

## **THE INSECTICIDE CHLORPYRIFOS: A NEW ENDOCRINE DISRUPTOR.**

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Among pesticides used for agriculture and domestic use (such as household pests) chlorpyrifos (CPF) is one of the most used organophosphorus insecticides.

CPF neurotoxic effects are well known, in fact U.S. Environmental Protection Agency banned CPF domestic use. CPF, as all the organophosphorus insecticides, is an acetylcholinesterase inhibitor; acetylcholinesterase is an enzyme that degrades (through its hydrolytic activity) the neurotransmitter acetylcholine in central and peripheral nervous system. Chronic exposure to organophosphorus insecticides may lead to memory loss, depression and insomnia. CPF effects are particularly relevant when vulnerable population group, such as pregnant women, fetuses and children, are exposed. Experimental data shows that in such vulnerable phases CPF may interfere, permanently, with neurobehavioural development (Veronesi et al, 2008). Several pesticides have the ability to act as endocrine disruptors (ED) (Mantovani et al 2008) but, so far it was not clear if Organophosphorus insecticides could modify hormonal mechanisms.

Studies carried out in our Unit show that pregnancy and/or neonatal exposure to CPF in mouse model proved:

1) hypothyroidism in dams exposed, with a reduction of thyroid hormone levels and clear damage at thyroid tissue. In F1 generation thyroid tissue and hormone levels alterations are evident, both in perinatal and sexual maturity stages, as it was observed in dams (De Angelis et al, 2009).

2) irreversible effects related to oxytocin and vasopressin production, two neuroendocrine regulators hormones released by the human posterior pituitary gland to act at a distance. In particular, oxytocin levels result increased while vasopressin levels are reduced (Tait et al, 2009).

Such alterations are observed at CPF dose levels below nervous system toxicity thresholds.

Our data concern mostly animals in adult lifestage exposed in the first lifestages mostly during pregnancy: therefore, it is a matter of irreversible modified organism programming; moreover, males seem to be more susceptible for both thyroid and neuroendocrine effects.

It is important to remark that thyroid alterations, in dams and F1 generation, may involve dysregulation in developmental and growth processes, with possible relapses also on other systems, including reproductive system that, so far, is not an important CPF target. Moreover, alteration in levels of hypothalamic neurotransmitters suggest an effect on regulation mechanisms, in particular on dialogue between hypothalamus and other endocrine system component, starting from pituitary gland.

Our data demonstrate, for the first time, that CPF is an ED, with unexpected and unforeseen mechanisms and long term effects on neuroendocrine and thyroid regulation.

Other organophosphorus could have the same mechanisms, with relapses for the safeguard of food safety from at least two points of view:

- it is important to take into account recent scientific concerns concerning definitions of maximum residues for pesticides in food, more focused on fetuses and children safeguard

- Evaluation, through suitable experimental models, of concomitant effects due to contemporaneous presence of several pesticides with analogous mechanism in food is needed.

### **References**

- De Angelis S, Tassinari R, Maranghi F, Eusepi A, Di Virgilio A, Chiarotti F, Ricceri L, Venerosi Pesciolini A, Gilardi E, Moracci G, Calamandrei G, Olivieri A, Mantovani A. (2009) Developmental exposure to chlorpyrifos induces alterations in thyroid and thyroid hormone levels without other toxicity signs in cd1 mice. *Toxicol Sci.* 108(2):311-9.

- Mantovani A, Maranghi F, La Rocca C, Tiboni GM, Clementi M. (2008) The role of toxicology to characterize biomarkers for agrochemicals with potential endocrine activities. *Reprod Toxicol.* 26(1):1-7.
- Tait S, Ricceri L, Venerosi A, Maranghi F, Mantovani A, Calamandrei G. Long-term effects on hypothalamic neuropeptides after developmental exposure to chlorpyrifos in mice. *Environ Health Perspect.* 2009 Jan;117(1):112-6.
- Venerosi A, Cutuli D, Colonnello V, Cardona D, Ricceri L, Calamandrei G. Neonatal exposure to chlorpyrifos affects maternal responses and maternal aggression of female mice in adulthood. *Neurotoxicol Teratol.* 2008 Nov-Dec;30(6):468-74.