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Increasing evidence supports the potential contribution of endocrine-disrupting chemical (EDC) exposure to the development of endocrine and metabolic disorders.[1] In particular, persistent organic pollutant (POP) pesticides and industrial solvents, plasticisers and by-products, and non-persistent pesticides have been suggested to have a role in obesity and diabetes.[2,3] Most studies done to investigate this association (and its implications) have focused on high-income countries.[1,2,4] However, in countries in the WHO South-East Asia region (further termed South-East Asia; figure), the use of EDCs seems to be more widespread, less well regulated, and therefore of greater potential importance with respect to the increasing incidence of diabetes. Unfortunately, little direct data on EDCs in this region exist.[1–3] Moreover, in South-East Asia, the diabetes epidemic has a greater effect on morbidity and mortality. Compared with other world regions, people from South-East Asia are at increased risk of developing type 2 diabetes at a lower BMI, developing it at a younger age, and having a more aggressive progression to macrovascular and microvascular complications.[5] According to the International Diabetes Foundation's Diabetes Atlas, South-East Asia has the highest mortality and lowest health-care expenditure per patient with diabetes in the world.[5,6]

Investigators have noted a close association between the rise in diabetes prevalence and production of synthetic compounds over the past 60 years in the USA.[2,3] Studies in the USA, Sweden, and Egypt have looked at low-level EDC exposure, proposing an association between increased insulin resistance and diabetes with chronic exposure to pesticides and industrial chemicals.[2,3,7] Epidemiological data have linked historical high-level exposures to several pesticides, solvents, and plasticisers with diabetes.[3] Results from in-vitro studies have shown that EDCs can disrupt energy metabolism, β-cell glucose sensing, and hepatic and skeletal muscle insulin sensitivity, operating via several homeostatic disruptions affecting the thyroid and glucocorticoid axes, oestrogen–androgen balance, and metabolic pathways such as peroxisome proliferator–activated receptor-γ suppression.[3,7] In studies in rats, bisphenol A, dioxins, and some fungicides have been shown to cause impaired glucose tolerance mediated through pro-inflammatory adipokine release and decreased adiponectin, and organophosphorus insecticides have been shown to impair hepatic insulin sensitivity.[3,7]

The European Union and Saudi Arabia have recently imposed bans on the import of some vegetables and fruits from India because of high pesticide residues,[8] suggesting that environmental exposure to EDCs (appendix) associated with diabetes is high in South-East Asia. Data from the Indian Government's Ministry of Chemicals and Fertilizers from 2001–12 show a roughly 38·5 times increase in imports of pesticides.[9] This increased use is out of proportion with economic and population growth in the region.[10] Improved regulatory enforcement is needed; several banned organochlorine pesticides are still in use despite prohibitions across South-East Asia.[11] Historical dumping of POPs and suboptimum storage of banned, legacy pesticides (especially in Pakistan) might have caused a rise in concentration of these compounds in fresh water (appendix). The ubiquitous nature and suboptimum regulation of pesticides in rural South-East Asia is shown by the high incidence of pesticide poisoning. According to estimates from WHO, pesticide poisoning accounts for about 160 000 deliberate and 56 000 unintentional cases of fatal poisoning per year in South-East Asia.[13]

Some non-modifiable factors might also play a part in high population exposure to EDCs. The warm climate of much of Asia is punctuated by monsoon rains, which drive the airborne mobilisation of POPs and transport them to the Himalayas, where they condense.[11] These

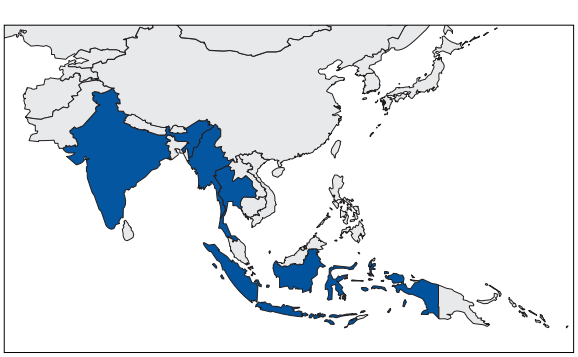

Figure: **Countries in the WHO South-East Asia region**

pollutants are then spread across large areas of South-East Asia by surface and sub-surface water flows. POPs can persist for years, moving all over the Indian subcontinent and leading to high concentrations in food and water.[11] The high population density in many urban areas of South-East Asia confers susceptibility to contaminated food and water supplies, and makes appropriate disposal of waste containing EDCs problematic.[10] Additionally, the hot, humid climate in much of South-East Asia means that people working with EDCs are less likely to wear protective clothing than in other parts of the world.[10]

The escalating use of EDCs in South-East Asia has been borne out of a desire for profitable manufacturing, efficient farming, and disease prevention. EDCs have been important to the sustained economic growth of the past few decades. If this growth accelerates as predicted, the issue of the potential harm EDCs can cause needs to be tackled.[14,15]

Six years ago, the Endocrine Society reviewed the scientific evidence for endocrine morbidity and mortality due to EDCs.[4] It described strong evidence for adverse reproductive outcomes from EDCs and some evidence for effects on other endocrine systems, including insulin and glucose homeostasis. In their statement,[4] the Endocrine Society concluded that comprehensive research was needed to identify means of exposure and mechanisms of endocrine disruption, and recommended that policies be urgently implemented to reduce exposure and prevent disease. WHO responded with a report on the state of the science on EDCs in 2012,[15] which echoed the Endocrine Society's conclusions. However, in both publications there was a paucity of discussion of an association between diabetes and EDC exposure, and an absence of studies from South-East Asia.

It is possible that with the advent of industrialisation and the increased distribution of industrial and agricultural chemicals across South-East Asia,[15] chronic exposure to EDCs has increased substantially, perhaps making a genetically susceptible population more prone to diabetes at a given age and BMI. Important efforts to reduce the diabetes epidemic, such as healthy eating campaigns, education, screening, pharmaceutical innovations, treatment guidelines, patient-centred care, and support networks could be undermined if EDC exposure continues to rise unchecked.

Addressing the possible threat of EDCs will depend on further characterisation of their population effects and development of relevant experimental models. The many thousands of chemicals released into the environment make quantifying low-level chronic human exposure and linking this exposure to endocrine disease difficult. Nevertheless, addressing EDC exposure might be important for confronting the diabetes epidemic in southeast Asia. Means of manufacturing and pest control that are not associated with diabetes are needed. Community-based intervention studies will also be necessary to find effective ways to reduce exposures and to identify the effect of these reductions on endocrine disease. Some of the vast sums of money spent worldwide on diabetes interventions could be effectively redeployed in the study of exposure to these neglected potential diabetogens.

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We declare no competing interests.

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