Press release – for immediate release

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The organophosphate Monocrotophos as cause of the India school lunch deaths: an editorial to be published in Archives of Toxicology by members of the ESNATS consortium

Poisoning through environmental chemicals has been with humans for a long time: from lead poisoning in ancient Rome over workplace exposure to mercury in 19th century Britain to multiple tragedies due to environmental poising in the 20th century. Most recently, on July 16th 2013, 23 Indian schoolchildren died in the Gandaman village after eating a contaminated school lunch. The deaths were more than likely caused by an acute intoxication from the pesticide monocrotophos. Forensic analysis reported high levels of monocrotophos in the cooking oil used for preparing the school lunches, and a container previously used to store pesticides was found in the kitchen area. Following this incident, an improved understanding of the impact of pesticides on human health is essential.

In an editorial to be published in Archives of Toxicology, appearing online in mid-August and in print around September 15th, toxicology and stem cell scientist members of an EUFP7 funded consortium to develop alternative human stem cell based models for toxicology (ESNATS) comment on Gandaman village tragedy. Monocrotophos is a chemical belonging to the group of organophosphates. The pesticide is insecticidal, but also highly toxic to other animals, including birds and mammals. Its use has therefore been banned in many Western countries. It is however still used in South America, Africa and Asia, including India. The apparently high efficacy of crop protection by monocrotophos probably explains the continued use of this dangerous pesticide in certain countries. To put things in context, malnutrition in India is very common. According to UNICEF, one in every three malnourished children in the world lives in India (UNICEF website). India desperately needs food and its poor depend heavily on affordable mass production, which includes the use of cheap and potentially very toxic pesticides. Such pesticides will therefore stay around for the foreseeable future.

Following the Gandaman incident, the superintendent of the Medical College hospital in Patna (a city close to Gandaman) downplayed the effects of acute poisoning , saying that children who survived the acute intoxication will have “no remnant effects on them” (Huffington Post 2013/07/18). Professor of Medicine Karl-Heinz Krause, Geneva/Switzerland says: *“This statement is misleading as long-term consequences of organophosphates poisoning include organophosphate-induced delayed polyneuropathy and chronic organophosphate-induced neuropsychiatric disorder. Such long term toxicity of organophosphates may even occur in the absence of documented acute intoxication and such cases might be much more frequent than fatal acute intoxications. In addition, low-level prenatal exposure is associated with reduced IQ scores and deficits in working memory.”*

To the best of present medical knowledge, monocrotophos is not devoid of this long-term organophosphate toxicity, but reports are more sketchy than for other pesticides. Toxicologists

Professor Jan Hengstler and Dr Christoph van Thriel, Dortmund/Germany say: *"When it comes to protecting the legal rights of victims and their families, our present medical knowledge is not good enough. Toxicity mechanisms need to be demonstrated and unequivocal cause/consequence chains need to be established."*
"Understanding the mechanisms of organophosphate toxicity is critical in two respects. First, therapeutic strategies for patients exposed to these toxics can be developed. Second, such studies should allow legislators to create legal frameworks that encourage the use of pesticides with the least unfavorable toxicology profile.", says Professor Marcel Leist, Konstanz/Germany.
It is crucial to identify low cost pesticides with as little long-term toxicity as possible. To achieve this goal, collaboration between clinical, epidemiological, and experimental toxicologists is necessary. Toxicologists need to study the impact of toxic compounds in physiologically relevant model systems, rather than using only immortalized cell lines, and to study the impact of toxics in human model systems, instead of relying exclusively on results obtained in other species.
Dr. Paul de Sousa, University of Edinburgh/UK explains: *"The advent of pluripotent stem cells (PSC) provides significant opportunities for such studies. The impact of toxics on virtually all types of cell types can be studied without recourse to immortalized cell lines."* The European consortium ESNATS *(Embryonic Stem cell-based Novel Alternative Testing Strategies)*, a partnership of scientists from 29 organisations from all over Europe and Israel receives funding from the European Commission's 7th Framework Programme for Research and Development to develop pluripotent stem cell-based toxicity tests. First results demonstrate that such test systems may indeed become powerful tools. The use of PSC technology is threefold. It allows for ethnic diversity of humans to be included in analysis, for toxics to be tested on tissues rather than on isolated cells, and for mice to be generated with humanized organs, advancing the level of complexity required for translatable experimental toxicology research.

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