



Standardised RT assay of HTLV-III infected lymphocytes.

the RT activity of infected cultures. At a 1% concentration about 65% of the cells remained viable throughout the experiment.

The RT activity of HTLV-III infected, nonoxynol-9 treated cultures was significantly less than that of untreated infected cultures (figure). Cultures were monitored for RT activity for 25 days.

Thus nonoxynol-9 at concentrations of 0.05% or more inactivated HTLV-III in vitro, while 1% or more reduced the live counts of the target lymphocytes. Commercially available spermicides contain 1–5% nonoxynol-9 and are often included in contraceptive jellies and foams used by women in combination with a diaphragm. Sexual transmission of HTLV-III via sperm may account for some cases of AIDS and when prevention is being considered a protective effect of nonoxynol-9 containing spermicides should be assessed.

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- Spire B, Barré-Sinoussi F, Montagnier L, Chermann JC. Inactivation of lymphadenopathy-associated virus by chemical disinfectants. *Lancet* 1984; **i**: 899–901.
- McDougal JS, Cort SP, Kennedy MS, et al. Immunoassay for the detection and quantitation of infectious human retrovirus, lymphadenopathy-associated virus (LAV). *J Immunol Meth* 1985; **76**: 171–83.
- Martin LS, McDougal JS, Loskaski SL. Disinfection and inactivation of the human T lymphotropic virus type III/lymphadenopathy-associated virus. *J Inf Dis* 1985; **152**: 400–03.
- Singh B, Cuthler JC, Utudjiam HMD. I. Studies on the development of a vaginal preparation providing both prophylaxis against venereal disease and other genital infections and contraception. II: Effect in vitro of vaginal contraceptive and on-contraceptive preparations on *Treponema pallidum* and *Neisseria gonorrhoeae*. *Br J Vener Dis* 1972; **48**: 57–62.
- Singh B, Posti B, Cutler JC. Virucidal effect of certain chemical contraceptives on type 2 herpesvirus. *Am J Obstet Gynecol* 1976; **126**: 422–25.
- Postic B, Singh B, Squeglia NL, Guevarra LO. Inactivation of clinical isolates of herpesvirus hominis types 1 and 2 by chemical contraceptives. *Sex Transmitted Dis* 1978; **5**: 22–24.
- Asculai SS, Weis MT, Rancourt MW, Kupferberg AB. Inactivation of herpes simplex viruses by nonionic surfactants. *Antimicrob Agents Chemother* 1978; **13**: 686–690.
- Poesz BJ, Ruscetti FW, Gadzar AF, Bunn PA, Minna JD, Gallo RC. Detection and isolation of type C retrovirus particles from fresh and cultured lymphocytes of a patient with cutaneous T-cell lymphoma. *Proc Natl Acad Sci USA* 1980; **77**: 7415

IN-VITRO INHIBITION OF LAV/HTLV-III INFECTED LYMPHOCYTES BY DITHIOCARB AND INOSINE PRANOBE

SIR,—LAV/HTLV-III selectively attacks T-helper cells.¹ Dithiocarb (sodium diethyldithiocarbamate, 'Imuthiol'; Institut Mérieux) and inosine pranobex ('Isoprinosine'; Delalande Laboratories) have been reported to prevent viral infections. Both

are thought to increase T-helper cells,^{2–4} and have been reported to restore in vitro the impaired T-helper cell population from patients with AIDS-related complex.⁵ We show here that these immunomodulators, at low concentration, inhibit LAV/HTLV-III expression and reverse transcriptase (RT) activity in HTLV-III infected H9 cells and normal human peripheral blood lymphocytes (PBL).

PBL were isolated on 'Ficoll-Hypaque' from three normal donors. H9 cells were treated with polybrene (2 µg/ml) for 30 min at 37°C and then washed with RPMI 1640 containing 20% fetal calf serum. PBL (1–2 million cells) or H9 cells (2 million cells) were simultaneously infected with 2×10^8 LAV/HTLV-III virus particles and treated with imuthiol or isoprinosine at different concentrations. The positive controls did not receive any drug. After 4 days of culture, cell growth (cell number) and virus expression (RT activity and immunofluorescence assays for p15 and p24⁶) were done.

As shown in the table, a 67% reduction in RT activity was induced in PBL by imuthiol 0.75 µg/ml and a 48% decrease by isoprinosine 200 µg/ml. The expression of HTLV-III p15 fell by 50% and that of p24 by 33% (imuthiol) and 42% (isoprinosine) at the above concentrations. These concentrations of isoprinosine and imuthiol were not toxic to PBL. The results in H9 infected cells were, on the whole, less striking than those in PBL. No reproducible inhibitory effects have been obtained by preincubation of the cells or the virus 4 h before virus infection (data not shown).

INHIBITION* OF REVERSE TRANSCRIPTASE AND VIRUS EXPRESSION BY IMUTHIOL OR ISOPRINOSINE

Experiment	RT	Anti-p15	Anti-p24
<i>Infected PBL</i>			
Imuthiol 0.25 µg/ml	27	75	83
Imuthiol 0.75 µg/ml	33	50	67
Isoprinosine 100 µg/ml	76	75	67
Isoprinosine 200 µg/ml	52	50	58
<i>Infected H9 cell line</i>			
Imuthiol 2.5 µg/ml	79	69	75
Imuthiol 7.5 µg/ml	70	65	56
Isoprinosine 100 µg/ml	123	113	87
Isoprinosine 200 µg/ml	109	69	92

*Expressed as % of activities in infected PBL and H9 cells without addition of immunomodulators.

Our results suggest that these two immunomodulators are only active during the first steps of viral infection of T-helper cells by LAV/HTLV-III—perhaps at the stage of viral transduction through the membrane and/or DNA integration in the nucleus.⁴ At a clinical level this means that these drugs may prove helpful in the early stages of AIDS, when the virus, though present in serum,⁵ has infected only a few helper T cells.

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- Popovic M, Sarngadharan MG, Read E, Gallo RC. Detection, isolation and continuous production of cytopathic retrovirus (HTLV-III) from patients with AIDS and pre-AIDS. *Science* 1984; **224**: 497–99.
- Pompidou A. In vitro effect of methisoprinol on human peripheral blood lymphocytes. *EOS* 1984; **4**: 112–14.
- Pompidou A, Duchet N, Cooper MD, et al. The generation and regulation of T-lymphocytes by imuthiol. *Int J Immunopharmacol* 1985; **7**: 561–66.
- Pompidou A, Delsaux TC, Telvi L, et al. Isoprinosine and imuthiol, two potentially active compounds in patients with AIDS-related complex symptoms. *Cancer Res* 1985; **45**: 4671s–73s.
- Zagury D, Fouchard M, Vol JC, et al. Detection of HTLV-III/LAV virus in cell-free plasma from AIDS patients. *Lancet* 1985; **ii**: 505–06.
- Sarin PS, Taguchi Y, Sun D, et al. Inhibition of HTLV-III/LAV replication by Foscarnet. *Biochem Pharmacol* (in press).