COT organophosphate statement lay summary

Organophosphates are a class of chemicals, some of which can bind to and inactivate an enzyme, acetylcholinesterase, which is important to the function of the nervous system. This property has been exploited in their use as insecticides in agriculture and horticulture, as veterinary medicines to prevent or treat infestations (e.g. sheep dips), as human medicines (malathion only – as a treatment for head lice), and as public hygiene products (e.g. for control of cockroaches). However, it poses a hazard to people who are exposed to them inadvertently during their manufacture or as a consequence of their use. In addition, intentional human poisoning has occurred as a result of deliberate self-harm, and through the use of some organophosphates (different from those in pesticides and medicines) as chemical warfare agents.

Poisoning by over-exposure to organophosphates that bind acetylcholinesterase causes rapid onset of illness, which in severe cases can be fatal. Moreover, people who survive such poisoning are at increased risk of subtle, long-term effects on brain function.

This statement considers whether long-term, harmful effects on the nervous system can result from exposure of adults to lower levels of cholinesterase-inhibiting organophosphates that are insufficient to cause overt short-term poisoning. When this question was last considered by the COT as part of a report published in 1999, the evidence was judged to be inconclusive.

The statement was drafted by a working group, who carried out a systematic review of relevant research that had published in peer-reviewed scientific journals up to September 2013. Preliminary consideration indicated that the most pertinent evidence would come from epidemiological investigations in human populations, and that toxicological studies in animals and in vitro would be less telling. The search was therefore limited to studies in humans, and reports of other types of research were not reviewed systematically.

Since 1999, 13 new papers have been published on the relation of low-level exposure to organophosphates to peripheral neuropathy (i.e. impaired function of the nerves outside the brain and spinal cord). These added to 13 studies that were already available at the time of the last COT report. The current balance of evidence suggests that there is no long-term risk of clearly demonstrable peripheral neuropathy from exposure to organophosphates that does not cause overt short-term poisoning; a conclusion that has strengthened with the passage of time.

There is uncertainty as to whether long-term low level exposure to organophosphates causes detectable impairment of people's ability to perceive sensory stimuli (such as light touch, hot and cold), but if there is an effect then it is likely to be small.

Few studies have looked for effects of low-level exposure to organophosphates on background patterns of electrical activity in the brain (electroencephalography or EEG), patterns of brain activity in response to standardised sensory stimuli (event-related evoked potentials), or the electrical activity in muscles (electromyography or EMG). In general, these studies do not suggest a hazard, but the evidence base is slim. One study has suggested impairment in the brain's processing of auditory information, but without independent replication, little can be drawn from this isolated finding.

Since the last COT review, 22 investigations have been published that looked for neuropsychological consequences of low-level exposure to organophosphates, adding to the nine that were available in 1999. Overall, there is no consistent evidence that low-level exposure to organophosphates has adverse effects on any specific aspect of cognitive function. If organophosphates do cause long-term neuropsychological impairment in the absence of overt poisoning, then the effects, at least in the large majority of cases, must be minor and subtle.

Evidence on whether, in the absence of acute poisoning, low-level exposure to organophosphates can cause long-term structural changes in the brain is insufficient for any firm conclusions.

The overall balance of evidence from 11 studies suggests no increased risk of Parkinson's disease from exposure to organophosphates that is insufficient to cause overt acute poisoning, although a small elevation of risk cannot be ruled out.

Findings from the only two studies on the relation of organophosphates to later dementia are not strongly suggestive of a hazard, but point to a need for further research.

Fourteen studies (including 10 published since 1999) have investigated the association of low-level exposure to organophosphates with depression and anxiety. Overall, there is no consistent evidence of a link. The balance of evidence suggests that low-level exposure to organophosphates does not lead to an increased risk of suicide.

Despite limitations of individual studies, current evidence suggests that there is an excess of multiple neuropsychiatric symptoms in people who have been exposed to organophosphates at levels insufficient to cause overt acute poisoning. However, it does not support the existence of a specific syndrome of "chronic organophosphate-induced neuropsychiatric disorder (COPIND)", as has previously been hypothesised. It is unclear whether the observed excess of symptoms is a consequence of chemical toxicity or occurs through psychological mechanisms, and it is possible that people who are aware of having been exposed to potentially toxic chemicals are more inclined to notice and report symptoms. Studies on the relationship of symptoms to differences in people's capacity to metabolise organophosphates have not clearly established a causal link with poorer ability to detoxify

organophosphate compounds, as might be expected if the illness were a consequence of toxicity.

Collectively, the evidence reviewed is reassuring. It suggests that exposures to cholinesterase-inhibiting organophosphates that are insufficient to cause overt acute poisoning do not cause important long-term neurological toxicity in adults, and that if toxic effects on the nervous system do occur then they are minor and subtle.

The most important gap in the current evidence base concerns the relation between low-level exposure to organophosphates and later dementia. An association of such exposure with dementia has some biological plausibility, and has been suggested (although not strongly) by the two studies that have looked at the question to date. Moreover, dementia is a major and growing public health problem, and even a small proportionate increase in risk could have important implications at a population level. However, further research on this should be conducted only through studies with adequate rigour that are statistically robust.

Given the evidence that is now available, it seems unlikely that further research on neurophysiological, neuropsychological and psychiatric outcomes would identify any important hazard from low-level exposure to organophosphates. Research to explore the possibility of more subtle, minor effects would require rigorous assessment of exposure, and better methods for assessment of the health outcomes than are currently available.

Glossary of technical terms

Epidemiological investigations: Studies that assess and compare the occurrence of specified health outcomes in defined populations or groups of people, and explore their statistical association with possible causes.

In vitro studies: Studies in experimental biology that use components of an organism (e.g. cells) that have been isolated from their usual biological surroundings.

Metabolise: Chemically transform within the body.

Neuropsychological: Concerning the structure and function of the brain as they relate to specific psychological processes and behaviours.

Toxicological studies: Studies investigating the occurrence and mechanisms of toxicity

The full COT statement can be found at: http://cot.food.gov.uk/sites/default/files/cot/cotstate.pdf

Lay summary to COT Statement 2014/01