Ehrlichia and *Anaplasma* are bacteria related to *Rickettsiae*. They are obligate intracellular bacteria that grow within membrane-bound vacuoles in human and animal leukocytes. The obligate intracellular bacteria proliferate in white blood cells (monocytes: *E. chaffeensis*) or granulocytes [*Ehrlichia* sp. related to *E. equi* (horses) and *E. phagocytophila* (cattle)].

Historical note

The generic name refers to Paul Erhlich (1854-1915), the famous German bacteriologist (Nobel Chemistry Prize 1908), the discoverer of salvarsan, an arsenical preparation active against syphilis. In 1954 the first human ehrlichiosis was described in Japan, caused by *E. sennetsu*. Since this initial report, several tick-borne infections have now been recognized. Human monocytic ehrlichiosis (HME) was first described in 1986 and is caused by *Ehrlichia chaffeensis*. The name refers to the American army base Fort Chaffee in Arkansas.

Human granulocytotropic anaplasmosis (HGA) was described in 1993 and is caused by *Anaplasma phagocytophilia*. *Ehrlichia ewingii* was described in 1999 as an agent of human ehrlichiosis. *E. ewingii* provokes “human granulocytic ehrlichiosis “.

Transmission and symptoms

The organisms are transmitted by ixodid ticks. *Amblyomma americanum* (Lone star tick) is the main vector for *E. chaffeensis*. In the USA white-tailed deer and coyotes form the most important reservoir. It has been shown that ticks on migrating birds can be infected with *Erhlichia* sp. and can thus be transported over long distances. *Anaplasma phagocytophila* in the broad sense is found in rodents such as the dusky-footed wood rats and mice. The reservoir of *E. ewingii* is still unknown. Transmission occurs predominantly by the bite of infected ticks, but mother-to-child transmission and transmission by blood transfusion or slaughtering of infected animals is reported.

Common symptoms include fever with or without chills, headache, myalgia, arthralgia, weakness, nausea, leukopenia and thrombocytopenia. Rash is uncommon. Liver test abnormalities can be found in about 50% of cases. In rare cases human monocytic ehrlichiosis can be associated with neurological lesions or meningitis. Post-infection asthenia can continue for months. In HIV patients infection can be overwhelming.

Diagnosis

White blood cell and platelet abnormalities are almost always present, so normal values virtually rule out this infection. Anemia is commonly present, so pancytopenia can be suggestive of anaplasmosis or ehrlichiosis.

Probably many infections are missed since laboratory testing is not widely available. The diagnosis of human granulocytic anaplasmosis is made by microscopic examination of a peripheral blood smear or serologic testing. A 4-fold rise in antibody titer between the acute an convalescent phases of infection confirms the diagnosis. Microscopy is labor intensive and the sensitivity of microscopy ranges from 20 to 80% depending on the degree of expertise: bacteria are observed in the cytoplasm of leukocytes as 0.5 to 1.5 µm large inclusions which are combined in groups (morulae). Today, PCR has gained diagnostic importance in high resource settings. Culturing of this intracellular bacteria is complex and it’s the most accurate method, and it is reserved for research purposes.

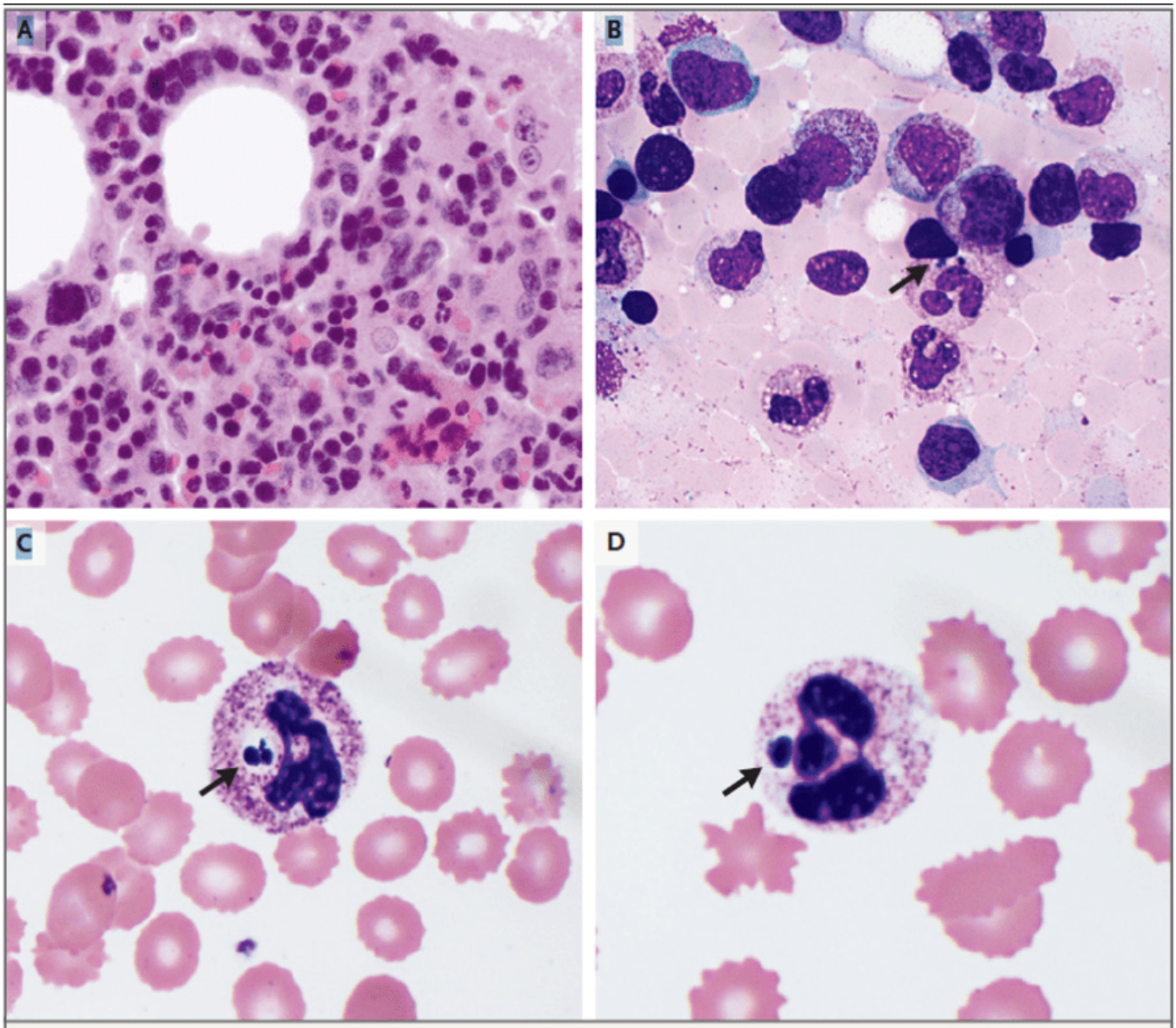
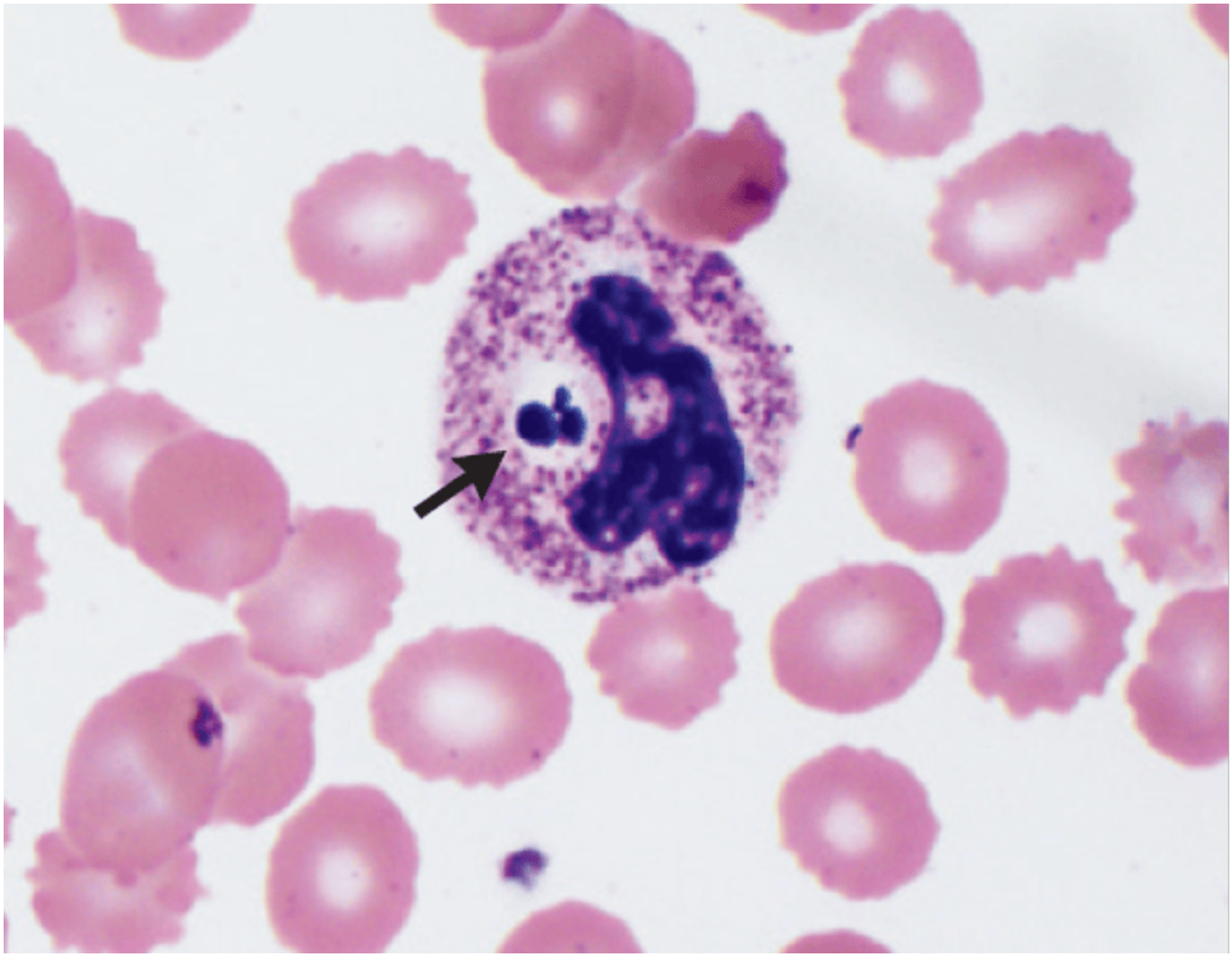


Figure 2. Bone Marrow–Biopsy Specimen, Bone Marrow Aspirate, and Peripheral-Blood Specimen.

Hematoxylin and eosin staining of a bone marrow core-biopsy specimen (Panel A) and Wright–Giemsa staining of a bone marrow aspirate smear (Panel B) show maturing trilineage hematopoiesis. On the bone marrow aspirate smear (Panel B) and on Wright's staining of a peripheral-blood smear (Panels C and D), most neutrophils show nonspecific toxic granulation; rare ones have intracytoplasmic inclusions (arrows), which are suggestive of human granulocytic anaplasmosis.



Human granlulocytic anaplasmosis: Wright's staining of a peripheral blood smear. Neutrophils show nonspecific toxic granulation and some have intracytoplasmic inclusions (arrow).
Source: N Engl J Med 2020;382:1258-66. DOI: 10.1056/NEJMcpc1916

Differential diagnosis:

The differential diagnosis includes rickettsiosis, typhoid fever and several arboviral infections, such as dengue.

The diagnosis of HGA can be overlooked if there is simultaneous infection with *B. burgdorferi*. In such cases, the typical rash of early Lyme disease (erythema migrans) may mislead the clinician into ignoring possible coinfection with ehrlichia or anaplasma. Findings that may

suggest coinfection include leukopenia, thrombocytopenia, and high fever (all relatively uncommon in Lyme disease) and abnormal liver enzyme tests accompanying the erythema migrans.

Treatment

Treatment is based on administration of tetracyclines, e.g. doxycycline 100 mg twice daily for 7 days.