

## **A Pig Model of Dimethoate Pesticide Poisoning**

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**Objective :** Dimethoate pesticide poisoning is a major clinical problem in rural Asia. Unlike poisoning with other OPs, the majority of dimethoate deaths result from delayed cardiovascular shock after early respiratory failure. The reason for this different clinical presentation is unclear. We set up a pig model of dimethoate poisoning to explore the pathophysiology of this poisoning. **Methods :** Gottingen minipigs were anaesthetized before placement of central arterial and venous lines. They were then poisoned with standard agricultural dimethoate (40% emulsifiable concentrate [EC40]) or dimethoate 25% active ingredient in ethanol. Atropine, pralidoxime, noradrenalin and fluids were administered as required. Blood samples were taken for pharmacokinetic/dynamic studies; neuromuscular junction (NMJ) function was assessed by mechanomyography. **Results :** 2.5 ml/kg dimethoate EC40 caused severe hypotension due to peripheral vasodilatation that was similar to human poisoning. High doses of noradrenaline were required to maintain a mean arterial blood pressure above 55 mmHg; this was associated with a blood lactate that rose over 10 hrs to 15  $\mu\text{mol/L}$ . The red cell acetylcholinesterase activity fell to <20% of normal by 4hrs; there was minimal response to pralidoxime (25  $\mu\text{mol/L}$ ). NMJ function failed by 12 hrs. 1.25 ml/kg dimethoate EC40 caused identical inhibition of red cell acetylcholinesterase and NMJ failure, but no severe hypotension or hyperlactataemia. Unformulated dimethoate active ingredient similarly inhibited red cell acetylcholinesterase but did not cause severe hypotension, hyperlactataemia, or NMJ failure. **Conclusion :** This study showed that severe red cell acetylcholinesterase inhibition was not necessarily associated with severe illness. The identical red cell acetylcholinesterase inhibition without clinical illness in pigs administered unformulated dimethoate suggests that the coformulants - solvents (such as cyclohexanone and xylene) and surfactants- may be important. Further studies are needed to determine whether these findings remain true for other OP pesticides and to clarify the mechanisms of cardiovascular shock.