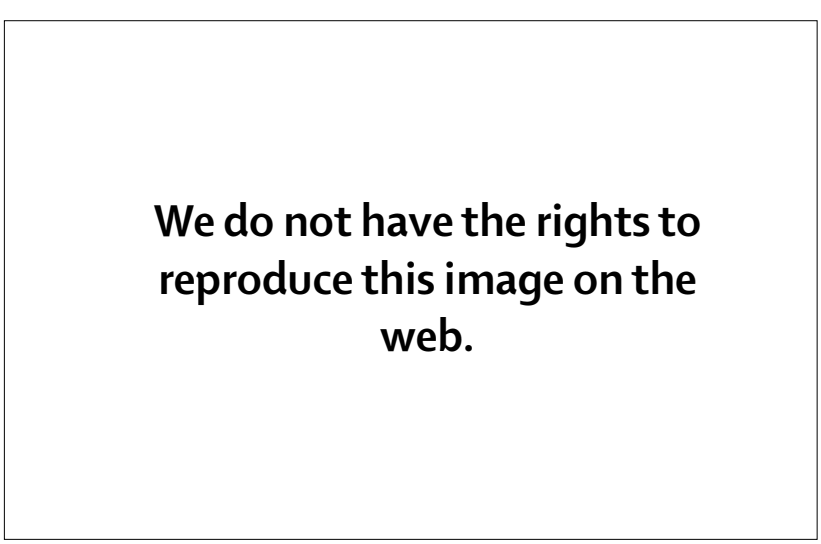
Persistent organic pollutants and the burden of diabetes

Studies from the USA[1,2] have drawn attention to the possibility that persistent organic pollutants might contribute to cause diabetes.[3-6] Dioxins, polychlorinated biphenyls, dichlorodiphenyldichloroethylene (DDE, the main degradation product of the pesticide dichlorodiphenyltrichloroethane [DDT]), trans-nonachlor, hexachlorobenzene, and the hexachlorociclohexanes (including lindane) are some of the persistent organic pollutants most commonly found in human beings.[7,8] Lipophilic and highly resistant to degradation, these pollutants are present in many fatty foods, usually at low concentrations.[9] Because they contaminate virtually all people, even if they confer only a low individual risk of diabetes, these pollutants might have a substantial overall population effect.[10]

Dae-Hee Lee and colleagues' recent study[1] is the first to analyse serum concentrations of persistent organic pollutants and fasting plasma-glucose concentrations in a random sample of a general population. Previous studies have focused on selected populations, often occupationally or accidentally exposed to high levels of such pollutants. Not studying a less-exposed group might have led to a blurring of risks. Widely prevalent exposures are particularly difficult to isolate as causal agents.[3] Concentrations of persistent organic pollutants in the study are typical of levels in many societies globally, and the risk of diabetes seems higher than ever. After adjustment for age, sex, race, income, lipids, body-mass index, and waist circumference, Lee and colleagues showed that the prevalence of diabetes was more than five times higher in groups with higher concentrations of polychlorinated biphenyl 153, oxychlordane, or trans-nonachlor than in those with lower concentrations. The prevalence of diabetes doubled and tripled in those in the upper quintiles of DDE and other compounds.[1]



Still Pictures

Lee and co-workers adjusted their results by multiple factors.[1] Such adjustment is fine if we wish to isolate the "pure" effect of persistent organic pollutants on diabetes separately from that of obesity, age, or income. However, adjustment by body-mass index and waist circumference might be an overadjustment, because dietary fats are the main source of persistent organic pollutants for human beings, and the body burden of these lipophilic chemicals often increases with increasing body-mass index. Crude or less adjusted prevalence odds ratios would provide information about the actual prevalence of diabetes in people with specific concentrations of these pollutants. Indeed, a priority should be to assess the validity of the study's[1] main finding: diabetes might be several times more prevalent in people with higher concentrations of these pollutants than in those with lower or no detectable levels. Causal inferences need to be extremely cautious. The cross-sectional nature of Lee's study, in particular, prompts assessment of the direction of the association: might diabetes cause a higher accumulation of persistent organic pollutants? Unfortunately, data for the toxicokinetics of these pollutants in patients with diabetes are scarce, while many studies indicate that most persistent organic pollutants are resistant to active metabolism.[1,7,8] Even if diabetes is some day shown to be the first major disease favouring accumulation of persistent organic pollutants, patients and clinicians would need to cope with the consequences: individuals with diabetes would be more likely to experience the adverse effects of these pollutants.[6]

Another striking finding in Lee and co-workers' study is that there was no association between obesity and diabetes in individuals with non-detectable levels of persistent organic pollutants. Obesity was a risk factor for diabetes only if people had blood concentrations of these pollutants above a certain level. This finding might imply that virtually all the risk of diabetes conferred by obesity is attributable to persistent organic pollutants, and that obesity is only a vehicle for such chemicals. This possibility

is shocking. Standard measures were used for body-mass index, but weight changes were not considered. Weight gains and weight losses in individuals with and without diabetes will be difficult to measure in large studies. But cohort studies with repeated measurements of individual weight and blood could help solve the puzzle.

An association between diabetes and blood concentrations of polychlorinated biphenyls has also been reported in a study from Michigan.[2] Although the study was prospective, diabetes was self-assessed and participants had had accidental food contamination 30 years previously. Women in groups with higher serum concentrations of polychlorinated biphenyls had a twofold increased incidence of diabetes (again adjusted by several factors, including age and body-mass index). The crude incidence also doubled in men with the highest levels of polychlorinated biphenyls, but adjusted results were non-significant.

Exposure to many persistent organic pollutants has fluctuated in the past 60 years: birth cohort and period effects are plausible. But time-series and age-period cohort analyses of the potential link between persistent organic pollutants and diabetes are not available. Ecological and individual-based studies would allow estimations to be made of the fraction of diabetes that is influenced by persistent organic pollutants, other environmental agents, genetic factors such as susceptibility haplotypes, and by their interactions.[3-6]

The causal role of persistent organic pollutants in diabetes is more likely to be contributory and indirect—eg, through immunosuppressant, non-genotoxic, perhaps epigenetic mechanisms.[3-7,11,12] A proper understanding of how genes and persistent organic pollutants interact to cause diabetes is important both for primary prevention and to advance basic knowledge on diabetogenic mechanisms. When assessing the mechanisms linking diet, fat intake, obesity, and diabetes, persistent organic pollutants should also be considered. We need a better understanding of the burden of diabetes that these pollutants might contribute to cause.

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I declare that I have no conflict of interest.

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UK classification of drugs of abuse: an un-evidence-based mess

It is extremely fortuitous that the UK House of Commons' Science and Technology Committee decided to pick classification of drugs of abuse as one of its case studies into the Government's handling of scientific advice, risk, and evidence in policymaking. Their concluding report, *Drug classification: making a hash of it?*,[1] has made public verbal, written, and scientific evidence in the stop, start, put on hold, and do not disclose efforts of the Government to date. The report's title hints at the Committee's opinion of the current classification system, but is not strong enough. The report highlights a situation that almost defies belief.

There is so much to focus on in the report that it is easy to get side-tracked. Some of the UK mass media majored on the written evidence submitted by David Nutt, chair of the Advisory Council on the Misuse of Drugs (ACMD) Technical Committee which showed that, with a semi-scientific scoring system, alcohol and tobacco are more harmful to health than cannabis and LSD. But as the Committee pointed