Chronic pesticide exposure may increase the risk for obesity by suppressing diet-induced thermogenesis

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Madam, the unregulated and injudicious use, or rather overuse, of pesticides in Pakistan is alarming. Pesticides are predominantly used in the agricultural industry, and Pakistan, being an agricultural country, is one of the largest consumers of pesticides in South Asia. The use of pesticides has increased by 1169% in the past two decades (more than 10 sprays per crop), raising great concerns and posing a grave threat to the ecosystem.[1] According to the pre-existing literature, the urinary levels of biomarkers for chlorpyrifos (an organophosphate pesticide) and diazinon are high in workers of the pesticide industry, and general residents of areas around these industries, due to the pesticide loading onto dust. Thus pesticides engender significant health risks to occupational workers such as farmers and pesticide industry workers and residential populations.[2] Apart from the well-recognized dermatological, gastrointestinal, respiratory, carcinogenic, neurological and endocrine effects of pesticide exposure,[3] a novel consequence in recent studies is the reduction of diet-induced thermogenesis in those chronically exposed to pesticides. Some of the most commonly used pesticides, such as chlorpyrifos, may thus be the yet-neglected precursors of obesity in the developing world. A recent ground-breaking study has hypothesized (with sufficient evidence) that the pesticide chlorpyrifos promotes obesity by suppressing diet-induced thermogenesis in brown adipose tissue. Obesity is responsible for multiple pathological conditions, including insulin resistance, high blood pressure, non-alcoholic fatty liver disease (NAFLD) and dyslipidaemias. The study has thus sparked major concerns.

So, the question arises: What is the specific mechanism that would likely explain the possible role of pesticides in obesity?

Uncoupling protein 1 (UCP1) is a well-documented protein that has a vital role in adaptive thermogenesis. Its role has been validated by prior studies involving the experimental removal of the UCP 1 gene in mice and the resulting obesity, insulin resistance, and NAFLD observed on administration of a high-fat diet and thermoneutral environment[5]. During the study under discussion, analysis of food contaminants at concentrations as low as 1 pM revealed the gene repression of UCP1 by chlorpyrifos. It does this by a twofold mechanism, namely the reduction of UCP1 promoter activity and mRNA expression, ultimately suppressing UCP1 protein. In addition, chronic exposure to even small quantities disrupted brown adipose tissue mitochondrial functions such as fatty acid oxidation regulation and cytochrome c oxidase assembly factor. Higher concentrations inhibit plasma butyryl cholinesterase and brain acetylcholinesterase, disrupts glucose metabolism, and thus may cause obesity by mechanisms that may involve increased energy intake and/or gut microbiome alterations. These findings suggest the contribution of common pesticides like chlorpyrifos in obesity.[4]

This discovery demands special attention in the context of the Pakistani population, a quarter of which was found to be in the overweight or obese category in a study conducted in 2006.[5] The condition is particularly concerning in Pakistan because of the enormous volumes of people directly involved in the agricultural industry. Even greater numbers are indirectly exposed to pesticides either from dust or from ingestion of contaminated foods. Most of the general population also lacks proper education and awareness on the harms of excess pesticides, further worsening.

In August 2021, the U.S. Environmental Protection Agency banned the use of chlorpyrifos on all food crops because of its already notorious neurological and environmental effects. Ideally, a similar response towards this pesticide is needed in Pakistan after the recent revelations. However, due to chlorpyrifos' inexpensive and efficacious nature, its use is rampant in the developing nations. The least that can be done on a governmental scale is to enforce the safe use of pesticides. Most pesticide producers over advertise their products but provide limited instructions on their use and virtually no knowledge of the possible detrimental effects. Farmers must be properly educated to use protective clothing and gloves while using the

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pesticide and avoid eating during this time. It is advisable to keep the place ventilated if used indoors.

Moreover, pesticide load must be calculated beforehand to avoid excessive spraying of pesticides. There is no governmental incentive for these efforts, and they may put more strain on the already limited resources of the farmers; therefore, monetary support and education of the farmers are imperative to achieve any success.

Additionally, the government must work to regulate pesticide use and effectively implement existing legislation. The 1971 Agricultural Pesticide Ordinance and the 1973 Agricultural Pesticide Rules provided some groundwork for the safe use of pesticides, but unfortunately, no substantial practical steps have been implemented. A more promising reform by the government would be to establish research institutes to determine the toxic effects of various pesticides so that any harmful substance may be pre-emptively removed and resources can be directed towards safer alternatives.

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