

(typhus group) or spread from cell to cell (spotted fever group). The widespread endothelial dysfunction can cause shock, peripheral and pulmonary edema, and disseminated intravascular coagulation, as well as renal failure and a variety of CNS manifestations that can include coma.

The innate immune response to rickettsial infection is mounted by NK cells, which produce IFN- γ , reducing bacterial proliferation. Subsequent cytotoxic T lymphocyte responses are critical for elimination of rickettsial infections. IFN- γ and TNF produced by activated NK cells and T cells stimulate the production of bactericidal nitric oxide derivatives. Cytotoxic T cells lyse infected cells, reducing bacterial proliferation.

MORPHOLOGY

Typhus Fever. In mild cases the gross changes are limited to a rash and small hemorrhages due to the vascular lesions. In more severe cases, there may be areas of necrosis of the skin and gangrene of the tips of the fingers, nose, earlobes, scrotum, penis, and vulva. In such cases, irregular ecchymotic hemorrhages may be found internally, principally in the brain, heart muscle, testes, serosal membrane, lungs, and kidneys.

The most prominent microscopic changes are small vessel lesions and focal areas of hemorrhage and inflammation in various organs and tissues. Endothelial swelling in the capillaries, arterioles, and venules may narrow the lumens of these vessels. A cuff of mononuclear inflammatory cells usually surrounds the affected vessel. The vascular lumens are sometimes thrombosed. Necrosis of the vessel wall is unusual in typhus (compared with Rocky Mountain spotted fever). Vascular thromboses lead to gangrenous necrosis of the skin and other structures in a minority of cases. In the brain, characteristic typhus nodules are composed of focal microglial proliferations with an infiltrate of mixed T lymphocytes and macrophages (Fig. 8-40).

Scrub typhus, or mite-borne infection, is usually a milder version of typhus fever. The rash is usually transitory or might not appear. Vascular necrosis or thrombosis is rare, but there may be a prominent inflammatory lymphadenopathy.

Rocky Mountain Spotted Fever. A hemorrhagic rash that extends over the entire body, including the palms of the hands and soles of the feet, is the hallmark of Rocky Mountain spotted

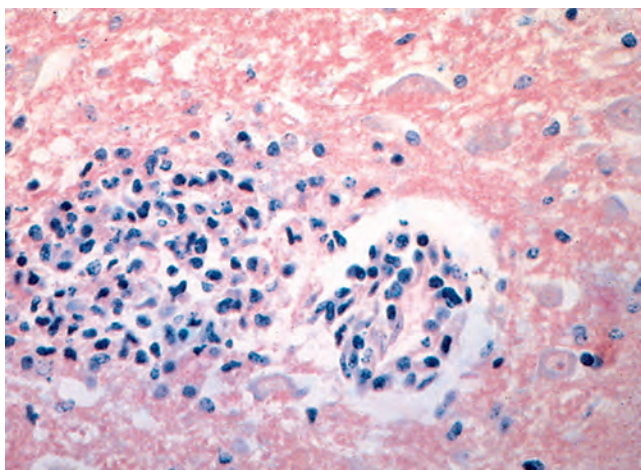


Figure 8-40 Typhus nodule in the brain.

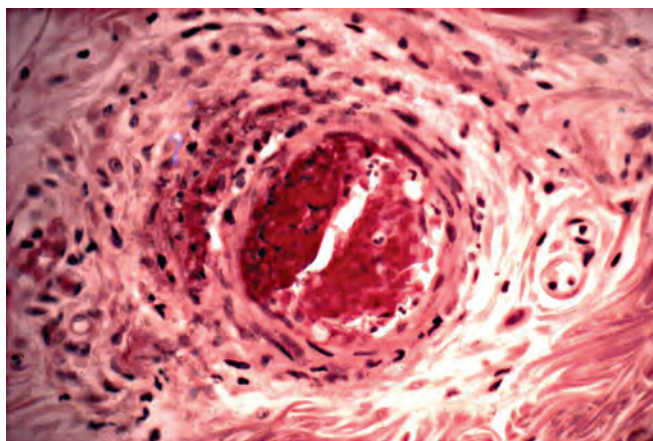


Figure 8-41 Rocky Mountain spotted fever with a thrombosed vessel and vasculitis.

fever. An eschar at the site of the tick bite is uncommon with Rocky Mountain spotted fever but is often seen with *R. akari*, *R. africae*, and *R. conorii* infection. The vascular lesions that underlie the rash often lead to acute necrosis, fibrin extravasation, and occasionally thrombosis of the small blood vessels, including arterioles (Fig. 8-41). In severe Rocky Mountain spotted fever, foci of necrotic skin appear, particularly on the fingers, toes, elbows, ears, and scrotum. The perivascular inflammatory response, similar to that of typhus, is seen in the brain, skeletal muscle, lungs, kidneys, testes, and heart muscle. The vascular lesions in the brain may involve larger vessels and produce microinfarcts. A noncardiogenic pulmonary edema causing adult respiratory distress syndrome is the major cause of death in patients with Rocky Mountain spotted fever.

Fungal Infections

Fungi are eukaryotes with cell walls that grow as multicellular filaments (mold) or individual cells alone or in chains (yeast). Cell walls give fungi their shape. Yeasts are round to oval and mainly reproduce by budding. Some yeasts, such as *Candida albicans*, can produce buds that fail to detach and become elongated, producing a chain of elongated yeast cells called *pseudohyphae*. Molds consist of threadlike filaments (hyphae) that grow and divide at their tips. They can produce round cells, called *conidia*, that easily become airborne, disseminating the fungus. Many medically important fungi are dimorphic, existing as yeast or molds, depending on environmental conditions (yeast form at human body temperature and a mold form at room temperature). Fungal infections can be diagnosed by histologic examination, although definitive identification of some species requires culture.

Fungal infections, also called *mycoses*, are of four major types:

- *Superficial and cutaneous mycoses* are common and limited to the very superficial or keratinized layers of skin, hair, and nails.
- *Subcutaneous mycoses* involve the skin, subcutaneous tissues, and lymphatics and rarely disseminate systemically.