later the dose was reduced to 30 mg, 2 days later to 20 mg, and after 2 more days to 10 mg, all 6-hourly. The dose was then reduced to 5 mg twice daily and he was extubated. Within 5 h he became agitated, paranoid, and aggressive and began spitting at the nurses with the expressed intention of giving them AIDS. The episode culminated when he bit a nurse on the finger.

Methylprednisolone was immediately discontinued and within 24 h his mental state was normal. Although the patient had received sedative drugs, muscle relaxants, and antibiotics it was felt that the psychotic behaviour was most probably caused by the high-dose corticosteroids. Those giving high-dose corticosteroids to patients with AIDS should be particularly aware of this well-known complication which, interestingly, did not appear among the AIDS patients so treated and recently described in *The Lancet* (June 27, p 1477; Aug 29, p 519).

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PEPTIDE $T_{[4-8]}$ IS CORE HIV ENVELOPE SEQUENCE REQUIRED FOR CD4 RECEPTOR ATTACHMENT

SIR,—Dr Sodroski and his colleagues (June 20, p 1428) report their failure to find effects of peptide T on HIV envelope-CD4 interactions. The potent antiviral effects of peptide T[1] have been independently confirmed[2] and extended[3] while the negative results of Sodroski et al are readily explained.

Sodroski et al assert that "not one of the eight aminoacids was conserved in all 15 HIV strains sequenced", in contrast to our findings.[1,4] The second variable region of gp120 in all 20 HIV isolates available to us contains a core pentapeptide sequence, known as peptide $T_{[4-8]}$, which is highly conserved. Tyrosine (Y) is always in position 7, and the pentapeptides are clearly pharmacological analogues when shared steric and physicochemical properties of aminoacids are considered (eg, serine [S] or threonine [T] differ by a single methylene and always occupy position 5):

Isolate	*Peptide T_{4-8} homologues*	*Isolate*	*Peptide T_{4-8} homologues*
ARV	TTNYT	BH102	TTSYT
HXB3	TTSYT	BRU	TTSYT
MAL	NSSYR	HXB2	TTSYS
RFENV	NTSYG	CDC42	NTKYR
Z3	SSTYR	WMJ3	SSTYR
LAV	TTSYT	BH8	TTSYT
H9M	TTSYT	B10	TTSYT
ELI	STNYR	WMJ2	SSRYR
HAT3	NTSYG	Z6	STNYR
WMJ1	SSTYR	NY5	NTSYG

These homologous pentapeptides are potent CD4 receptor ligands[5] which can block HIV infectivity and inhibit the specific binding of [^{3}H]-D-Ala^1-peptide T to a human T-cell line. All viral peptide $T_{[4-8]}$ homologues display very potent CD4 or L3T4 receptor-mediated activity; the same single D-aminoacid substitutions greatly diminish bioactivity:[5-7]

—	*Reverse transcriptase** (^{32}P *cpm per 10 µl)*	*Binding† (cpm)*
Control (no peptide)	7335 (280)	1394 (195)
gp120–IIIB (1 nmol/l)	not tested	404 (17)
Peptides		
TTNYT	1786 (382)	414 (2)
TTSYT	1990 (603)	539 (39)
NTSYG	1275 (280)	957 (96)
STNYT	1052 (394)	540 (30)
D-Ala^1-peptide T-NH_2	1968 (372)	825 (162)
D-Ala^1-D-Thr^8-peptide T-NH_2	5738 (629)	1447 (102)
TTNdYT	5177 (626)	1120 (9)

Results as mean (and SEM)

*A3.01 cells (10^6 in 1.0 ml) preincubated with peptides at 1 nmol/l for 45 min at 37°C in serum-free RPMI. Infections were initiated by adding virus (LAV) (stock endpoint titration of 1–2 × 10^6 $TCID_{50}$) to final concentration of 100 $TCID_{50}$ with a further 60 min incubation. Residual virus was removed by washing three times and 2 × 10^5 cells were established in 2·0 ml RPMI/10% FCS in 24-well tissue trays in triplicate. Cells were fed/split 1:1 every 4 days. Supernatants assayed for reverse transcriptase at day 14.

†^{3}H-DAla peptide T (20 Ci/mmol) at 0·5 nmol/l incubated with 10^5 A3. 01 cells in Hank's balanced salt solution, pH 7·4, for 2 h at 31°C in presence of 10 nmol/l peptides: bound ligand was separated on Whatman GFC filters by vacuum and washed within 7 s with 3·5 ml incubation buffer containing 0·1% serum albumin.

Two critical variables for the detection of receptor-limiting processes mediating viral entry were emphasised at a National Institute of Mental Health workshop on June 30, 1987—namely, the concentration of virus and the concentration of receptor. The formation of virus-receptor complex must be rate-limiting: if peptide T competitively inhibits HIV binding to its CD4 receptor the effect will be most readily observed at low concentrations of virus and receptor and excess of either could make it difficult or impossible to observe inhibition. Sodroski et al used undiluted supernatants from a cell line engineered to produce large amounts of virus, and reverse transcriptase activity was 120 000 cpm/ml after only 5 days of culture. Furthermore, Sodroski et al selected target cells for their high receptor densities. Syncytial assays rely on a high local density of virus and receptor, conditions not met in vivo. In syncytial assays gp120 itself is ineffective in blocking infection so failure to detect inhibition by peptide T would be predicted. The detection of peptide T inhibition of viral infectivity diminishes with increasing virus concentration,[2,3] and at the NIMH workshop we showed that even with an appropriate virus concentration peptide T did not inhibit in Sup T1 cells while the lower CD4-expressing line (A3·01) used in the studies reported here did show this effect.

Similar considerations apply to attempts to characterise direct gp120 receptor binding to CD4. A low concentration of radiolabelled envelope protein is critical. We have detected high affinity, stereospecific, peptide T-displaceable ^{125}I-gp120 binding to rat brain CD4 receptors[1] (and human T cells, unpublished) which is displaced by low (0·1 µg/ml) concentrations of two anti-CD4 monoclonal antibodies. Displacement by peptide T and its active and inactive analogues is closely correlated with biological activity. Clearly, the peptide T-insensitive, monoclonal anti-CD4 insensitive bimolecular interactions reported by Sodroski et al and by Lundin et al,[8] using unspecified, high concentrations of viral envelope and CD4 target cells and 1000-fold higher monoclonal antibody concentrations, display very different properties. Since such high concentrations of virus are probably never attained, the slow intercellular spread of HIV most probably happens, at low virus concentrations, via the stereospecific, high-affinity peptide-T-sensitive binding process.[1]

If the above pharmacological principles are adhered to, the potent effects of peptide T can be demonstrated. Failure to detect activity in assays of uncertain physiological relevance should not be grounds for postponement of clinical trials of peptide T, particularly since compassionate use of peptide T in four AIDS patients showed no toxicity and some improvement.[9]

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