

## Long-term harms

Like many drugs, *diethylstilbestrol* (*DES*) was initially prescribed on the basis of pharmacological reasoning and rather encouraging results from non-comparative trials.

Like all too many drugs, it continued to be prescribed and dispensed by healthcare professionals who were unaware of or overlooked the fact that a more rigorous clinical evaluation showed an unfavourable harm-benefit balance.

Like so many drugs taken during pregnancy, it can provoke malformations in the unborn child. And over the past decades, it has emerged that *DES* provokes other adverse effects, including cancers in adulthood in “DES daughters” who were exposed to the drug in utero.

More and more evidence is accumulating that the children of these “DES daughters” are also subjected to the harms of this drug taken for just a few weeks or months by their grandmothers (see pp. 294-298).

Is *DES* an exception? Or do many other drugs have harmful effects decades after their use and over several generations?

As of 2016, nobody knows.

It seems likely that *DES* is not an exception, given the near-absence of robust long-term studies and the slow pace at which knowledge emerges. Another example is the length of time it took for the risk of autism associated with in utero exposure to *valproic acid* to be taken into account.

When prescribing or dispensing a drug, the hope of efficacy usually prevails over the fear of risks presumed to occur very rarely. Irreparable harm is not contemplated. Large numbers of patients are thus exposed to a highly uncertain fate. How could we do better?

Those who train health professionals can certainly do more to help their students become aware that the power of drugs should not be thought of in terms of efficacy alone but also as a potential source of harm, and that the harmful effects of drugs, especially over the long term, are poorly understood.

Health authorities can certainly do more to stimulate public-sector research in pharmacovigilance. They can provide patients and healthcare professionals with easily accessible information about the harms and benefits of drugs more rapidly and more frequently, updating this information without delay.

Patients and healthcare professionals can certainly become more aware of the long-term and possibly very long-term effects of the choices they make. Including effects on the lives of generations yet unborn.

For this to happen, healthcare professionals will need, among other things, to find the time to address this issue in their working lives, and have access to reliable sources of information and continuing education.

**Prescrire**