presence or absence of 10 ng/ml of recombinant TNF-alpha (rTNF). The culture supernatant was harvested and examined for p24 (Abbott HIV antigen EIA). HIV replication was enhanced by TNF in PBMC from patients 1 (CDC status IV C-1), 2 (III), and 4 (IV C-1) but not from patient 3 (IV C-1) (table).

This demonstration that freshly isolated PBMC from HIV-infected patients respond to rTNF supports the hypothesis that TNF might be one of the cofactors which augment HIV replication. The enhancement of HIV replication was blocked by the inclusion of zidovudine 5 μmol/l in the culture (table).

Previously, Wong et al[9] reported that cotreatment with TNF and gamma-interferon blocks HIV infection. In response to this report, we suggested[10] a cautious approach because of the possible hazards of TNF use, based on our finding that TNF enhances HIV replication. However, the present study suggests that it is possible to administer TNF to HIV-infected patients together with an anti-HIV substance such as zidovudine.

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MERCURY POISONING FROM DENTAL AMALGAM THROUGH A DIRECT NOSE-BRAIN TRANSPORT

SIR,—The toxicity of mercury from dental amalgam is the subject of vigorous debate in many countries. In Sweden an expert committee from the National Board of Health has published a report on low-dosage exposure to mercury from amalgam.[1] However, expert opinion remains divided. In my view amalgam toxicity should not be discussed without addressing the matter of how mercury from amalgam can reach the brain. Regrettably the debate has neglected this key issue—namely, the direct pathway for transport of mercury from the oro-nasal to the cranial cavity.

Dental amalgam, containing about 50% mercury, is not stable. 50 years ago the German chemist A. Stock demonstrated that dental amalgam gives off mercury that may be inhaled and so reach the circulation and pass into the body, including the brain. However, far more dangerous are mercurial fumes, which settle on the mucous membranes in the upper region of the nasal cavity, from where the mercury is transported directly to the brain and pituitary gland. The pathways are the olfactory nerves or the valve-less cranial venous system that provides an open communication between the oronasal cavity and the intracranial cavity,[2,3] bypassing the general arterial bloodstream and the liver and its detoxifying processes. The direct nose-brain pathway is valid for other materials (eg, micro-organisms, toxins, and aminoacids) besides metals such as aluminium,[4] cadmium,[5] and mercury. Moreover, neuronal transport along trigeminal nerves to the brain has long been recognised for herpesvirus, and horseradish peroxidase inserted into a tooth-pulp readily spreads to the brainstem.[6]

MERCURY CONCENTRATION IN PITUITARY GLAND AND BRAIN

Case*	Mercury ng/g wet weight: Pituitary gland	Occipital cortex	Ratio
Occupationally exposed			
1	4040	300	14:1
2	3650	84	43:1
3	2700	16	169:1
4	350	40	9:1
5	350	5	70:1
6	300	17	18:1
7	135	19	7:1
8	1300	18	72:1
Not occupationally exposed			
With amalgam (n = 15)	28 (7–77)	11 (3–23)	2·5:1
Without amalgam (edentulous) (n = 2)	10; 5	6; 6	..

Source: Nylander and colleagues.[7,8]
*Cases 1–7, dentists; case 8, dental nurse.

Surprisingly high concentrations of mercury have been found post mortem in the pituitary glands of dentists[7]—concentrations out of all proportion to the mercury found elsewhere in the brain (table), especially the occipital cortex. This disparity in mercury concentration between the pituitary and the occipital cortex can only be explained by different routes by which the metal arrived at these sites. Through the general arterial circulation both pituitary and occipital cortex receive a small amount of mercury but the pituitary has an extra "dose" by direct transport from the nasal cavity.

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EFFECT OF SURAMIN IN A PATIENT WITH ADRENOCORTICAL CARCINOMA

SIR,—Patients with inoperable adrenocortical cancer face a grim prognosis. For the past 30 years mitotane (*o,p'*-DDD) has been the most widely used drug in these patients, albeit with limited success. Suramin, an antitrypanosomal agent, has adrenotoxic properties.[1,2] It has been linked to the development of adrenal failure in a patient with AIDS[3] and exerts a toxic effect on the adrenal cortex in monkeys.[4] We have studied the potential therapeutic effect of suramin in a patient with metastasising adrenocortical cancer.