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Murine Cytomegalovirus Genomic Material in Marrow Cells: Relation to Altered Leukocyte Counts During Sublethal Infection of Mice

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To investigate infection of hematopoietic cells by murine cytomegalovirus (MCMV), we used *in situ* hybridization to detect MCMV genomic material in marrow cells during sublethal infection of three-week-old mice. MCMV genomic material was present in femoral marrow cells on days 3, 5, 7, and 14, and detection of MCMV genomes correlated strongly with recovery of infectious virus. Peak infection occurred on day 5, when 0.003%–0.185% of the marrow cells contained MCMV genomic material. At peak infection, MCMV genomic material was observed predominantly in marrow mononuclear cells. Coincident with marrow infection, mice experienced significant leukopenia, whereas cessation of MCMV replication in marrow cells was associated with leukocytosis and restoration of normal peripheral blood leukocyte counts.

Cytomegalovirus (CMV) infections of humans are often associated with alterations in the hematologic profile. Infants with congenital cytomegalic inclusion disease may develop thrombocytopenia, leukocytosis, leukopenia, or hemolytic anemia [1–4]. In some infants the changes in the peripheral blood are severe enough to mimic a primary hematologic disorder. Older patients with acquired CMV infections, such as the CMV mononucleosis syndrome, usually develop an atypical lymphocytosis and may have thrombocytopenia as well [5, 6].

In spite of the fact that these hematologic abnormalities have been recognized clinically for many years, the pathogenesis of CMV-induced abnormalities in hematopoiesis has not as yet been completely elucidated. Direct CMV infection of human hematopoietic elements is assumed to occur, but this assumption is based largely on the histological appearance of marrow elements and not on detecting CMV replication in hematopoietic cells [7].

Of the various animal models, murine cytomegalovirus (MCMV) infection has been the most extensively studied. Osborn and Shahidi [8] observed that

thrombocytopenia and leukopenia developed in MCMV-infected mice, and Petursson et al. [9] noted that MCMV infection was associated with reduced numbers of granulocyte and megakaryocyte precursors. Both groups of investigators attributed these abnormalities to CMV infection of hematopoietic cells, because MCMV antigen could be detected in splenic megakaryocytes and because progenitor cells were reduced by infection of marrow cells *in vitro*.

In the experiments described in this report, we have used *in situ* hybridization to pursue similar questions regarding the pathogenesis of CMV-induced hematologic abnormalities. Our principal objectives were to detect MCMV genomic material in marrow cells of mice undergoing sublethal infection and to relate the appearance of MCMV genomic material to the changes that occur in the peripheral blood leukocyte counts.

Materials and Methods

Animals. Three-week-old female Swiss-Webster mice (Biolab Breeding Laboratories, Minneapolis, Minn) were maintained in a controlled environment (12-hr light-dark cycle, food and water *ad libitum*) during these experiments. Infected and control mice were housed separately.

Virus. The Smith strain of MCMV, obtained originally from Dr. Earl R. Kern, University of Utah, Salt Lake City, Utah, was used to prepare virus pools. As previously described [10], MCMV was prepared

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from MCMV-infected mice as a 10% wt/vol homogenate of salivary gland tissues in Eagles' MEM containing 10% fetal calf serum, penicillin (100 U/ml), and streptomycin (50 µg/ml). The MCMV pools contained 10^7 pfu of MCMV/ml when titrated under agarose on mouse embryo fibroblast (MEF) cell monolayers. For control inoculations, a normal salivary gland pool was prepared in a similar manner by using salivary glands from uninfected mice.

Experimental protocol. In preliminary experiments, mice were inoculated ip with serial dilutions of the MCMV pool. A 0%–20% mortality consistently occurred at an inoculum of 10^5 pfu per mouse. This inoculum was used in subsequent experiments and infected all mice, as indicated by ruffled fur, diminished activity, and subsequent positive cultures of virus. Control mice received an equivalent dilution of normal salivary gland homogenate ip.

On days 1, 3, 5, 7, 14, and 21 after inoculation, mice were killed, and specimens of blood, spleen tissues, and femoral marrow cells were obtained for culture of virus and in situ hybridization studies. Blood was collected into a heparinized syringe (10 U/ml) by direct cardiac puncture, and blood mononuclear cells were harvested by using previously described techniques [11]. Spleen tissues were prepared as 10% wt/vol homogenates in MEM with 10% fetal calf serum and antibiotics. Marrow cells were collected by flushing the shaft of the right femur with 1 ml of MEM containing fetal calf serum and antibiotics. Aliquots of cell suspensions and spleen homogenates for virus culture were frozen at -70 C until assayed.

Marrow cells for in situ hybridization experiments were prepared by centrifugation (Cytospin 2[®]; Shandon Southern Instruments, Sewickley, Pa) of $\sim 10^5$ cells onto acetylated microscope slides treated with Denhardt's medium [12]. Slides were then fixed with ethanol:acetic acid (3:1) and 95% ethanol and stored at 4 C.

Virus assay. Tissues and cell suspensions were assayed for MCMV on confluent monolayers of MEF cells grown in 24-well plates by using an agarose overlay, as previously described [10]. Culture results were expressed as log pfu of MCMV per gram of spleen tissue or infectious foci per 10^6 marrow or peripheral blood mononuclear cells.

Blood leukocyte determinations. Blood was obtained by tail-vein sampling from ten MCMV-infected and ten control animals on days 0, 1, 3, 5, 7, 14, and 21. Total and differential white blood cell

counts were determined by using the Unopette[®] microcollection system (Becton-Dickinson, Rutherford, NJ) and blood smears stained with Hemacolor[®] (Harleco, Gibbstown, NJ). Platelet counts were determined from blood diluted 1:40 in formalin (2%), acetic acid (2.9%), and crystal violet (0.05%) by using a hemacytometer under phase-contrast microscopy (magnification, $\times 400$).

In situ hybridization. Nucleic acid hybridization studies were performed by using modifications of techniques described by Haase et al. [12]. Immediately before hybridization, cytocentrifuge cell preparations were treated with 0.2 N HCl, proteinase K, and RNase, and were post-fixed in 5% paraformaldehyde. Cells hybridized with biotinylated probes were also pretreated with hydrogen peroxide and methanol to inactivate endogenous peroxidase activity. The probe consisted of cloned MCMV DNA fragment *Hind*III A [13] labeled by nick-translation procedures either with ³⁵S to specific activities of $2\text{--}4 \times 10^8$ cpm/µg of DNA or with biotin. Slides were hybridized at room temperature (~ 23 C) for 72 hr (5-ng probe in 5 µl of reaction mixture) and then washed for 6 hr with 50% formamide, 0.6 M NaCl, 1 mM EDTA, and 10 mM phosphate buffer, pH 6.0. Slides hybridized with ³⁵S-labeled probes were dipped in NTB 2 photoemulsion (Eastman Kodak, Rochester, NY) and exposed for 24 hr at 20 C. Cells hybridized with biotinylated probes were developed by using the Vectastain[®] ABC kit (Vector Laboratories, Burlingame, Calif), diaminobenzidine, and 0.03% hydrogen peroxide. After development, slides were lightly counterstained with either Harris hematoxylin or Hemacolor.

Statistical methods. Data regarding total and differential leukocyte counts from infected and control animals were compared by using two-tailed *t* tests. *P* values $< .05$ were considered significant.

Results

Detection of MCMV genomic material in marrow cells. As summarized in table 1, MCMV genomic material was detected, by using ³⁵S-labeled probes, in the marrow cells harvested on days 3, 5, 7, and 14 of infection. On days 3 and 5, 100% of the animals studied (*n* = 13) had MCMV genomic material in marrow cells, whereas by day 21, only one of four animals was positive. The number of positive cells per marrow ranged from a low of < 1 per 10^6 marrow cells on day 0 to a high of 1,900 per 10^6 cells

Table 1. Detection of MCMV in marrow cells by in situ hybridization.

Day	No. of animals positive/ total no. (%)	Positive cells (range)*
Uninfected	0/4 –	0
1	0/4 –	0
3	4/4 (100)	259 ± 172 (84–413)
5	9/9 (100)	541 ± 604 (4–1,900)
7	5/9 (56)	32 ± 58 (0–180)
14	3/4 (75)	3 ± 2.6 (0–7)
21	1/4 (25)	0.8 ± 1.6 (0–3)

* Numbers (mean ± SD) of cells showing specific hybridization for MCMV genomic material per 10⁶ marrow cells.

on day 5. Peak infection, in terms of the number of positive cells, occurred on day 5, with a mean of 541 ± 604 positive cells per 10⁶ marrow cells. Infection diminished rapidly thereafter, such that by day 7, the mean number of cells containing MCMV genomic material was only 32 ± 58 per 10⁶ marrow cells. Figure 1 shows representative marrow cells hybridized with ³⁵S-labeled probes.

We next attempted to determine the types of cells that contained MCMV genomic material. In these experiments, slides from days 3–7 from animals with positive hybridization with ³⁵S were hybridized with biotin-labeled probes and counterstained with Harris hematoxylin. Biotinylated probes did not obscure cellular morphology, but proved to be slightly less sensitive than were ³⁵S-labeled probes and detected

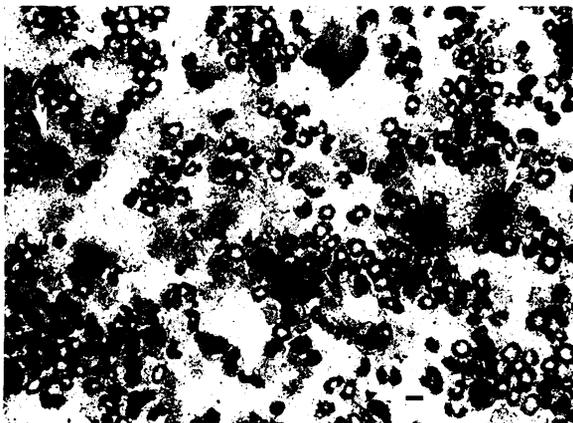


Figure 1. A photomicrograph of a marrow-cell preparation obtained from an MCMV-infected animal; the cells were harvested on day 5 and reacted with the ³⁵S-labeled MCMV DNA probe. This field contains three positive cells (arrows) containing numerous autoradiograph grains. Bar = 10 μm.



Figure 2. A high-power photomicrograph of an MCMV-infected marrow mononuclear cell that contains intranuclear pigment consistent with the presence of MCMV DNA. Bar = 1 μm.

~75% of the cells positive with radioactive probes. By biotin-labeled probes, 85%–90% of the cells containing MCMV genomic material were mononuclear (figure 2). MCMV genomic material was occasionally observed in marrow cells that could be identified morphologically as megakaryocytes and was infrequently observed in mature granulocytes.

Correlation of in situ hybridization results with recovery of infectious MCMV. As summarized in figure 3, MCMV was recovered from marrow cells on days 3–14, with peak levels on day 5. By compar-

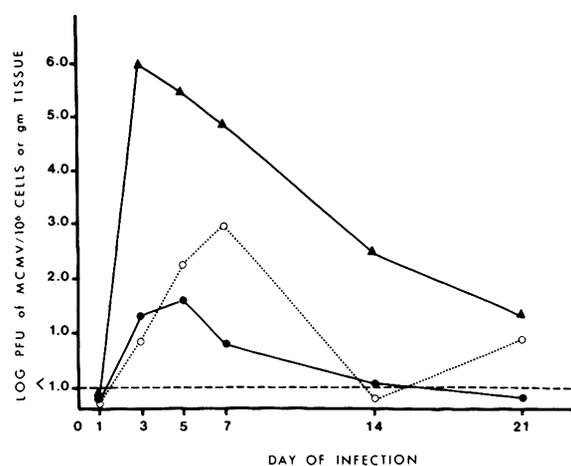


Figure 3. Recovery of infectious MCMV from spleen tissues (▲), marrow cells (●), and peripheral blood mononuclear cells (○). Each point represents mean data from 4 to 10 animals.

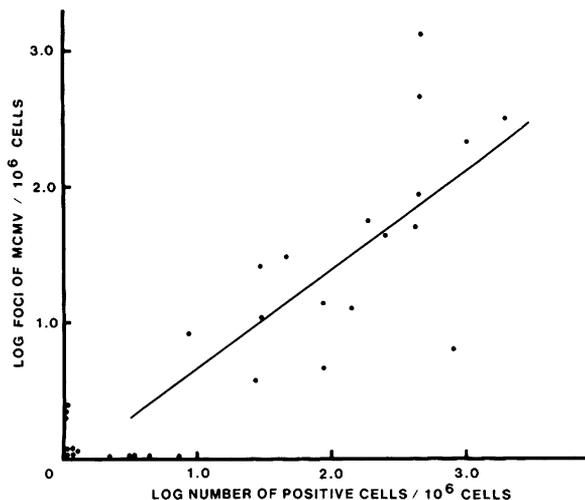


Figure 4. Correlation of the results of in situ hybridization using ^{35}S -labeled MCMV DNA probes with detection of infectious virus by using an infectious-center assay ($P < .001$, $r = .87$). Data include all MCMV-infected animals studied on days 1-21. Each dot represents data from an individual animal.

ison, MCMV was isolated from spleen tissues on days 3-21 (peak on day 3) and from peripheral blood mononuclear cells on days 3-7 and 21 (peak on day 7). The amounts of MCMV in peripheral blood mononuclear cells peaked at levels 10- to 100-fold higher than did the amounts in marrow cells, whereas the peak titers of MCMV in spleen tissues were $\sim 10^6$ pfu/g.

As shown in figure 4, there was a strong positive correlation between detection of MCMV genomic material in marrow cells and isolation of infectious

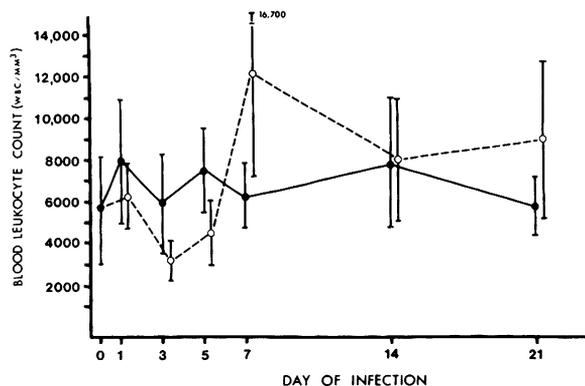


Figure 5. Summary of total peripheral blood leukocyte counts in MCMV-infected (○) and control (●) mice. Each point represents mean data ± 1 SD for groups of ten MCMV-infected and ten control mice per day.

virus from marrow cells. Samples negative by culture assay were generally negative by in situ hybridization techniques, whereas samples containing considerable amounts of infectious virus had large numbers of cells that hybridized with the ^{35}S probes.

Relation of marrow infection to changes in hematologic profile. Mice infected with MCMV experienced a biphasic alteration in total peripheral blood leukocyte count (figure 5). On days 3 and 5, the leukocyte count in infected mice was significantly lower ($P < .01$) than that of control animals; however, by day 7, a significant leukocytosis occurred.

Table 2 summarizes the results of differential counts in infected animals and controls. MCMV-infected animals experienced a significant reduction in the numbers of lymphocytes on days 1-5. Neutrophil and monocyte counts in MCMV-infected mice were reduced on days 3 and 5 when compared with days 1 and 7 of infection, although the differences from control mice were not significant. By day 7, MCMV-infected mice had increasing numbers of neutrophils and monocytes, and by day 21, lymphocytes were also increased when compared with controls. When platelet counts were compared, MCMV-infected mice had a modest reduction on day 5 ($743,000/\text{mm}^3$ in MCMV-infected versus $831,000/\text{mm}^3$ in controls), but no significant differences were observed on this or other days of infection.

These data indicate that during the period of maximum MCMV replication in marrow cells (days 3 and 5 of infection), MCMV-infected mice had significant reductions in the numbers of circulating lymphocytes and moderate reductions in neutrophils. MCMV replication in marrow cells, possibly mature megakaryocytes, may also be associated with a slight decrease in the numbers of circulating platelets. By contrast, when MCMV replication ceased in marrow cells, a rebound leukocytosis occurred, first with increased numbers of granulocytes and monocytes and later, by day 21, with increased numbers of lymphocytes as well.

Discussion

In these studies we used in situ hybridization techniques to detect MCMV genomic material in marrow cells of mice during sublethal infection. MCMV DNA could be detected in marrow cells during acute infection, particularly during days 3 and 5, and the numbers of cells positive by in situ hybridization were approximately equal to the numbers of cells produc-

Table 2. Peripheral blood leukocyte counts during MCMV infection.

Day	Lymphocytes*		Neutrophils*		Monocytes*	
	MCMV	Control	MCMV	Control	MCMV	Control
0	-	4383 ± 1998	-	1136 ± 487	-	221 ± 258
1	3264 ± 1090†	6628 ± 2624	2658 ± 1090‡	937 ± 504	378 ± 220	454 ± 344
3	2235 ± 716†	4354 ± 1962	885 ± 568	1274 ± 615	128 ± 126	239 ± 220
5	3845 ± 1305†	6055 ± 1701	898 ± 410	1397 ± 629	146 ± 108	142 ± 183
7	6957 ± 3482	5219 ± 1098	2371 ± 1744§	765 ± 218	682 ± 485†	73 ± 82
14	5872 ± 2318	6386 ± 2947	1653 ± 669§	923 ± 765	586 ± 408§	180 ± 99
21	7543 ± 2785§	4991 ± 1399	1640 ± 740‡	597 ± 193	528 ± 344†	145 ± 98

* Data are mean ± SD for nine or 10 animals per group per day.

† $P < .01$.

‡ $P < .001$.

§ $P < .05$.

ing infectious virus, as determined by infectious-center assay. Furthermore, during the period of MCMV replication in marrow cells, MCMV-infected mice had significant alterations in the numbers of circulating leukocytes.

The pattern of leukocyte differential counts was consistent with transient marrow suppression and corresponded with the timing of MCMV replication in marrow cells. During days 1–5, MCMV-infected mice had significant leukopenia, and then beginning on day 7 they experienced a rebound leukocytosis. The transient leukopenia was due predominantly to lymphopenia, but MCMV-infected mice had trends toward reduced numbers of circulating granulocytes as well. Beginning on day 7, the rebound leukocytosis was characterized by an initial granulocytosis and monocytosis, and by day 21, the number of circulating lymphocytes also increased. As shown by the studies of Cheung et al. [14], the period of leukocytosis correlates with the appearance of atypical lymphocytes in the peripheral blood of infected animals.

There are several possible explanations for the peripheral leukopenia that accompanies MCMV infections: (1) lytic infection of mature cells in the marrow, (2) lytic infection of precursor cells, (3) abortive infection of marrow cells, or (4) other factors, such as sequestration of cells in organs or migration of cells to the infected peritoneal cavity. On the basis of the relatively small numbers of marrow cells that contained MCMV DNA, it is unlikely that the leukopenia was the result of lytic destruction of mature cells. For example, leukocyte counts in MCMV-infected mice on day 3 were ~50% less than those of controls, yet only 0.026% of the marrow cells contained MCMV DNA. In addition, MCMV DNA was infrequently

observed in mature granulocytes. Moreover, because the marrow is not the principal repository of lymphocytes, it is unlikely that the profound lymphopenia observed in MCMV-infected mice was mediated through effects of virus on the marrow.

Although we cannot disprove that abortive infection or sequestration of cells could account for MCMV-induced leukopenia, the current results suggest that lytic infection of progenitor cells may have an important role, particularly in reducing the numbers of circulating granulocytes and monocytes. Destruction of certain precursor cells by MCMV could account for decreases in mature cells and would also be consistent with the observations of Petursson et al. [9]. These investigators noted significant reductions in granulocyte-macrophage progenitor cells beginning on days 2 and 3 of MCMV infection, a time that corresponds to our detecting MCMV DNA in marrow cells.

We did not observe significant thrombocytopenia and did not detect MCMV DNA in large numbers of mature megakaryocytes. This contrasts with the results of Osborn and Shahidi [8] who observed significant thrombocytopenia, beginning on day 3 of infection, and identified MCMV antigen in splenic megakaryocytes. These conflicting results may be explained in part by the severity of MCMV infection in the experimental animals. In the studies of Osborn and Shahidi, peak titers of MCMV in spleen exceeded 10^8 pfu of MCMV/g of tissue, whereas the titers in the current experiments were considerably less, $\sim 10^6$ pfu/g. More-severe infection may be associated with more-striking thrombocytopenia and increased numbers of infected megakaryocytes.

This study provides additional data relevant to the

mechanisms by which MCMV infection may enhance susceptibility to secondary bacterial infections. We observed previously that MCMV-infected mice had reduced inflammatory responses to a localized bacterial infection [15]. This abnormal inflammatory response in MCMV-infected mice correlated with an increased severity of *Escherichia coli* bacteremia and was due principally to reduced numbers of granulocytes migrating into sites of bacterial infection [15]. Reduced inflammatory responses occurred on days 3 and 5 of MCMV infection, a time that corresponds to the timing of maximum MCMV replication in marrow cells, as shown in the current studies. We postulated previously that reduced inflammatory responses could be the result of altered granulocyte functions or depleted stores of neutrophils in marrow cells. Although functional defects of neutrophils have been described in MCMV-infected animals [10, 16], marrow suppression caused by viral replication in certain leukocyte precursors may be an important contributing factor in the pathogenesis of CMV-associated immunosuppression.

References

1. Weller TH, Hanshaw JB. Virologic and clinical observations on cytomegalic inclusion disease. *N Engl J Med* 1962; **266**: 1233-44
2. Pass RF, Stagno S, Meyers GJ, Alford CA. Outcome of symptomatic congenital cytomegalovirus infection: results of long-term longitudinal follow-up. *Pediatrics* 1980; **66**:758-62
3. Panjvani ZFK, Hanshaw JB. Cytomegalovirus in the perinatal period. *Am J Dis Child* 1981; **135**:56-60
4. McCracken GH Jr., Shinefield HR, Cobb K, Rausen AR, Dische MR, Eichenwald FR. Congenital cytomegalic inclusion disease. A longitudinal study of 20 patients. *Am J Dis Child* 1969; **117**:522-39
5. Jordan MC, Rousseau WE, Stewart JA, Noble GR, Chin TDY. Spontaneous cytomegalovirus mononucleosis: clinical and laboratory observations in nine cases. *Ann Intern Med* 1973; **79**:153-60
6. Fiala M, Kattlove H, Lemkin S. Cytomegalovirus mononucleosis with severe thrombocytopenia. *Ann Intern Med* 1973; **79**:450-1
7. Chesney PJ, Taher A, Gilbert EMF, Shahidi NT. Intranuclear inclusions in megakaryocytes in congenital cytomegalovirus infection. *J Pediatr* 1978; **92**:957-8
8. Osborn JE, Shahidi NT. Thrombocytopenia in murine cytomegalovirus infection. *J Lab Clin Med* 1973; **81**:53-63
9. Petursson SR, Chervenick PA, Wu B. Megakaryocytopoiesis and granulopoiesis after murine cytomegalovirus infection. *J Lab Clin Med* 1984; **104**:381-90
10. Bale JF Jr., Kern ER, Overall JC Jr., Baringer JR. Impaired migratory and chemotactic activity of neutrophils during murine cytomegalovirus infection. *J Infect Dis* 1983; **148**: 518-25
11. Sell MS, Bale JF Jr., Giller RH. T-lymphocyte subpopulations and function during murine cytomegalovirus infection. *Pediatr Res* 1985; **19**:583-7
12. Haase A, Brahic M, Stowring L, Blum H. Detection of viral nucleic acids by in situ hybridization. *Methods Virol* 1984; **7**:189-226
13. Ebeling A, Keil GM, Knust E, Koszinowski UH. Molecular cloning and physical mapping of murine cytomegalovirus DNA. *J Virol* 1983; **47**:421-33
14. Cheung KS, Li JH, Falletta JKK, Wagner JL, Lang DJ. Murine cytomegalovirus infection: hematological, morphological, and functional study of lymphoid cells. *Infect Immun* 1981; **33**:239-49
15. Bale JF Jr., Kern ER, Overall JC Jr., Glasgow LA. Enhanced susceptibility of mice infected with murine cytomegalovirus to intranasal challenge with *Escherichia coli*: pathogenesis and altered inflammatory response. *J Infect Dis* 1982; **145**:525-31
16. Lineaweaver W, Balliro J, McMorris S, Howard RJ. Neutrophil migration under agarose in healthy and cytomegalovirus-infected mice. *J Surg Res* 1984; **36**:184-9