INFECTION OF SALIVARY GLANDS, KIDNEYS, ADRENALS, OVARIENS AND EPITHELIA BY MURINE CYTOMEGALOVIRUS

C. A. MIMS AND JANINE GOULD

Department of Microbiology, Guy's Hospital Medical School, London Bridge, London SE1 9RT

PLATES V AND VI

Since the original description of the pathology of murine cytomegalovirus (CMV) infection more than 40 years ago (McCordock and Smith, 1936), there have been few studies of basic features in the pathogenesis of the infection. In early virus-titration studies (Medearis, 1964) the salivary gland was identified as a prime target organ, and this group of viruses was originally referred to as the salivary gland viruses. But the salivary glands have not often been investigated (Ruebner et al., 1966; Henson and Strano, 1972) and the immunofluorescence technique has not been used. Occasional reports have dealt with events in the liver (Henson, Smith and Gehrke, 1966), inner ear (Davis and Hawnisiak, 1977), brain (Margolis and Kilham, 1976) or placenta (Johnson, 1969) but much recent work has understandably focussed on immunological aspects of the infection (Osborn, Blazkovec and Walker, 1968; Selgrade et al., 1976; Olding, Kingsbury and Oldstone, 1976; Starr and Allison, 1977; Jordan, Shanley and Stevens, 1977).

Investigations of the behaviour of CMV in the mouse spleen (Mims and Gould, 1978a) and liver (Mims and Gould, 1978b) have been reported elsewhere. In the present study, infection of salivary glands, kidneys, adrenals, ovaries and epithelial surfaces was investigated by fluorescent-antibody staining, routine histology, and virus titration.

MATERIALS AND METHODS

Virus. The strain of CMV used was kindly sent by Dr June Osborn (Dept. of Medical Microbiology, University of Wisconsin, Madison, USA) who had developed it from the Smith strain by many serial passages through mouse salivary gland in vivo. It was further passaged in this laboratory up to four times in 3-wk-old mice, the salivary glands being harvested, on each occasion, 3 wk after intraperitoneal (i.p.) inoculation of $10^{3.5}$–$10^{4.5}$ plaque-forming units (p.f.u.) of virus. Stock virus was prepared in this way and contained $10^{6.5}$–$10^{7}$ p.f.u./ml. Similar titres were obtained, 3 wk after infection with the same dose of virus, whether mice were inoculated when 1 day, 1 wk, 3 wk or 3 mth old. In some experiments the virus was used after attenuation by seven or eight serial passages in mouse-embryo fibroblasts (Osborn and Walker, 1971), a procedure that decreased its lethality for newborn and 3-wk-old mice.

Received 8 Aug. 1978; accepted 1 Sept. 1978.

J. MED. MICROBIOL.—VOL. 12 (1979) 113
Titration of virus was carried out by plaque assay in either microtitre plates (Nunc, UK) or in "Multiwell" dishes (Falcon Plasticware, Oxnard, California, USA) (Mims and Gould, 1978b).

Mice. These were specific-pathogen-free, outbred CD1 mice bred in the Guy's Hospital Medical School SPF unit.

Immunofluorescent technique. The indirect method was used with a hyperimmune mouse serum and a fluorescein-conjugated goat anti-mouse globulin (Nordic Immunological Laboratories, Maidenhead, Berkshire, England). Mouse tissues were frozen in liquid nitrogen and sections cut in a cryostat. Observations were made with a Leitz Orthoplan microscope equipped for epi-illumination, with an HBO 200 lamp and water-immersion objectives.

RESULTS

Salivary glands

The salivary glands are known to be involved at a late stage of murine CMV infection; very little virus is detectable within the first 5–6 days, after i.p. infection of adult mice, and peak titres are not reached until 3 wk later (Henson et al., 1967; Ruebner et al., 1966). In the present experiments, virus titres of $10^{6.5} \text{ p.f.u./g}$ were found in the salivary glands of mice infected (i.p.) with $10^3 \text{ p.f.u.}$ of CMV at 3 wk of age and examined 3 wk later (table I). This had fallen to $10^{5.6} \text{ p.f.u./g}$ by 30 days, and virus was undetectable (<$10^{2.0} \text{ p.f.u./g}$) by 50 days. Histological examination by fluorescent-antibody staining demonstrated infection of occasional interstitial cells by the fourth day, often in a perivascular position. Isolated acinar cells were first involved on the fifth day (fig. 1), the infection subsequently spreading to adjacent cells to produce "acinar foci" of infection. Viral antigen was initially confined to the acinar cells, which were often swollen, but after 10 days large collections of antigen

<table>
<thead>
<tr>
<th>Interval after infection (days)</th>
<th>Virus titre (log_{10} plaque-forming units/g)† in</th>
<th>salivary glands</th>
<th>saliva‡</th>
</tr>
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<tbody>
<tr>
<td>7</td>
<td>&lt;2.0</td>
<td>ND</td>
<td></td>
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<tr>
<td>14</td>
<td>ND</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>6.5</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>5.7</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>ND</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>&lt;2.0</td>
<td>&lt;1.3</td>
<td>&lt;1.3</td>
</tr>
<tr>
<td>58</td>
<td>&lt;2.0</td>
<td>2.1</td>
<td>&lt;1.3</td>
</tr>
<tr>
<td>72</td>
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<td>&lt;1.3</td>
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<td>79</td>
<td>&lt;2.0</td>
<td>&lt;1.3</td>
<td>&lt;1.3</td>
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<tr>
<td>97</td>
<td>&lt;2.0</td>
<td>&lt;1.3</td>
<td>&lt;1.3</td>
</tr>
<tr>
<td>189</td>
<td>&lt;2.0</td>
<td>&lt;1.3</td>
<td>&lt;1.3</td>
</tr>
</tbody>
</table>

* Inoculum dose was $10^2$–$10^3 \text{ p.f.u.}$.
† Determined on pooled tissue or saliva from two mice.
‡ Collected as an oral washing into 1 ml of phosphate-buffered saline (virus titres in pure saliva were 50–100-fold higher).
ND = not done.
began to appear in the acinar lumen (fig. 2) and the intensity and extent of the staining increased to reach a maximum by about 14 days. The appearances remained essentially unchanged during the next 7 days, but by 28 days the antigenic material in the acini and ducts had contracted in volume, as if inspissated. The submaxillary glands were heavily involved, the sublinguals less so, and the parotids least of all. The virus content of these glands, separately, 3 wk after infection, was $10^6.5$, $10^5.6$ and $10^3.5$ p.f.u./g, respectively; each titration was made on the pooled glands from two mice. Local (cervical) lymph nodes, embedded in the salivary glands, contained $10^3.0$ p.f.u./g. Circulating antibody was detectable 3 wk after infection, by neutralisation, complement fixation, and immunofluorescence tests, when peak titres of virus were present in the salivary glands.

Large amounts of virus were present in saliva for at least 41 days after infection (table I), and virus was still detectable at 58 days, but not subsequently. An attempt was made, 3 wk after initial infection, to “flush out” into the saliva the large amounts of antigen present in the acinar and duct lumina, by administering to the mice 1-0 mg of pilocarpine subcutaneously. This induced, within 5-10 min., copious salivation and, occasionally, diarrhoea. However, the amount of virus in the saliva fell to $10^3$ p.f.u./ml, presumably because of dilution by the increased output of saliva. Mice killed 45 min. after receiving pilocarpine showed no significant differences either in the distribution of antigen in the salivary glands, as observed by fluorescent-antibody staining of histological sections, or in the virus content, when compared with infected mice that had not received pilocarpine.

An attempt was made to involve the salivary glands at an earlier stage of infection by infecting the mice with a large dose ($10^6$ p.f.u.) of virus intravenously (i.v.). However, immunofluorescence-staining failed to detect infected cells after three days and only occasional, isolated interstitial cells were visibly infected after five days, when the salivary glands contained $10^3.9$ p.f.u./g of virus. In view of the possibility that the bulk of the virus entering the blood stream is taken up by reticuloendothelial macrophages lining the sinusoids of the liver and spleen, thus severely limiting the chance of infection of the salivary glands, 0-3 ml of thorotrast (Testagar and Co. Inc., Detroit, Michigan) was given i.v. 3-5 h before the virus inoculum, to block the activity of the phagocytic cells. This, however, failed to increase the extent of salivary gland infection, demonstrable either by virus titration or by immunofluorescence.

Similar peak titres of virus were obtained in the salivary glands, 3 wk after i.p. infection, in both sexually active males and sexually active females. Nevertheless, it was noticed, during tests of the lethality of CMV for newborn mice, that salivary-gland-virus stocks prepared in sexually active adult mice were less virulent than those prepared in 3-wk-old-mice, suggesting that sexual factors were present in salivary glands that affected the virulence of CMV. This was examined in newborn mice. Two litters, each of 10 newborn mice, were given i.p. injections of $10^4$ and $10^3$ p.f.u., and the mortality was 85% and 35%, respectively. When the experiment was repeated with the same two doses of virus mixed with an equal volume of a 10% tissue-suspension of salivary glands from
sexually active 3-mth-old female mice, the mortality was, in each case, reduced to zero. Similar experiments with virus mixed with salivary gland suspension from sexually active 3-mth-old male mice gave mortalities of 25% and zero. Salivary gland suspensions from 3-wk-old mice were not tested.

**Ovaries**

When non-pregnant mice were infected i.v. with $10^{4.7}$ p.f.u. of virus, the ovaries contained $10^5$ p.f.u./g after five days. Foci of infection were demonstrable, by immunofluorescence, in corpora lutea (fig. 3) and an occasional follicle was involved, but viral antigen was never observed in ova. The susceptibility of the ovary was greatly increased in 16-day-pregnant mice, virus titres reaching $10^{6.2}$ p.f.u./g five days after i.v. infection with the same dose of virus. The ovaries were not often infected, even in pregnant mice, when virus was given by the i.p. route.

**Adrenals**

Foci of infection were present in the adrenal cortex 3–4 days after i.p. or i.v. infection of adult mice, sometimes involving 25% of the entire cortex (fig. 4). Occasional infected cells also appeared in the medulla, but extensive medullary infection was seen only in suckling mice (fig. 5).

**Other tissues**

In 3-wk-old mice given $10^3$ p.f.u. of virus i.p., there was no obvious involvement of the mammary glands either one wk or three wk later. This was also the case when larger doses of virus ($10^6$ p.f.u.) were given i.p. to 17-day-pregnant mice; virus could not be detected in their mammary glands nor in milk removed from the stomachs of the suckling infants four days after birth. Non-pregnant and 16-day-pregnant mice were then infected with $10^6$ p.f.u. of CMV by the i.v. route, but, again, the mammary glands contained no significant amounts of virus five days later. Treatment of these mice with thorotrast (0.3 ml) 3 h before infection, to reduce reticuloendothelial-cell clearance of circulating virus, did not affect the result.

In suckling mice, but not in older mice, foci of infected cells were commonly formed in brown fat, and small foci were also seen in striated muscle, heart muscle and cartilage. An occasional, infected acinar cell was seen in the pancreas in mice infected when newborn or at three wk of age. The islets of Langerhans were not involved, and infected cells were at no time observed in the Harderian glands. The thyroids were not affected in any of 12 8-wk-old mice given $10^5$ p.f.u. of CMV i.p. and examined, by immunofluorescence staining, three wk later.

**Epithelia**

Although epithelial cells in the salivary glands were readily and abundantly infected by CMV, they were rarely involved in other tissues. Thus, infected epithelial cells were never seen, by immunofluorescence, in the mucosa of the
nose, mouth or respiratory tract of suckling or adult mice. This was so even after direct intranasal inoculation of large doses of virus. The skin was readily infected in both newborn and adult mice, by intradermal or subcutaneous injection, but only cells of the dermis, of unidentified nature, were involved and never epithelial cells. When less virulent virus, harvested from sexually active (pregnant) female mice infected i.p. (see above), was administered (10⁵.⁵ p.f.u.) to newborn mice, some of them died at 10–15 days and most developed running and bald patches on the skin. There were as many as 30 bald patches, each up to 1 mm diameter, on each mouse, without erythema or breakage of skin; each skin lesion contained up to 10⁶ p.f.u. of virus per g and foci of infection were demonstrable only in the dermis. The bald patches were obvious six days after infection, but by 14 days began to disappear, as the fur grew again.

There was no evidence of infection, by fluorescent-antibody staining, of the epithelium of the bladder or ureter or of the endometrium, in adult mice. The vagina and uterus, removed from pairs of mice infected i.p. with 10⁴ p.f.u. of virus at three wk of age and killed 14 or 26 days later, were homogenised and tested for virus, but none was detected.

Endothelial cells were occasionally infected by CMV. They were seen in the endocardium and also in venular endothelium (fig. 6), including the intima of coronary vessels, in newborn mice infected i.p. and in adult mice infected i.v.

Persistence of CMV in the salivary glands, kidneys and adrenals

Table II shows the amounts of virus present in the salivary glands, kidneys and adrenals of mice infected i.p. when newborn with 10³.⁵ p.f.u. of stock CMV and then killed after 1 wk, 3 wk and 3 mth. By immunofluorescent staining, the interstitial tissues and glomeruli of the kidneys were seen to be sparsely infected, and very occasional epithelial cells of the tubules were involved. This was in contrast to adult mice, in which interstitial tissues and glomeruli were infected but, in as many as 21 kidneys examined, the tubular epithelium was never involved, even after injection of large doses of virus i.v. One of the newborn mice was examined 50 days after infection and virus was still present in the salivary glands, at a titre of 10⁵.⁵ p.f.u./g, and viral antigen was seen in the lumen of occasional acini; in one of the acini, there was also a fine

<table>
<thead>
<tr>
<th>Interval after infection</th>
<th>Virus titre (log₁₀ p.f.u./g)* in</th>
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<tbody>
<tr>
<td></td>
<td>salivary glands</td>
<td>kidneys</td>
</tr>
<tr>
<td>1 wk</td>
<td>7·9</td>
<td>5·5</td>
</tr>
<tr>
<td>3 wk</td>
<td>7·5</td>
<td>7·0</td>
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<tr>
<td>3 mth</td>
<td>&lt;1·0</td>
<td>3·1</td>
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* Determined on pooled organs from three mice.
speckling of antigen in the neighbouring acinar cells. Three mth after infection, although small amounts of virus were still detectable in the kidneys, none was found in the salivary glands or adrenals.

Newborn mice were also infected i.p. or intracerebrally with $10^{2.5-3.5}$ p.f.u. of a strain of CMV that had been attenuated by 7–8 serial passages in mouse embryo tissue cultures, and they were compared, over a period of 12–26 months, with newborn mice infected with the same dose of stock, salivary-gland-passaged virus (table III). From among the mice infected with tissue-culture-passaged virus 22 were killed at intervals for examination, but only small numbers of the mice infected with stock virus survived over comparable periods. Significant differences were not found in the long-term carriage of virus, in either the salivary glands or kidneys, between the two groups of mice. Three out of five of the stock-virus-infected mice were positive for virus in the kidneys after 12–18 mth and six out of 12 of the tissue-culture-virus-infected mice; three out of eight of the latter group that survived for 20–26 mth still showed the presence of active virus. Only two of the 23 mice examined for virus in the salivary glands were positive. No mouse had detectable virus in kidneys and in salivary glands. All the kidneys and salivary glands that yielded active virus were also examined by immunofluorescence staining, but infected cells were never seen.

Twelve of the mice that had been infected at birth with the attenuated strain of virus and killed 12–26 mth later were also examined by routine histological methods. In all these mice, the kidneys showed severe, hyaline eosinophilic degeneration of glomeruli, but this was also sometimes found to be present.

Table III

Cytomegalovirus content of kidneys and salivary glands 12–26 mth after neonatal infection of mice with virulent, salivary-gland-passaged (SG) virus or attenuated, tissue-culture-passaged (TC) virus

<table>
<thead>
<tr>
<th>Virus</th>
<th>Interval after infection (months)</th>
<th>Virus titre ($\log_{10}$ p.f.u./g) in</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>kidneys</td>
<td>salivary glands</td>
</tr>
<tr>
<td>SG</td>
<td>12</td>
<td>3.7</td>
<td>ND</td>
</tr>
<tr>
<td>TC</td>
<td>12 (2 mice examined)</td>
<td>0, 0*</td>
<td>0, 4.0</td>
</tr>
<tr>
<td>SG</td>
<td>13</td>
<td>5.5</td>
<td>ND</td>
</tr>
<tr>
<td>TC</td>
<td>13 (3 mice)</td>
<td>2.4, 4.0, 0</td>
<td>0, 0, ND</td>
</tr>
<tr>
<td>TC</td>
<td>15 (2 mice)</td>
<td>4.7, 2.4, 2.0</td>
<td>0, 0</td>
</tr>
<tr>
<td>SG</td>
<td>17</td>
<td>0</td>
<td>ND</td>
</tr>
<tr>
<td>TC</td>
<td>17 (2 mice)</td>
<td>0</td>
<td>0, 0</td>
</tr>
<tr>
<td>SG</td>
<td>18 (2 mice)</td>
<td>4.5, 0</td>
<td>0, 0</td>
</tr>
<tr>
<td>TC</td>
<td>18 (3 mice)</td>
<td>0, 0, 0</td>
<td>0, 0, 0</td>
</tr>
<tr>
<td>TC</td>
<td>18 (2 mice)</td>
<td>3.6, 5.8</td>
<td>0, 0</td>
</tr>
<tr>
<td>SG</td>
<td>19</td>
<td>0</td>
<td>2.9</td>
</tr>
<tr>
<td>TC</td>
<td>20 (2 mice)</td>
<td>0, 3.1</td>
<td>0, 0</td>
</tr>
<tr>
<td>TC</td>
<td>22 (4 mice)</td>
<td>0, 0, 3.7, 3.2</td>
<td>0, 0, 0, 0</td>
</tr>
<tr>
<td>TC</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TC</td>
<td>26</td>
<td>0</td>
<td>ND</td>
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</table>

* $0 = < 10^2$ p.f.u./g. ND = not done.
in uninfected mice of the same age. Striking changes were observed in the adrenals and salivary glands of some of the mice. Thus, in three of five mice examined, the adrenals were small and pale, the cortex was depleted, and there was a zone of hyaline, eosinophilic, acellular material between the cortex and the medulla (fig. 7). Three out of 15 salivary glands examined were small in size, and histologically, the submaxillary portion was reduced to scattered collections of secretory and duct tissue within hyaline, acellular areas; in another six of the glands the same histological changes were restricted to the parotid division (fig. 8); the sublingual division was unaffected. The adrenals and the salivary glands were stained for amyloid with congo red and thioflavine T, but the hyaline acellular areas failed to give a convincingly positive reaction. Uniformly negative results were obtained in tests for the presence of mouse immunoglobulins in the acellular areas of the salivary glands, by immunofluorescence staining with anti-mouse globulin antiserum. These various changes in the adrenals and salivary glands were not seen in uninfected mice of the same age.

**DISCUSSION**

Our results confirm that the salivary gland is a prime target organ for CMV in the mouse, and that this is so whether the mouse is infected when newborn, 3 wk old, or adult. The salivary gland is also commonly involved in human infants, cytomegalic cells having been recognised in 5–10% of routine paediatric autopsies (McCordock and Smith, 1934). In mice infected soon after birth, the tubular epithelium of the kidney is affected, and human infants commonly excrete CMV in the urine (Rowe et al., 1958). However, it may be misleading to draw parallels between the CMV infections of humans and mice. For example, humans excrete CMV in milk (Hayes et al., 1972) and semen (Lang, Kummer and Hartley, 1974), but in the present mouse experiments there was no evidence of infection of the mammary glands, and similarly negative results have been obtained for semen and the male reproductive organs of mice, even after direct injection of virus into the testis, into seminal vesicles and into the prostate via the bladder (unpublished observations). CMV infected the dermis in suckling mice, to produce bald patches, and there is a recent report of skin involvement by CMV in a renal-transplant patient (Minars et al., 1977); the patient developed skin ulcers with cytomegalic cells localised to the dermis and affecting mainly endothelial cells—apparently a CMV vasculitis. In the mouse the placenta is infected only sporadically or at a late stage of pregnancy, and the fetus does not contain infectious virus (unpublished observations; Dr K. P. Johnson, 1969), whereas in man the placenta is infected as a prelude to fetal infection. The present experiments were, of course, carried out with only one strain of virulent, salivary-gland-adapted, murine CMV and one strain of mouse.

When CMV was injected intravenously into pregnant mice the ovary was heavily infected. This might be explained by the vascular changes that occur in the ovary in pregnancy and which are known to lead to increased localisation of intravenously injected particles (Morris and Sass, 1966). The ova themselves
were not infected, but the infection of corpora lutea could lead to changes in
the secretion of pregnancy hormones.

CMV is highly adapted to replication in salivary glands, especially in the
acinar epithelial cells, and this probably accounts for the predominantly salivary
method of spread of the virus among mice. Our observations demonstrate a
possibly important effect of mouse salivary gland components on the virulence
of CMV, but this was not investigated further. Epithelial cells of other glands
and of other organs and tissues of the body did not appear to be infected by
CMV, either in the infant or adult mouse, except for the kidney tubules in the
infant mouse. On the other hand, endothelial cells in blood vessels and the
heart were sometimes involved.

After neonatal infection, some mice were still actively infected 12-26 mth
later, i.e., into old age, and this was seen with virulent, salivary-gland-adapted
virus and with attenuated, tissue-culture-passaged virus. The kidneys and
salivary glands were sites for such persistent infection, but the infected cells
were presumably sparsely distributed since they could not be located by
fluorescent-antibody staining. It is likely that in the salivary glands the infection
persists in acinar cells, as was seen to be the case in the mouse killed 50 days
after neonatal infection. Not all the mice showed evidence of persistent infec-
tion, and the reasons for this are not known. The persistent infection in these
experiments was active and could be recognised by the finding of infectious virus
in the supernates of organ extracts. This differs from the latent CMV infection
demonstrated in lymphoid cells by Olding, Jensen and Oldstone (1975) who
induced the cells to differentiate and multiply in vitro, causing reactivation of the
latent infection and the synthesis of infectious virus.

The mice that survived neonatal infection for more than a year often de-
veloped characteristic lesions in the adrenals and salivary glands. The dis-
appearance of secretory tissues was presumably due to long-term cytopathic
effects, but the nature of the acellular hyaline deposits is obscure. These did not
appear to be amyloid or to contain immunoglobulin. The significance of the
chronic glomerulonephritis seen in most of the kidneys is not clear, but immune
complexes are known to be deposited in glomeruli in latent CMV infection of
the mouse (Olding et al., 1976).

**Summary**

Cytomegalovirus (CMV) infection of CD1 mice was investigated by im-
munofluorescence and virus titration. The salivary glands were obviously
prime targets for the virus, infection involving initially perivascular interstitial
cells and then spreading to acinar cells. The submaxillary gland was the most
affected and, in mice infected at 3 wk of age, virus was recoverable from
saliva for up to 58 days. The ovaries became infected, especially after intra-
venous injection of virus into pregnant mice, but it was corpora lutea and not
ova that were involved. In the adrenals, the medulla was most heavily infected
in suckling mice, the cortex in older mice. Virus was not recoverable from
mammary glands or milk. Infection of respiratory epithelial cells did not occur,
MIMS AND GOULD PLATE V

MURINE CYTOMEGALOVIRUS INFECTION

FIG. 1.—Section of submaxillary salivary gland 5 days after intraperitoneal infection with CMV of a 3-wk-old mouse, showing infected acinar cells. Immunofluorescence (IF). × 500.

FIG. 2.—Section of submaxillary salivary gland 14 days after intraperitoneal infection of a 3-wk-old mouse, showing the presence of CMV antigen in acinar lumina. The arrow demonstrates an infected acinar cell. IF. × 200.

FIG. 3.—Section of ovary 6 days after intravenous infection of an adult mouse, showing foci of infection in corpora lutea. IF. × 100.

FIG. 4.—Section of adrenal gland 3 days after intravenous infection of an adult mouse with CMV, showing numerous foci of infection in the cortex (above) and two small foci in the medulla (below). IF. × 80.
FIG. 5.—Section of adrenal gland 8 days after intracerebral infection of a 2-day-old mouse, showing a large focus of infection in the medulla, extending into adjacent cortex. IF. × 80.

FIG. 6.—Section of vein in subcutaneous tissue of skin 11 days after intracerebral infection of a newborn mouse, showing extensive involvement of intima and vessel wall. IF. × 250.

FIG. 7.—Section of adrenal gland 17 months after intraperitoneal infection of a newborn mouse with attenuated, tissue-culture-passaged CMV. A zone of hyaline, acellular material separates cortex from medulla. Haematoxylin and eosin (HE). × 50.

FIG. 8.—Section of parotid gland 18 months after intracerebral infection of a newborn mouse with tissue-culture-passaged CMV, showing secretory and duct tissue surrounded by hyaline, acellular areas. HE × 300.
and in the skin only the dermis became infected, leading to the appearance of bald patches.

Among mice surviving neonatal infection, about half continued to carry infectious virus in the kidneys for 12–26 mth, and a smaller number carried virus in the salivary glands. This was seen after infection with a virulent, salivary-gland-passaged strain of virus and also with an attenuated tissue-culture-passaged strain. Nearly all these surviving mice had chronic glomerulonephritis and hyaline acellular deposits of unknown nature in the adrenals and salivary glands.

We thank Cecilia Callis for expert technical assistance. The work described here was carried out with the help of a Project Grant (no. G972/751/C) from the Medical Research Council.

REFERENCES


