Figure Legend: Figure 1 Bone marrow in a female F344/N rat from a chronic study. Increased numbers of pale-staining vacuolated histiocytes (arrows) can be seen among the hematopoietic cells. Figure 2 Bone marrow in a female F344/N rat from a chronic study. Increased numbers of pale-staining vacuolated histiocytes can be seen among the hematopoietic cells. Figure 3 Bone marrow in a female F344/N rat from a chronic study. Increased numbers of pale-staining vacuolated histiocytes containing cholesterol crystals can be seen among the hematopoietic cells. Figure 4 Bone marrow in a female F344/N rat from a chronic study. Increased numbers of pale-staining vacuolated histiocytes can be seen among the hematopoietic cells.
Comment: Histiocytic infiltration is defined as an increase in the numbers of macrophages or histiocytes in the bone marrow. These macrophages may be vacuolated and/or contain variable amounts of cellular debris, cholesterol clefts, or pigment (e.g., hemosiderin) and are usually found in ill-defined, unorganized aggregates (Figures 1–4). Use of the term “histiocytic infiltration” is reserved for those instances when macrophage infiltration is present without other evidence of inflammation. The presence of (a) epithelioid or multinucleated macrophages, which may form organized aggregates (granulomas), (b) other inflammatory cells in the area, or (c) vascular changes, such as edema, warrants a diagnosis of granulomatous inflammation.

Histiocytic infiltration usually represents a reactive process, the reasons for which are not well defined in rodents. Compounds that are cytotoxic and cause necrosis of the bone marrow may result in increased numbers of macrophages, which serve to remove the cellular debris. In addition, any condition capable of causing bone marrow injury or inflammation can result in increased macrophages. In other species (humans and dogs), noninflammatory histiocytic infiltrates have been associated with bone marrow hyperplasia, ineffective hematopoiesis, or increased breakdown of blood cells.

Recommendation: Histiocytic infiltration should be consistently recorded and graded for all animals in a study. Grading is based on the degree of infiltration and/or numbers of aggregates.
References:


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