Using cross-sectional data from the 1999–2002 US National Health and Examination Survey, Duk-Hee Lee and colleagues reported a strong correlation between insulin resistance and serum concentrations of persistent organic pollutants, especially for organochlorine compounds. This result was a surprise for many people working in diabetes research, because most studies to date have focused on the effects of genetics and the westernisation of dietary habits and lifestyle, while ignoring the potential effect of xenobiotics. Nevertheless, as discussed by Porta, an increasing number of reports suggest that chronic dietary exposure to, and accumulation of, low concentrations of environmental pollutants within the body might also be associated with diabetogenesis. Ignoring the potential effects of xenobiotics therefore risks ignoring a potentially crucial component in the study of type 2 diabetes, obesity, and the metabolic syndrome.

Lee and co-workers note two important findings related to obesity. The first was that the expected association between obesity and diabetes was absent in people with low concentrations of persistent organic pollutants in their blood. The second was that the association between obesity and diabetes became stronger as the concentrations of such pollutants in the blood increased. Interestingly, this report is not the first time that the presence of persistent organic pollutants and other organochlorine compounds in blood have been associated with diabetes. Rylander and colleagues analysed the concentrations of 2,2’,4,4’,5,5’-hexachlorobiphenyl (CB-153) and 1,1-dichloro-2,2-bis (p-chlorophenyl) -ethylene (p,p'-DDE, a breakdown product of DDT) in the serum of 196 men and 184 women in a fishing community in Sweden. Both compounds showed a strong association with the occurrence of diabetes. Much the same results were seen in a population-based study in Belgium. Studies of US Air Force veterans of the Vietnam War exposed to Agent Orange also suggest an adverse relation between dioxin exposure and symptoms of diabetes.

The potential of xenobiotics to disrupt glucose and lipid metabolism in mammals is a well-developed theory in toxicology. Indeed, many of the early toxicity responses in animal studies with a range of pollutants note glucosuria, dyslipidaemia, increased gluconeogenesis, and fatty liver. The versatility of high-throughput screening in metabolomics and metabonomics is an especially useful way of monitoring metabolic changes caused by disease or exposure to toxicants (eg, heavy metals) in animal models. Although most studies have tested acute exposure (ie, less than 2 weeks), in the few chronic exposure studies (ie, more than 3 months), glucosuria was recorded as long-term effect. This result suggests that diabetes could be exacerbated by chronic exposure to xenobiotics that disrupt normal metabolism of glucose and lipids.

Although correlation does not necessarily prove the existence of a causal relation, biologically plausible explanations exist for this association. For instance, dioxin-like compounds exert their effects through binding to the aryl-hydrocarbon receptor. This receptor is thought to antagonise peroxisome proliferator-activated receptors. One plausible hypothesis, therefore, is that the aryl-hydrocarbon receptor promotes diabetogenesis by antagonism of peroxisome proliferator-activated receptors. However, no data are available to support this.
argument. Some chemicals disrupt the ability of the body to metabolise fats directly, thereby inducing symptoms, such as weight gain, that can lead to diabetes. For instance, the polyaromatic hydrocarbon benzo[a]pyrene impairs lipolysis in adipose tissue, causes weight gain in mice, and profoundly impairs catecholamine-induced lipolysis in murine and human adipocytes. Our research is financially supported by the European Union. JLG is supported by the Royal Society (UK) and MLM is funded by the Medical Research Council (UK). We declare that we have no conflict of interest.


Retraction—A growing, bleeding, violet mole

On Oct 13, 2007, The Lancet published a Case Report by Michael Sand and Falk Bechara on cutaneous endometriosis.1 We accepted the paper after having been informed in writing, by the authors, that it had not been submitted for publication elsewhere. In fact, however, the same case had already been reported by the same authors in Muenchener Medizinische Wochenschrift Fortschritte der Medizin, a German medical journal.1 We were alerted to this fact by Prof Benno Mann, who was a coauthor of the paper published in German but who was not named as an author of the paper we published and was unaware of the decision to submit the paper to us. Because the Case Report in The Lancet is a duplicate publication, we retract it in full.

Richard Horton
The Lancet, London NW1 7BY, UK