

## Papaverine, a vasodilator with antiviral activity

We read with interest the excellent case report of Speich et al. concerning a 37-year-old patient with pulmonary arterial hypertension and HIV infection [1]. The patient's pulmonary hypertension improved clinically after treatment with a combination of a nucleoside analogue and a protease inhibitor, and no vasodilatory therapy was necessary. However, if a vasodilator is considered of potential use in HIV patients with pulmonary arterial hypertension, papaverine may be a suitable therapeutic approach.

Papaverine, a potent non-selective phosphodiesterase inhibitor, has shown itself to be effective in pulmonary arterial hypertension [2, 3]. The compound has additional antiviral activity against respiratory syncytial virus, cytomegalovirus or measles [4, 5]. Moreover, HIV replication is significantly inhibited by papaverine [5, 6], a finding consistent with the

clinical observation that papaverine may improve immunological cutaneous responsiveness in acquired immunodeficiency syndrome [7]. The antiviral effect of papaverine is obviously independent of the increase in intracellular C-AMP and affects neither Il-2 production nor Il-2 receptor expression. Although its biological antiviral mechanism is not completely elucidated, papaverine may offer an alternative warranting further investigation in HIV patients with pulmonary hypertension.

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## Author's reply

The effects of papaverine on HIV infection have mainly been observed in in-vitro experiments. The only clinical data derive from a letter concerning two patients whose Cd4 cell counts improved on oral papaverine. These findings, however, have nowhere been reproduced to date, and papaverine is not used by any other HIV specialists. The same is true of pulmonary hypertension. Since papaverine, like theophylline, is only a non-specific phosphodiesterase inhibitor, problems with side effects are foreseeable. Moreover, there are no sound data on the pharmacokinetics of papaverine. On the other hand, a favourable acute response to oral administration of sildenafil, a specific inhibitor of phosphodiesterase isoform 5, has recently been

demonstrated in two patients with HIV-related pulmonary arterial hypertension. One of them has been treated for more than 3 months with a persistent clinical improvement and decrease in pulmonary artery pressures.

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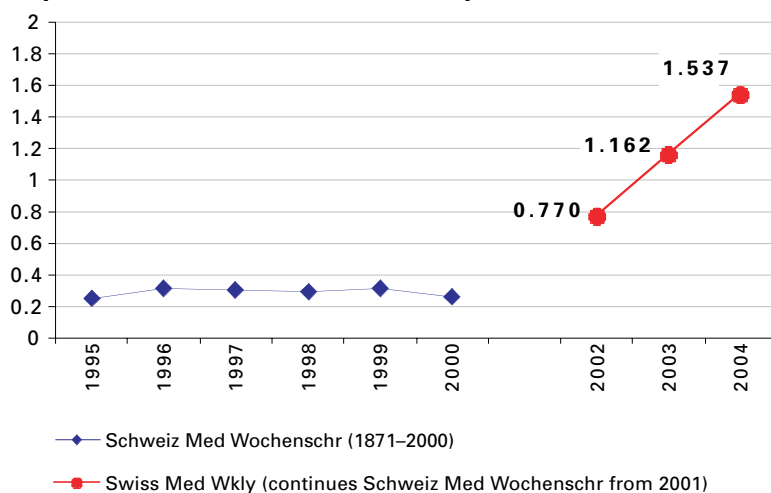
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