

# Infectious Mononucleosis in the Community Hospital

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The clinical records from three community hospitals of 161 patients with a diagnosis of infectious mononucleosis were reviewed. Epidemiological, clinical, and laboratory findings were compared with previous studies of selected populations and age groups as well as with those from referral centers. The purpose of this study was to obtain information on infectious mononucleosis as it presents to primary care physicians in the community setting. Infectious mononucleosis can pose diagnostic difficulties, demonstrated by the variety of admission diagnoses made by physicians prior to the laboratory confirmation of the illness. Although often a benign and self-limited illness, hospitalization was often required for minor and rare major complications. Ampicillin-related rash did not occur so frequently as previously reported. The use of steroids in treatment of complications was felt to be appropriate. With few exceptions, epidemiological, clinical, and laboratory findings generally agreed with previous studies.

Most clinical and epidemiological studies of infectious mononucleosis have been carried out on selected populations<sup>1-10</sup> and age groups<sup>11-15</sup> as well as in referral centers.<sup>16-19</sup> This paper describes infectious mononucleosis in three community hospitals in Saginaw, Michigan, during a five-year period from 1977 through 1981. Epidemiological, clinical, and laboratory findings are compared with those of previous studies. Emphasis is placed on features of importance to the primary care physician.

## Methods

The hospital records from 1977 through 1981 of all patients with the discharge diagnosis of infectious mononucleosis were reviewed. Three community hospitals (St. Mary's, St. Luke's, and Saginaw General Hospital, with a total capacity of 981 beds) were used in this study. One hundred seventy-five patients cared for by various primary care physicians had a discharge diagnosis of infectious mononucleosis; of these, 161 patients had findings felt to be consistent with infectious mononucleosis. The criteria necessary for diagnosis of infectious mononucleosis included (1) a clinical picture compatible with infectious mononucleosis, such as pharyngitis, lymphadenopathy, and fever, and (2) a positive Monospot or differential heterophil agglutination test (Paul-Bunnell-Davidsohn test), two tests the

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specificity of which approaches 99 percent.<sup>20</sup> In none of the 175 cases initially reviewed were studies for antibodies to Epstein-Barr virus obtained.

Clinical records were studied retrospectively. Patient age, sex, race, admission diagnoses, prior antibiotic treatment, symptoms, and reason for admission were determined from the medical history. The physical examination was reviewed for significant physical findings. Laboratory studies, including complete blood count, Monospot test, differential heterophil test, liver function studies, erythrocyte sedimentation rate, cold agglutinins, and throat cultures, were noted, if performed. Complications and use of steroids were obtained from the discharge summary.

For the purpose of this study, leukocytosis, anemia, and thrombocytopenia were determined by the ranges of normal given by the laboratory involved in the care of the patient. Absolute lymphocytosis was considered to be a lymphocyte count of 5,000/mm<sup>3</sup> or greater. A relative lymphocytosis was defined as lymphocytes making up 50 percent or greater of the total leukocyte count. Normal ranges of laboratory tests were age adjusted.

**Results**

*Epidemiology*

One hundred sixty-one patient records met the criteria for diagnosis of infectious mononucleosis. There were 81 male (50.3 percent) and 80 female (49.7 percent) patients, with age ranges from 2 to 58 years. Age distribution revealed a peak incidence at 18 years. Racial distribution included 146 whites (90.7 percent) and 15 blacks (9.3 percent). Interestingly, in those under ten years of age (n = 15), there were 4 whites (26.7 percent) and 11 blacks (73.3 percent). The ratio of whites to blacks who are hospitalized in the three community hospitals is approximately four to one. No significant seasonal variation was seen.

*Admission Diagnoses and Reasons for Admission*

Infectious mononucleosis was suspected in 84 patients prior to serological confirmation of the disease. This admission diagnosis was followed in frequency by nonspecific pharyngitis or tonsillitis (27 cases), dehydration (19 cases), hepatitis (10 cases), and gastroenteritis (10 cases). There was a multiplicity of other admission diagnoses, and in

**Table 1. Admission Diagnoses prior to Serological Confirmation of Infectious Mononucleosis (n = 161)\***

Diagnosis	Number
Infectious mononucleosis	84
Tonsillitis, pharyngitis	27
Dehydration	10
Hepatitis	10
Nausea, vomiting, gastroenteritis	10
Pneumonia, pneumonitis	6
Respiratory distress, airway obstruction	6
Meningitis, encephalitis	4
Cervical adenitis	3
Abdominal pain, appendicitis	3
Diabetes, diabetic complications**	3
Lymphadenopathy	2
Sinusitis, upper respiratory infection	2
Otitis media, ear infection	2
Bleeding diathesis, Henoch-Schoenlein purpura	2
Internal injuries, ruptured spleen	2
Other	19

\*There may be more than one diagnosis per patient  
 \*\*Condition previously diagnosed

four cases patients hospitalized for problems unrelated to infectious mononucleosis were diagnosed as having infectious mononucleosis during their hospitalization. The various admission diagnoses are listed in Table 1.

It was not always apparent from the admission diagnoses what factors necessitated hospitalizing a patient; therefore, an effort was made to determine the reasons the physician felt hospitalization was necessary. In 99 cases (61.5 percent) treatment or prevention of dehydration was given as the reason for hospitalization. Causes of dehydration were most commonly secondary to severe dysphagia and less commonly secondary to vomiting and diarrhea. In 42 cases (26.1 percent) investigation of abnormal clinical or laboratory findings was given as the reason for hospitalization. Six patients (3.7 percent) were hospitalized for impending airway obstruction. Four patients (2.5 percent) were hospitalized for problems unrelated to infectious mononucleosis. The specific reason for hospitalization could not be determined in ten cases (6.2 percent).

**Table 2. Symptoms in Infectious Mononucleosis (n = 161)**

Symptom	No. (%)
Sore throat	128 (79.5)
Feverishness	79 (49.1)
Fatigue	72 (44.7)
Dysphagia	71 (44.1)
Headache	52 (32.3)
Nausea	47 (29.2)
Anorexia	39 (24.2)
Malaise	35 (21.7)
Nasal congestion	34 (21.1)
Abdominal pain	33 (20.5)
Chills	33 (20.5)
Cough	31 (19.3)
Weakness	31 (19.3)
Earache	21 (13.0)
Myalgias	15 (9.3)
Rhinorrhea	12 (7.5)
Neck pain	10 (6.2)
Diarrhea	9 (5.6)
Dizziness	8 (5.0)
Dark urine	6 (3.7)
Lethargy	3 (1.9)
Pruritis	3 (1.9)
Frequency, dysuria	3 (1.9)
Diaphoresis, night sweats	3 (1.9)
Chest pain	2 (1.2)
Diplopia, blurred vision	2 (1.2)
Shakiness	1 (<1.0)
Weight loss	1 (<1.0)

### Antibiotic Use and Throat Culture Findings

Seventy-eight patients (48.4 percent) received antibiotics before serological confirmation of infectious mononucleosis. Fifty-nine patients (36.6 percent) received antibiotics after serological diagnosis of infectious mononucleosis. Thirty-six patients (22.4 percent) received ampicillin during their illness, of whom 10 (27.8 percent) developed a rash attributed to the drug's administration.

Eighty patients (49.7 percent) had throat cultures during their hospitalization. Two of these 80 throat cultures (2.5 percent) were positive for group A  $\beta$ -hemolytic streptococci.

### Clinical Findings

The most common presenting symptom was sore throat in 128 cases (79.5 percent). This was followed in frequency by a subjective feeling of fever (feverishness) in 79 cases (49.1 percent),

**Table 3. Physical Findings in Infectious Mononucleosis (n = 161)**

Physical Finding	No. (%)
Lymphadenopathy	134 (83.2)
Pharyngitis	123 (76.4)
With exudate	102/123 (82.9)
Without exudate	21/123 (17.1)
Fever	122 (75.8)
Splenomegaly	56 (34.8)
Hepatomegaly	32 (19.9)
Jaundice	11 (6.8)
Rash	10 (6.2)
Rash attributed to ampicillin use	10 (6.2)
Periorbital edema	6 (3.7)
Palatine petechiae	5 (3.1)
Otitis media	2 (1.2)
Ecchymoses, petechiae	2 (1.2)
Abdominal tenderness	2 (1.2)
Conjunctivitis	1 (<1.0)
Tender epididymis	1 (<1.0)
Flank tenderness	1 (<1.0)

fatigue in 72 cases (44.7 percent), dysphagia in 71 cases (44.1 percent), and headache in 52 cases (32.3 percent). Other presenting symptoms are listed in Table 2.

Like the numerous presenting symptoms, there were a large variety of presenting physical findings (Table 3). The most common physical finding was adenopathy in 134 cases (83.2 percent), which was followed by pharyngitis in 123 cases (76.4 percent), usually accompanied by an exudate (82.9 percent of patients with pharyngitis). Other physical findings included fever in 122 cases (75.8 percent), splenomegaly in 56 cases (34.8 percent), and hepatomegaly in 32 cases (19.9 percent).

### Laboratory Findings

The presence of atypical lymphocytes (Downey cells) was the most common hematological abnormality seen in this study. These atypical lymphocytes were seen in 132 of 161 cases (82.0 percent). The relative percent of atypical lymphocytes was not determined in the majority of cases. The second most common presenting hematological abnormality was a relative lymphocytosis, noted in 126 of 161 cases (78.3 percent). This was followed by an absolute lymphocytosis (5,000/mm<sup>3</sup> or greater), found in 103 of 161 cases (64.0 percent). Leukocytosis (a leukocyte count of 10,000/mm<sup>3</sup> or greater)



was noted in 92 of 161 cases (57.1 percent). Also included among the hematological abnormalities was prolongation of the Westergren erythrocyte sedimentation rate (ESR) in 11 of 19 cases (57.9 percent) and cold agglutinin positivity in 2 of 5 cases (40 percent). Anemia was seen in 12 of 161 cases (7.5 percent), and thrombocytopenia was seen in 9 of 161 cases (5.6 percent).

Lactic acid dehydrogenase elevation was the most common liver function abnormality seen with 122 of 140 cases (87.1 percent) showing elevations. Serum glutamic-oxaloacetic transaminase was elevated in 113 of 138 cases (81.9 percent) and glutamic-pyruvic transaminase was elevated in 74 of 99 cases (74.7 percent). Elevation of alkaline phosphatase was noted in 62 of 131 cases (47.3 percent). Total bilirubin was elevated in 33 of 139 cases (23.7 percent).

Of the 175 cases reviewed for inclusion in this study, only two did not have a differential heterophile or Monospot test performed. One hundred sixty-one of the 175 cases (92.0 percent) had positive tests. Twelve of 175 cases (6.9 percent) were heterophile negative. In 64 cases, 61 positive and 3 negative, both a Monospot and a differential heterophile test were obtained, and in all cases the results of the two tests correlated.

### Complications

Three patients (1.7 percent) were reported as having suppurative cervical adenitis or neck abscess; one of these had positive cultures for *Staphylococcus aureus*. The causative bacteria in the other two were not determined. Three patients (1.7 percent) had airway obstruction resulting in mild to moderate respiratory distress not requiring intubation. Peritonsillar abscess was diagnosed in two patients (1.1 percent), one of whom had a positive culture for group B  $\beta$ -hemolytic streptococci. One patient (<1.0 percent) developed Guillain-Barré syndrome, resulting in residual neurological deficits including lower extremity weakness and cranial nerve palsies. A ruptured spleen was sustained by one patient (<1.0 percent) after falling from a ladder.

### Steroid Use

Thirty-seven patients (23.0 percent) received steroids during therapy. Twenty-five of these 37 patients (67.6 percent) received steroids for severe dysphagia, which required intravenous fluids. In

four cases (10.8 percent) the reason for steroid use could not be determined. Another three patients (8.2 percent) required steroids for treatment of airway obstruction. One patient each (2.7 percent) was treated with steroids for persistent fever, uncontrolled pruritis, and "recurrent" infectious mononucleosis (authors' quotes). One patient with Guillain-Barré syndrome and one patient with a ruptured spleen were treated with steroids.

### Discussion

The epidemiological results of this study are in agreement with findings of prior studies. The absence of a predilection for either sex by infectious mononucleosis<sup>1,5,21</sup> and peak age incidence during the late adolescent and early adult years are well known.<sup>5,16,21</sup> The higher incidence of clinically recognized disease in whites during the adolescent and adult years and in blacks during the infant years confirms other investigations.<sup>10</sup> This difference in incidence of infectious mononucleosis among blacks and whites is thought to be due to socioeconomic factors rather than racial factors.<sup>9,10,22</sup> No significant seasonal variation was seen in this study. Previous reports of seasonal variation are conflicting<sup>9,23</sup>; some studies show no variation,<sup>5</sup> while others demonstrate increases of infectious mononucleosis during fall and spring.<sup>1,21</sup>

The variety and number of different admission diagnoses prior to serological confirmation of infectious mononucleosis demonstrate the difficulty in diagnosing this illness. Although infectious mononucleosis was suspected in a great number of patients, a significant number of other illnesses were also considered by physicians. This may serve to reinforce the thought that physicians must have a high index of suspicion for infectious mononucleosis, especially in age groups that are prone to atypical presentations.<sup>11-15</sup> For example, it is known that young children frequently lack a heterophile antibody response<sup>7,11-13,16</sup> and may present clinically with a picture of pneumonia or hepatitis.<sup>12</sup> On the other hand, elderly patients have been reported to not develop an atypical lymphocytosis or lymphadenopathy to the same degree as younger patients and may develop liver function abnormalities that are more marked than in their younger counterparts.<sup>14</sup>

This study demonstrates that although infectious mononucleosis is usually considered to be a benign, self-limited illness, hospitalization is often

required for minor complications, such as dehydration. The need to investigate unusual clinical or laboratory findings may also prompt hospitalization; however, the clinician may be able to reduce the hospitalizations by being aware of the broad spectrum of clinical manifestations of infectious mononucleosis.

Infectious mononucleosis can often be confused with bacterial infections, particularly streptococcal pharyngitis and peritonsillitis, as shown by the great number of patients receiving antibiotics. Over one third of the patients in this study received antibiotics subsequent to the serological diagnosis of infectious mononucleosis, although only 2 of 80 throat cultures (2.5 percent) were positive for group A  $\beta$ -hemolytic streptococci. Interestingly enough, this conflicts with previous reports showing that up to one third of cases of infectious mononucleosis were associated with streptococcal infection.<sup>24</sup> The reason for such a low rate of positive throat cultures is uncertain, but may represent antibiotic treatment of some patients prior to hospitalization. The low number of patients who had throat cultures despite the most common presenting symptom's being sore throat is also surprising. However, the number of patients who had throat cultures done in the physicians' offices also is not known. Antibiotics have been used prophylactically with the hope that they would help prevent secondary bacterial infection during the use of steroids.<sup>4</sup> Nevertheless, penicillin has not been shown to alter the course of the disease<sup>25</sup>; therefore, routine use of antibiotics is discouraged. Certainly the routine use of ampicillin in the treatment of pharyngitis should be avoided because of the well-recognized rash it may precipitate in association with infectious mononucleosis.<sup>24,26,27</sup>

Ampicillin-associated rash was not seen so frequently as previously reported. Only 10 of 36 patients in this study developed rash associated with ampicillin therapy, while various studies have placed the incidence at 69 to 100 percent.<sup>24,26,27</sup>

The symptoms seen in this investigation are in general agreement with other studies.<sup>2,4,28</sup> Abdominal pain, cough, and chills were noted in a larger number of patients in this series than in two prior reports.<sup>2,28</sup>

This study confirms earlier ones demonstrating that the frequency and duration of symptoms can be quite variable.<sup>28,29</sup> Differences in subjective

complaints, however, may also reflect variability of expression of infectious mononucleosis among age groups.<sup>1,13-15,29</sup>

The physical findings reported in this study also tend to be similar to those noted by other investigators.<sup>2,4,5,28</sup> The characteristic periorbital edema (Hoagland's sign) and palatal enanthem of infectious mononucleosis were not seen so frequently as previously reported.<sup>2,28</sup> Differences with which the various physical findings are seen may well reflect their transient nature.<sup>28</sup>

Laboratory findings—hematological, serological, and chemical—were in agreement with other reports.<sup>4,30</sup> Again, it should be noted that the laboratories of the three hospitals studied did not report the relative number of atypical lymphocytes, a helpful diagnostic feature in differentiating infectious mononucleosis from many other illnesses.<sup>25,30,31</sup> Thrombocytopenia was not seen so frequently as in other reports<sup>30</sup>; however, in many cases only an estimate of the platelet number was given, and quantitative counts were not performed.

The Monospot test, along with the complete blood count, was the test most often ordered by community physicians in diagnosing infectious mononucleosis. Although the Monospot test can give false-positive results, the number is small, and the test is highly specific as well as sensitive.<sup>20,25,31-33</sup> This study showed that the Monospot test and the differential heterophil test correlated in 64 patients. It is felt that utilizing both tests probably will not add significant clinical information.<sup>31</sup>

Epstein-Barr virus (EBV) antibody titers were not obtained in any patients in this study. Since other illnesses, such as cytomegalovirus infections, may mimic infectious mononucleosis,<sup>34</sup> in clinically suspected cases of infectious mononucleosis with a negative heterophil test, EBV antibody titers should be obtained to rule out more serious conditions.

Liver function abnormalities seen in the majority of patients in this study represent a well-recognized finding.<sup>30</sup> Some experts feel that in the absence of liver function abnormalities, other diagnoses should be strongly considered.<sup>35</sup> On the other hand, if it is not clinically apparent that infectious mononucleosis is responsible for elevated liver function results, other causes of hepatitis should be ruled out.

The rate of serious complications in this investigation was comparable to other reports.<sup>28,36,37</sup> Al-



though the complication rate in infectious mononucleosis is relatively low, one must be alert for complication recognition and management.<sup>36,37</sup>

Steroids were used in less than 25 percent of the patients hospitalized for infectious mononucleosis. No deleterious short-term effects were ascribed to their use. Nevertheless, it is recommended that their use be restricted for treatment of the more serious complications.<sup>25</sup>

## Summary

From this study of infectious mononucleosis in the community hospital setting, it is clear that the primary care physician should maintain a wide perspective when dealing with this illness; this is especially true of the family physician who deals with all age groups and who must be aware of differences in presentation of infectious mononucleosis among these age groups. This study also indicates that the use of antibiotics by some physicians may be indiscriminate, particularly in the treatment of pharyngitis of obvious viral etiology and with negative throat cultures. The various manifestations of infectious mononucleosis can pose diagnostic difficulties for the clinician. The findings of this study imply, however, that many needless hospitalizations can be avoided by maintaining a high index of suspicion and by being aware of the numerous manifestations of the illness.

## References

1. Evans AS: Infectious mononucleosis in University of Wisconsin students: Report of a five-year investigation. *Am J Hyg* 71:342, 1960
2. Hoagland RJ: Infectious Mononucleosis. *Am J Med* 13:158, 1952
3. Pannuti CS, Carvalho RP, Evans AS, et al: A prospective clinical study of the mononucleosis syndrome in a developing country. *Int J Epidemiol* 9:349, 1980
4. Mason WR, Adams EK: Infectious mononucleosis: An analysis of 100 cases with particular attention to diagnosis, liver function tests, and treatment of selected cases with prednisone. *Am J Med Sci* 236:447, 1958
5. Hubble MP, Lai PK, Mackay-Scollay EM, et al: Epidemiology of infectious mononucleosis in Western Australia: A retrospective study, 1966-1972. *Med J Aust* 2:863, 1974
6. Evans AS: Infectious mononucleosis in the Armed Forces. *Milit Med* 135:300, 1970
7. Evans AS, Niederman JC, McCollum RW: Seroepidemiologic studies of infectious mononucleosis with EB virus. *N Engl J Med* 279:1121, 1968
8. Sawyer RN, Evans AS, Niederman JC, et al: Prospective studies of a group of Yale University freshmen: Occurrence of infectious mononucleosis. *J Infect Dis* 123:263, 1971
9. Hallee TJ, Evans AS, Niederman JC, et al: Infectious mononucleosis at the United States Military Academy: A prospective study of a single class over four years. *Yale J Biol Med* 3:182, 1974
10. Sumaya CV, Henle W, Henle G, et al: Seroepidemiologic study of Epstein-Barr virus infections in a rural community. *J Infect Dis* 131:403, 1975
11. Tamir D, Benderly A, Levy J, et al: Infectious mononucleosis and Epstein-Barr virus in childhood. *Pediatrics* 53:330, 1974
12. Krabbe S, Hesse J, Uldall P: Primary Epstein-Barr virus infection in early childhood. *Arch Dis Child* 56:49, 1981
13. Henle G, Henle W: Observations on childhood infections with Epstein-Barr virus. *J Infect Dis* 121:303, 1970
14. Horowitz CA, Henle W, Henle G: Clinical and laboratory evaluation of elderly patients with heterophil-antibody positive infectious mononucleosis: Report of seven patients, ages 40 to 78. *Am J Med* 61:333, 1976
15. Sumaya CV: Primary Epstein-Barr virus infections in children. *Pediatrics* 59:16, 1977
16. Joncas J, Chiasson JP, Turcotte J, et al: Studies on infectious mononucleosis: Clinical data, serological and epidemiologic findings. *Can Med Assoc J* 98:848, 1968
17. Niederman JC: Infectious mononucleosis at the Yale-New Haven Medical Center, 1946-1955. *Yale J Biol Med* 28:629, 1956
18. Fisher M, Shenker IR, Nussbaum MP: Infectious mononucleosis: Review of complications in a hospitalized series. *NY State J Med* 80:929, 1980
19. Dunnet WN: Infectious mononucleosis. *Br Med J* 1:1187, 1963
20. Lee CL, Davidsohn J: The clinical serology of infectious mononucleosis. In Carter RL, Penman HG (eds): *Infectious Mononucleosis*. Oxford, Blackwell Scientific, 1969, pp 177-200
21. Heath CW, Brodsky AL, Potalsky AI: Infectious mononucleosis in a general population. *Am J Epidemiol* 95:46, 1972
22. Nye FJ: Social class and infectious mononucleosis. *J Hyg* 71:145, 1973
23. Pollack TM: Epidemiology of infectious mononucleosis. In Carter RL, Penman HG (eds): *Infectious Mononucleosis*. Oxford, Blackwell Scientific, 1969, pp 63-81
24. Patel BM: Skin rash with infectious mononucleosis and ampicillin. *Pediatrics* 40:910, 1967
25. Karzon DT: Infectious mononucleosis. *Adv Pediatr* 22:231, 1976
26. Brown LG, Kanwar BS: Drug rashes in glandular fever. *Lancet* 2:1418, 1967
27. Pullen H, Wright N, Murdock JM: Hypersensitivity reactions to antibacterial drugs. *Lancet* 2:1176, 1967
28. Finch SC: Clinical symptoms and signs of infectious mononucleosis. In Carter RL, Penman HG (eds): *Infectious Mononucleosis*. Oxford, Blackwell Scientific, 1969, pp 19-46
29. Niederman JC, McCollum RW, Henle G, et al: Infectious mononucleosis: Clinical manifestations in relation to EB virus antibodies. *JAMA* 203:205, 1968
30. Finch SC: Laboratory findings in infectious mononucleosis. In Carter RL, Penman HG (eds): *Infectious Mononucleosis*. Oxford, Blackwell Scientific, 1969, pp 47-62
31. English EC, Geyman JP: The efficiency and cost effectiveness of diagnostic tests for infectious mononucleosis. *J Fam Pract* 6:977, 1978
32. Lee CL, Davidsohn E, Panczyzyn O: Horse agglutinins in infectious mononucleosis: The spot test. *Am J Clin Pathol* 49:12, 1968
33. Tests for infectious mononucleosis, editorial. *Br Med J* 10:1153, 1980
34. Klemola E, Von Essen R, Henle G, et al: Infectious mononucleosis-like disease with negative heterophil agglutination test: Clinical features in relation to EB virus and cytomegalovirus antibodies. *J Infect Dis* 121:608, 1970
35. Schlepupner CJ, Overall JC: Infectious mononucleosis and Epstein-Barr virus: Clinical picture, diagnosis, and management. *Postgrad Med* 65:95, 1979
36. Evans AS: Complications of infectious mononucleosis: Recognition and management. *Hosp Med* 3:24, 1967
37. Dalrymple W: Infectious mononucleosis: Implications of serious complications in medical management. *Postgrad Med* 35:243, 1964