The Release of Lactate Dehydrogenase from Chick Embryo Cells Infected with Semliki Forest Virus

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During the course of an investigation into changes in host-coded enzymes of chick embryo cells (CEC) following infection with Semliki Forest virus (SFV) (Cassells & Burke, 1973) it was observed that, after an initial increase, there was a decrease in the activity of cellular lactate dehydrogenase (LDH: EC 1.1.1.27) which coincided with an increase in LDH activity in the growth medium. Further investigation showed that the release of LDH by the cells was an indicator of SFV growth. It was also found that treatment of CE cells with actinomycin D (AMD) resulted in LDH release.

The time course of LDH release is compared in Fig. 1 with other indicators of SFV growth, namely virus RNA synthesis as measured by [3H]-uridine incorporation, virus haemagglutinin production and the release of infective virus. For these experiments, cells were prepared and infected, and the activities measured as previously described (Wroblewski & LaDue, 1955; Burke, Skehel & Low, 1967; Walters, Burke & Skehel, 1967) except that, actinomycin D was omitted from the culture medium in the LDH experiment (see below). The peaks of [3H]-uridine incorporation and virus haemagglutinin production were at 5 and 8 h after infection respectively, LDH release and the appearance of infective virus continued to increase up to 24 h after infection. It was shown (Fig. 2) that LDH release was related to the multiplicity of infection. The maximum effect at 5 h after infection was obtained for 5 or more p.f.u./cell. The pretreatment of CE cells for 1 h with 0·5 #g/ml AMD resulted in the release of LDH in the absence of infection, the release of LDH from AMD-treated infected cells exceeding that of untreated infected cells (Fig. 3).

Although this is the first report of LDH release from cells infected with an arbovirus,
Fig. 2. The effect of increasing multiplicity of infection on LDH released from CE cells at 5 h after infection. Conditions as for Fig. 1.

Fig. 3. The release of LDH from cells treated with actinomycin D in the presence and absence of SFV infection. •—•, Control cells; ○—○, actinomycin D-treated cells; ■—■, SFV infected cells; △—△, actinomycin D and virus infected cells. Conditions as for Fig. 1.
the observation that enzymes are released by virus infected cells is not new (Notkins et al. 1962; Gilbert, 1963; Mahy et al. 1964; Notkins, 1965; Reeve et al. 1971). The release of LDH is not specific, since the above authors have shown that virus infection leads to a general release of soluble enzymes. However, LDH is a suitable marker for following virus growth and cell permeability changes, because of its high level in the cell and relatively high stability in the growth medium. Warren & Glick (1968) showed that the protein components of L-cell surface membranes underwent rapid turnover and that this depended on cellular protein synthesis. It is suggested that the release of LDH by CE cells may be related to the inhibitory effects of virus infection and AMD treatment on protein synthesis in the host.

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REFERENCES


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