Effects of neonicotinoid insecticides on mammalian nicotinic acetylcholine receptors.

Duzguner, V., Edogaan, S. Acute oxidant and inflammatory effects of *imidacloprid* on the mammalian central nervous system and liver in rats. *Pest. Biochem. Physiol.* **97**, 13-18 (2010). *This shows that imidacloprid has acute oxidant and inflammatory effects on the mammalian CNS and liver.*

Kimura-Kuroda J., Hayashi, M., Kawano, H. Nicotine-like effects of neonicotinoids on rat cerebellar neurons. *Neuroscience Research*, **71**, suppl, (2011). *This is a study to determine to what extent the neonicotinoids imidacloprid and acetamiprid affected the nAChRs of rat cerebellar neurons and to compare their effects with nicotine by using in vitro excitatory Ca-influx assay. Although nicotine excited rather higher proportions of neurons and a higher peak of Ca-influx compared with the two neonicotinoids, both had higher binding to the neurons and were significantly inhibited with nAChR antagonists. The authors suggested that the neonicotinoids could have adverse effects on human health, especially in the developing foetus.*

Bal, R. *et al* Insecticide imidacloprid induces morphological and DNA damage through oxidative toxicity on the reproductive organs of developing male rats. *Cell. Biochem. Funct.* (2012) DOI: 10.1002/cbf.2826. *The weights of the epididymis, vesicula seminalis, epididymal sperm concentration, body weight gain, testosterone and reduced glutathione values were lower in the imidacloprid-treated groups than that in the controls. All treated groups had increased lipid peroxidation, fatty acid concentrations and higher rates of abnormal sperm. Apoptosis and fragmentation of seminal DNA were higher in rats treated at the two higher doses of imidacloprid. These results show that this compound has a negative effect on sperm and testis of rats.*

Bal, R. *et al*. Effects of clothianidin exposure on sperm quality, testicular apoptosis and fatty acid composition in developing male rats. Cell Biol Toxicol DOI 10.1007/s10565-012-9215-0. *It is concluded that low doses of CTD exposure during critical stages of sexual maturation had moderate detrimental effects on reproductive organ system and more severe effects are likely to be observed at higher dose levels. In addition, the reproductive system may be more sensitive to exposure of CTD even earlier in development (prenatal and early postnatal), and therefore it could be expected that more severe effects could also be observed at the NOAEL dose levels, if dosing had occurred in utero or early postnatal.*

Abou-Donia M.B. *et al*. Imidacloprid induces neurobehavioral deficits and increases expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats following in utero exposure. J. Toxicol. Environ. Health A. 2008; 71 (2) 119-130. *Gestational exposure to a single large, non-lethal, dose of imidacloprid produces significant neurobehavioral deficits an and increased expression of glial fibrillary acidic protein in several brain regions of the offspring on postnatal day 30, corresponding to human early adolescent age. These changes may have long-term adverse effects in the offspring.*

Li, P., Ann, J., Akk, G. Activation and Modulation of Human α4β2 Nicotinic Acetylcholine Receptors by the Neonicotinoids Clothianidin and Imidacloprid. *J. Neuroscience Research* DOI:10.1002/jnr.22644 (2011). *Since the clinical manifestations of neonicotinoid poisoning clearly involved the nicotinic receptors, studies of the effects of clothianidin and imidacloprid on human neuronal-type α4β2 nAChRs were undertaken. Both chemicals had effects on human receptors, but imidacloprid more so than clothianidin.*

Mondal, S., Ghosh, R.C., Mate, M.S., Karmakar, D.P. Effects of Acetamiprid on Immune System in Female Wistar Rats. *Proc. Zool. Soc*. **62** (2), 109-117 (2009).
A subacute toxicity study of acetamiprid was undertaken in 72 female wistar rats in four groups (18 each). Three different concentrations of acetamiprid (25, 100 and 200 mg/kg of body weight) were administered orally to rats. The results indicated that acetamiprid suppressed both CMI and antibody forming ability of lymphocytes.

Marıa Elena Calderon-Segura *et al* Evaluation of Genotoxic and Cytotoxic Effects in Human Peripheral Blood Lymphocytes Exposed In Vitro to Neonicotinoid Insecticides News. *Journal of Toxicology* Volume 2012, Article ID 612647, doi:10.1155/2012/612647
Abstract: *Calypso (thiacloprid), Poncho (clothianidin), Gaucho (imidacloprid), and Jade (imidacloprid) are commercial neonicotinoid insecticides, a new class of agrochemicals in Mexico. However, genotoxic and cytotoxic studies have not been performed. In the present study, human peripheral blood lymphocytes (PBL) were exposed in vitro to different concentrations of the four insecticides. The genotoxic and cytotoxic effects were evaluated using the alkaline comet and trypan blue dye exclusion assays. DNA damage was evaluated using two genotoxicity parameters: tail length and comet frequency. Exposure to 9.5 $\times 10^{-6}$ to 5.7 $\times 10^{-5}$ M Jade; 2.8 $\times 10^{-4}$ to 1.7 $\times 10^{-3}$ M Gaucho; 0.6 $\times 10^{-1}$ to 1.4 $\times 10^{-1}$ M Calypso; 1.2 $\times 10^{-1}$ to 9.5 $\times 10^{-1}$ M Poncho for 2 h induced a significant increase DNA damage with a concentration-dependent relationship. Jade was the most genotoxic of the four insecticides studied. Cytotoxicity was observed in cells exposed to 18 $\times 10^{-3}$ M Jade, 2.0 $\times 10^{-3}$ M Gaucho, 2.0 $\times 10^{-1}$ M Calypso, 1.07M Poncho, and cell death occurred at 30 $\times 10^{-1}$ M Jade, 3.3 $\times 10^{-3}$ M Gaucho, 2.8 $\times 10^{-3}$ M Calypso, and 1.42M Poncho. This study provides the first report of genotoxic and cytotoxic effects in PBL following in vitro exposure to commercial neonicotinoid insecticides.*

Cai, B., Deitch, E.A., Ulloa, L. Novel insights for systemic inflammation in sepsis and haemorrhage. *Mediators of Inflammation* 2010 ID 642462 (2010). *Human clinical studies in 2010 demonstrated a connection between the nAChRs and the immune system. In the process of trying to treat severe inflammatory responses in sepsis and haemorrhage (which are a major cause of death in patients in Critical Care), a specific anatomical and physiological connection was proved between the nicotinic acetylcholine anti-inflammatory receptors in the central nervous system, via the vagus nerve, to the innate immune system. This system protects humans against infection and tissue injury.*

30th December 2011; Geoffrey Lean, Environment Correspondent of the Telegraph, marks the end of the UN's Year of Chemistry. "*The usually cautious US President's Cancer Panel has reported that synthetic chemicals can cause grievous harm and that the number of cancers for which they are responsible had been grossly underestimated. The Standing Committee of European Doctors, including the BMA, added: "Chemical Pollution represents a serious threat to children, and to Man's survival."*

I wrote to both the US President's Cancer Panel and the BMA about these statements suggesting the neonicotinoid pesticides might be responsible. The US cancer panel said they only reported and the BMA never replied.