group patients also had a factor VIII:V ratio of 30 or above at 72 h but all seven patients survived, one developing transient encephalopathy.

This study suggests that, if measured less than 72 h post overdose, a factor VIII:V ratio of 30 or above and/or a factor V concentration of 10% or below are not reliable early prognostic indicators in paracetamol poisoning, unless accompanied by grade III/IV encephalopathy.[1]

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Boxer disqualified for taking selegiline

SIR—The case of Gianfranco Rosi, a 38-year-old Italian boxer, who defeated Verno Phillips at the World Boxing Organisation superwelterweight final on May 17 in Perugia has recently received attention from the press. The day after he became champion, Rosi was disqualified because he was found positive for amphetamine and metamphetamine in urine. Upon advise from his general practitioner, he had taken selegiline (Deprenyl) to prevent boxer's encephalopathy. Selegiline, is a monoamine oxidase (MAO) inhibitor widely used to treat Parkinson's disease and is registered in Italy as an adjutant to prevent brain ageing. Selegiline is metabolised to l-metamphetamine and l-amphetamine, which may be responsible for some of its clinical effects.[1]

The effect of selegiline on patients with Parkinson's is partly due to a potentiation of levodopa.[2] After the observation that nigral-cell degeneration induced by MPTP could be prevented by MAO inhibitors, Birkmayer suggested that selegiline may also slow the progression of motor signs in Parkinson's disease.[3] This indication has not been unequivocally confirmed, mainly due to difficulties in designing appropriate clinical studies.[4] Selegiline, however, is currently used as a neuroprotective not only for Parkinson's disease, but for Alzheimer's disease, multiple system atrophy, and motor neuron disease. In all such conditions, the anti-oxidant properties of selegiline are believed to slow neural degeneration. Furthermore, based on the observation that brain MAO activity increases with ageing, hints have appeared on the possibility that MAO inhibitors, such as selegiline, may prevent brain ageing.[5]

Selegiline is not classified as a doping drug. However, an Italian drug reference handbook of sport medicine lists it as a stimulant to be avoided. Rosi, who never denied he had taken selegiline was disqualified as world champion and was suspended for 2 years by the Italian boxing federation. On appeal, based on the proven champion's good faith and on medical literature supporting the use of selegiline as a neuroprotective agent, Rosi's suspension was reduced to 1 year. This unfortunate story supports our belief that selegiline must be used in medical practice only for well documented indications.

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Dipyridamole augmentation of response to nitric oxide

SIR—Inhaled nitric oxide (NO) improves oxygenation and lowers pulmonary vascular resistance in hypoxaemic neonates with severe pulmonary hypertension.[1] Some neonates, including some with congenital diaphragmatic hernia, have partial or absent clinical responses to inhaled NO therapy. Poor response to inhaled NO is commonly due to insufficient lung inflation Since NO causes vasodilation by stimulating production of cyclic guanosine monophosphate (cGMP) in vascular smooth muscle, responses to inhaled NO may be partly limited by an inability to sustain cGMP concentrations in pulmonary vascular smooth muscle. Laboratory studies have demonstrated that inhibitors of cGMP-specific (type V) phosphodiesterase (PDE5), which hydrolyses cGMP in vascular smooth muscle, augments pulmonary vasodilation.[2-5] To examine the clinical effects of PDE5 inhibition on the response to inhaled NO, we studied the response of a neonate with severe congenital diaphragmatic hernia requiring extracorporeal membrane oxygenation (ECMO) due to poor cardiac performance with severe lung hypoplasia.

Despite prolonged ECMO therapy, cardiac function remained poor and systolic pulmonary artery pressure (PAP) (based on echocardiographic measurement of tricuspid regurgitant jet) was suprasystemic. Bleeding complications led to an urgent need to discontinue ECMO support with a trial of inhaled NO to expedite decannulation. Although inhaled NO at 1, 5, and 20 parts per million (ppm) decreased systolic PAP by 30% (figure), high pulmonary vascular resistance and right-to-left shunting at the ductus arteriosus persisted. With dipyridamole treatment (0·6 mg/kg), the response to inhaled NO was enhanced, decreasing systolic PAP by 45%, reversing the ductus arteriosus shunting from right-to-left to left-to-right, and allowing for transition away from ECMO.

From these findings, we speculate that PDE5 inhibition may enhance the response to low-dose NO therapy in selected neonates with severe pulmonary hypertension.

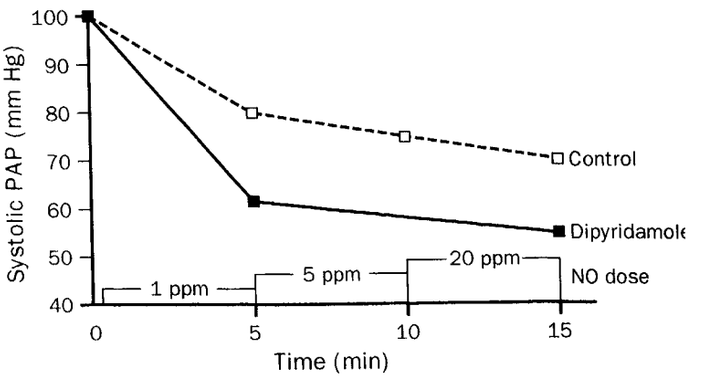

Figure: **Augmentation of response to NO by PDE5 enzyme inhibitor dipyridamole**