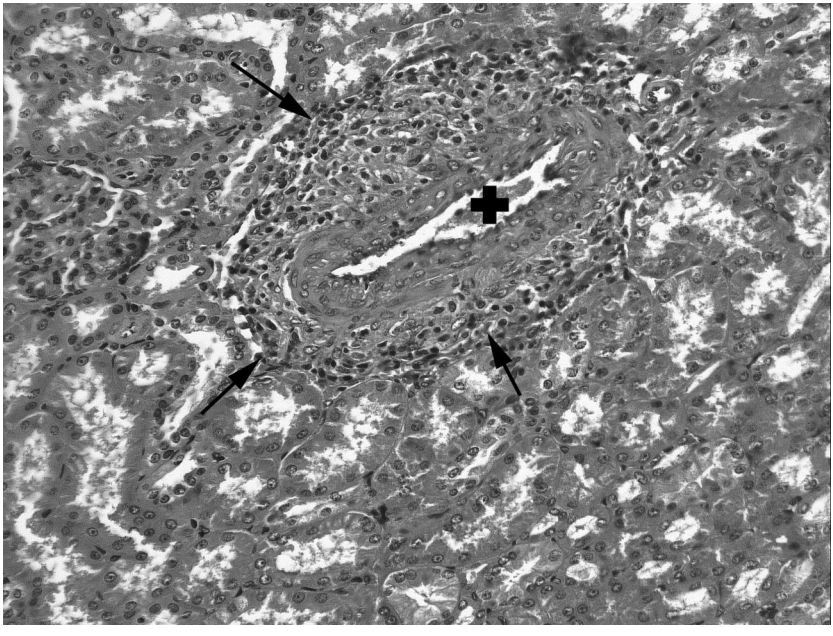

Figure 10 Kidney: Vasculitis—Inflammatory cells (→) mainly around a small blood vessel (+). The surrounding renal tubules are normal. (*See color insert p. 6.*)

particularly but not exclusively in nonrodents, and can jeopardize the outcome of toxicity studies (123–125).

4. TYPICAL NON-NEOPLASTIC ALTERATIONS SEEN IN TOXICITY STUDIES

4.1. Organ Toxicology

Typical *nonneoplastic alterations* seen in toxicity studies with rodents, dogs, monkeys, and minipigs are summarized in Table 7. For further details, a number of good histopathology atlases (70–72,126) and textbooks (127,128) are available.

Toxicity manifests itself often in single *target organs*, but can also affect whole systems, (e.g., the reticuloendothelial system). For this reason, storage diseases (e.g., phospholipidosis) are seen throughout the body and are manifest in lung, liver, lymphatic system, and partly also in other organs (129).

The target organ also depends on the physical characteristics of the test compound. This is best illustrated by inhalation studies: test compounds in powder form with particle sizes $>5\,\mu$ are deposited in the nose and, therefore, may exert an irritative potential only locally. Particles of $1–5\,\mu$ deposit in the airways and $<1\,\mu$ particles reach the alveoli (130,131).

(*text continued on p. 491*)