Key References in Infectious Diseases

AN ANNOTATED GUIDE

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Preface

Many physicians have access to computerized reference services that allow exhaustive literature searches of any clinical topic. Generally such lists are nonselective; although helpful when writing an authoritative review, they often prove overwhelming to the busy medical student, house officer, or practicing physician. In the collection of references that follows, we have selected infectious disease topics and references with these physicians in mind. The references are clinically oriented. When it was possible, we have included major reviews of each topic. To assist the reader who desires more literature on a given topic, we have included the number of references cited in each article. In our brief annotations we have attempted to summarize important diagnostic and management points. In general, we have included only papers from major journals available in most hospital libraries. We hope that the many hours we have spent selecting and summarizing the current infectious disease literature will make it easier for physicians to maintain an up-to-date knowledge in this important medical field.

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Key References in Infectious Diseases

INFECTIONS CLASSIFIED BY ETIOLOGIC AGENT

Viral Diseases

Herpes Simplex

General

Nahmias AJ and Roizman B: Infection with herpes simplex viruses 1 and 2. *N Engl J Med*, 289:667–674; 719–730; 781–789, 1973.

A comprehensive review of the structure, molecular biology and clinical manifestations of herpes simplex viruses 1 and 2. 234 refs.

Schaeffer HJ, Beauchamp L, deMiranda P, Elion GB et al.: 9-

(2-hydroxyethoxymethyl) guanine activity against viruses of the herpes group. *Nature*, 272:583–585, 1978.
Acyclovir, a new antiviral agent, is currently undergoing clinical testing for use in herpes simplex and herpes zoster infections. It is likely that this agent will prove to be a major advance over currently available anti-herpetic agents. 13 refs.

Encephalitis

Whitley RJ, Soong SJ, Dolin R, Galasso GJ et al.: Adenine arabinoside therapy of biopsy proven herpes simplex encephalitis. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study. *N Engl J Med*, 297:289–294, 1977.
In a prospective, randomized, double-blinded, placebo-controlled trial adenine arabinoside reduced the mortality in biopsy proven herpes simplex encephalitis from 70 percent in the placebo group to 28 percent in the ara-A treated group. 40 percent of patients who were begun on ara-A prior to the onset of semicoma were able to return to work. Although the diagnosis of herpes simplex encephalitis is supported by localization of pathology by brain scan, EEG and on angiogram, definitive diagnosis is only possible by brain biopsy. A significant number of patients felt to have herpes simplex encephalitis prior to biopsy were found to have other treatable illnesses. In a center in which a brain biopsy can be safely performed, patients should undergo brain biopsy prior to institution of antiviral chemotherapy. 34 refs.

Davis JM, Davis KR, Kleinman GM et al.: Computed tomography of herpes simplex encephalitis, with clinicopathologic correlation. *Radiology*, 129:409–417, 1978.
9 patients with biopsy proven herpes simplex encephalitis underwent computed cranial tomography. A low absorption defect in the temporal or parietal lobes was the most frequent finding, but this finding was not seen within the first 5 days of the onset of neurologic signs or symptoms. In at least 2 instances the 99-^{Tc} radionuclide scan was positive before the computed tomographic study. 12 refs.

Genital

Spruance SL, Overall JC, Kern ER, Krueger GG et al.: The natural history of recurrent herpes simplex labialis. Implications for antiviral therapy. *N Engl J Med*, 297:69–75, 1977.
Quantitative measures of pain, swelling and viral sheddding were undertaken in 80 patients with recurrent herpes labialis.

The study indicates that although the highest titers of virus are recovered from vesicular lesions, virus is still isolated from two-thirds of crusted lesions and may be isolated for up to 10 days after onset of the attack. The prolonged viral shedding and virus isolation from crusted lesions has implications for nurses, dentists and other health care personnel at risk for herpetic whitlow. 25 refs.

Blough HA and Giuntoli RL: Successful treatment of human genital herpes infections with 2-deoxy-d-glucose. *J Am Med Assoc*, 241:2,798–2,801, 1979.

A frequently cited study suggesting efficacy for 2-deoxy-d-glucose in the treatment of herpes genitalis. Close perusal of the data suggests that the apparent differences between control and treated patients may relate more to prolongation of the disease by the placebo than to improvement by 2-deoxy-d-glucose. 20 refs.

Corey L, Reeves WC, Chiang WT et al.: Ineffectiveness of topical ether for the treatment of genital herpes simplex virus infection. *N Engl J Med*, 299:237–239, 1978.

In addition to being ineffective in the therapy of herpes genitalis, topical ether is extremely painful. 19 refs.

Adams HG, Benson EA, Alexander ER et al.: Genital herpetic infection in men and women: Clinical course and effect of topical application of adenine arabinoside. *J Infect Dis*, 133A:151–159, 1976.

Topical ara-A is ineffective in the treatment of herpes genitalis. 7 refs.

Spruance SL, Crumpacker CS, Haines H et al.: Ineffectiveness of topical adenine arabinoside 5'monophosphate in the treatment of recurrent herpes simplex labialis. *N Engl J Med*, 300:1,180–1,184, 1979.

Topical ara-A monophosphate is also ineffective in treatment of recurrent herpes simplex labialis. 32 refs.

Caplan LR, Kleeman FJ and Berg S: Urinary retention probably secondary to herpes genitalis. *N Engl J Med*, 297:920–921, 1977.

An association between urinary retention and herpes genitalis was demonstrated in 11 patients aged 19 to 38 years. The syndrome consisted of fever, parasthesias or pain of the perineum or lower extremities, inguinal lymphadenopathy and vesicular genital skin lesions. The syndrome is self-limited and should not be treated with corticosteroids. 12 refs.

Cytomegalovirus

Weller TH: The cytomegaloviruses: Ubiquitous agents with protean clinical manifestations. *N Engl J Med*, 285:203–214; 267–274, 1971.
This extensive review provides an excellent summary which integrates basic information about the virus with the epidemiology and clinical manifestations of CMV infection. 186 refs.

Nankervis GA and Kumar ML: Diseases produced by cytomegaloviruses. *Med Clin North Am*, 62:1,021–1,035, 1978.
This excellent review summarizes recent advances in the knowledge of clinical manifestations of CMV infections. 88 refs.

Horwitz CA, Henle W, Henle G et al.: Heterophile negative infectious mononucleosis and mononucleous-like illnesses. Laboratory confirmation of 43 cases. *Am J Med*, 63:947–957, 1977.
Extensive serologic testing of 43 patients with heterophile negative infectious mononucleous syndrome revealed that 30 were due to CMV. Compared to patients with EBV induced disease, these patients tended to be older, have less cervical adenopathy or pharyngitis and less marked LFT elevations. 36 refs.

Lee FK, Nahmias AJ and Stagno S: Rapid diagnosis of cytomegalovirus infection in infants by electron microscopy. *N Engl J Med*, 299:1,266–1,270, 1978.
Particles consistent morphologically with CMV were demonstrated in 18 of 20 CMV infected infants examined before 6 months of age. Positive electron microscopy correlated with the presence of CMV infectivity (titers of $\geq 10^4$/ml of urine). The method is proposed as a rapid means for identification of infants infected with CMV during the perinatal period. 23 refs.

Murray HW, Knox DL, Green WR, and Susel RM: Cytomegalovirus retinitis in adults. A manifestation of disseminated infection. *Am J Med*, 63:574–584, 1977.
The authors suggest that a distinctive series of ophthalmoscopic observations allow the diagnosis of CMV retinitis. These ophthalmic manifestations often precede other evidence of disseminated infection seen in immunosuppressed individuals. 36 refs.

Phillips CA, Fanning WL, Gump DW and Phillips CF: Cytomegalovirus encephalitis in immunologically normal adults.

Successful treatment with vidarabine. ***JAMA*****, 238:2,299–2,300, 1977.**
2 adults with presumed CMV encephalitis are presented. In one of the patients the virus was isolated from a brain biopsy specimen. The presentation and course of the illness was similar to that manifested by HSV except that it was less severe and slower in evolution. 12 refs.

Myers JD, Spencer HC, Watts JC et al.: Cytomegalovirus pneumonia after human marrow transplantation. ***Ann Intern Med*****, 82:181–188, 1975.**
In a retrospective study of 85 patients undergoing bone marrow transplantation, 35 developed interstitial pneumonia. Of these, 23 died. Autopsies of 17 of these patients suggested that CMV played a major role in the development of interstitial pneumonia in at least 50 percent of the patients who died. 32 refs.

Tolkoff-Rubin NE, Rubin RH, Keller EE et al.: Cytomegalovirus infection in dialysis patients and personnel. ***Ann Intern Med*****, 89:625–628, 1978.**
This study suggests that freezing of blood prior to transfusion decreases the risk of CMV transmission. 42 refs.

Rubin RH, Cosimi AB, Tolkoff-Rubin NE et al.: Infectious disease syndromes attributable to cytomegalovirus and their significance among renal transplant recipients. ***Transplantation*****, 28:458–464, 1977.**
In a prospective evaluation of 68 consecutive renal transplant recipients, clinically overt CMV disease was detected in 38. The peak incidence in the onset of these illnesses occurred 1 to 4 months posttransplantation. Disease manifestations include fever, pneumonia, leukopenia and hepatitis. 49 refs.

Treatment

Glazer JP, Friedman HM, Grossman RA et al.: Live cytomegalovirus vaccination of renal transplant candidates. A preliminary trial. ***Ann Intern Med*****, 91:676–683, 1979.**
In a study of 12 seronegative renal transplant candidates, live attenuated CMV vaccine was found to be immunogenic and apparently safe, but did not protect renal transplant recipients from CMV related morbidity. 33 refs.

Cheeseman SH, Rubin RH, Stewart JA et al.: Controlled trial of prophylactic human-leukocyte interferon in renal transplantation. ***N Engl J Med*****, 300:1,345–1,349, 1979.**
In a prospective, double-blinded, placebo-controlled trial in-

volving 45 renal transplant recipients, interferon was shown to delay the onset of CMV excretion and to decrease the incidence of CMV viremia. 32 refs.

Meyers JD, McGuffin RW, Neiman PE et al.: Toxicity and efficacy of human leukocyte interferon for treatment of cytomegalovirus pneumonia after marrow transplantation. *J Infect Dis*, 141:555–562, 1980.
8 bone marrow transplant recipients with CMV pneumonia diagnosed at open lung biopsy were treated with human leukocyte interferon. All patients died of the pneumonia. Virus was isolated from lung tissue postmortem examination in 3 of 5 patients in whom isolation was attempted. 27 refs.

Epstein-Barr Virus

Sawyer RN, Evans AS, Niederman JC and McCallum RW: Prospective studies of a group of Yale University freshmen. I. Occurrence of infectious mononucleosis. *J Infect Dis*, 123:263–270, 1971.
This article remains the best source of information relating to the epidemiology of EBV in the college population. Approximately 10 percent of the EBV seronegative population acquired infection each year. With the close clinical monitoring at the Yale Student Health Services about three-fourths of the cases were clinically recognized as infectious mononucleosis. EBV seronegative roommates of IM patients developed IM no more frequently than the EBV seronegative college population at large, thus confirming the relatively low communicability of the virus. 17 refs.

Horwitz CA, Henle W, Henle G et al.: Clinical and laboratory evaluation of elderly patients with heterophile-antibody positive infectious mononucleosis. Report of seven patients, ages 40–78. *Am J Med*, 61:333–339, 1976.
The authors retrospectively reviewed 7 cases of heterophile positive infectious mononucleosis occurring in patients over 40. The clinical and laboratory features were similar to those manifested by younger patients. 36 refs.

Andiman WA: The Epstein-Barr virus and EBV virus infections in childhood. *J Pediatr*, 95:171–182, 1979.
In children, primary EBV infection is often subliminal. Children are less likely than adolescents to manifest a heterophile antibody response. 75 refs.

Henle W, Henle G and Horwitz CA: Epstein-Barr virus specific

diagnostic tests in infectious mononucleosis. *Hum Pathol*, 5:551–565, 1974.
This excellent review outlines the available serologic tests for EBV. Although technically difficult to perform, the EBV viral capsid antigen IgM titer is the most sensitive and specific test for documentation of primary EBV infection. 82 refs.

Horwitz CA, Moulds J, Henle W et al.: Cold agglutinins in infectious mononucleosis and heterophile antibody negative mononucleosis syndromes. *Blood*, 50:195–202, 1977.
The authors studied sera from 150 patients with heterophile positive infectious mononucleosis, 38 patients with heterophile negative infectious mononucleosis and 500 healthy individuals. Cold agglutinins (CA) were found in 85 pefcent of patients with heterophile positive infectious mononucleosis. 25 percent of these were of anti-i specificity. In contrast, anti-i specific CA were found in only 0.8 percent of control sera. In the heterophile negative infectious mononucleosis group, 3 patients had anti-i CA's and all 3 had EBV induced disease. 31 refs.

Grose C, Henle W, Henle G and Feorino PM: Primary Epstein-Barr virus infections in acute neurologic disease. *N Engl J Med*, 292:392–395, 1975.
7 of 24 young patients with Guillain-Barre syndrome and 3 of 16 with facial palsies had definite serologic evidence of recent primary EBV infection. In addition, 2 patients with transverse myelitis and 2 with meningoencephalitis had evidence of recent primary EBV infection. Only 1 of the patients had other typical manifestations of infectious mononucleosis. The authors suggest that acute neurologic syndromes of young adults are often associated with primary EBV infection. 23 refs.

Ellman L, Carvalho A, Jacobson BM and Colman RW: Platelet autoantibody in a case of infectious mononucleosis presenting as thrombocytopenic purpura. *Am J Med*, 55:723–726, 1973.
A patient is presented in whom the only clinical manifestation of primary EBV infection was thrombocytopenic purpura. The authors demonstrated the presence of an anti-platelet antibody in the patient's serum. The platelet count was only minimally responsive to prednisone, but returned promptly to normal after splenectomy. The patient was studied prior to the advent of plasmaphoresis. 19 refs.

Hammond WP, Harlan JM and Steinberg SE: Severe neutropenia in infectious mononucleosis. *West J Med*, 131:92–97, 1979.
The authors present 3 patients with primary EBV infection

complicated by profound granulocytopenia. At present, the pathophysiology of the mild granulocytopenia seen in almost half of patients with infectious mononucleosis and of rare cases associated with profound granulocytopenia is unknown. Treatment is supportive. 28 refs.

Purtilo DT, Bhawan J, Hutt LM et al.: Epstein-Barr virus infection in the X-linked recessive lymphoproliferative syndrome. *Lancet*, 1:798–801, 1978.

One of a series of articles relating to a kindred with an immunodeficiency to EBV which results in either fatal primary infection, lymphoproliferation or severe immunologic sequelae in affected males. 24 refs.

Robinson JE, Brown N, Andiman W et al.: Diffuse polyclonal B-cell lymphoma during primary infection with Epstein-Barr virus. *N Engl J Med*, 302:1,293–1,297, 1980.

The authors present an intensively studied case of primary EBV infection in a 4-year old girl with multiple congenital anomalities which evolved into a polyclonal B-cell lymphoma. The accompanying editorial is an excellent summary of the current information relating to the immune response to EBV. 22 refs.

Cheeseman SH, Henle W, Rubin RH et al.: Epstein-Barr virus infection in renal transplant recipients. Effects of antithymocyte globulin and interferon. *Ann Intern Med*, 93:39–42, 1980.

In a prospective, placebo-controlled trial, human leukocyte interferon was shown to decrease rates of EBV excretion. 4 of 41 patients developed febrile illnesses associated with rises in titers of antibody to EBV early antigen. It is suggested that EBV reactivation can lead to syndromes similar to those evoked by CMV in the immunosuppressed patient population. 19 refs.

Marker SC, Ascher NL, Kalis JM et al.: Epstein-Barr virus antibody responses and clinical illness in renal transplant recipients. *Surgery*, 85:433–440, 1980.

In a retrospective study of 88 renal transplant recipients, the authors conclude that EBV can cause prolonged unexplained fever in immunosuppressed patients. 2 patients are presented in whom the appearance of lymphoproliferative disorders was accompanied by rises in antibody titers to EBV. 28 refs.

Varicella Zoster

Dolin R, Reichman RC, Mazur MH and Whitley RJ: Herpes zoster—varicella infections in immunosuppressed patients. *Ann Intern Med*, 89:375–388, 1978.

This review of the impact of varicella zoster virus on the immunosuppressed population includes an excellent discussion of the neurologic complications of varicella zoster infection. The syndrome of ophthalmic zoster with contralateral hemiplegia which may follow ophthalmic zoster accounts for one-third of reported cases of herpes zoster encephalitis. The mortality rate of 25 percent associated with herpes zoster encephalitis contrasts with the mortality rate of 70 percent in untreated herpes simplex encephalitis. 113 refs.

Mazur M and Dolin R: Herpes zoster at the NIH: A 20 year experience. *Am J Med*, 65:738–744, 1978.
In a retrospective review of 107 episodes of herpes zoster seen in the NIH patient population, dissemination followed dermatomal zoster by 4 to 11 days in 15 percent of patients. Although dissemination was associated with considerable morbidity, it directly accounted for only 1 death. 24 refs.

Peters ACB, Versteeg J, Lindeman J and Bots TAM: Varicella and acute cerebellar ataxia. *Arch. Neurol*, 35:769–771, 1978.
Examination of CSF in 2 cases of cerebellar ataxia associated with varicella revealed the presence of varicella zoster virus antigens in cerebrospinal fluid lymphocytes. This suggests that this complication of varicella may be caused by actual viral involvement of the CNS. 18 refs.

Mazur M, Whitley R and Dolin R: Serum antibody levels as risk factors in the dissemination of herpes zoster. *Arch Intern Med*, 139:1,341–1,345, 1979.
The sera obtained at the onset of dermatomal zoster in 67 immunosuppressed patients were examined for the presence of antibodies to varicella zoster viruses by immune adherence hemagglutination inhibition (IAHA), indirect immunofluoresence (IFA) and complement fixation (CF). IFA titers of <32 or undetectable IAHA titers were highly predictive of those patients and who subsequently developed disseminated zoster. 27 refs.

Prevention and Therapy

Merigan TC, Rand KH, Pollard RB et al.: Human leukocyte interferon for the treatment of herpes zoster in patients with cancer. *New Engl J Med*, 298:981–987, 1978.
In a prospective, double-blinded, placebo-controlled trial, human leukocyte interferon (5×10^5 U/kg/day) was shown to be effective in decreasing cutaneous and visceral dissemination and in decreasing the severity of postherpetic neuralgia. 27 refs.