

**Klemola E & Kääriäinen L.** Cytomegalovirus as a possible cause of a disease resembling infectious mononucleosis. *Brit. Med. J.* 2:1099-102, 1965; and, **Kääriäinen L, Klemola E & Paloheimo J.** Rise of cytomegalovirus antibodies in an infectious-mononucleosis-like syndrome after transfusion. *Brit. Med. J.* 1:1270-2, 1966. [Dept. Virol., Univ. Helsinki; Aurora Hosp.; and, First Dept. Med., Univ. Central Hosp., Helsinki, Finland]

**A significant rise in the titer of antibodies to cytomegalovirus was established in five previously healthy individuals experiencing a febrile disease hematologically resembling infectious mononucleosis, but without positive heterophil agglutination test and exudative pharyngitis. A similar disease, "cytomegalovirus mononucleosis," was demonstrated after blood transfusions in three patients. [The SC<sup>®</sup> indicates that these papers have been cited in more than 270 and 220 publications, respectively.]**

## Cytomegalovirus as a Cause of Atypical Mononucleosis

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I worked as a medical doctor in the Helsinki City Hospital for Contagious Diseases since 1945. In 1954, its name was changed to Aurora Hospital, and I was promoted to head the Department of Medicine. My main scientific interest was infectious mononucleosis.

The acute illness in January 1965 of the 33 year-old brother-in-law of Leevi Kääriäinen, my young colleague, started our studies on atypical mononucleosis. In his own *Citation Classic* commentary, Kääriäinen gave an excellent description of the early events of these studies.<sup>1</sup> In a short time, four other patients with Paul-Bunnell-negative mononucleosis and a significant rise in antibodies against cytomegalovirus (CMV) were hospitalized. Our observation was published in the *British Medical Journal* in 1965. A relative started this study, and a friend was of great help in getting the second article published in the same journal after six months. The chemist of the

Aurora Hospital had told me that his wife, who had received a substantial amount of fresh blood in connection with a gynecological operation, showed an atypical Paul-Bunnell-negative mononucleosis. There was a significant rise of antibodies against CMV after the operation. We started a systematic study on CMV infections in patients with open-heart surgery at the Helsinki University Central Hospital, in collaboration with Jorma Paloheimo. It soon became apparent that subclinical infections were quite common in those patients.<sup>2</sup> Harri Nevanlinna, head of the Finnish Red Cross Blood Transfusion Service, said: "It is insignificant if some of the mononucleosis cases are caused by cytomegalovirus, but it is of great concern that healthy blood donors can spread CMV infections."

Our collaboration with Kääriäinen lasted for two years until he went to the US as a post-doctoral fellow. For me, it had been fortunate to collaborate with an enthusiastic young virologist. The work was continued by Robert von Essen. Prospective studies on the role of CMV in the etiology of mononucleosis were started at the Aurora Hospital immediately after the first findings. Serum samples were taken from 500 mononucleosis patients during a period of eight years. From these cases, 33 had cytomegalovirus mononucleosis.<sup>3-5</sup>

We were very fortunate to have the keen interest and sympathy of Thomas Weller. At the International Conference on Cytomegalovirus Infections, held in St. Gall, Switzerland, in 1970, the topic of my keynote lecture was "Postnatal cytomegalovirus infections." We had several collaborations with Werner Henle, who, in 1968, had shown that the etiology of the typical infectious mononucleosis was Epstein-Barr virus.<sup>6</sup> I was honored to receive the "Matti Äyräpää Prize and Honorary Lecture," the most prestigious Finnish annual prize in medicine, in 1976. That same year, I was invited to Stockholm to give the "Justus Ström Honorary Lecture."

1. **Kääriäinen L.** A new disease for an old virus. *Citation Classic*. Commentary on *Brit. Med. J.* 2:1099-102, 1965 and *Brit. Med. J.* 1:1270-2, 1966. *Current Contents/Clinical Medicine* 19(34):10, 26 August 1991.
2. **Paloheimo J A, von Essen R, Klemola E, Kääriäinen L & Siltanen P.** Subclinical cytomegalovirus infections and cytomegalovirus mononucleosis after open heart surgery. *Amer. J. Cardiol.* 22:624-30, 1968. (Cited 100 times.)
3. **Klemola E, Kääriäinen L, von Essen R, Haltia K, Koivuniemi A & von Bonsdorff C-H.** Further studies on cytomegalovirus mononucleosis in previously healthy individuals. *Acta. Med. Scand.* 182:311-22, 1967. (Cited 80 times.)
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5. **Klemola E.** Cytomegalovirus infection in previously healthy adults. *Ann. Intern. Med.* 79:267-8, 1973.
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