

# EBV infection

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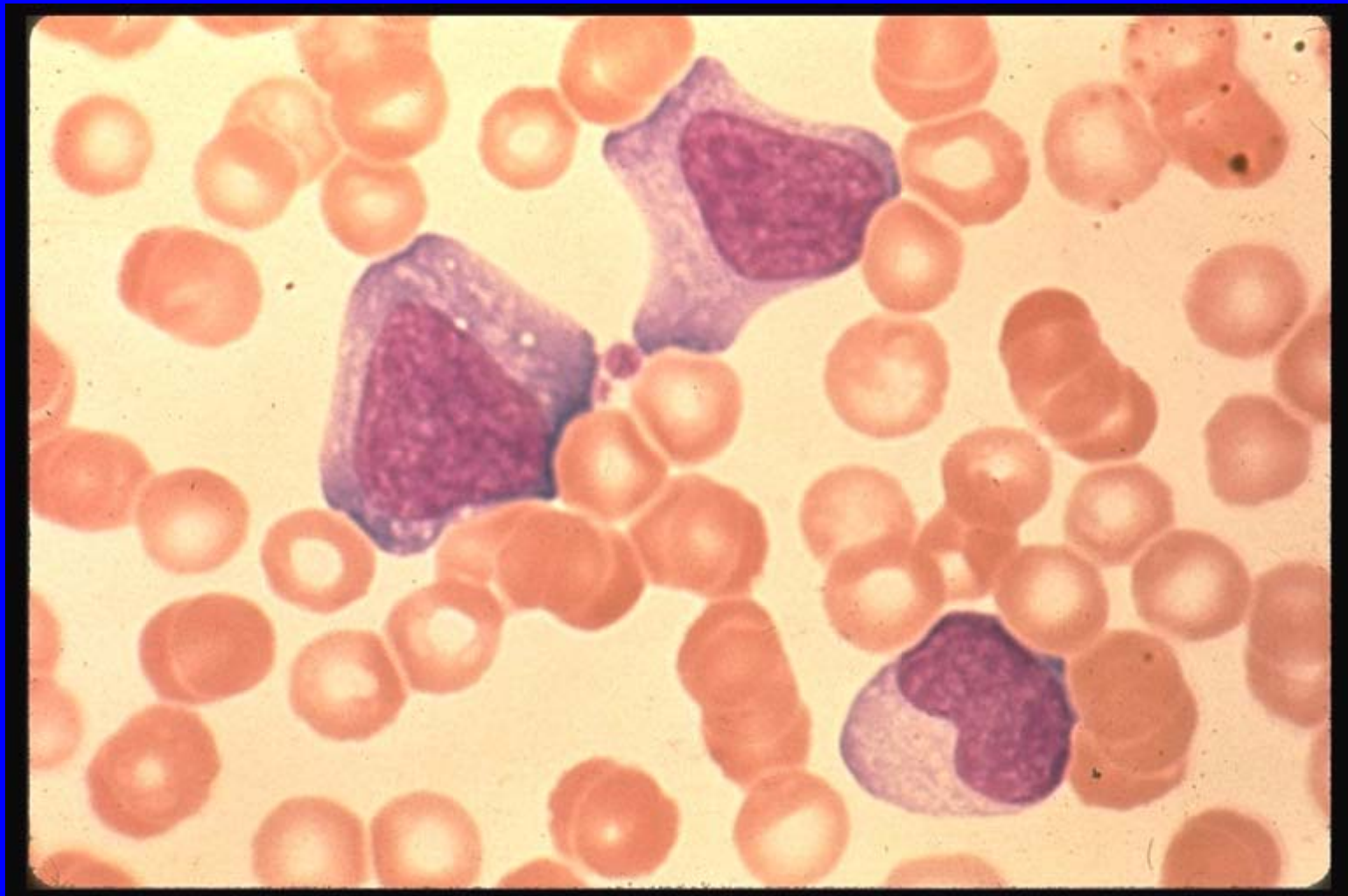
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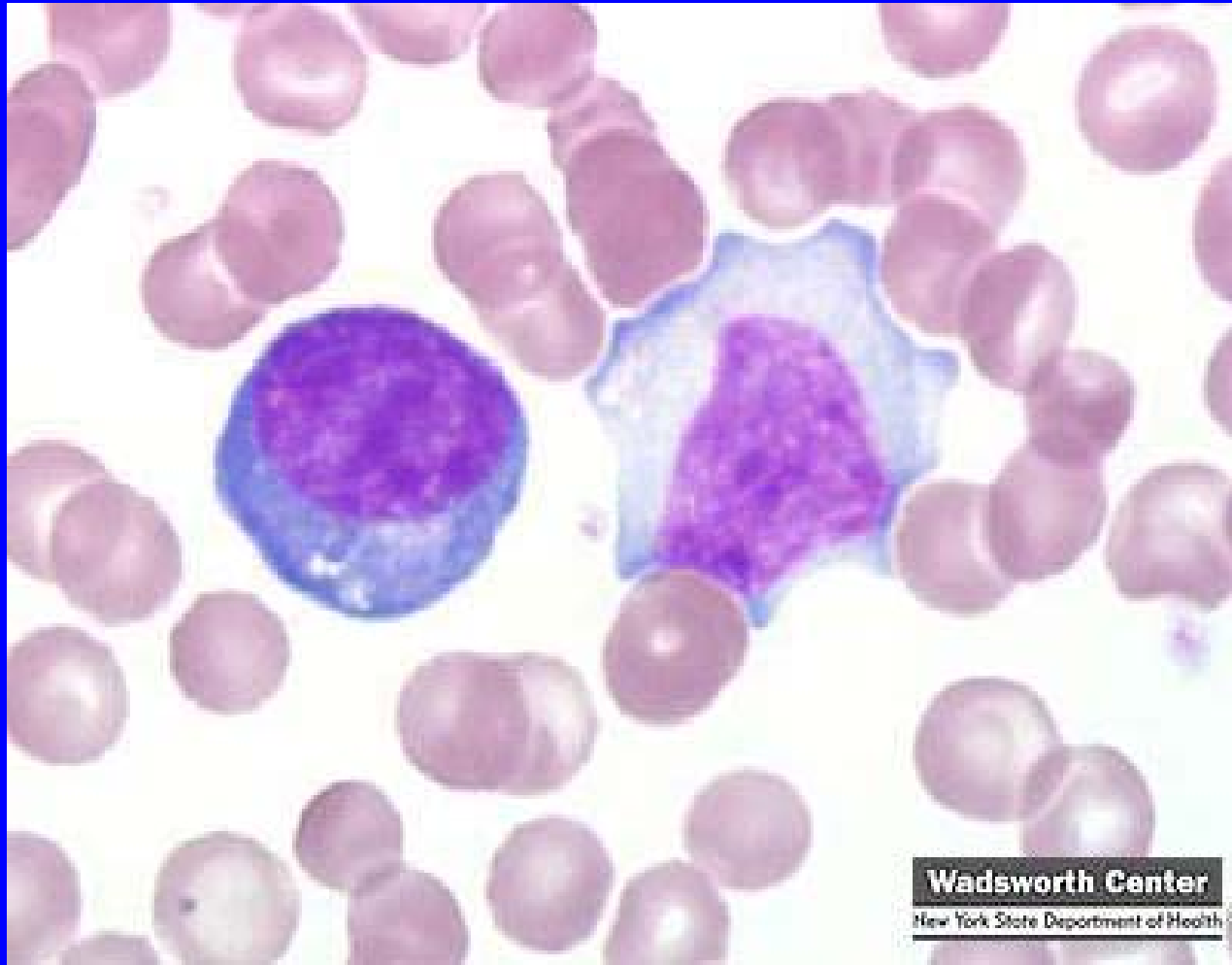
# History

- Late 1800's, Filatov and Pfeiffer simultaneously described an illness characterized by malaise, fever, hepatosplenomegaly, lymphadenopathy, and abdominal discomfort
- Was called “Drusenfieber” (glandular fever)

# History

- Was doubted as a clinical entity until 1921 when Sprunt and Evans described a syndrome involving fever, lymphadenopathy and prostration in 6 previously healthy young adults
- They observed a mononuclear lymphocytosis and contrasted the pathologic appearance of these lymphocytes with those of children with other infections





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# History

- 1921: Downey and McKinlay described additional cases of “infectious mononucleosis” and provided a more detailed morphologic description of the atypical lymphocytosis.
- 1932: Paul and Bunnell found the “heterophile antibody”. They were looking at immunologic mechanisms of serum sickness and surprisingly found high titers of sheep red cell agglutinins in the sera of patients with infectious mononucleosis.

# History

- 1958: Burkitt described an unusual lymphoma with a predilection for the head and neck. Since the distribution of the tumor paralleled certain mosquito-borne illnesses in Africa, he searched for a related arbovirus
- 1964: Epstein found particles that resembled herpesviruses in tissue cultures of biopsy specimens from patients with Burkitt's lymphoma

# History

- An indirect immunofluorescent antibody test was developed to the virus, now called Epstein-Barr virus
- High titers were found in Burkitt's patients
- 90% of American adults were also seropositive

# History

- A technician in Henle's lab developed infectious mononucleosis, and serial analyses of his sera suggested that acute EBV infection was associated with this illness
- Specific antibody tests for EBV enabled researchers to identify “heterophile-negative” mononucleosis (about 10-20% of cases); subsequently, other viruses (primarily CMV) were identified as causative agents.

# Epidemiology

- EBV is widespread; 90-95% of adults are seropositive
- Spread by intimate contact between susceptible persons and asymptomatic EBV shedders
- Most infections are asymptomatic and sub-clinical

# Epidemiology

- Incidence is highest in the 15-24-year-old age group
- College roommates of pt's with IM were not more likely to seroconvert than the general college population
- EBV can be cultured from the oropharynx for up to 18 months after resolution of illness
- Labile in the lab, not recovered from fomites
- Most illness is likely due to intimate contact between susceptibles and asymptomatic shedders

# Epidemiology

- Spread by kissing
- Sibling contact within families
- Cases reported from blood transfusion, after cardiac surgery (CMV) “postpump perfusion” syndrome
- Unlikely that epidemics occur
- Public health impact is greatest in the military and at universities

# Virology

- Host cells are lymphocytes (both B and T cells), epithelial cells, and myocytes
- Limited to humans and a few other primates: squirrel monkeys and cotton top marmosets
- Remains latent for life in most adults
- Unlike CMV and the other herpesviruses, EBV is capable of transforming cells
- Can be the causative agent of some B and T cell lymphomas, Hodgkin disease, and nasopharyngeal carcinoma

# Virology

- Not associated with reactivation disease late in life except in post-transplant patients
- This is in contrast to other herpesviruses

# Virology

- Likely route of infection is the oropharynx
- EBV DNA is found within epithelial cells by cytohybridization studies
- B cells are infected in local lymphoid tissue
- During the 30-50 day incubation period, viral replication and dissemination occur via the lymphoreticular system.

# Immune response

- Humoral response includes antibodies directed against viral antigens as well as unrelated antigens on sheep, horse, and beef red cells (the heterophile antibody--IgM).
- No correlation between heterophile antibody and severity of illness
- Cellular response is complex and includes both T cells and NK cells
- B cells also proliferate, though the response to EBV is more T cell mediated, humoral response is of questionable significance
- Atypical lymphocytosis resolves as illness does

# Clinical presentation

- Sore throat
- Fever
- LAD
- HSM
- Abdominal pain
- Myalgias
- HA





# Clinical presentation

- Malaise
- Anorexia
- Chills, Fever (>90%)
- Arthralgias

# Clinical Presentation

- In children, infection is often asymptomatic
- Children are more likely to exhibit rashes, neutropenia, or pneumonia
- Penicillin antibiotics may cause a pruritic maculopapular eruption

# Hematology

- Atypical lymphocytosis
- Cold agglutinins (IgM) present in 70-80% of rare cases of hemolytic anemia, usually becoming apparent in the 2<sup>nd</sup> or 3<sup>rd</sup> week of illness
- Mild thrombocytopenia is common, severe with bleeding is rare but reported

# Complications

- Splenic rupture
- Due to lymphocytic infiltration of the capsule, trabeculae, and vascular walls
- No contact sports
- Caution in splenic palpation

# Complications

- Transaminitis occurs in 80-90% of cases
- Fulminant hepatic failure reported, but rare
- Death is rare
- Duncan syndrome is an X-linked recessive congenital immunodeficiency involving dysregulation of induced killer cells (NK cells?)—poorly understood

# Clinical course

- Most cases resolve spontaneously over 2-3 weeks
- Sore throat lasts 3-10 days
- Fevers may last 10-15 days, though they gradually defervesce
- Recovery involves days of improved symptoms and days of recurrence.

# Treatment

- Supportive care
- Steroids are not helpful unless airway compromise
- Acyclovir reduces viral shedding but not course of illness
- INF-alpha, IL-2, IVIG not helpful in primary EBV infection
- Ongoing research to develop a vaccine

# Sources

- Mandell's *Infectious Diseases*, 3<sup>rd</sup> edition
- UpToDate: Clinical Manifestations and treatment of Epstein-Barr virus infection
- Goodman and Gilman's *The Pharmacologic Basis of Therapeutics*, 8<sup>th</sup> edition