uman Reproduction vol.9 no.6 pp.1001–1002, 1994

OPINION

Dioxin pollution and endometriosis in Belgium

P.R.Koninckx[1,3], P.Braet[1], S.H.Kennedy[2] and D.H.Barlow[2]

[1]Division of Gynaecologic Endoscopic Surgery, Department of Obstetrics and Gynaecology, University Hospital Gasthuisberg, K.U.Leuven, B-3000 Leuven, Belgium and [2]Nuffield Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford, UK

[3]To whom correspondence should be addressed

The WHO report (1989) showing that dioxin concentrations in breast milk in Belgium are amongst the highest in the world, has recently stirred some concern, emphasizing the problems of pollution in Belgium. A woman can excrete up to half of her accumulated amount of dioxin during lactation (Pluim *et al.*, 1993) since dioxin is concentrated in breast milk.

The incidence of endometriosis in Belgium is 60–80% in women with infertility and/or pain (Koninckx *et al.*, 1991), which is one of the highest reported incidences in the world. Also the first report and the largest series of deeply infiltrating endometriosis, a very severe form of endometriosis (Koninckx and Martin, 1992), originated from Belgium.

These unrelated observations on dioxin pollution and on the incidence and severity of endometriosis in Belgium, could become a cause of great concern if a causal relationship exists between them. At the moment, only indirect arguments favour such a causal relationship. Firstly, women with endometriosis were recently reported to have increased concentrations of polychlorodiphenyl compounds (PCBs) in their blood (Gerhard and Runnebaum, 1992). Secondly, the incidence of endometriosis is higher in developed than in developing countries, although this may be a racial effect. Reported racial differences, which recently have been questioned, could possibly be explained by duration of exposure to dioxin pollution. Similarly, the impression that the incidence of endometriosis is higher in 'career women' could equally be interpreted as a consequence of urban life in industrialized areas rather than as a consequence of lifestyle and delayed child birth. A third, indirect, argument is that the incidence of severe endometriosis has risen in developed countries over recent decades. This coincides with the increased industrial production of PCBs and the related dioxin pollution since World War II. The increasing incidence of endometriosis is generally interpreted as due to the increased awareness of subtle or non-pigmented lesions. This new awareness cannot be responsible for the observed increase in hysterectomies due to endometriosis, as these are performed for either cystic ovarian endometriosis or deeply infiltrating endometriosis. Indeed in the USA the number of hysterectomies performed for endometriosis increased from 150 000 in 1965 to 400 000 in 1984 (National Center for Health Statistics, 1987). This increase was specific, a[s]e proportion of hysterectomies performed for endometi[o]is increased steadily from <10% to >18% during that pe[r]d.

The recent report of a dose-dependent relationship bet[w]en dioxin exposure and both the subsequent development [a]nd severity of endometriosis in the rhesus monkey (Rier *et al.*, 1[9]3; Tryphonas *et al.*, 1991), after a latent period of >5 years r[e]s the question whether these data are applicable to humans. [I]s moreover tempting to speculate that this increased incidenc[e a]nd severity of endometriosis is mediated through the immune sy[s]n. Dioxin is known to decrease cell-mediated cytotoxicit[y] by reducing T helper cell numbers (Neubert *et al.*, 1991). I[n]o-metriosis is known to be associated with a polyclonal B-[c]ell activation (Barlow *et al.*, 1993). It is associated with a [c]ell-mediated immunodeficiency (Dmowski *et al.*, 1981) whic[h] we showed in Leuven to be a decreased natural killer cell ac[t]ity (Oosterlynck *et al.*, 1992). The severity of endometriosis ha[s a]lso been linked to the degree of natural killer cell suppressi[on].

In conclusion, although studies have failed to demonstrat[e a]ny significant long-term health effects of dioxin, at levels to w[hi]ch humans have been exposed (Leung *et al.*, 1991; Kamri[n a]nd Fischer, 1991), an attitude towards dioxin pollution as bein[g] 'too low to be harmful' could be over-optimistic. The subject de[se]rves further investigation.

References

Barlow,D.H., Kennedy,S.H., Fernandez-Shaw,S. and Starkey, M. (1993) Changes in humoral immunity in endometriosis. In Bro[s],I. and Donnez,J. (eds), *The Current Status of Endometriosis*. Part[ho]n, Carnforth, pp. 235–247.

Dmowski,W.P., Steele,R.W. and Baker,G.F. (1981) Deficient c[el]ular immunity in endometriosis. *Am. J. Obstet. Gynecol.*, **141**, 377–83.

Gerhard,I. and Runnebaum,B. (1992) Grenzen der Hormonsubst[itu]ion bei Schadstoffbelastung und Fertilitätsstörungen. *Zentralbl. für Gynäkologie*, **114**, 593–602.

Kamrin,M.A. and Fischer,L.J. (1991) Workshop on human [he]alth impacts of halogenated biphenyls and related compounds. *Env[ir]on. Health Perspect.*, **91**, 157–164.

Koninckx,P.R. and Martin,D. (1992) Deep endometriosis: a consen[sus] nce of infiltration or retraction or possibly adenomyosis externa? *Fertil. Steril.*, **58**, 924–928.

Koninckx,P.R., Meuleman,C., Demeyere,S., Lesaffre,E and Cornillie,F. (1991) Suggestive evidence that pelvic endometri[osis] is a progressive disease, whereas deeply infiltrating endometri[osis] is associated with pelvic pain. *Fertil. Steril.*, **55**, 759–765.

Leung,H.W., Murray,F.J. and Paustenbach,D.J. (1988) A pr[opo]sed occupational exposure limit for 2,3,7,8-tetrachlorodibenzo-p-[di]oxin. *Am. Ind. Hyg. Assoc. J.*, **49**, 466–474.

National Center for Health Statistics (1987) *Hysterectomies in the United States, 1965–84*. Vital and Health Statistics, Series 13, Dat[a fr]om