
Communications

Infectious Mononucleosis: Some New Observations from a 15-Year Study

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Although new developments have clarified somewhat the epidemiology and pathogenesis of infectious mononucleosis (IM), still there is much uncertainty.^{1,2}

The old homely label of glandular fever has been replaced by the more scientific term, infectious mononucleosis, with the discovery of the Epstein-Barr virus (EBV) and the demonstration of its association with IM.¹

Yet there are many unanswered questions. In spite of its title, IM rarely is infectious. In practice it is most unusual to discover any case-to-case contacts. Epidemics are not a feature of the condition, though on occasion clustering does seem to occur. The explanations that relate to the remarkable age incidence of IM (affecting teenagers and young adults predominantly), and its causation by delayed infection with EBV are not convincing.

Most reports on IM have come from short planned field studies by physicians, epidemiologists, and virologists. General practice offers opportunities for observing and following up a fairly static population with families and individuals

over long periods of time. This prospective study has been carried out in a family practice over a period of 15 years (1964 to 1979).

Methods

The practice is in a southeast London suburb, chiefly with social classes 2, 3, and 4.³ The population was stable at around 8,500 during the period of study. An age/sex register recorded all the persons at risk.

There was full access to pathology services at a nearby hospital (Beckenham Hospital). The diagnosis of infectious mononucleosis was made on the basis of positive Paul-Bunnell or Monospot tests and on reported presence of abnormal mononuclear (glandular fever) cells on blood checks carried out at the local hospital laboratory.

Prospective records were kept on all persons diagnosed as suffering from IM and it was possible to relate subsequent family and personal course and history.

Results

Incidence

During the 15 years, the annual incidence rate was 1.6 per 1,000 of the population (Table 1). This is much higher than the 0.2 to 0.6 per 1,000 rates quoted by Pullen.⁴ This suggests that in an average

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Table 1. Infectious Mononucleosis: Numbers and Rates per 1,000 in 1964 to 1979

Age (years)	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50+	Total
Male	0	2	30	41	21	9	0	1	104
Female	1	2	28	48	20	9	1	1	110
Persons	1	4	58	89	41	18	1	2	214
(Incidence per 1,000 persons)	1.7	5.0	90.0	121.6	34.2	14.4	0.8	0.8	23.8*

*This represents an annual incidence of 1.6 per 1,000

sized practice of 2,500, there may occur four new cases of IM in a year.

Table 1 also shows the age distribution of the 214 persons with IM (4 had two episodes). There was no appreciable sex difference. The highest incidence was in the 10- to 19-year age group.

Season

The seasonal distribution was that 64 were diagnosed in the January to March quarter, 59 in April to June, 41 in July to September, and 50 in October to December.

Infectivity

In no instance was there any reliable history of contact with any other known case of IM. There were, however, clusters of cases at times.

Family History

Among the 214 persons with IM, there were 32 from families in whom more than one person was diagnosed with IM during the 1964 to 1979 period.

There were 2 families in whom three siblings had IM; 11 families with two siblings with IM; 1 family where the mother and son had IM, and 1 family where the father and son had IM. Out of 38 siblings at risk in the 15 families, 30 (79 percent) had IM.

It is important to stress that in no family was there any evidence of cross infection. In each

family there was a two-year or longer spacing between the cases of IM.

The ages at which these family cases of IM occurred were: four at 10-to-14 years; twenty-four at 15-to-19 years; two at 20-to-29 years; and two parents were aged 32 years (mother) and 54 years (father) when they were diagnosed.

It was as though, when each sibling reached the vulnerable age for IM, each succumbed in turn.

Multiple Attacks

Four persons apparently had two episodes of IM. On each occasion the Paul-Bunnell or Monospot tests were positive, and there were atypical (GF) mononuclear cells in the blood. There was a lapse of nine months or longer between each episode.

One girl had her attacks at 15 and 16 years; one at 12 and 16 years; one at 13 and 15 years; and one at 4 and 11 years.

Clinical Course

All but 2 of the 214 were unremarkable and followed the recognizable pattern of illness with prolonged sore throat, tender palpable lymph glands in neck and elsewhere, and malaise and general disturbance that persisted for varying periods.

One girl developed jaundice during her second attack of IM. One boy, aged 19 years, was found dead in bed at home while being treated for IM. The autopsy report was that he died from "myocarditis due to infectious mononucleosis."

Association Between Infectious Mononucleosis and Lymphoma

There were two remarkable cases in which an initial diagnosis of IM was made in the early course of the patient's illness, but both subsequently were found to have lymphoma.

A female, aged 62 years, presented with a sore throat for over two weeks. On examination, she had a swollen left tonsil and enlarged, tender, left upper cervical lymph nodes. Monospot test was positive, and abnormal mononuclear blood cells were found. She continued to be unwell. Eventually, she was found to have lymphoma of her left tonsil and cervical lymph nodes. Treated with radiotherapy and chemotherapy, her condition was controlled. In addition, she had a long history of depression and she was found dead from an overdose of barbiturates two years from first diagnosis of IM.

A female, aged 21 years, had a neurological illness that was considered to be either a polyneuritis or multiple sclerosis. In hospital she was found to have a positive Paul-Bunnell test and atypical mononuclear blood cells. She was diagnosed as having "unusual glandular fever." She continued to deteriorate, developed evidence of widespread lymphomas, and died within a year of onset.

Discussion

IM is an intriguing and challenging syndrome. Its true nature still has not been explained completely. It is generally a benign but debilitating and prolonged illness, affecting teenagers and young adults. Until 1966, only 50 cases of death from IM complications were recorded.¹ This series records another fatality, totally unexpected (the boy of 19).

IM is not uncommon, and four new cases a year may be expected in a general practice, and many more in universities and military units where young adults are brought together.

In addition to confirmed cases of IM, during the teenage period also there is a high prevalence of non-specific sore throats and of streptococcal throat infections.³ Epidemiologically, there are two periods at which throat infections are most prevalent: the period from 4 to 8 years of age contains the highest prevalence rates, followed by a second peak from 10 to 19 years.³ Tonsillectomy is

most often carried out at the same periods and is further evidence of troublesome, recurrent sore throats.

It is likely that there are some immunological reasons for these high prevalence rates of infections affecting the lymphoid structures of the throat during the 4- to 8-year and the 10- to 19-year periods. In support of this hypothesis is the previously unreported observation that some families are particularly liable to suffer from IM on reaching the vulnerable age period. It is as though they have some unusual deficiency or hypersensitivity that renders them particularly susceptible to Epstein-Barr virus infection and infectious mononucleosis.

A relation between EBV and African (endemic) Burkitt lymphoma is well established,¹ but the relationship between an initial diagnosis of IM and subsequent lymphoma as recorded in the two persons in this paper does not appear to have been reported before.

These original findings from one family practice demonstrate the continuing value in modern times of what may have been old fashioned recording of clinical observations as practiced by Sydenham and Mackenzie in the past.

Such observations may not provide complete answers to current medical problems, but they do add small pieces of information. This is particularly so in a condition such as IM, which, after all, is very much a family practice disease.

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