Histopathology

The mouse liver is made up of a large number of hexagonal prisms, each representing an architectural unit or lobule. The liver lobule consists of a central vein from which cords or rows of cells radiate like spokes of a wheel. The liver tissue is made up of thousands of lobules which contain hepatic cells that are the basic metabolic cells of the liver. The liver has to perform certain important functions that include the breakdown of fats, production of urea, conversion of glucose derived from the food into glycogen, preparation of vital amino acids that are the building blocks of proteins.

In mouse liver the outlines of lobules are usually delineated by a connective tissue. Earlier reports state that metazoan parasitic infections not only alter the body physiology but also damage to the tissues like gastrointestinal tract, liver and other endocrine organs. The present investigations were aimed to understand the histopathological reactions in liver caused due to various doses (single and repeated) of infective, third stage, filariform larvae of *A. caninum*.

**In control group (a):** In normal (uninfected) mouse, the section of the liver showed large number of hepatic lobules. The hepatic lobule revealed numerous cords of hepatocytes radiating from the central vein to the periphery of the lobule. The hepatocytes are separated by narrow sinusoids as seen in liver sections. Hepatic cells are arranged concentrically around the central vein. The large hepatocytes have more or less centrally situated one large round nucleus and homogenous cytoplasm (*Plate 1, Fig.1-a*).

The tissue response of the mouse liver to infection with single doses of 500 (group A), 1000 (group B) and 2000 (group C) were studied.
500 dose (group A) (Plate 1)

Day 1 of infection (Fig. 1-A1): A clear pathological changes of infection with infective 500 dose of *A. caninum* was evident at day 1 of infection. T.S. of liver showed mild histopathological changes. Increase in sinusoidal spaces, hyalinisation of hepatocytes and dilation of central vein were observed. Hepatocytes showed distinct nuclei and cytoplasm.

Day 4 of infection (Fig. 1-A2): The normal arrangement of hepatocytes is slightly disturbed because of the congestion of blood vessels. Few liver cells damaged at certain places and showing vacuole degeneration. Heavy vacuolisation, hypertrophy and hyalinisation of hepatocytes were found. Hepatic cells lost their integrity and showed necrosis and infiltration. Central vein showed dilation and mild infiltration of cells.

Day 9 of infection (Fig. 1-A3): The first sign of pathological reaction is the cloudy appearance of the hepatic cells. Heavy necrosis of hepatic cells, hypertrophy, and loss of radial arrangement of hepatocytes, pycnotic nuclei and dilation of central vein with mild infiltration of cells were observed.

Day 16 of infection (Fig. 1-A4): The major pathological changes include loss of radial arrangement of hepatic cells. Hypertrophy, vacuolisation and pycnotic nuclei were evident. At certain places the presence of bi-nucleated hepatocytes were seen probably due to the increased rate of death of hepatocytes.

Day 30 of infection (Fig. 1-A5): On day 30 of infection the liver histological section showed complete atrophy and disorganisation of hepatocytes. Dilated central vein showed heavy infiltration of cells. Necrosis and heavy vacuolisation were observed.
1000 dose (group B) (Plate-2)

**Day 1 of infection (Fig. 2-B1):** A distinct pathological alteration of infection with infective 1000 dose of *A. caninum* was seen at day 1 of infection. Liver section showed mild histopathological changes. Central vein is dilated and showing cell infiltration. Increase in spaces among the sinusoids is observed. Vacuolisation is prominent.

**Day 4 of infection (Fig. 2-B2):** The normal liver cells lost their integrity. Central vein is dilated. Central veins are separated by wide scars at certain places. The hepatocytes lost their original shape (rounded or spherical).

**Day 9 of infection (Fig. 2-B3):** The prominent pathological observation in this group is necrosis of hepatocytes and the infiltration of inflammatory cells in the focal area. A high lesion is seen. Vacuolisation is evident.

**Day 16 of infection (Fig. 2-B4):** The first sign of pathological reaction is the dilated central vein and sinusoids. Highly infiltrated cells are accumulated near the dilated central vein.

**Day 30 of infection (Fig. 2-B5):** On the final day (30th day) of infection the liver histological sections showed dilated central vein and dilated sinusoids. Necrotised hepatocytes are clearly seen.

**2000 dose (group C) (Plate–3):**

**Day 1 of infection (Fig. 3-C1):** The histopathological changes in the liver tissue are evident from day 1 of infection. There was an increase in the lumen of veins and their
increase might have brought a change in the hepatic cellular arrangement. Hypertrophy and hyalinisation of hepatocytes are prominent. Dilated spaces of sinusoids are distinct.

**Day 4 of infection (Fig. 3-C2):** On histological examination of liver, the pathological symptoms include the appearance of hepatocytes undergoing necrosis. Pycnotic nuclei in some hepatocytes (at certain places) are prominent. Liver was atrophied. Vacuolization, hypertrophy and cellular infiltration are seen.

**Day 9 of infection (Fig. 3-C3):** The microscopic signs were associated with several histological changes. The major change includes loss of original shape of hepatocytes along with nuclei. Pycnotic nuclei in some hepatocytes at certain places are evident. Moderately dilated sinusoids and central vein are seen.

**Day 16 of infection (Fig. 3-C4):** The clinical signs of the liver are observed histopathologically and found that the hepatocytes are mildly infiltrated. Vacuolization and pycnotic nuclei are seen. Central vein is highly dilated and occupied by cell debris. Heavy necrosis of hepatocytes is prominent.

**Day 30 of infection (Fig. 3-C5):** Liver histopathological section showed prominent pathological aberrations. The normal arrangement of hepatic cells is disturbed. Hepatocytes lost their texture. Vacuolization and dilation of central veins are distinct. Sinusoids and central vein are moderately occupied by cell debris. Moderate infiltration of cells near the dilated central vein is clearly evident.
125+125+250 dose (group D) (Plate-4):

Day 1 of infection (Fig. 4-D1): A distinct or microscopic signs of infiltration with *A. caninum* larvae were evident in liver tissue. Disturbance is there in the arrangement of hepatic cords. Cellular integrity of hepatocytes and also mild dilation of sinusoids and central vein besides hemorrhagic conditions are observed.

Day 4 of infection (Fig. 4-D2): A clear histopathological change of infection with repeated dose (125+125+250) of *A. caninum* larvae was evident at day 4 of infection. T.S. of liver showed sequestration of cell debris and infiltrated cells at certain places. Dilated sinusoids and hypertrophic hepatocytes are observed.

Day 9 of infection (Fig. 4-D3): On day 9 of infection, histological sections of liver showed highly dilated central vein. Mild vacuolisation is seen. Accumulation of infiltrated cells near the dilated central vein is prominent. Hepatocytes lost their texture.

Day 16 of infection (Fig. 4-D4): The histopathological reactions in the mouse liver, which received repeated dose (125+125+250), showed loss of texture of hepatocytes, dilation of central vein and sinusoids. Hypertrophy of hepatocytes was seen; liver necrosis and heavy vacuolisation were observed.

Day 30 of infection (Fig. 4-D5): Over the period from 1 to 30 days of infection, clinical signs developed most notably in infected liver. The major changes include distortion and necrosis of hepatocytes. Appearance of two nuclei in some hepatocytes at certain places is observed. Heavy infiltration of hepatocytes is evident.
250+250+500 dose (group E) (Plate 5):

Day 1 of infection (Fig. 5-E1): The liver histology revealed diffusely scattered cell infiltration in the lobule especially in the perivenular area. Lymphocytes are predominant among neutrophils, eosinophills and plasma cells.

Day 4 of infection (Fig. 5-E2): The major pathological changes include dilated central vein and sinusoids. Moderate infiltration is evident. Vacuolisation and hyalinisation of hepatocytes and appearance of pycnotic nuclei are seen.

Day 9 of infection (Fig. 5-E3): A prominent pathological changes of infection like increase of sinusoidal spaces and mild infiltration. T.S. of liver showed mild form of central fibrosis and deposition of fine collagen fibres in the sinusoids.

Day 16 of infection (Fig. 5-E4): T.S. of liver showed heavy necrosis accompanied by inflammatory reaction. Vacuolisation and heavy dilation of sinusoids and central vein is evident. The dilated central vein is occupied by cell debris.

Day 30 of infection (Fig. 5-E5): Over the period from day 1 to 30 of infection, clinical signs developed prominently in infected liver. The entire lumen of central vein is occupied by debris. Central vein is dilated. Loss of texture of hepatocytes is clearly seen. Vacuolisation and infiltration of cells are seen.
500+500+1000 dose (group F) (Plate 6):

**Day 1 of infection (Fig. 6-F1):** Major histopathological findings are noticed. There was dilation and an increase in the lumen of central veins and sinusoids. Dilated central vein is occupied by cell debris.

**Day 4 of infection (Fig. 6-F2):** A distinct pathological change is evident at day 4 of infection. Moderate infiltration, hypertrophic hepatocytes and dilated central vein are observed. The lumen of the central vein is occupied by cell debris and few infiltrated cells.

**Day 9 of infection (Fig. 6-F3):** The T.S. of infected mouse liver showed the presence of scars among sinusoids. Dilation of central vein, moderate infiltration in hepatocytes and vacuolization are evident.

**Day 16 of infection (Fig. 6-F4):** A clear microscopic sign of infection in liver tissue is the congestion of sinusoids and the presence of collagen fibres in hypertrophied hepatocytes. Vacuolisation and hyalinisation of hepatocytes, dilation of central vein and heavy infiltration of central vein are seen.

**Day 30 of infection (Fig. 6-F5):** On day 30 of infection the liver histopathological sections showed complete atrophy. Dilation of central vein and sinusoids is seen. Heavy infiltration of cells is evident. Lumen of central vein is occupied by cell debris. Vacuolisation is clearly seen.

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