Title : ALTERATION OF VIRUS GROWTH BY HALOGENATED ANESTHETICS

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Introduction. Few studies have been concerned with the effect of anesthetics on virus replication. This is unfortunate since anesthetics are most likely to alter the host-parasite equilibrum in virus infection of man. Moreover, viral agents themselves may serve as a molecular probe to help ascertain the cellular effects of anesthetics. Previously, we reported inhibition of measles virus replication in halothane-treated cells. In the present study, we compare these results with those obtained using enflurane- and isoflurane-treated cells.

Methods. BSC cells, a continuous primate cell line, were grown to confluency in sealed 4 oz. glass prescription bottles. Cultures were exposed to 95% air-5% CO_2 with and without various doses of halothane, enflurane, or isoflurane. Anesthetic vapor concentrations were assessed by gas chromatography; losses from the sealed containers were approximately 5% over a 24 hour period. Virus was innoculated in these cultures just prior to exposure of the cells to the anesthetic. The cultures were harvested for progeny virus by sonic disruption at various times following inoculation. The cell extracts were then assayed for infectivity by determining the number of plaque forming units (PFU) per ml of extract. Viable cells were counted using the trypan blue dye exclusion technique.

Results. Production of viable new cells was markedly depressed in the cultures treated with halothane, enflurane, or isoflurane in doses of 1-2 MAC (as determined in human patients). This was not due, however, to an increase in cell death since the number of nonviable cells did not increase. Halothane, enflurane, and isoflurane caused a dose related inhibition of measles virus replication over a range of clinical concentrations. (Table 1.) The inhibition of virus replication was reversible if these agents were removed from the cultures up to 18 hours following innoculation and exposure to the anesthetic. Measles virus replication was almost completely inhibited when either 2 MAC doses of halothane, enflurane, or isoflurane were added within 24 hours following initiation of infection. Linear regression analysis demonstrated that halothane, enflurane, and isoflurane inhibited peak virus titers at 44 hours in a similar dose related manner and at equivalent MAC fractions.

Discussion. These data demonstrate that halothane, enflurane, and isoflurane inhibit measles virus replication in a dose-dependent and reversible manner. Also, the amount of inhibition of measles virus replication appears to be similar for clinically equipotent doses of halothane, enflurane, and isoflurane. These results suggest a similar site of action for the anesthetics tested in the measles virus replication cycle.

EFFECTS OF HALOTHANE, ENFLURANE, AND ISOFLURANE ON PEAK MEASLES VIRUS TITERS 44 HOURS FOLLOWING INITIATION OF INFECTION

dose required for:	minimum dose for depression		50% inhibition		100 fold decrease		10,000 fold decrease	
	%*	MAC	%*	MAC	%*	MAC	%*	MAC
Halothane	.2	.25	.15	.2	.39	.5	.77	1
Enflurane	.26	.15	.36	.2	1.68	1	3.24	1.8
Isoflurane	.33	.25	.26	.2	.98	.75	1.63	1.25

*Anesthetic concentration as % of a standard atmosphere

†linear regression equations:

I = Infectivity (% of control)

$I = -33\ MAC_{halothane} + 45$ n=50

$I = -41\ MAC_{enflurane} + 63$ n=60

$I = -39\ MAC_{isoflurane} + 58$ n=55

Regression equations for halothane, enflurane, and isoflurane did not differ statistically ($p > .05$).

Reference.

1. Knight PR, Nahrwold ML: Replication of measles virus in halothane-treated cells. (Abstr) American Society of Anesthesiologists Annual Meeting, 1976, pp 103-104