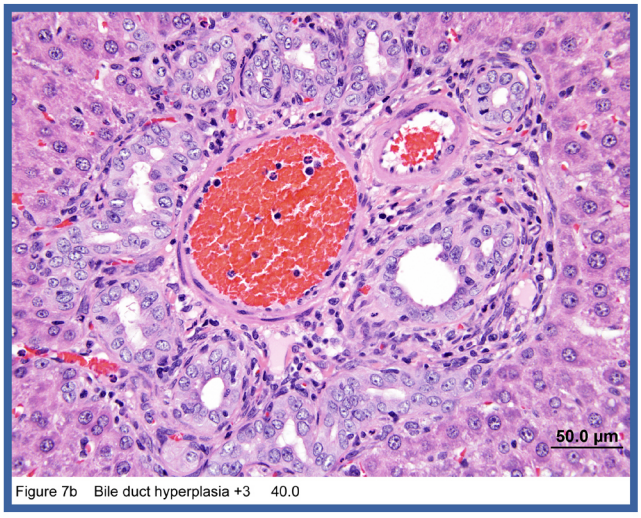

Figure 7b Bile duct hyperplasia +3 40.0

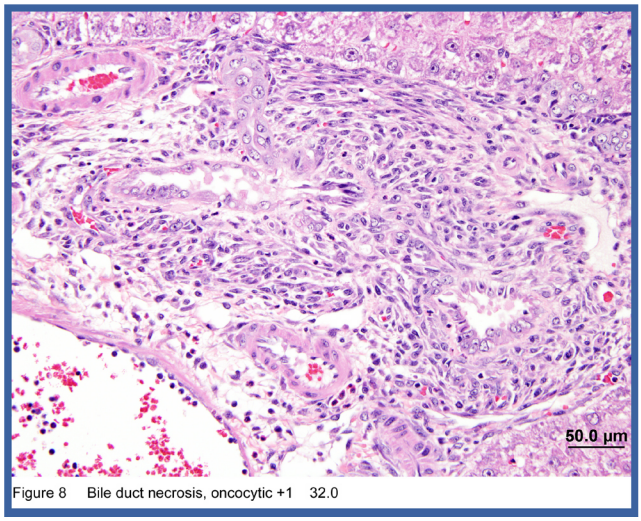

Figure 8 Bile duct necrosis, oncocytic +1 32.0

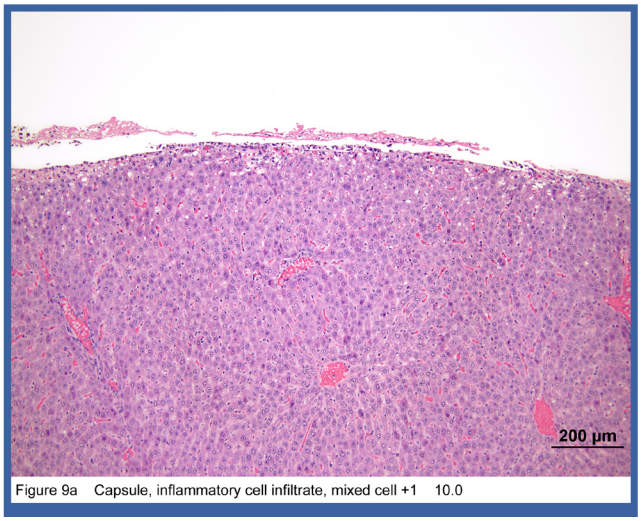

Figure 9a Capsule, inflammatory cell infiltrate, mixed cell +1 10.0

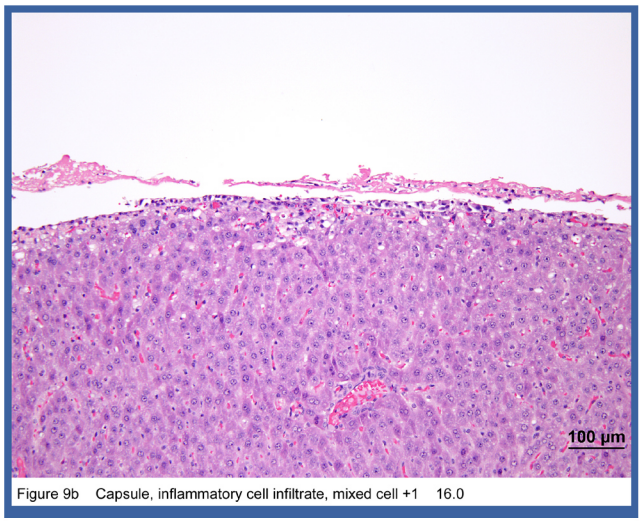

Figure 9b Capsule, inflammatory cell infiltrate, mixed cell +1 16.0

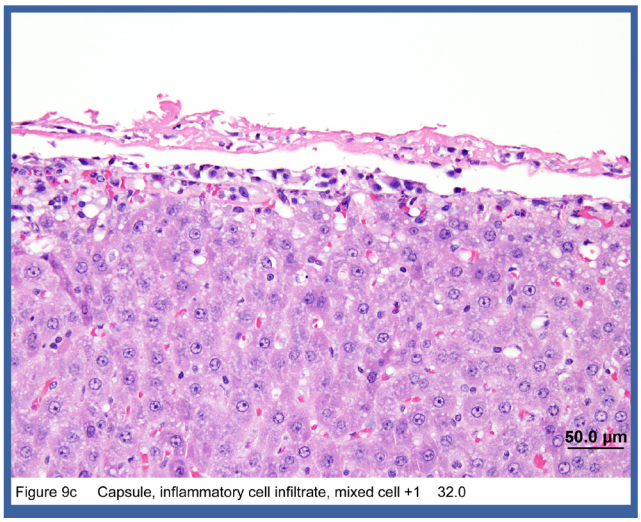

Figure 9c Capsule, inflammatory cell infiltrate, mixed cell +1 32.0

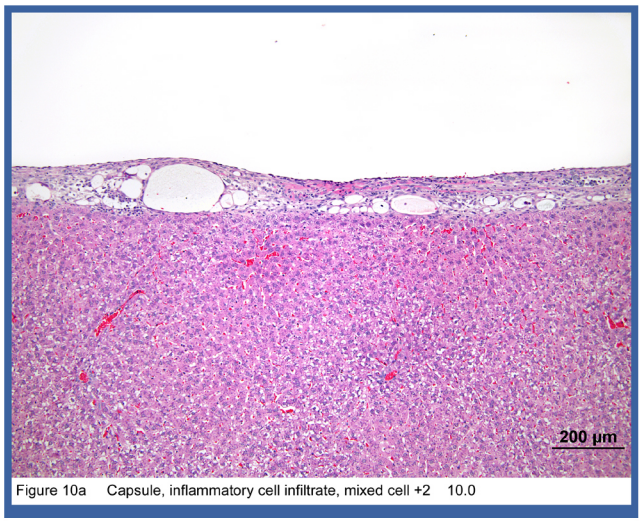

Figure 10a Capsule, inflammatory cell infiltrate, mixed cell +2 10.0

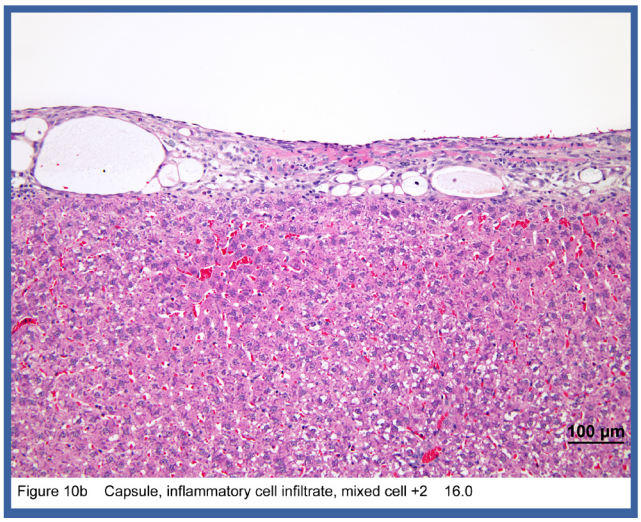

Figure 10b Capsule, inflammatory cell infiltrate, mixed cell +2 16.0

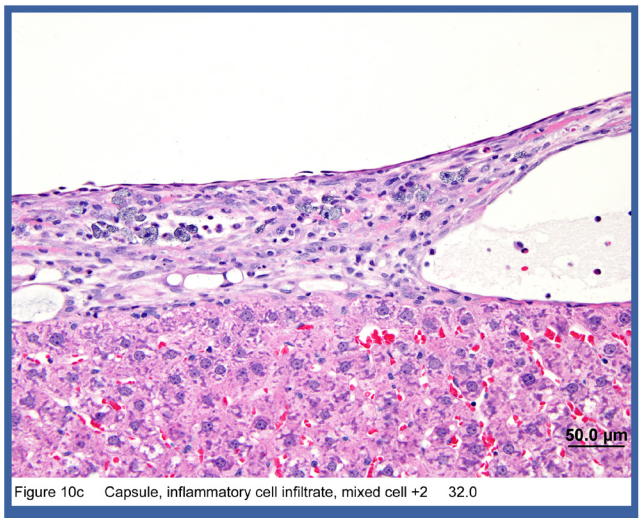

Figure 10c Capsule, inflammatory cell infiltrate, mixed cell +2 32.0

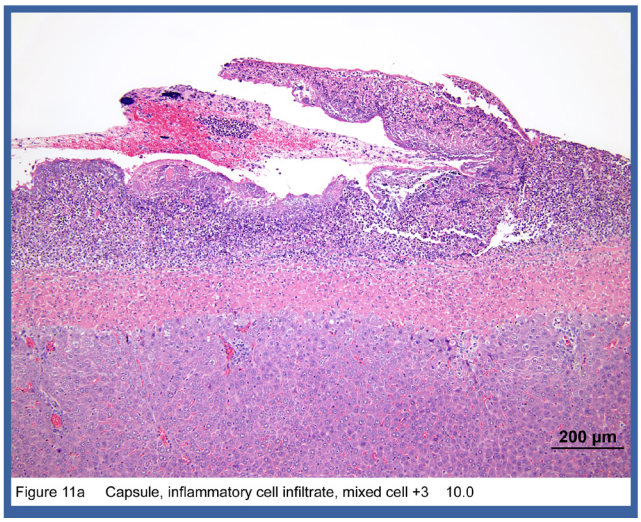

Figure 11a Capsule, inflammatory cell infiltrate, mixed cell +3 10.0

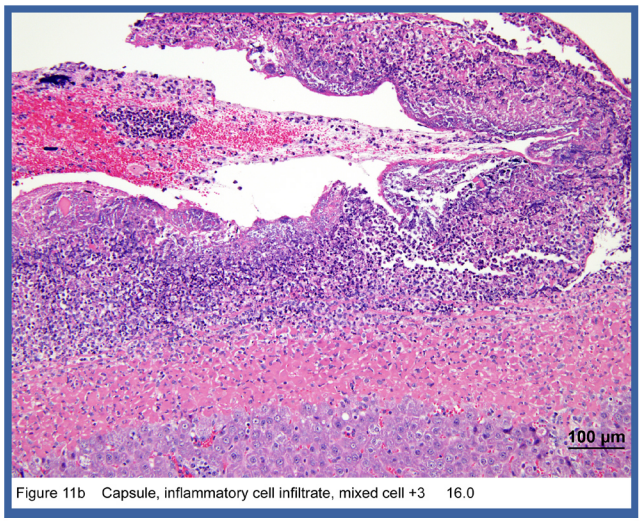

Figure 11b Capsule, inflammatory cell infiltrate, mixed cell +3 16.0

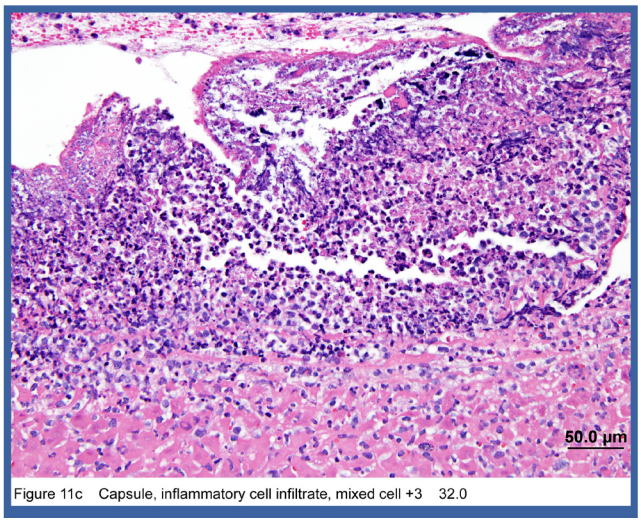

Figure 11c Capsule, inflammatory cell infiltrate, mixed cell +3 32.0

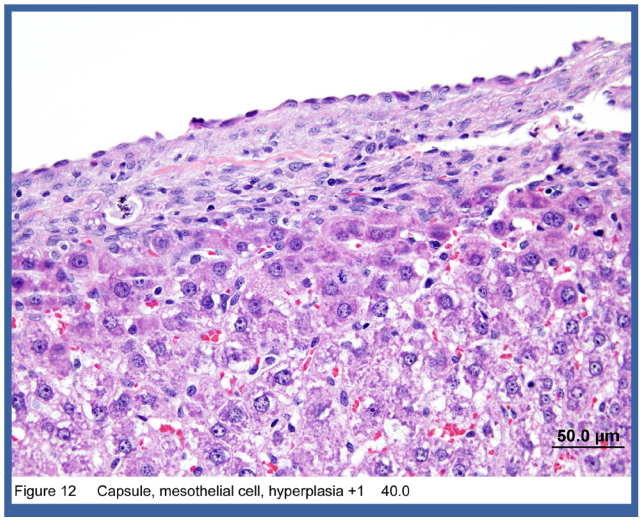

Figure 12 Capsule, mesothelial cell, hyperplasia +1 40.0

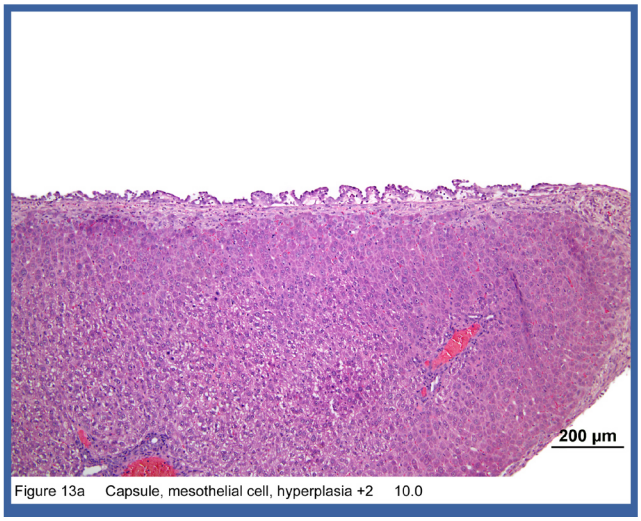

Figure 13a Capsule, mesothelial cell, hyperplasia +2 10.0

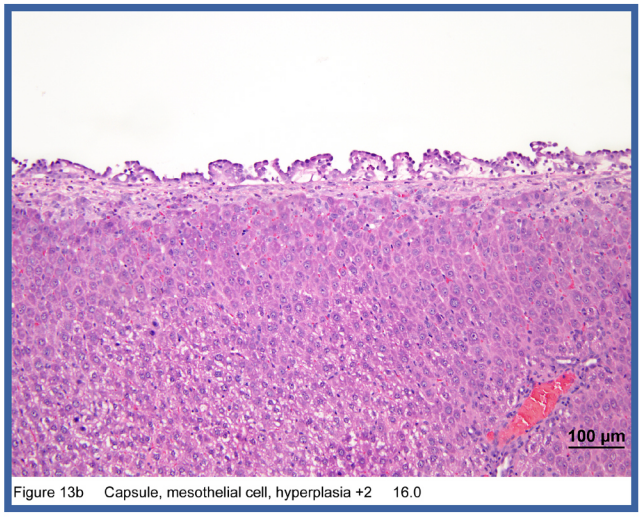

Figure 13b Capsule, mesothelial cell, hyperplasia +2 16.0

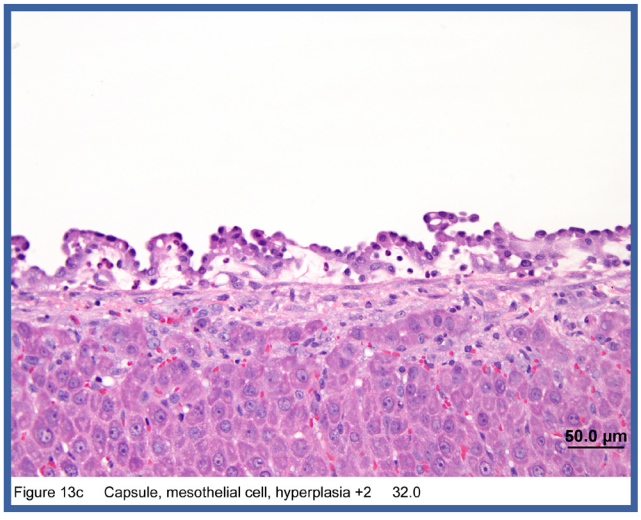

Figure 13c Capsule, mesothelial cell, hyperplasia +2 32.0

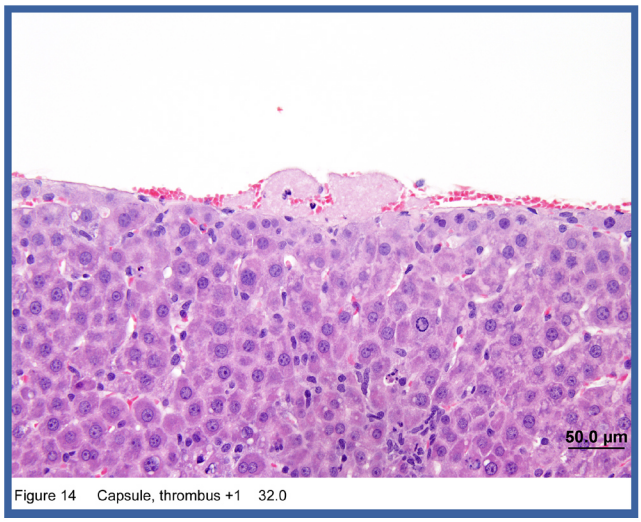

Figure 14 Capsule, thrombus +1 32.0

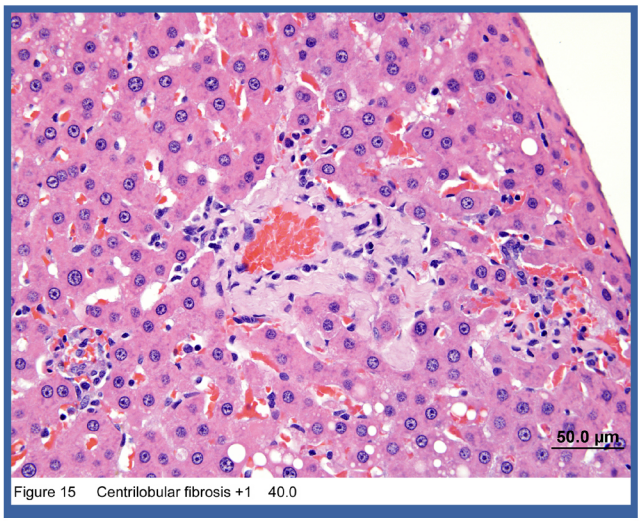

Figure 15 Centrilobular fibrosis +1 40.0

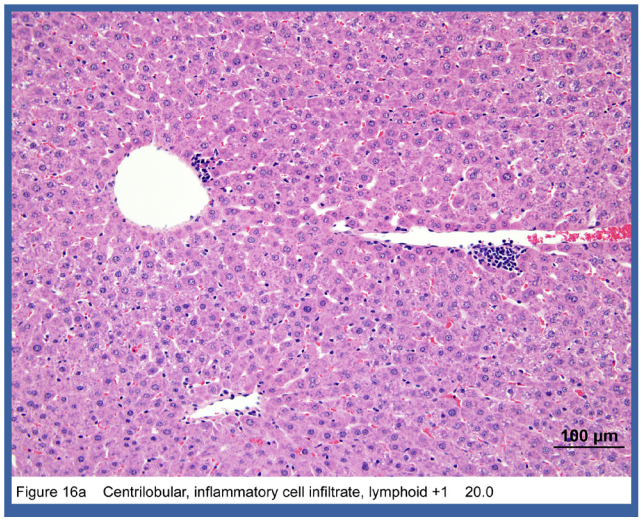

Figure 16a Centrilobular, inflammatory cell infiltrate, lymphoid +1 20.0

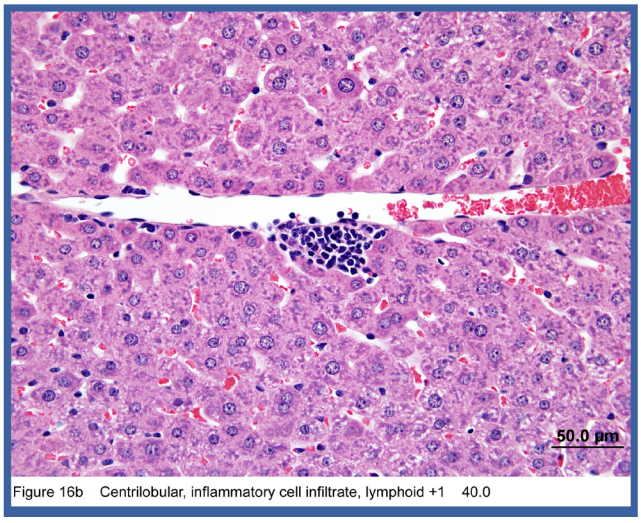

Figure 16b Centrilobular, inflammatory cell infiltrate, lymphoid +1 40.0

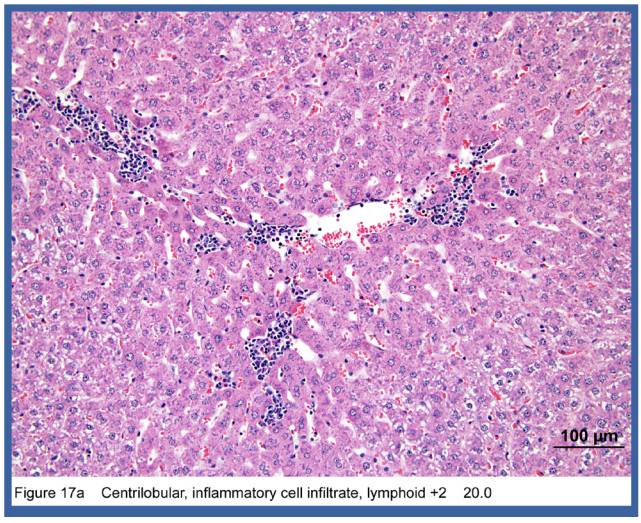

Figure 17a Centrilobular, inflammatory cell infiltrate, lymphoid +2 20.0

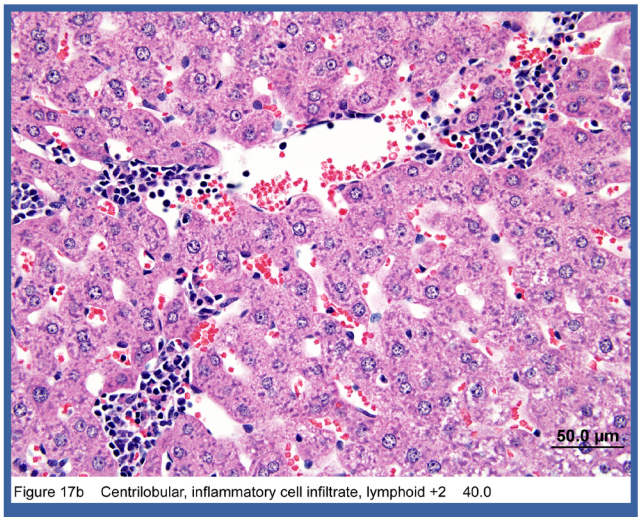

Figure 17b Centrilobular, inflammatory cell infiltrate, lymphoid +2 40.0

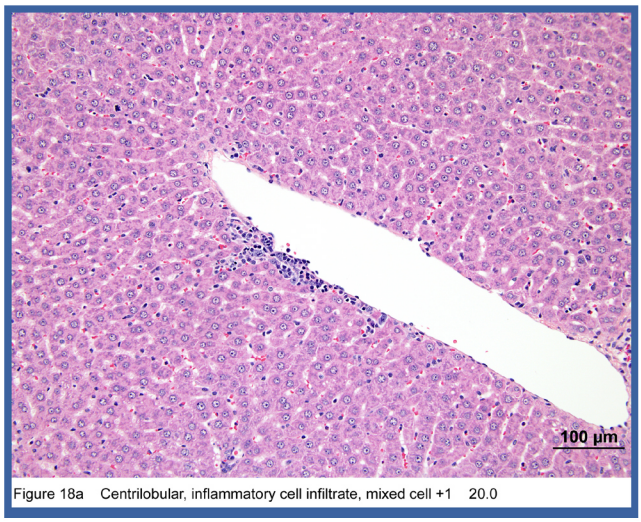

Figure 18a Centrilobular, inflammatory cell infiltrate, mixed cell +1 20.0

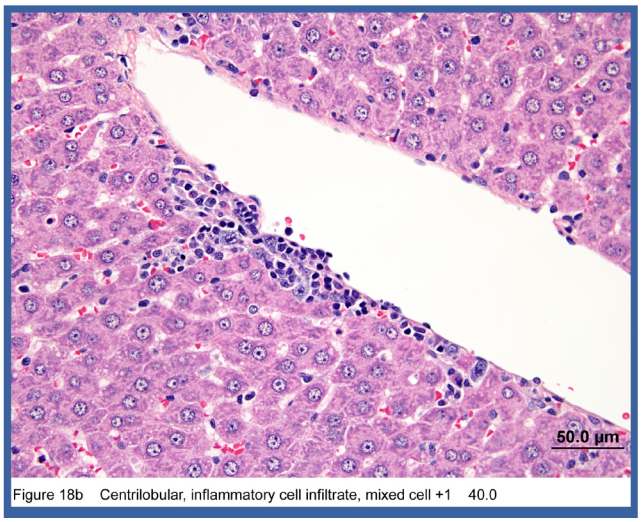

Figure 18b Centrilobular, inflammatory cell infiltrate, mixed cell +1 40.0

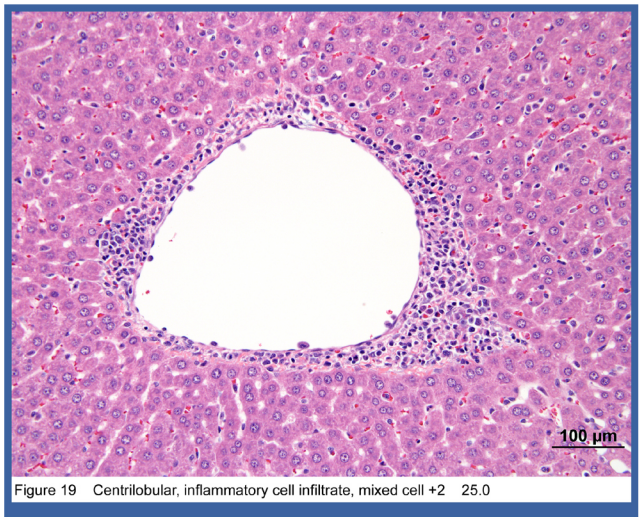

Figure 19 Centrilobular, inflammatory cell infiltrate, mixed cell +2 25.0

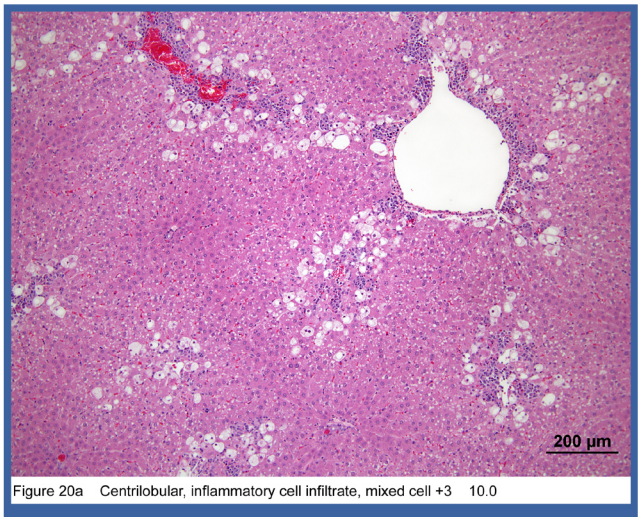

Figure 20a Centrilobular, inflammatory cell infiltrate, mixed cell +3 10.0

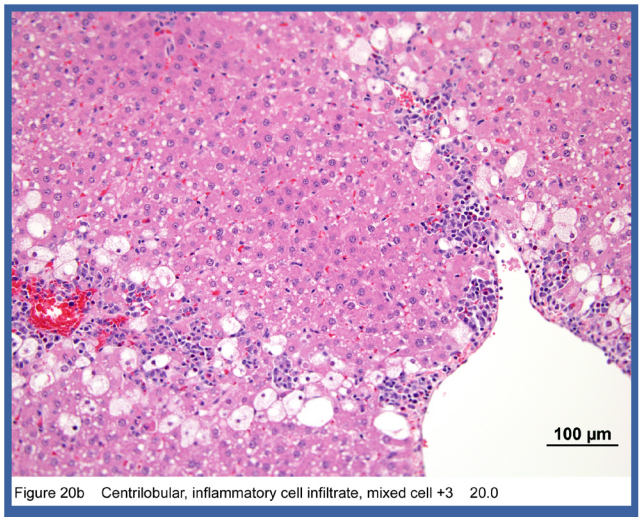

Figure 20b Centrilobular, inflammatory cell infiltrate, mixed cell +3 20.0

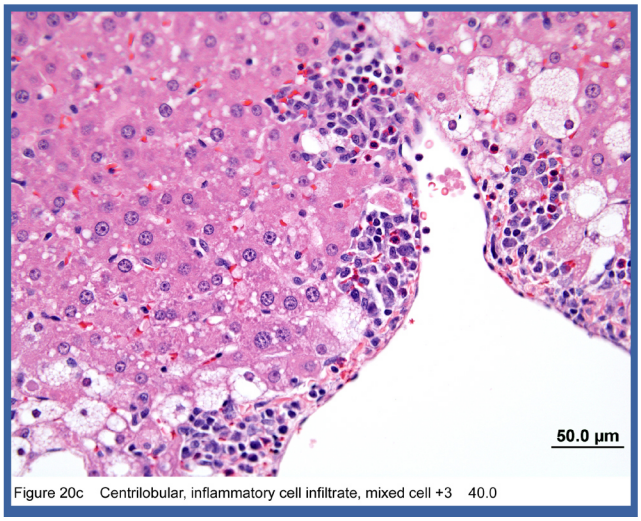

Figure 20c Centrilobular, inflammatory cell infiltrate, mixed cell +3 40.0

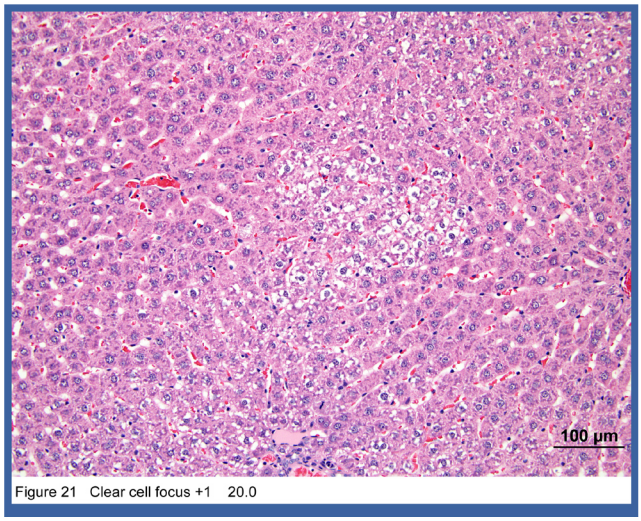

Figure 21 Clear cell focus +1 20.0

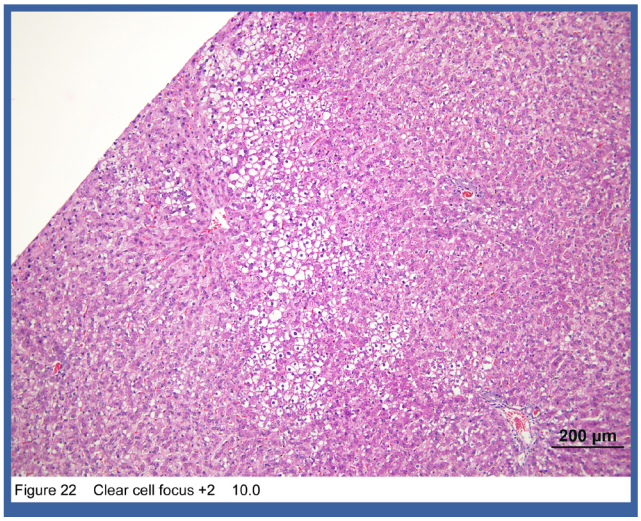

Figure 22 Clear cell focus +2 10.0

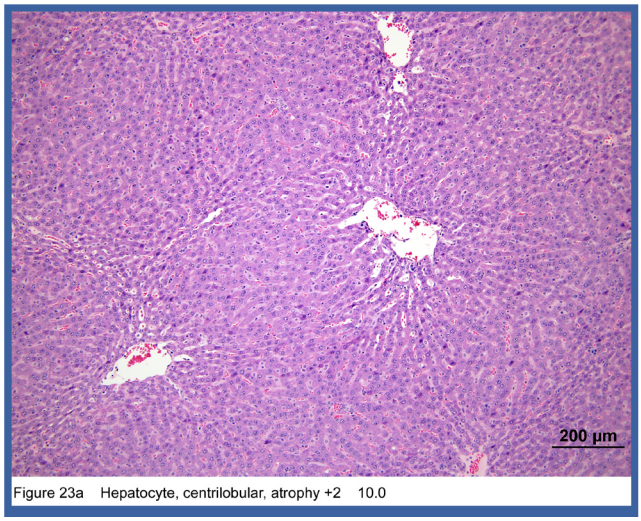

Figure 23a Hepatocyte, centrilobular, atrophy +2 10.0

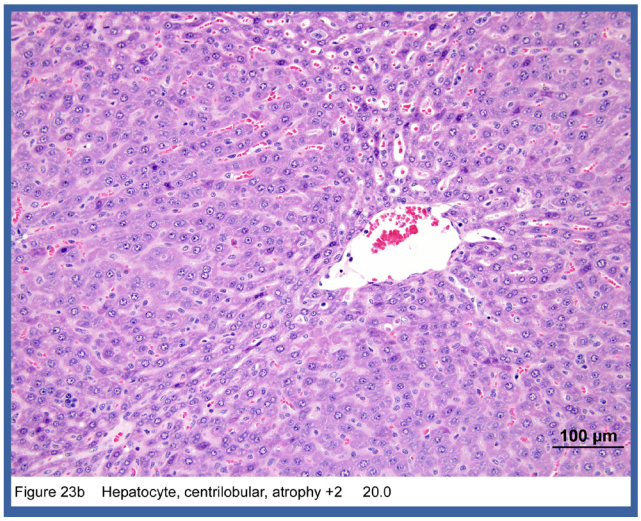

Figure 23b Hepatocyte, centrilobular, atrophy +2 20.0

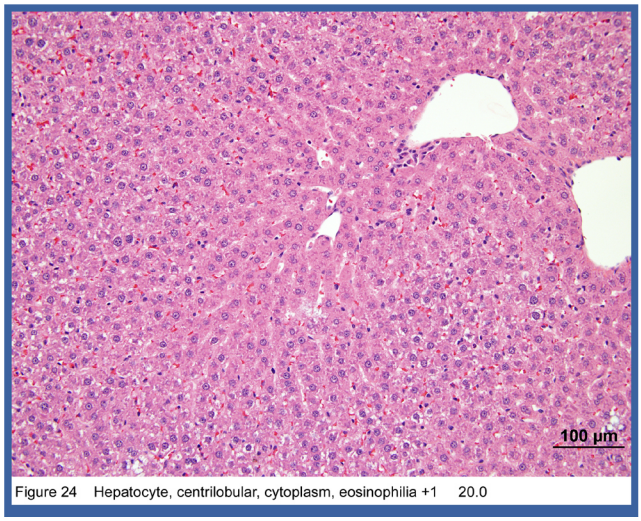

Figure 24 Hepatocyte, centrilobular, cytoplasm, eosinophilia +1 20.0

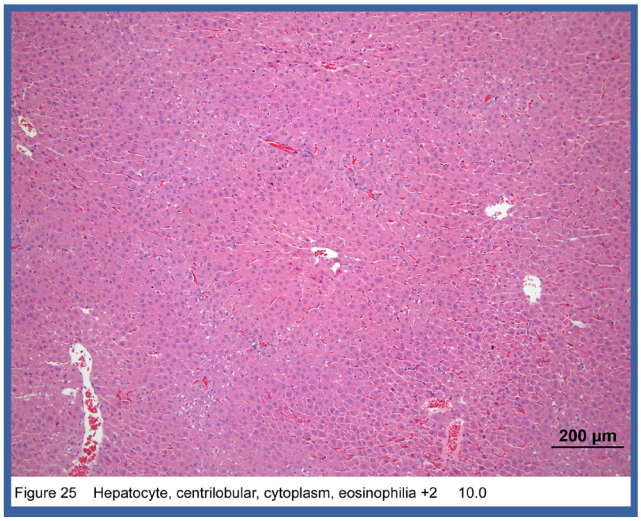

Figure 25 Hepatocyte, centrilobular, cytoplasm, eosinophilia +2 10.0

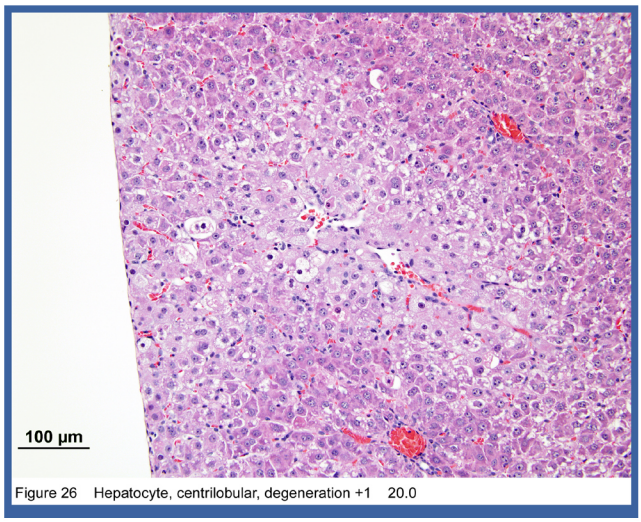

Figure 26 Hepatocyte, centrilobular, degeneration +1 20.0

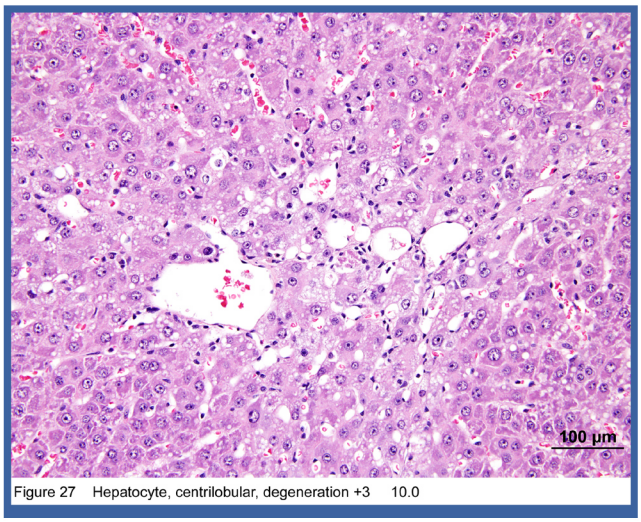

Figure 27 Hepatocyte, centrilobular, degeneration +3 10.0

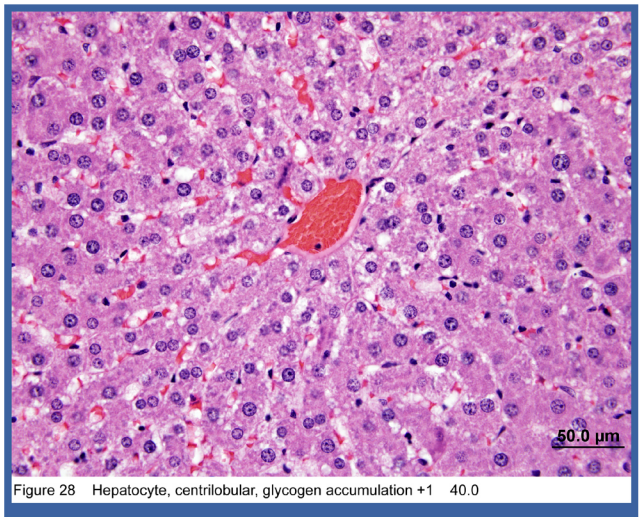

Figure 28 Hepatocyte, centrilobular, glycogen accumulation +1 40.0

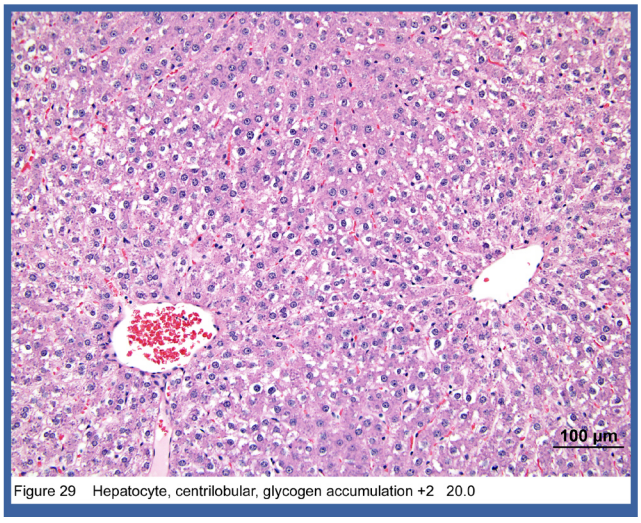

Figure 29 Hepatocyte, centrilobular, glycogen accumulation +2 20.0

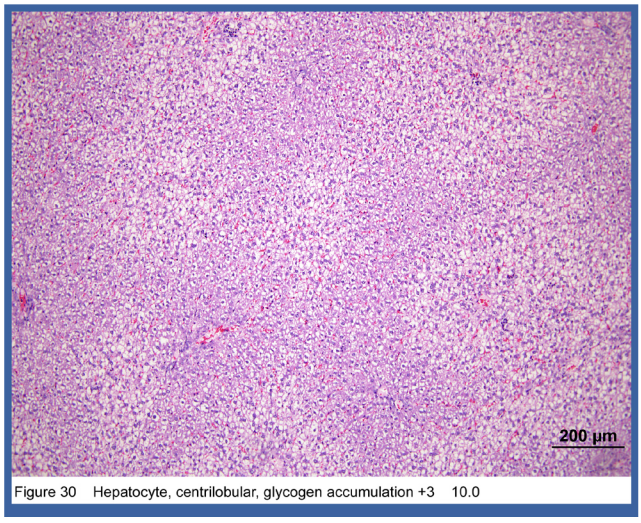

Figure 30 Hepatocyte, centrilobular, glycogen accumulation +3 10.0

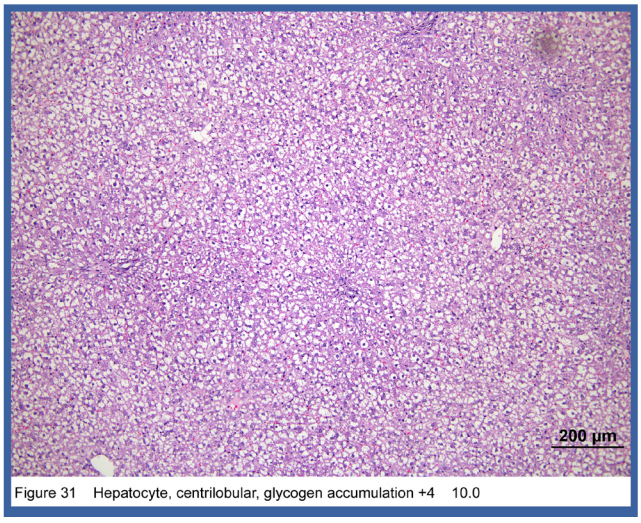

Figure 31 Hepatocyte, centrilobular, glycogen accumulation +4 10.0

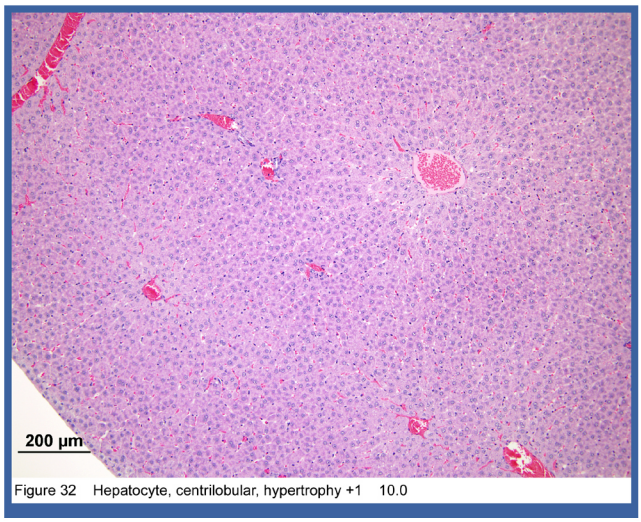

Figure 32 Hepatocyte, centrilobular, hypertrophy +1 10.0

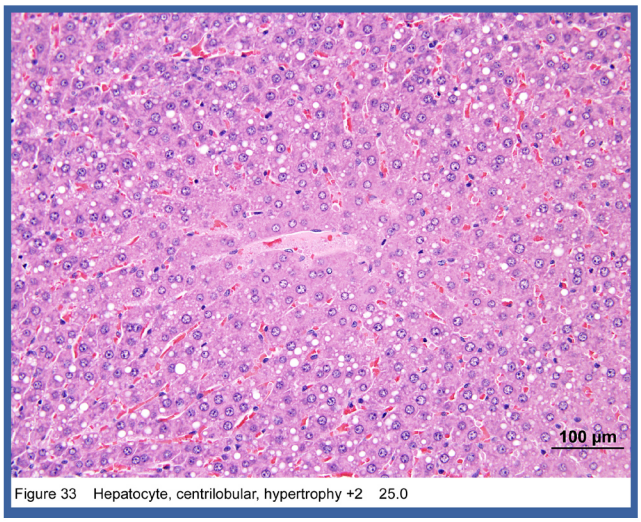

Figure 33 Hepatocyte, centrilobular, hypertrophy +2 25.0

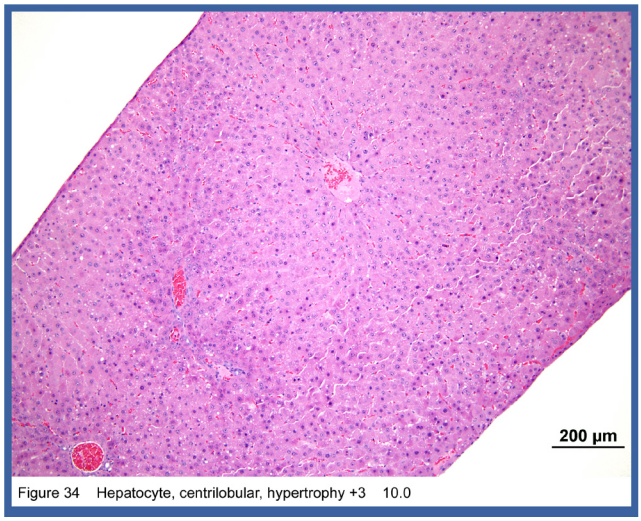

Figure 34 Hepatocyte, centrilobular, hypertrophy +3 10.0

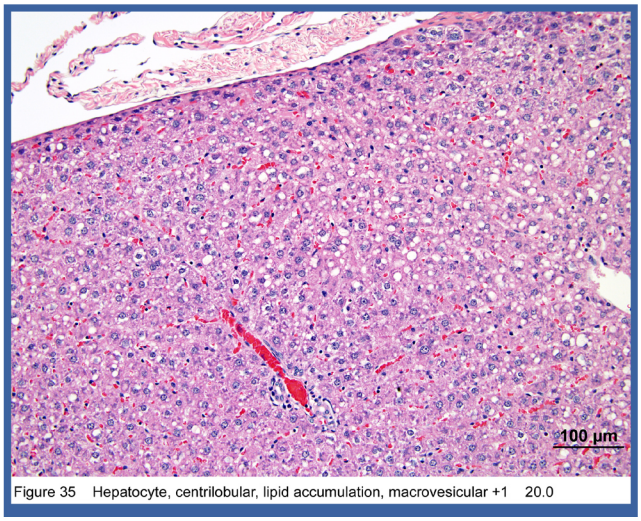

Figure 35 Hepatocyte, centrilobular, lipid accumulation, macrovesicular +1 20.0

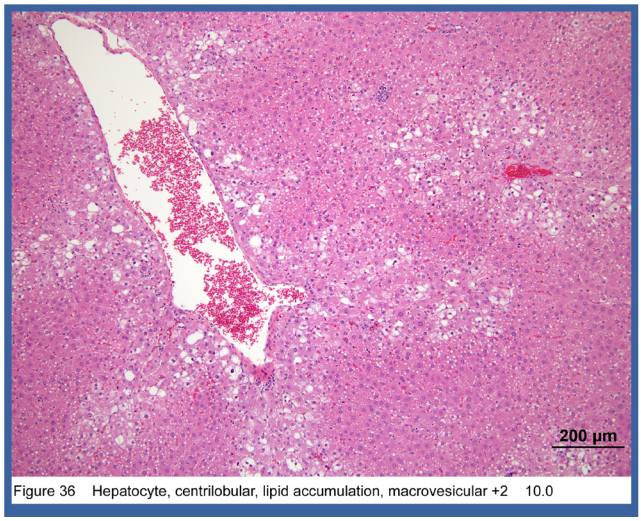

Figure 36 Hepatocyte, centrilobular, lipid accumulation, macrovesicular +2 10.0

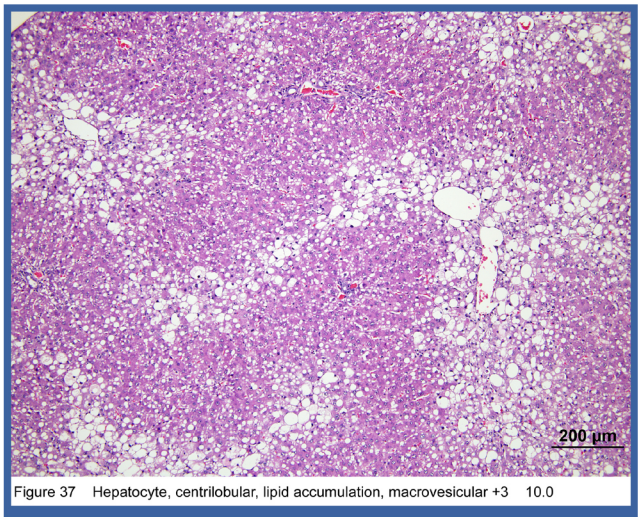

Figure 37 Hepatocyte, centrilobular, lipid accumulation, macrovesicular +3 10.0

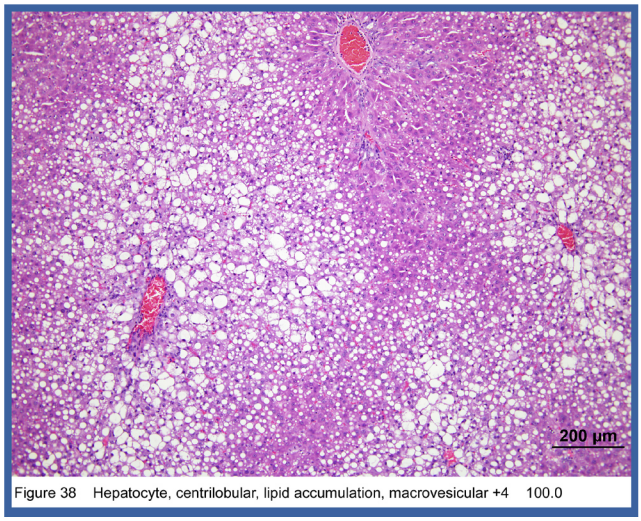

Figure 38 Hepatocyte, centrilobular, lipid accumulation, macrovesicular +4 100.0

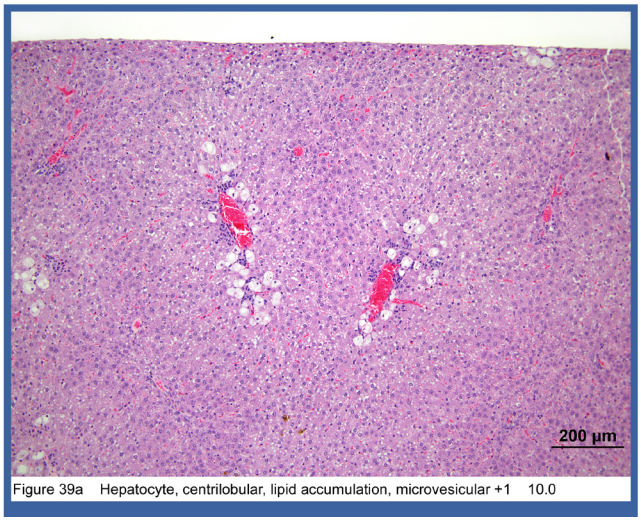

Figure 39a Hepatocyte, centrilobular, lipid accumulation, microvesicular +1 10.0

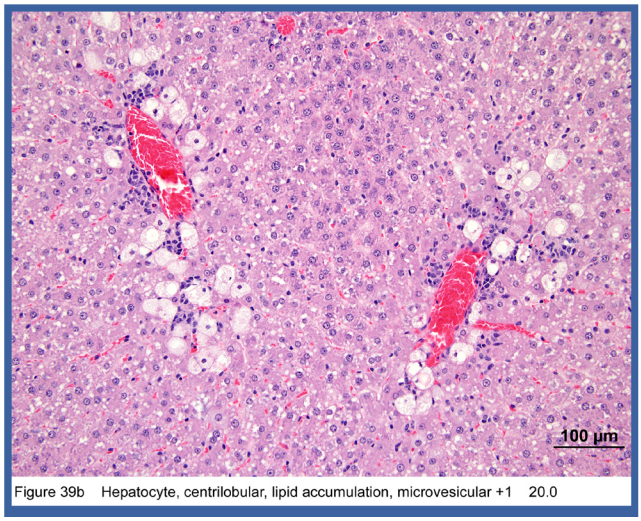

Figure 39b Hepatocyte, centrilobular, lipid accumulation, microvesicular +1 20.0

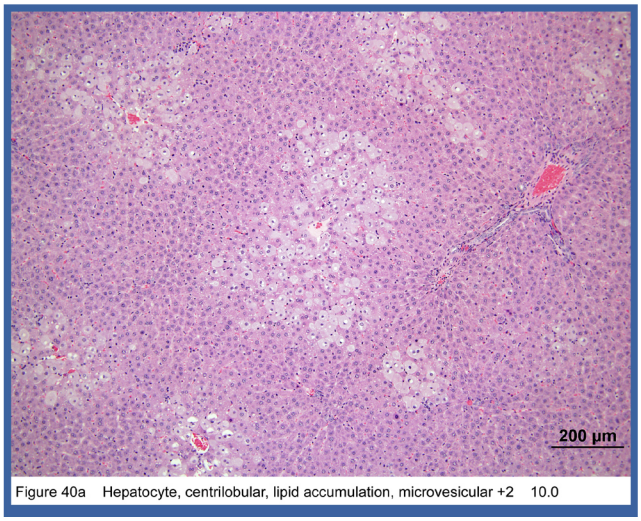

Figure 40a Hepatocyte, centrilobular, lipid accumulation, microvesicular +2 10.0

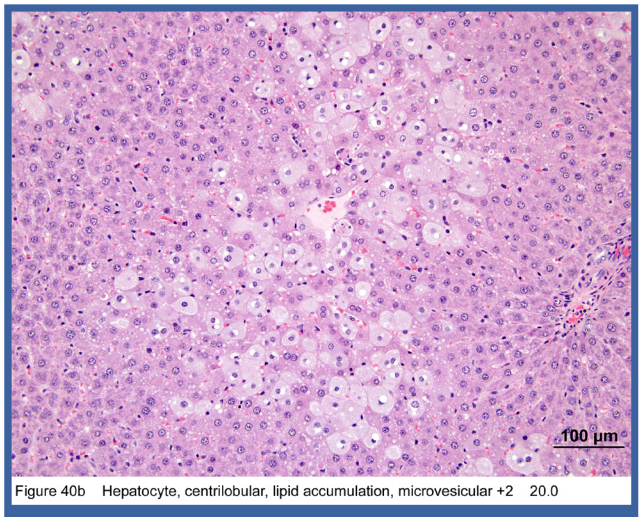

Figure 40b Hepatocyte, centrilobular, lipid accumulation, microvesicular +2 20.0

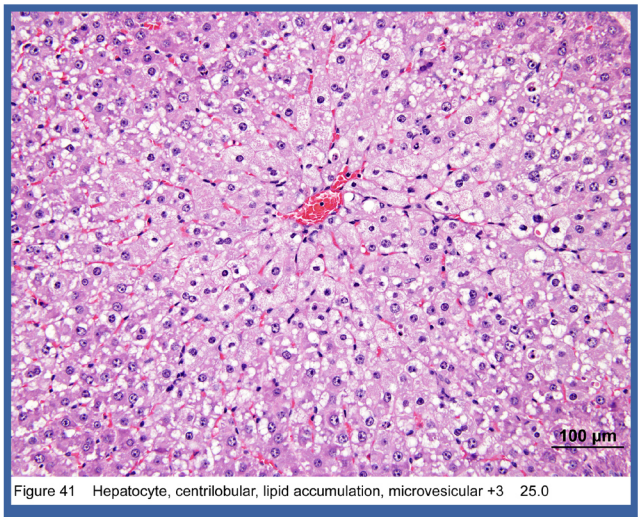

Figure 41 Hepatocyte, centrilobular, lipid accumulation, microvesicular +3 25.0

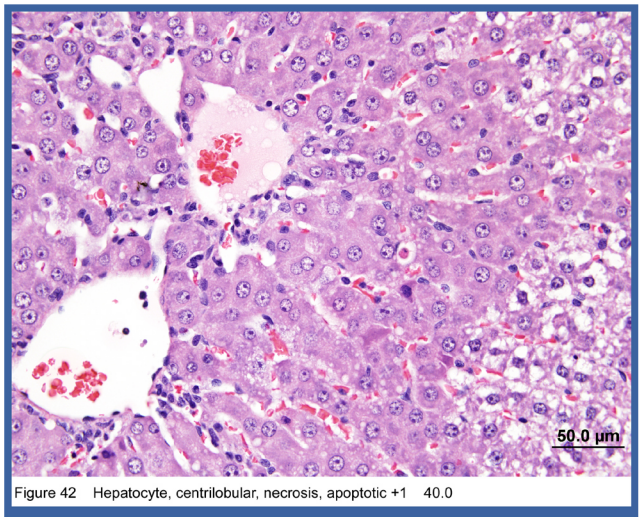

Figure 42 Hepatocyte, centrilobular, necrosis, apoptotic +1 40.0

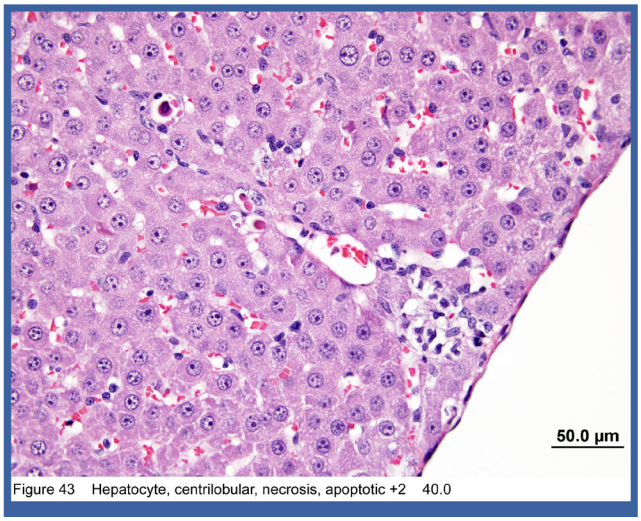

Figure 43 Hepatocyte, centrilobular, necrosis, apoptotic +2 40.0

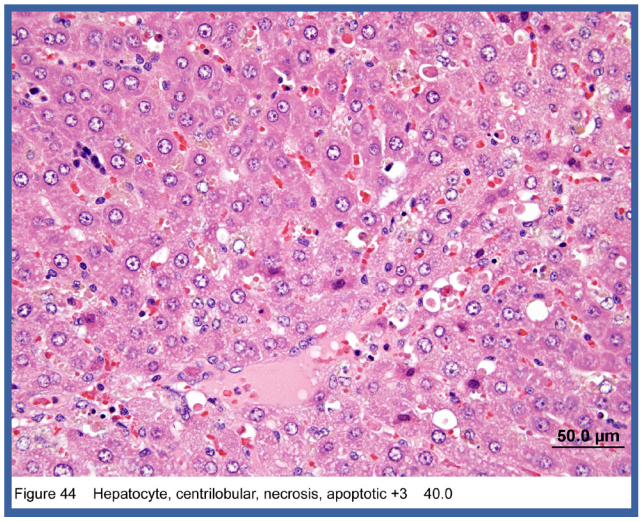

Figure 44 Hepatocyte, centrilobular, necrosis, apoptotic +3 40.0

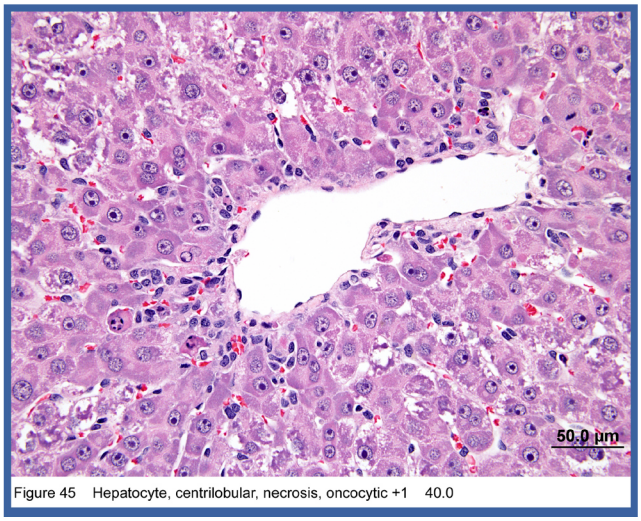

Figure 45 Hepatocyte, centrilobular, necrosis, oncocytic +1 40.0

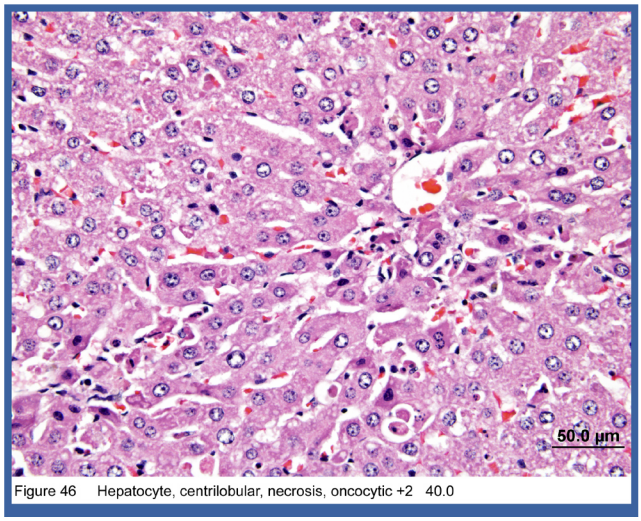

Figure 46 Hepatocyte, centrilobular, necrosis, oncocytic +2 40.0

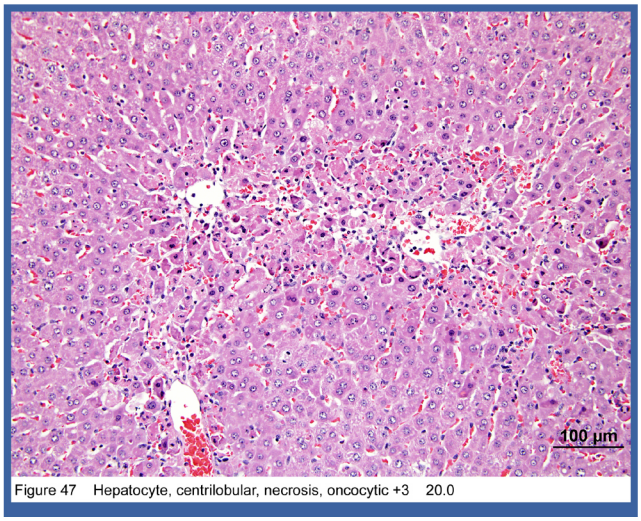

Figure 47 Hepatocyte, centrilobular, necrosis, oncocytic +3 20.0

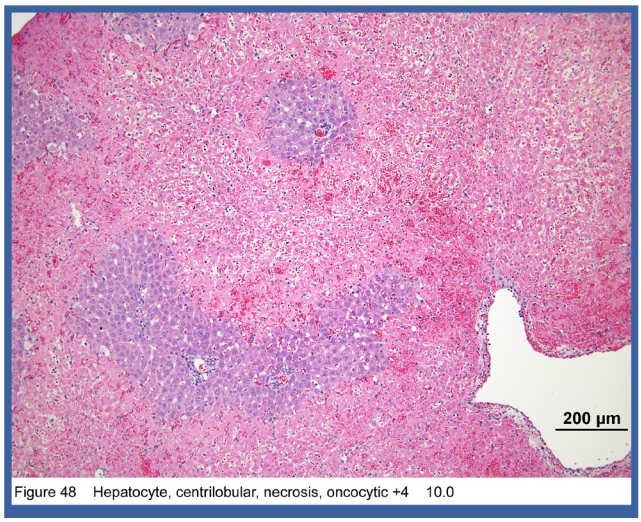

Figure 48 Hepatocyte, centrilobular, necrosis, oncocytic +4 10.0

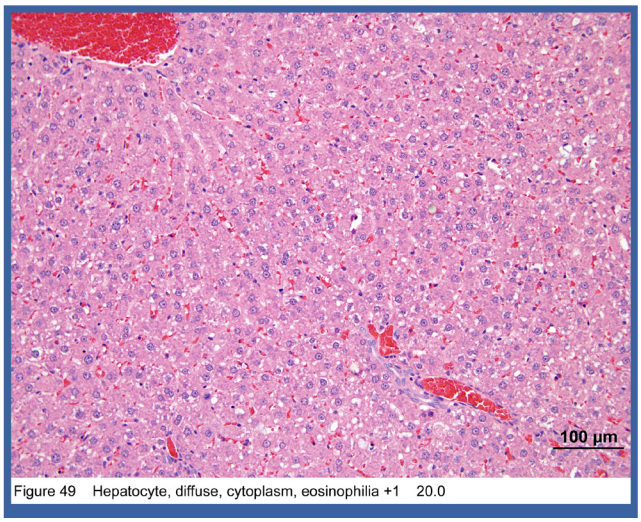

Figure 49 Hepatocyte, diffuse, cytoplasm, eosinophilia +1 20.0

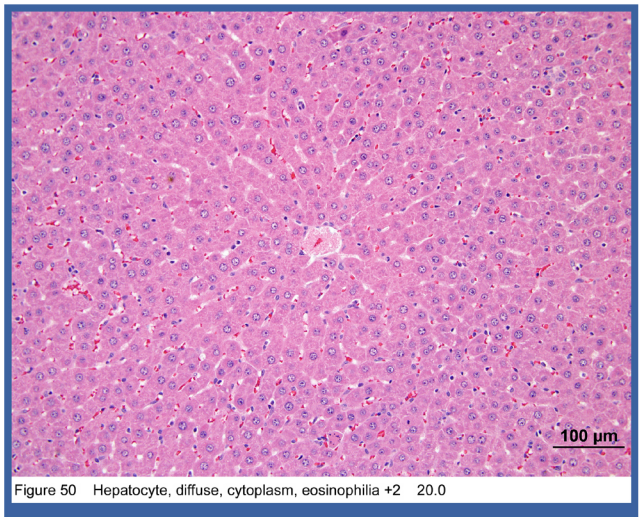

Figure 50 Hepatocyte, diffuse, cytoplasm, eosinophilia +2 20.0

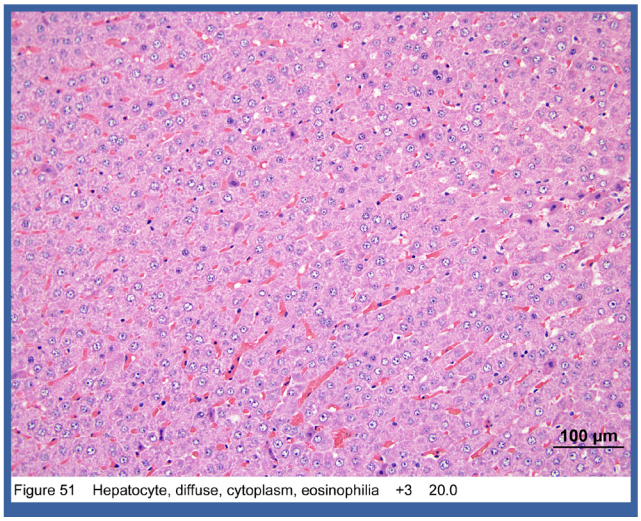

Figure 51 Hepatocyte, diffuse, cytoplasm, eosinophilia +3 20.0

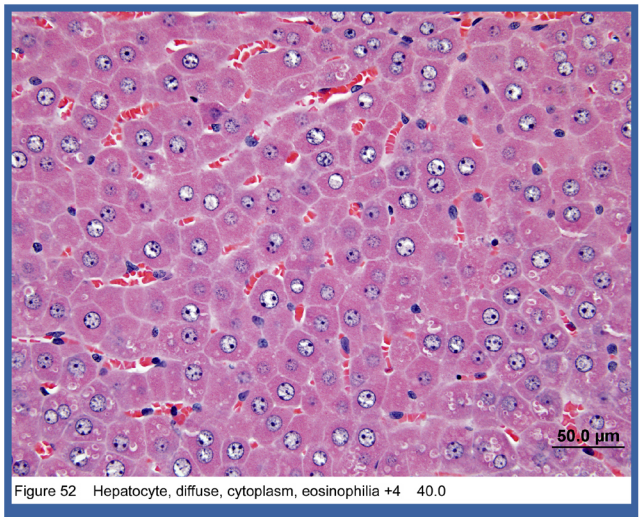

Figure 52 Hepatocyte, diffuse, cytoplasm, eosinophilia +4 40.0

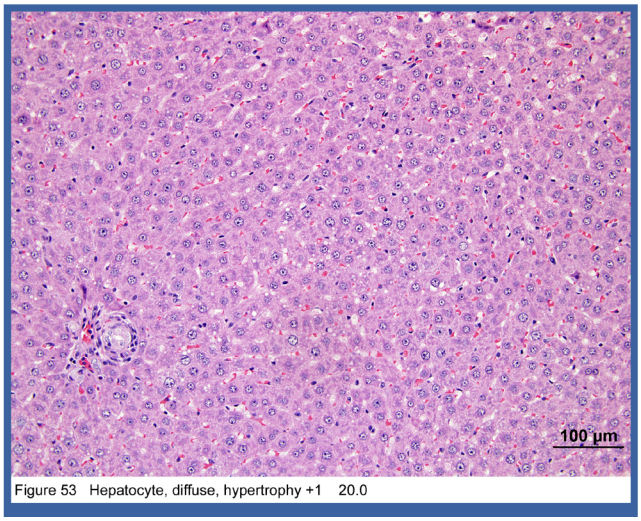

Figure 53 Hepatocyte, diffuse, hypertrophy +1 20.0

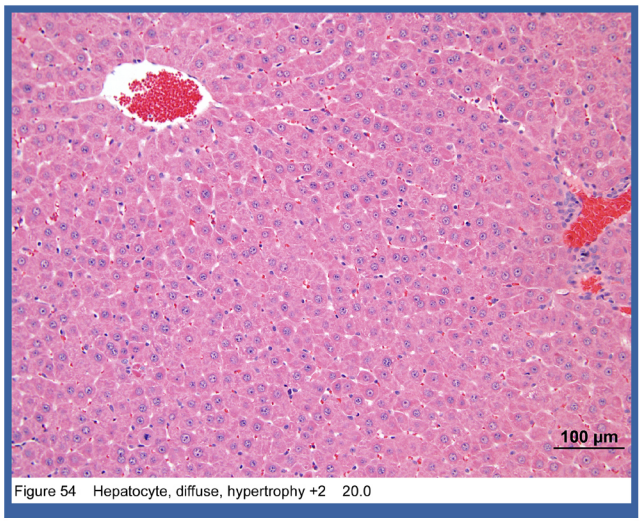

Figure 54 Hepatocyte, diffuse, hypertrophy +2 20.0

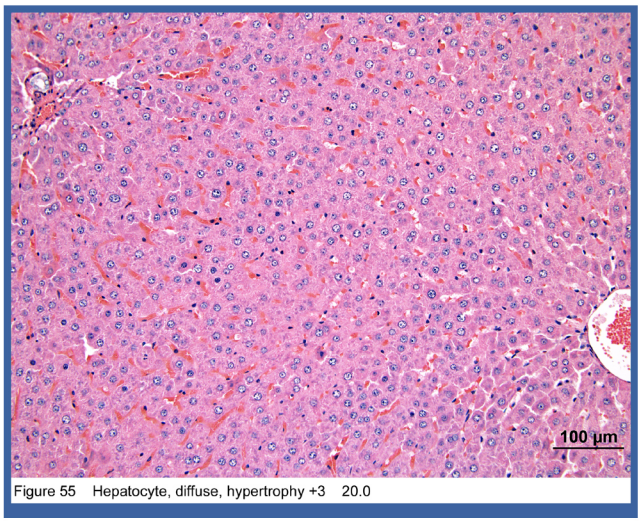

Figure 55 Hepatocyte, diffuse, hypertrophy +3 20.0

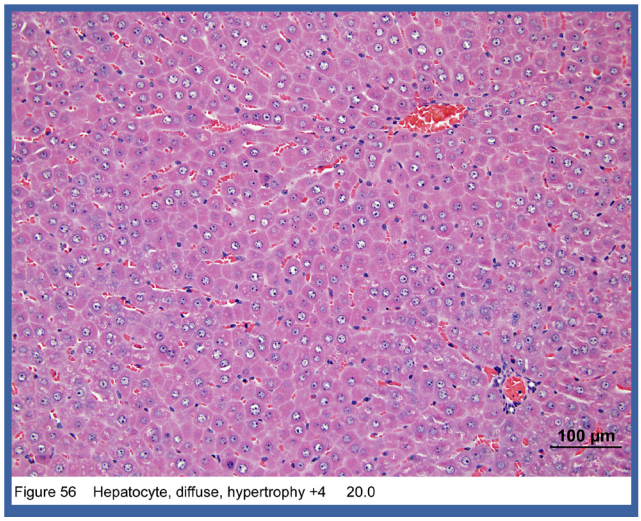

Figure 56 Hepatocyte, diffuse, hypertrophy +4 20.0

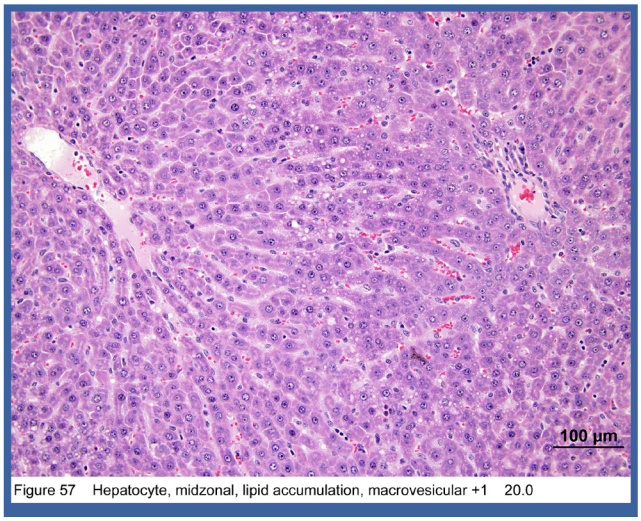

Figure 57 Hepatocyte, midzonal, lipid accumulation, macrovesicular +1 20.0

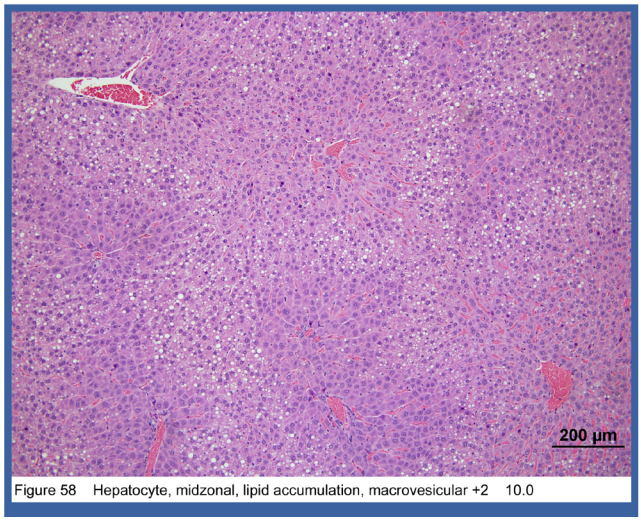

Figure 58 Hepatocyte, midzonal, lipid accumulation, macrovesicular +2 10.0

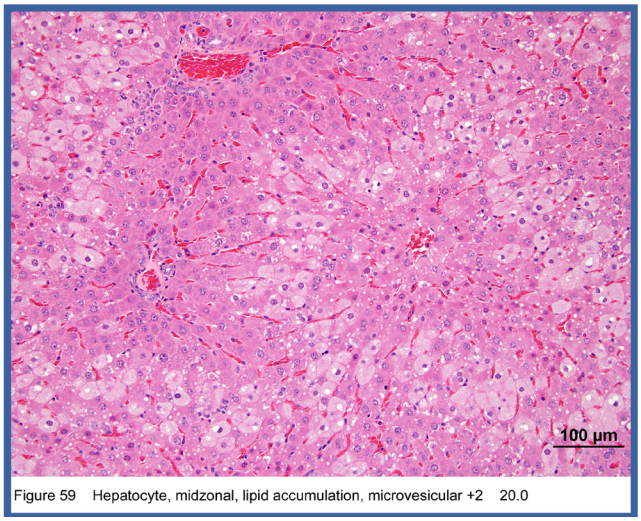

Figure 59 Hepatocyte, midzonal, lipid accumulation, microvesicular +2 20.0

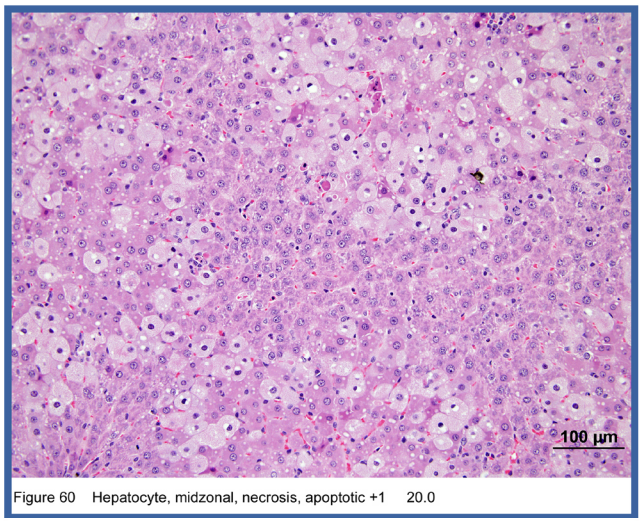

Figure 60 Hepatocyte, midzonal, necrosis, apoptotic +1 20.0

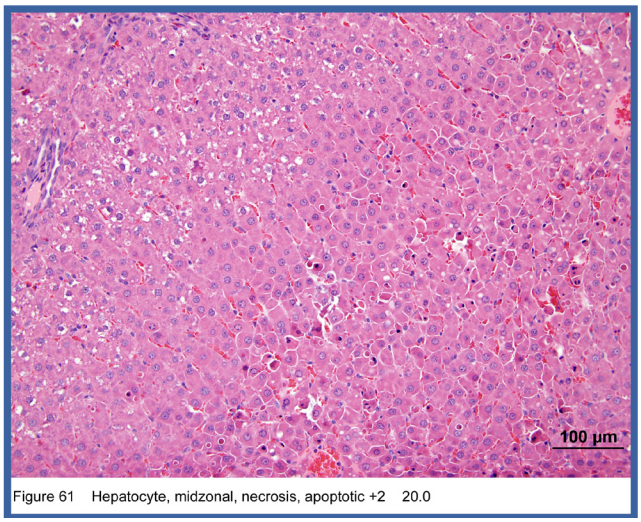

Figure 61 Hepatocyte, midzonal, necrosis, apoptotic +2 20.0

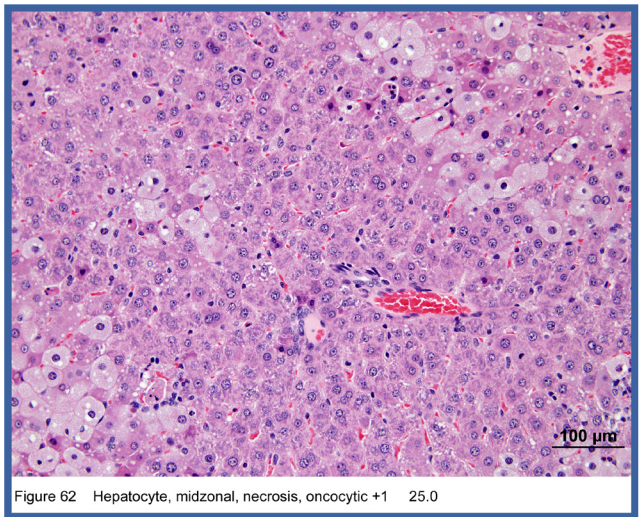

Figure 62 Hepatocyte, midzonal, necrosis, oncocytic +1 25.0

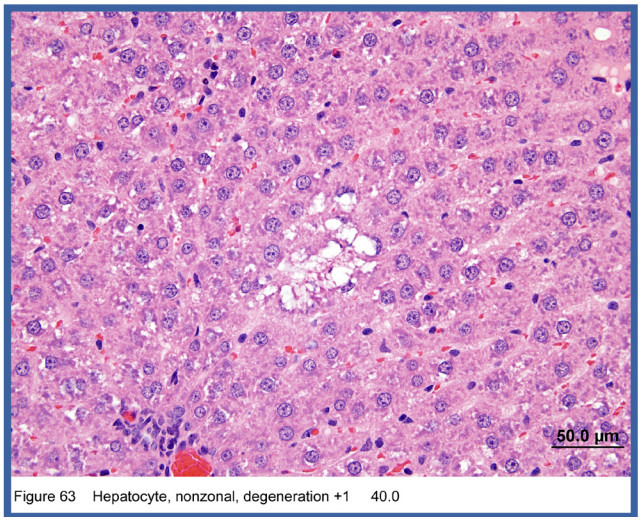

Figure 63 Hepatocyte, nonzonal, degeneration +1 40.0

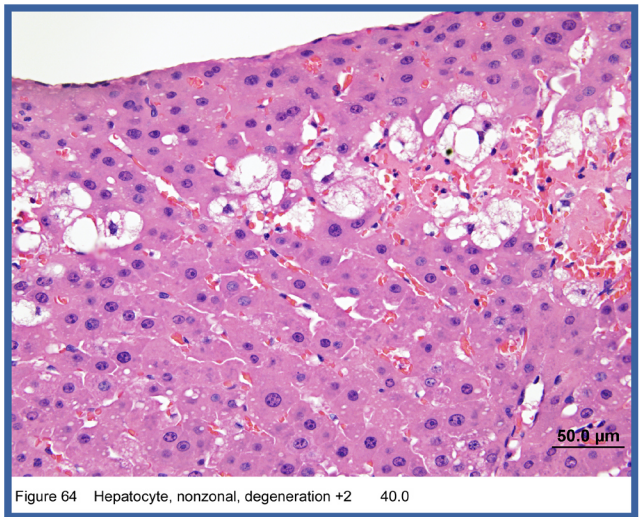

Figure 64 Hepatocyte, nonzonal, degeneration +2 40.0

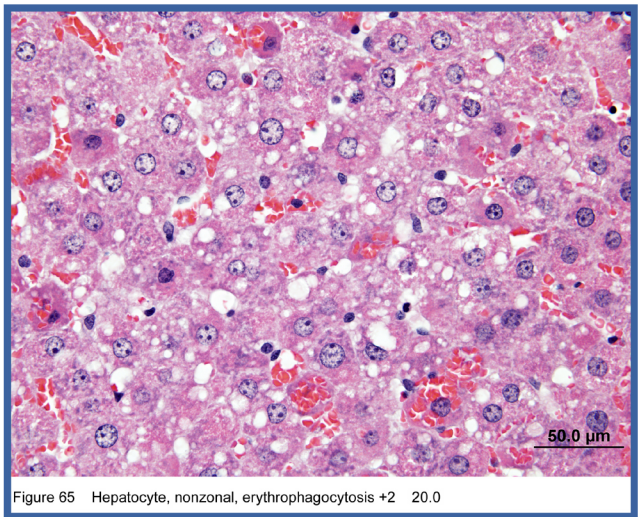

Figure 65 Hepatocyte, nonzonal, erythrophagocytosis +2 20.0

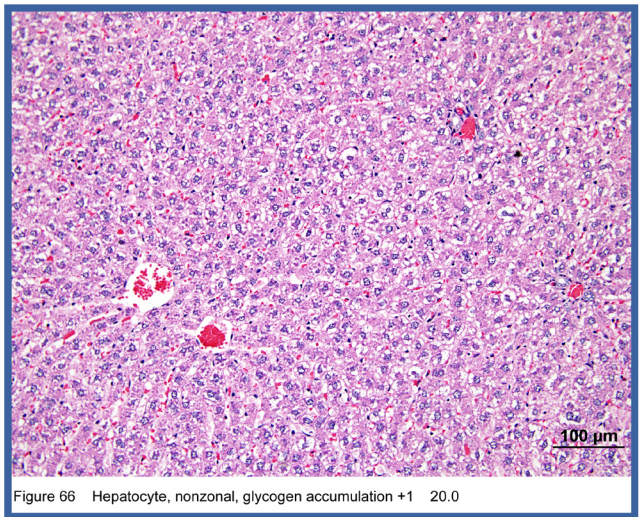

Figure 66 Hepatocyte, nonzonal, glycogen accumulation +1 20.0

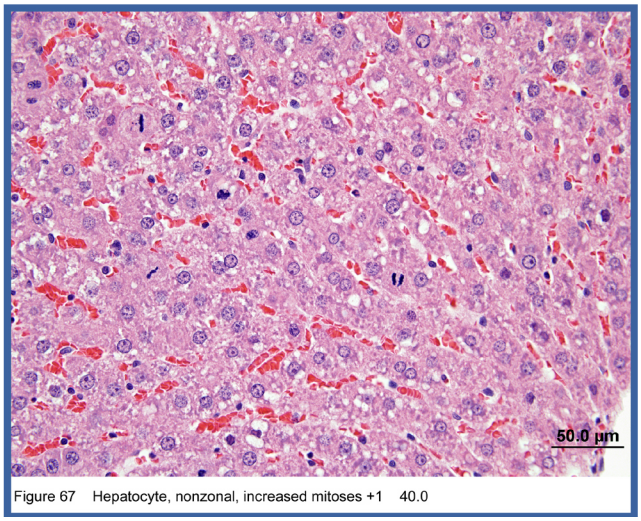

Figure 67 Hepatocyte, nonzonal, increased mitoses +1 40.0

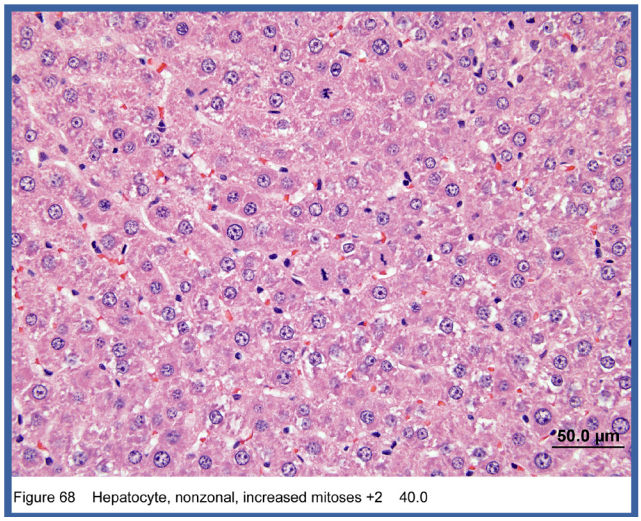

Figure 68 Hepatocyte, nonzonal, increased mitoses +2 40.0

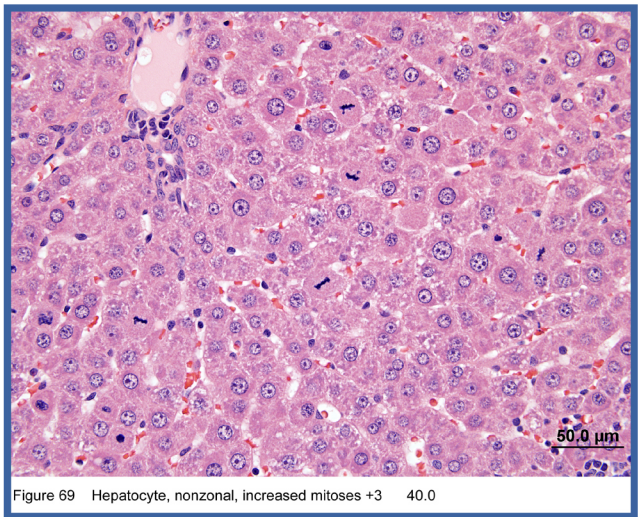

Figure 69 Hepatocyte, nonzonal, increased mitoses +3 40.0

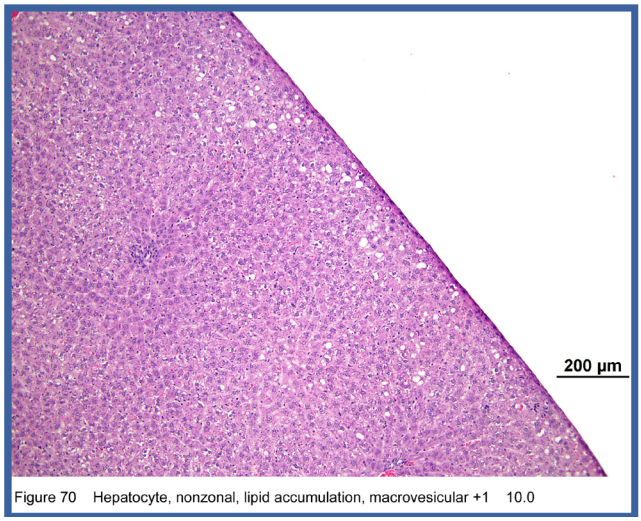

Figure 70 Hepatocyte, nonzonal, lipid accumulation, macrovesicular +1 10.0

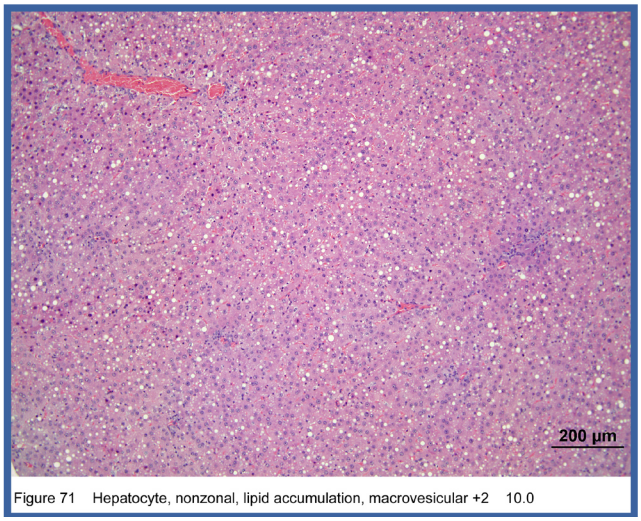

Figure 71 Hepatocyte, nonzonal, lipid accumulation, macrovesicular +2 10.0

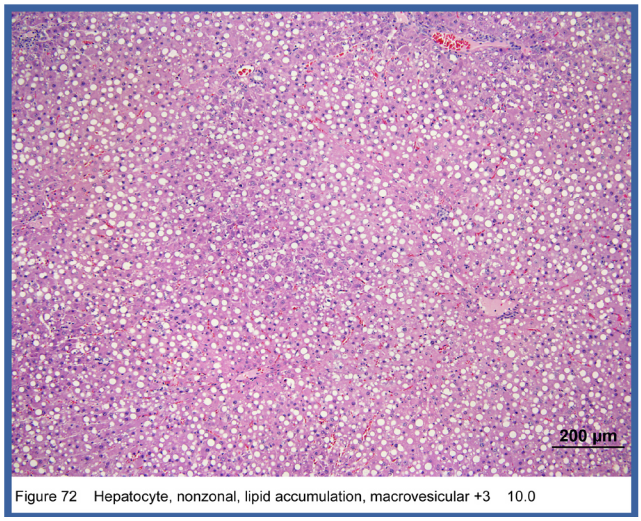

Figure 72 Hepatocyte, nonzonal, lipid accumulation, macrovesicular +3 10.0

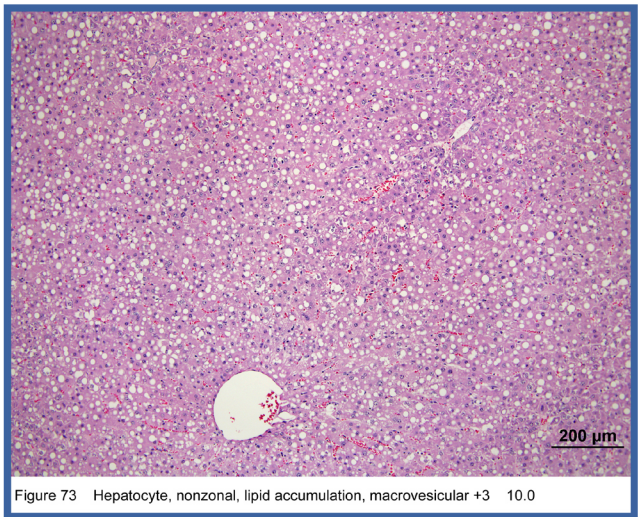

Figure 73 Hepatocyte, nonzonal, lipid accumulation, macrovesicular +3 10.0

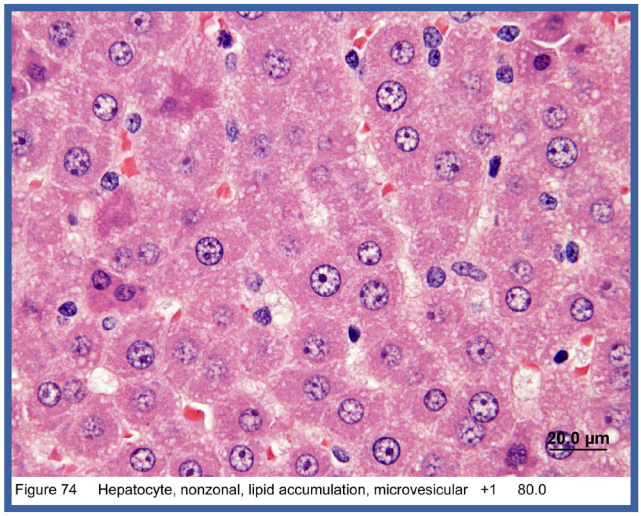

Figure 74 Hepatocyte, nonzonal, lipid accumulation, microvesicular +1 80.0

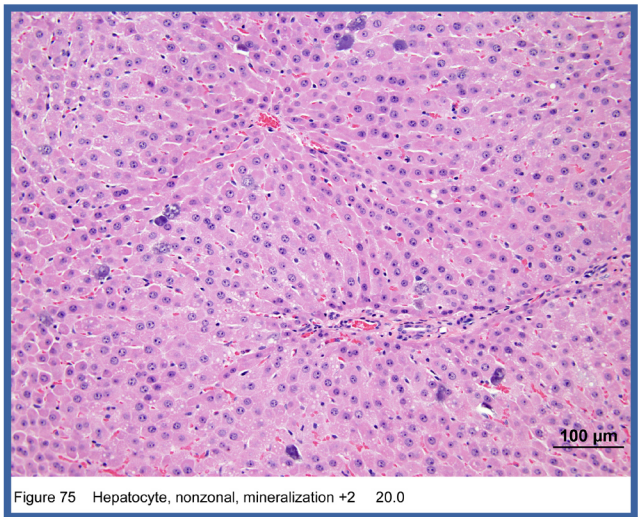

Figure 75 Hepatocyte, nonzonal, mineralization +2 20.0

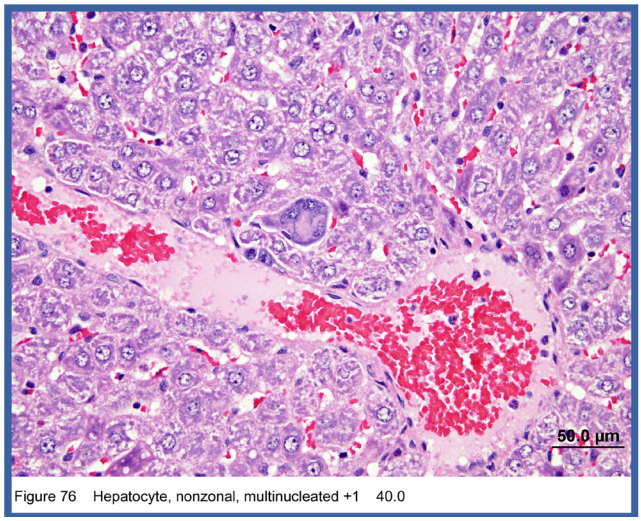

Figure 76 Hepatocyte, nonzonal, multinucleated +1 40.0

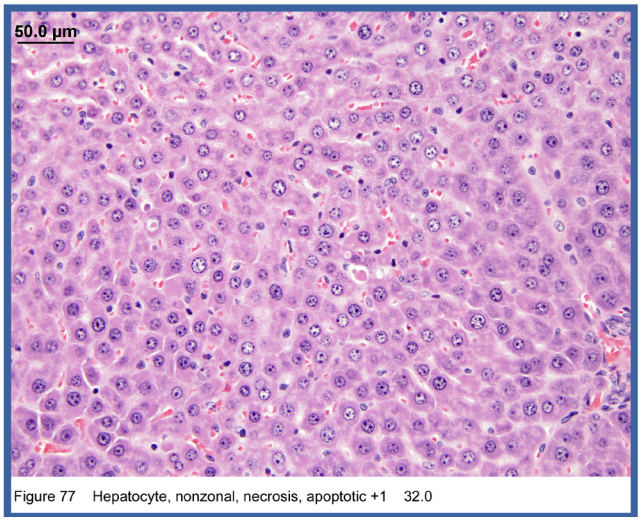

Figure 77 Hepatocyte, nonzonal, necrosis, apoptotic +1 32.0

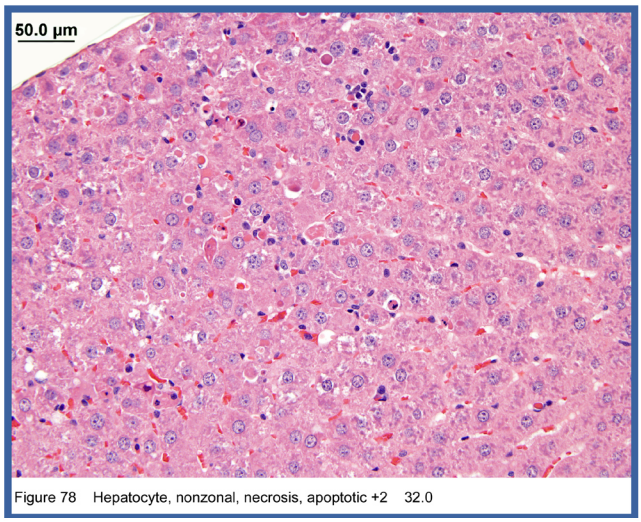

Figure 78 Hepatocyte, nonzonal, necrosis, apoptotic +2 32.0

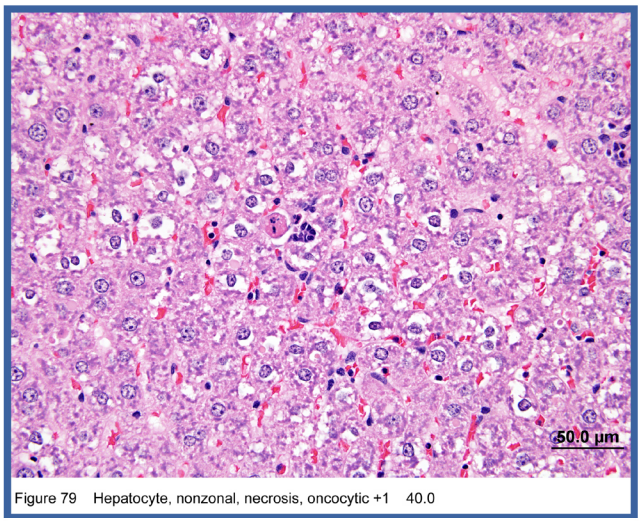

Figure 79 Hepatocyte, nonzonal, necrosis, oncocytic +1 40.0

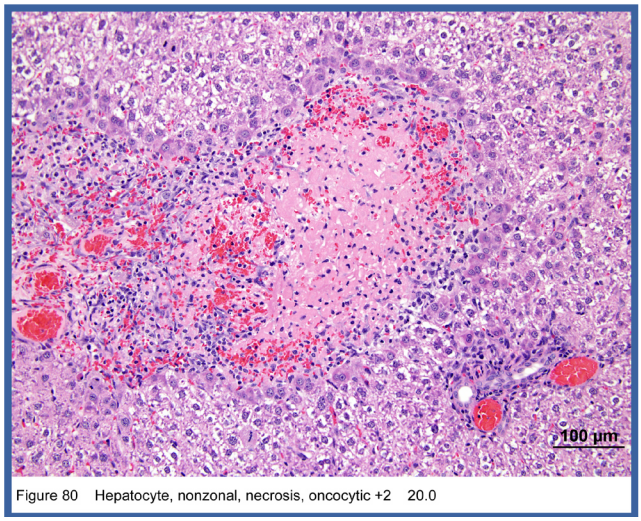

Figure 80 Hepatocyte, nonzonal, necrosis, oncocytic +2 20.0

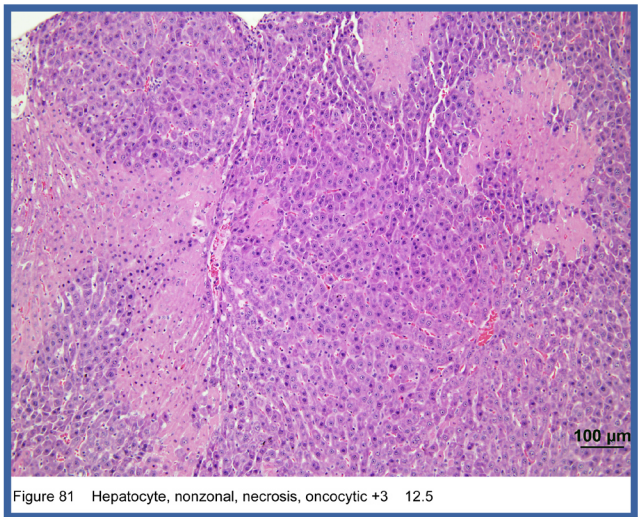

Figure 81 Hepatocyte, nonzonal, necrosis, oncocytic +3 12.5

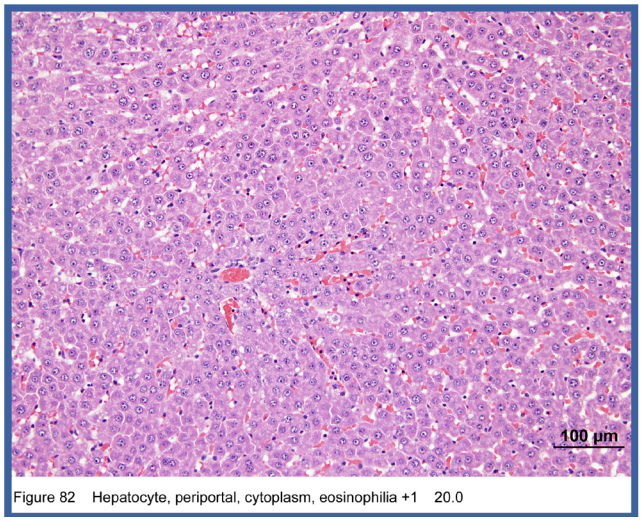

Figure 82 Hepatocyte, periportal, cytoplasm, eosinophilia +1 20.0

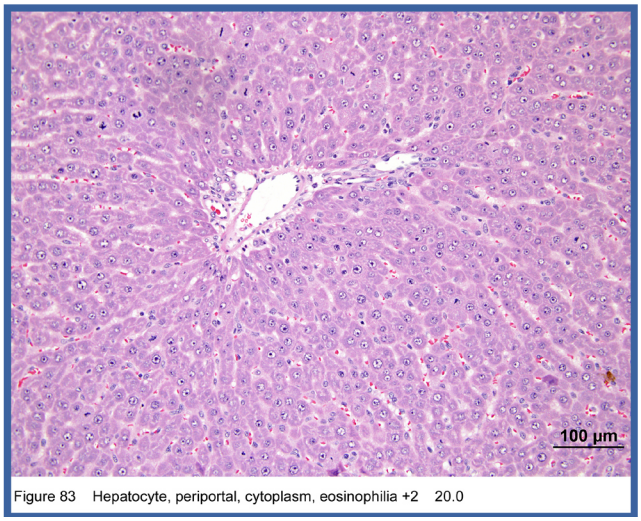

Figure 83 Hepatocyte, periportal, cytoplasm, eosinophilia +2 20.0

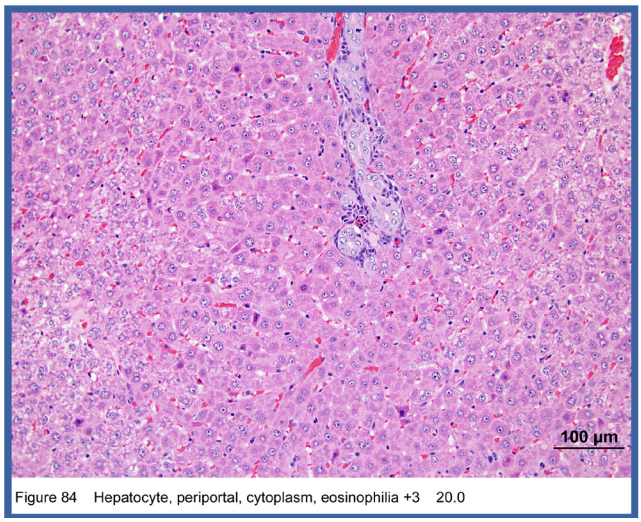

Figure 84 Hepatocyte, periportal, cytoplasm, eosinophilia +3 20.0

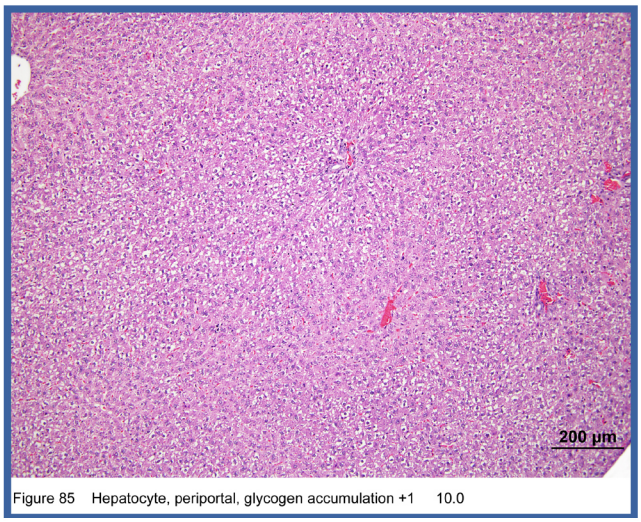

Figure 85 Hepatocyte, periportal, glycogen accumulation +1 10.0

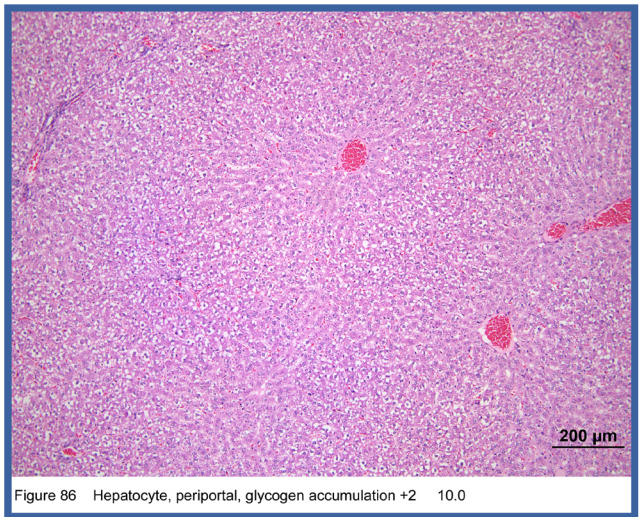

Figure 86 Hepatocyte, periportal, glycogen accumulation +2 10.0

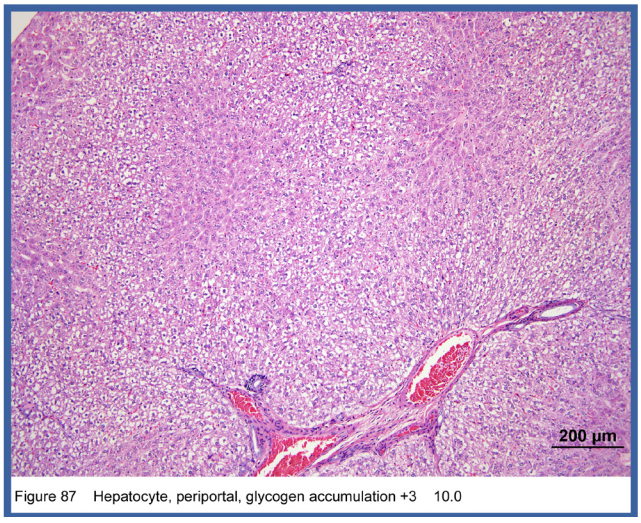

Figure 87 Hepatocyte, periportal, glycogen accumulation +3 10.0

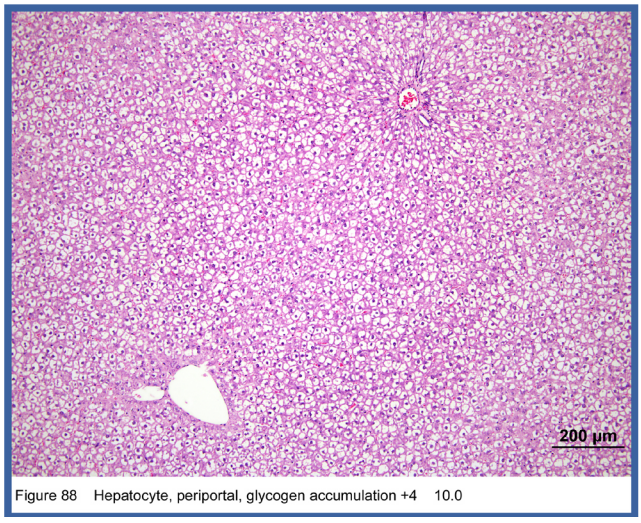

Figure 88 Hepatocyte, periportal, glycogen accumulation +4 10.0

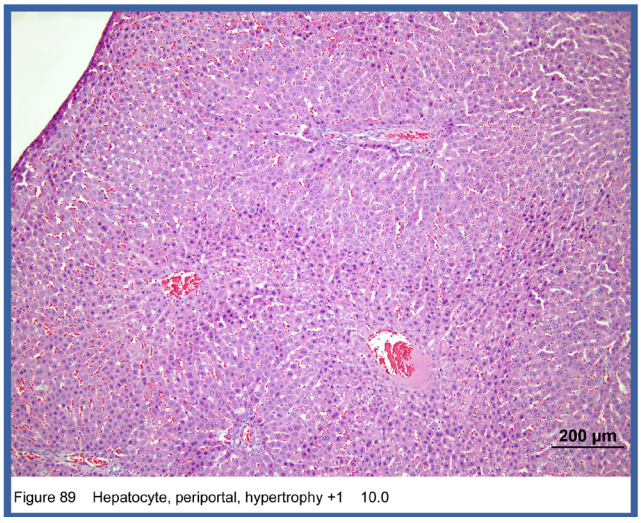

Figure 89 Hepatocyte, periportal, hypertrophy +1 10.0

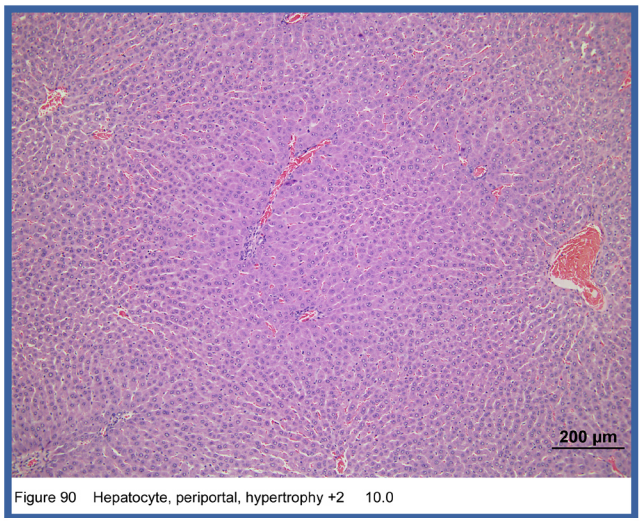

Figure 90 Hepatocyte, periportal, hypertrophy +2 10.0

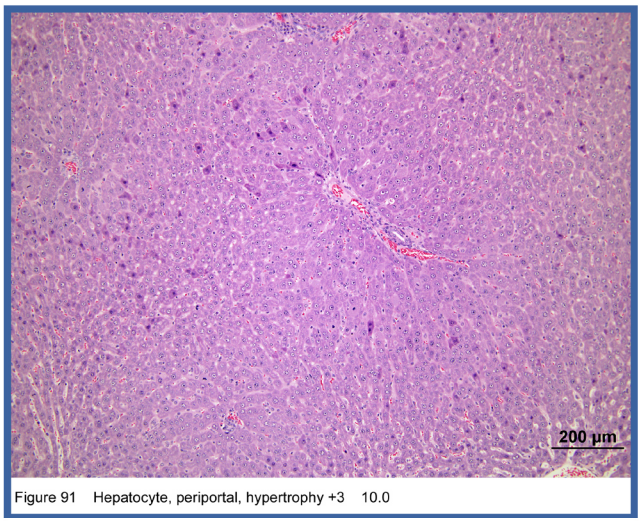

Figure 91 Hepatocyte, periportal, hypertrophy +3 10.0

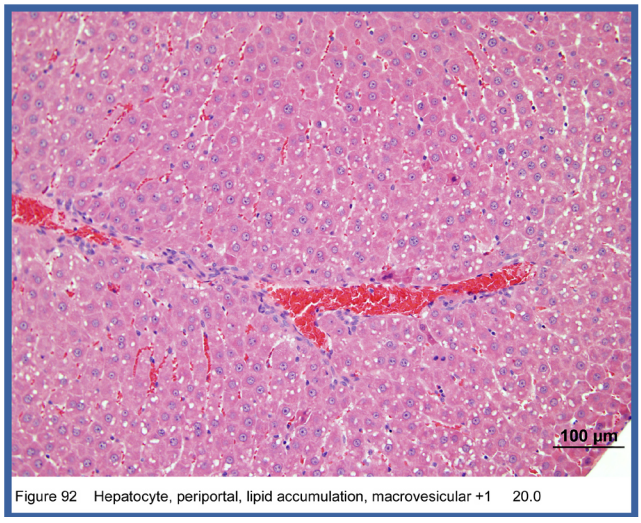

Figure 92 Hepatocyte, periportal, lipid accumulation, macrovesicular +1 20.0

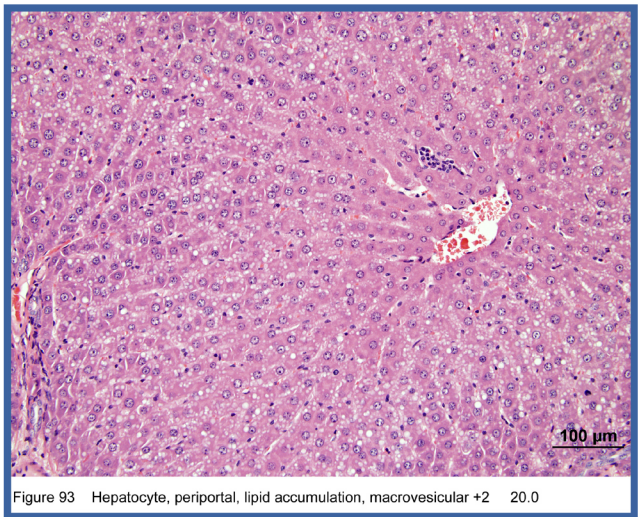

Figure 93 Hepatocyte, periportal, lipid accumulation, macrovesicular +2 20.0

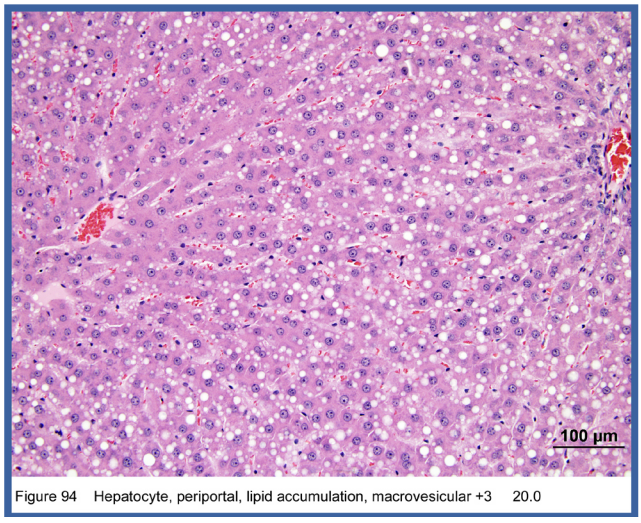

Figure 94 Hepatocyte, periportal, lipid accumulation, macrovesicular +3 20.0

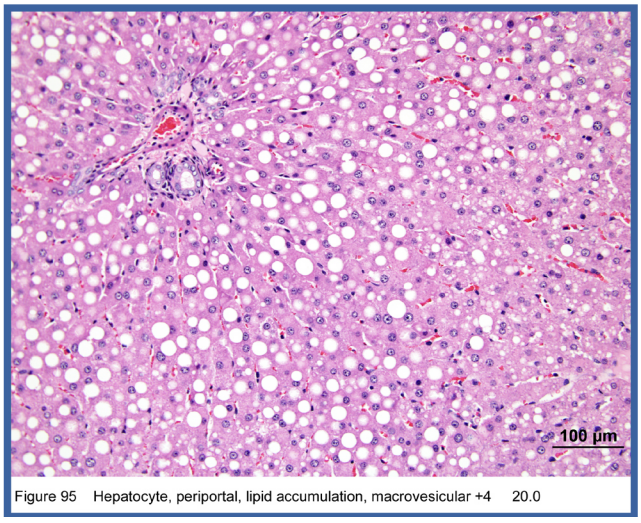

Figure 95 Hepatocyte, periportal, lipid accumulation, macrovesicular +4 20.0

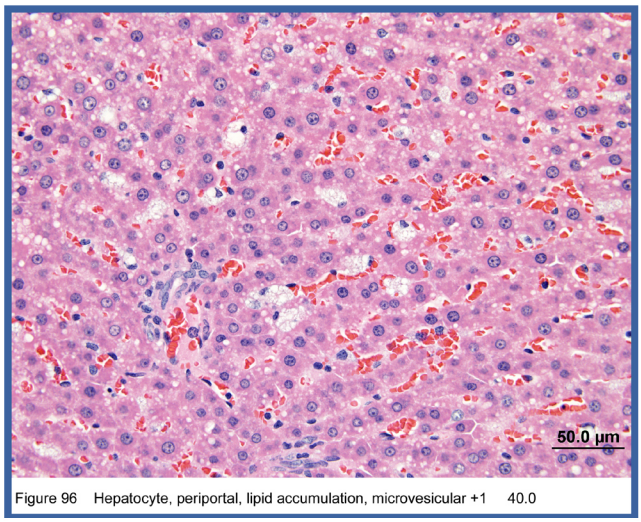

Figure 96 Hepatocyte, periportal, lipid accumulation, microvesicular +1 40.0

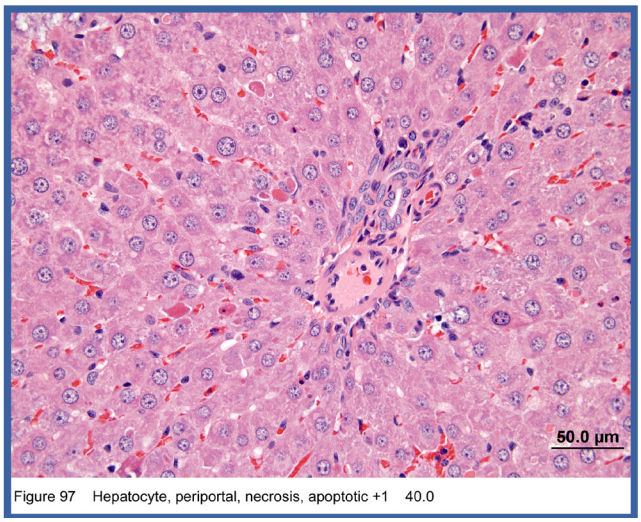

Figure 97 Hepatocyte, periportal, necrosis, apoptotic +1 40.0

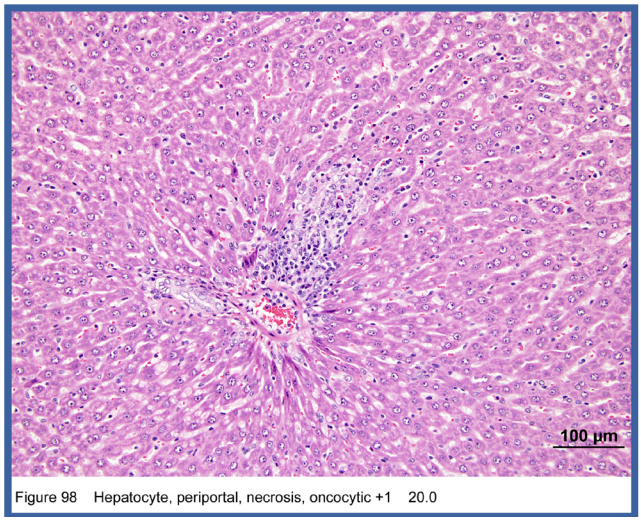

Figure 98 Hepatocyte, periportal, necrosis, oncocytic +1 20.0

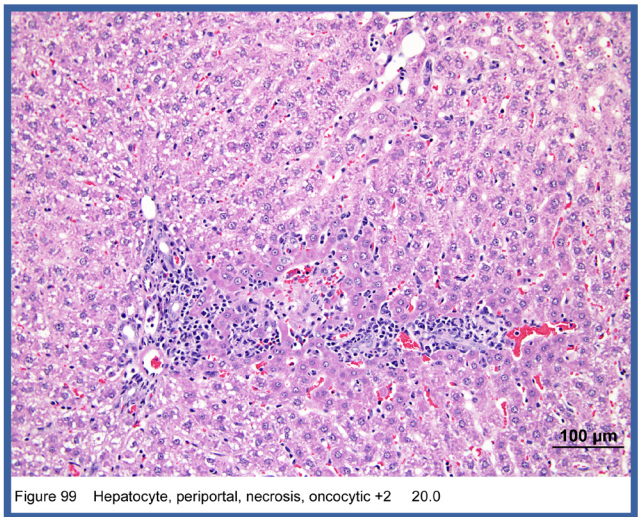

Figure 99 Hepatocyte, periportal, necrosis, oncocytic +2 20.0

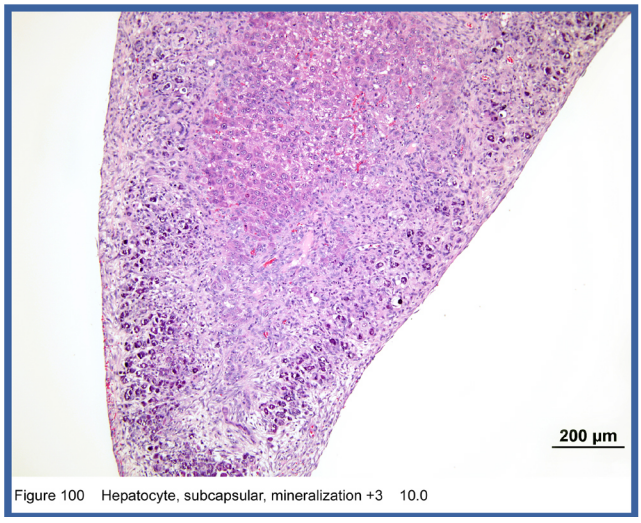

Figure 100 Hepatocyte, subcapsular, mineralization +3 10.0

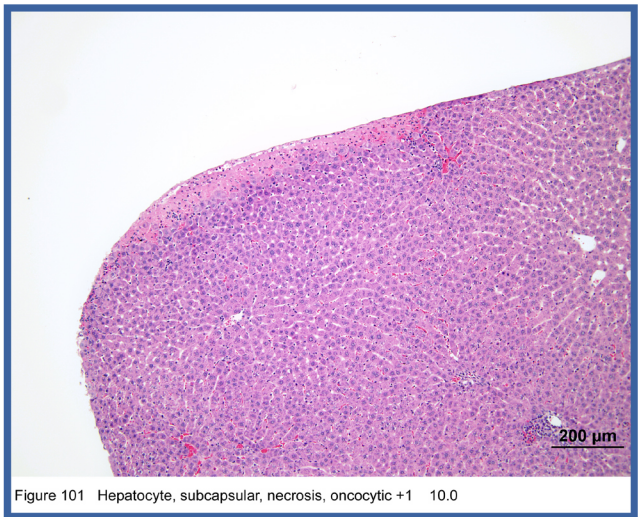

Figure 101 Hepatocyte, subcapsular, necrosis, oncocytic +1 10.0

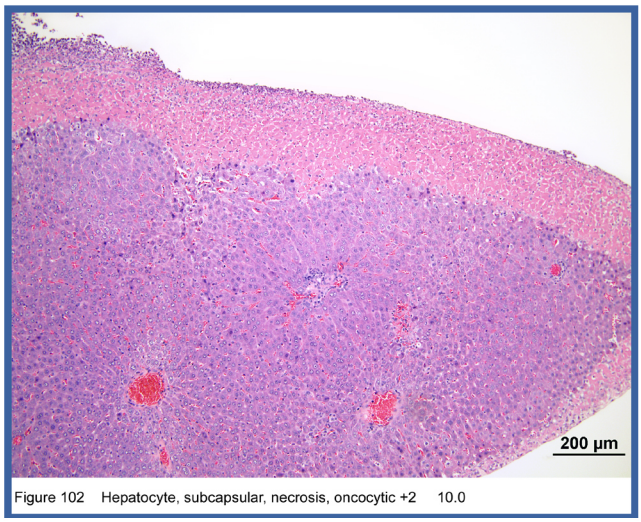

Figure 102 Hepatocyte, subcapsular, necrosis, oncocytic +2 10.0

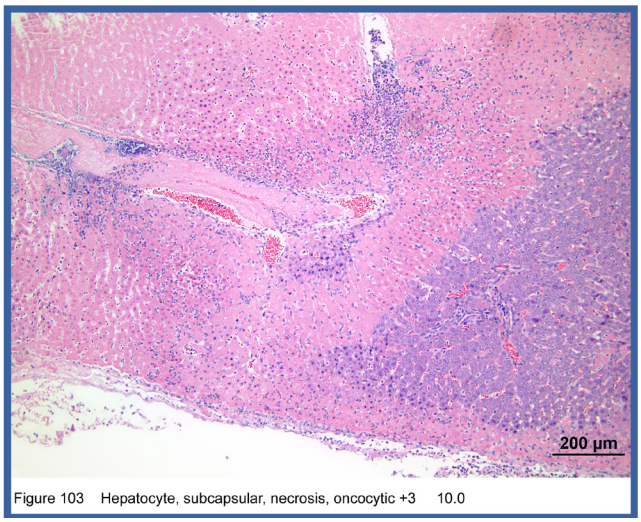

Figure 103 Hepatocyte, subcapsular, necrosis, oncocytic +3 10.0

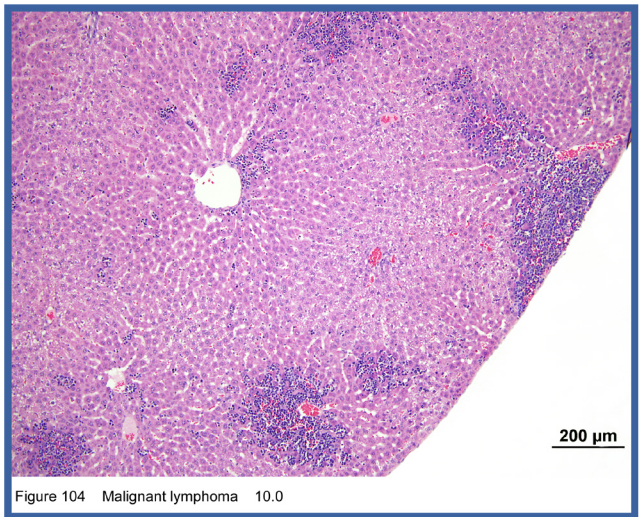

Figure 104 Malignant lymphoma 10.0

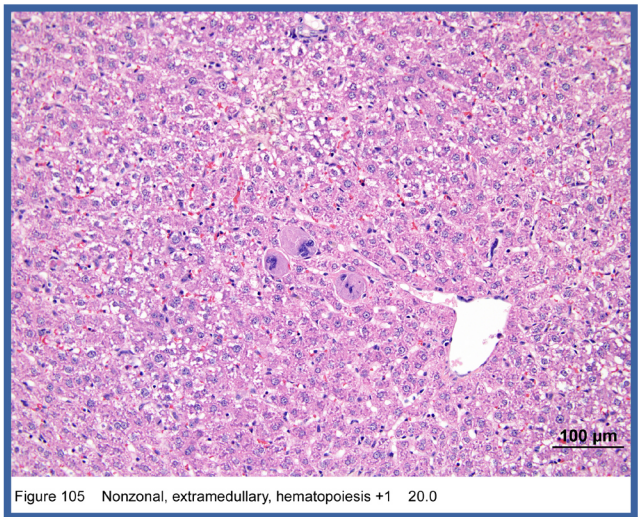

Figure 105 Nonzonal, extramedullary, hematopoiesis +1 20.0

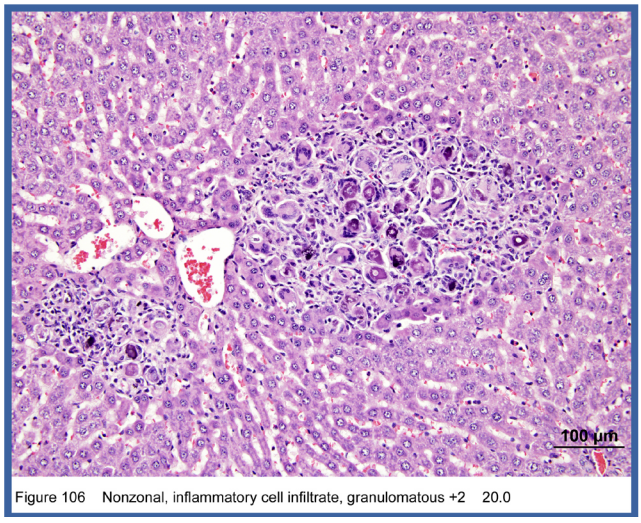

Figure 106 Nonzonal, inflammatory cell infiltrate, granulomatous +2 20.0

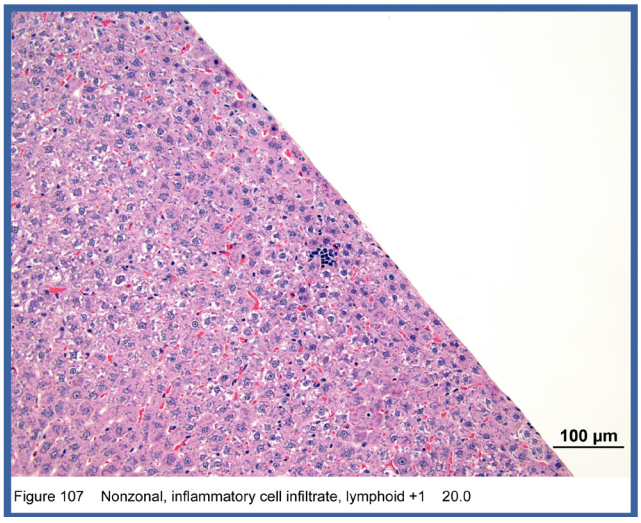

Figure 107 Nonzonal, inflammatory cell infiltrate, lymphoid +1 20.0

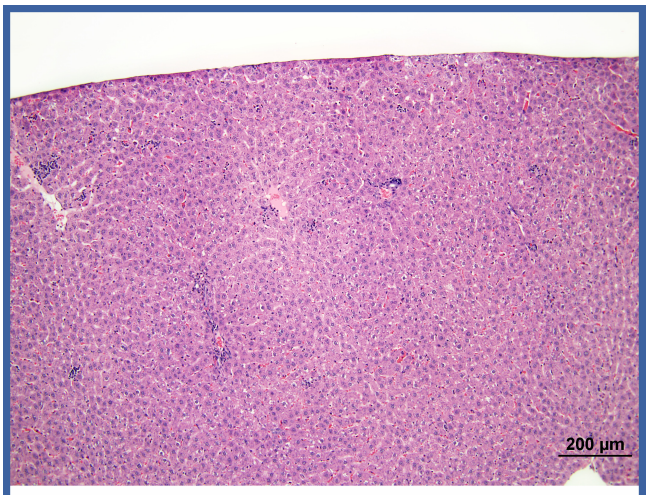

Figure 108 Nonzonal, inflammatory cell infiltrate, lymphoid +2 20.0

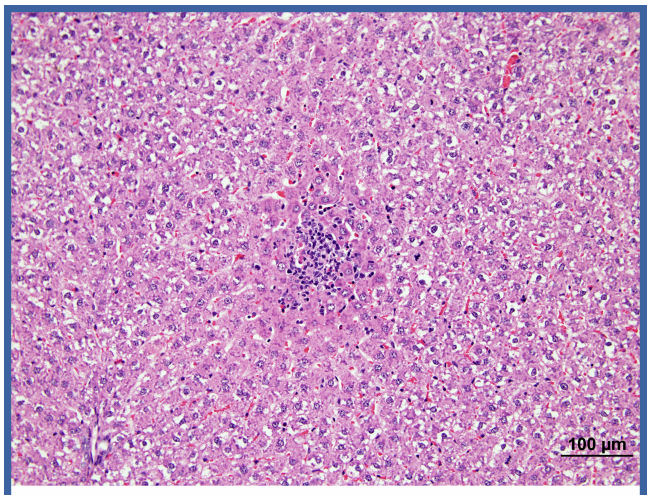

Figure 109 Nonzonal, inflammatory cell infiltrate, mixed cell +1 20.0

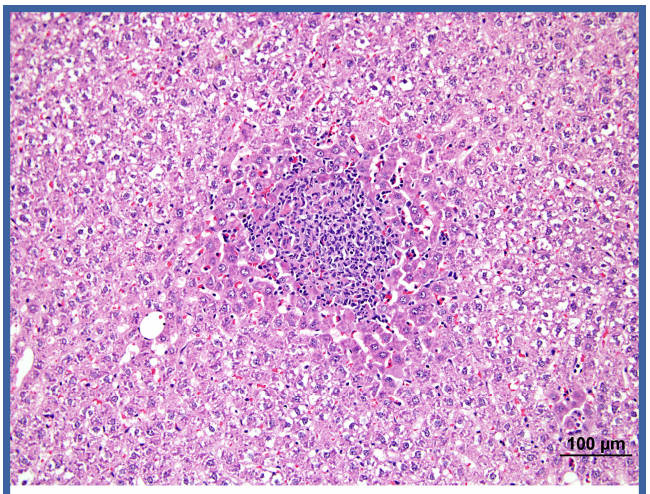

Figure 110 Nonzonal, inflammatory cell infiltrate, mixed cell +2 20.0

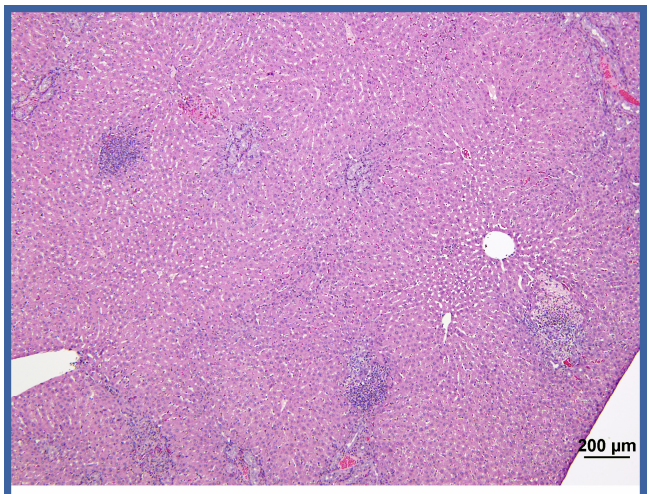

Figure 111 Nonzonal, inflammatory cell infiltrate, mixed cell +3 6.4

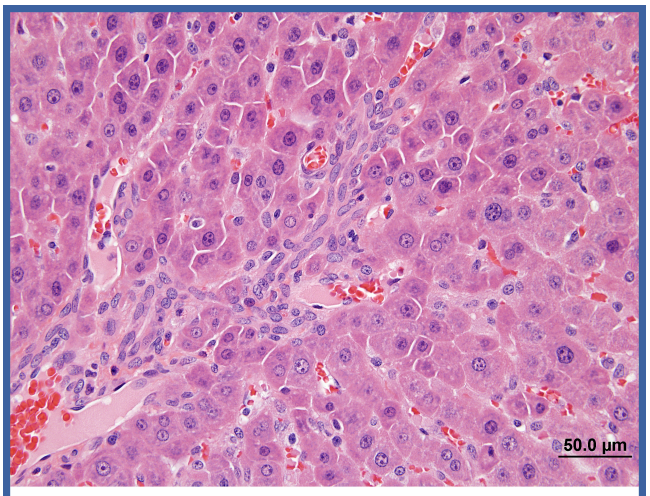

Figure 112 Oval cell, hyperplasia +1 40.0

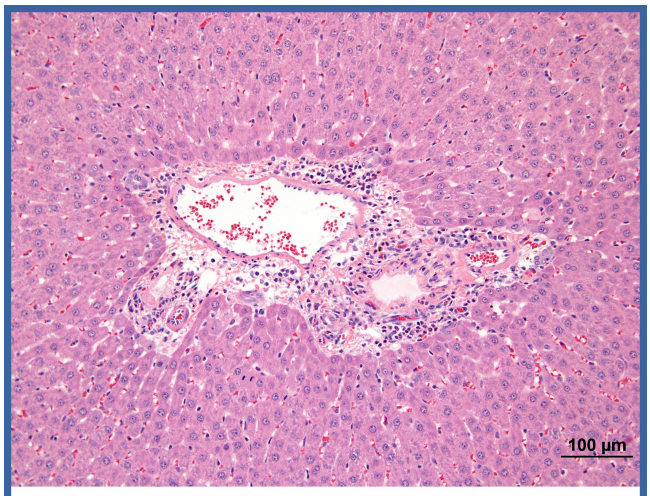

Figure 113 Periportal, edema +2 20.0

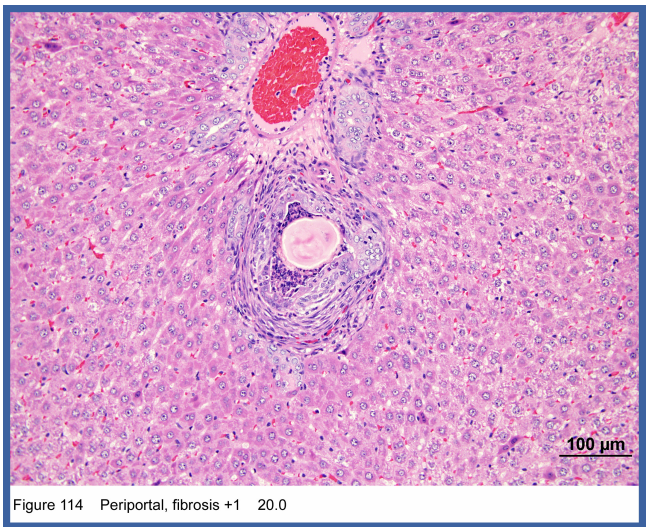

Figure 114 Periportal, fibrosis +1 20.0

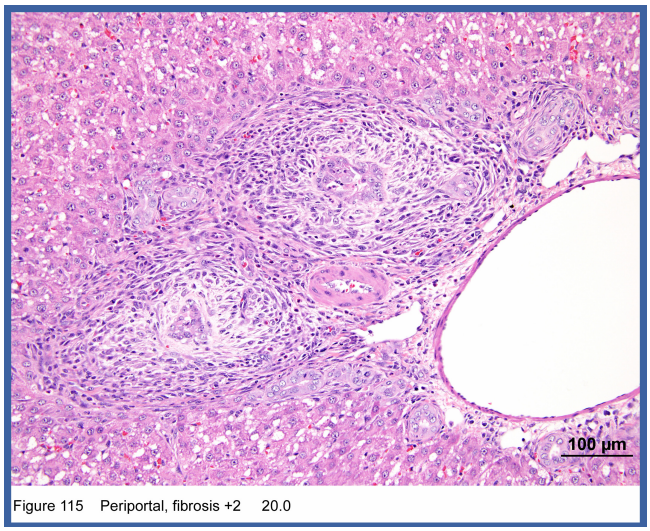

Figure 115 Periportal, fibrosis +2 20.0

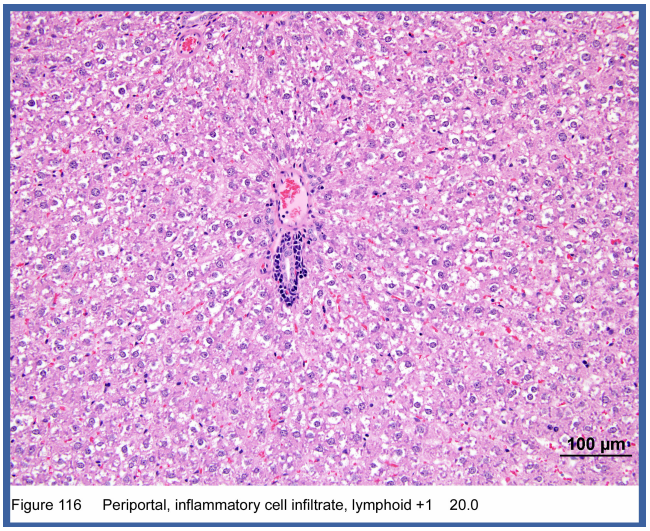

Figure 116 Periportal, inflammatory cell infiltrate, lymphoid +1 20.0

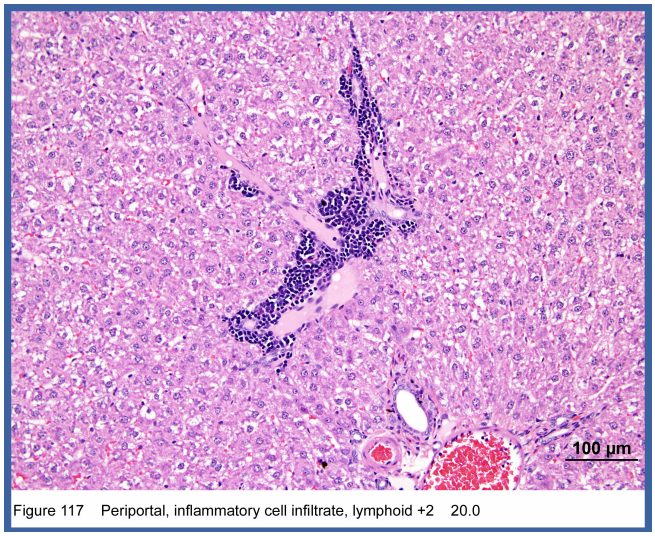

Figure 117 Periportal, inflammatory cell infiltrate, lymphoid +2 20.0

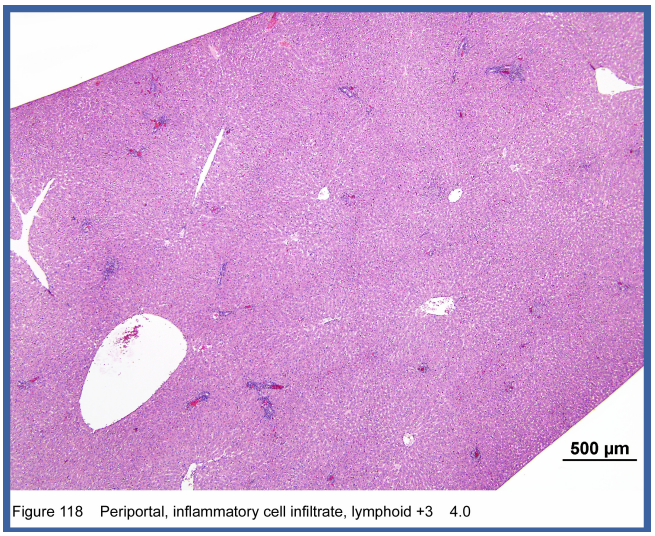

Figure 118 Periportal, inflammatory cell infiltrate, lymphoid +3 4.0

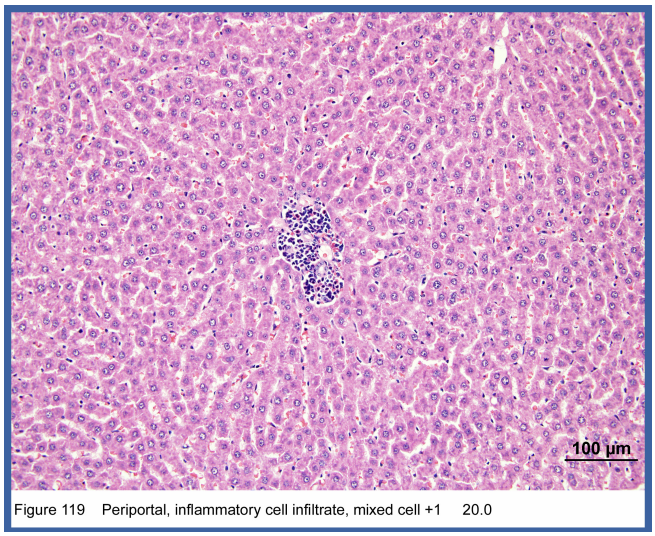

Figure 119 Periportal, inflammatory cell infiltrate, mixed cell +1 20.0

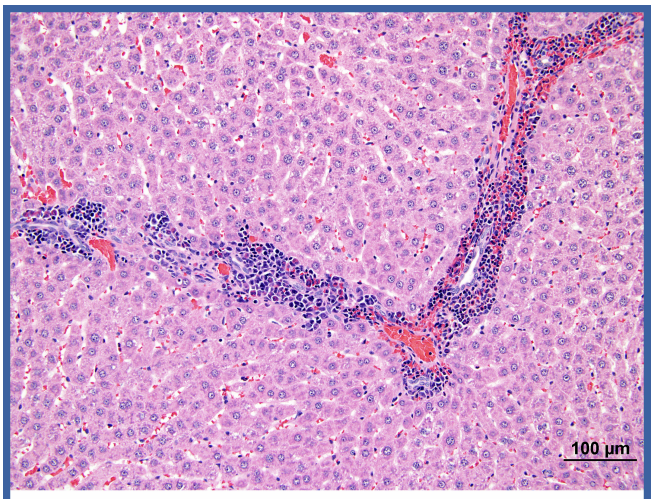

Figure 120 Periportal, inflammatory cell infiltrate, mixed cell +2 20.0

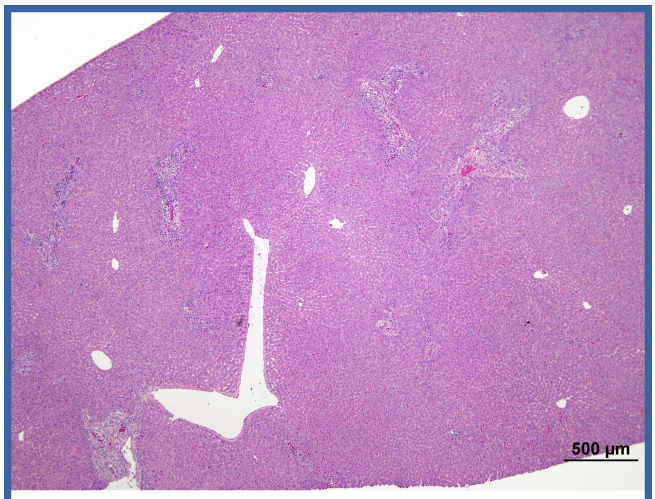

Figure 121a Periportal, inflammatory cell infiltrate, mixed cell +3 4.0

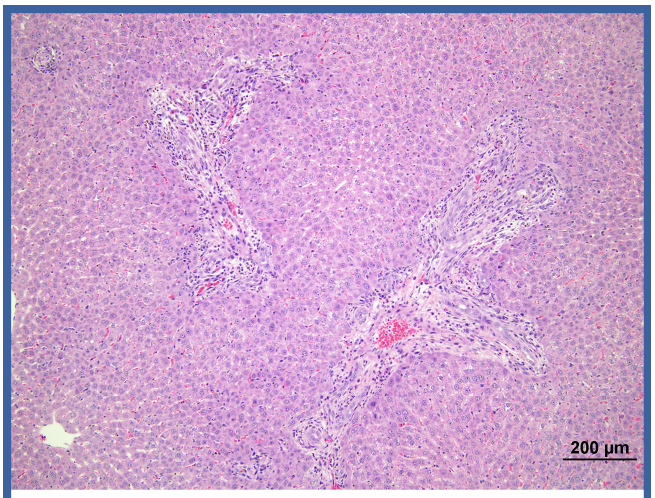

Figure 121b Periportal, inflammatory cell infiltrate, mixed cell +3 10.0

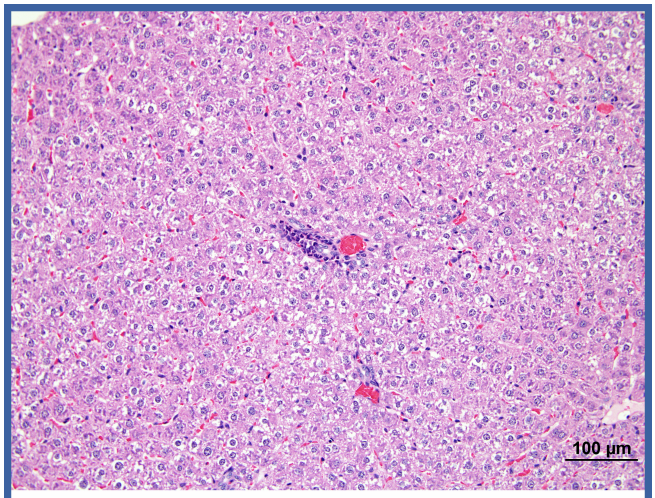

Figure 122 Periportal, inflammatory cell infiltrate, neutrophilic +1 20.0

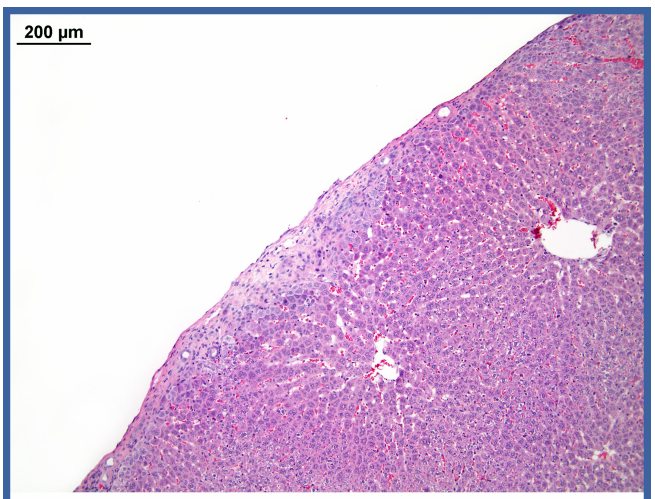

Figure 123 Subcapsular, fibrosis +1 10.0

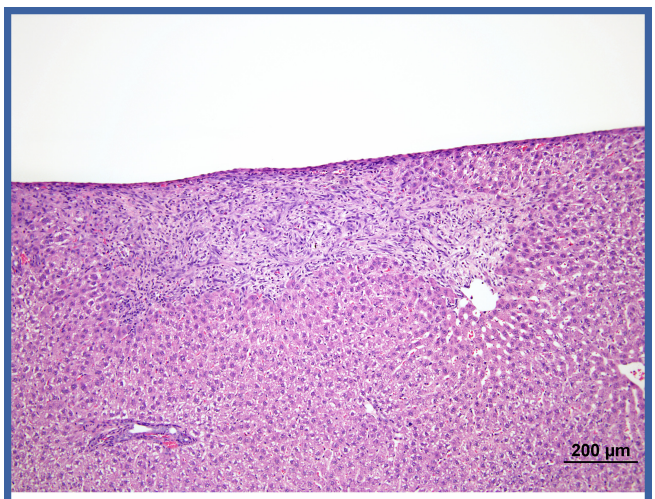

Figure 124 Subcapsular, fibrosis +2 10.0

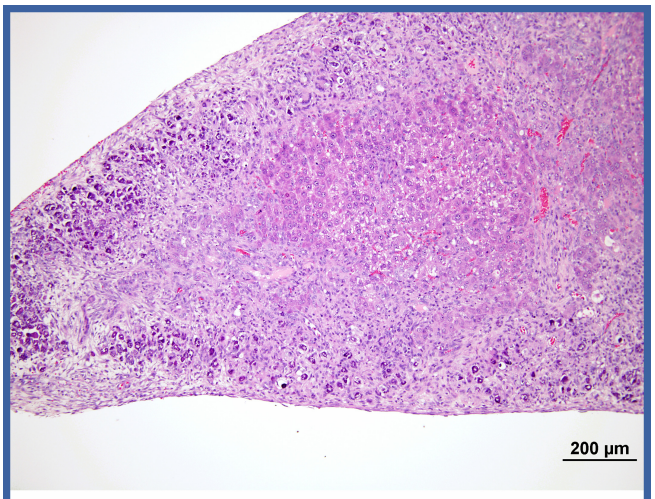

Figure 125 Subcapsular, fibrosis +3 10.0