

health issues are. The challenge to any government is how to respond to them.

To have reached this point is in itself a major achievement. If one party had run away with the Health for All ball we would have been faced with the usual British nonsense whereby good ideas are opposed just because the other party thought of them first. Something of this has been evident in the Labour party's response to the green paper and in what could be an interminable argument about who has stolen whose clothes. Such argument is a diversion; to a large extent they are WHO's clothes anyway, and the former director general, Halfdan Mahler, and the current European director, Jo Asvall, have a right to some of the credit. So too does the current chief medical officer, Sir Donald Acheson, whose hand is in there somewhere. At present the Labour party is attacking the wrong goal, and if it wins the next election it is likely to be more than happy to base its policy on the green paper. What it should be concentrating on now is the government's continuing weakness—the level of NHS funding and the mechanisms of accountability.

Those who have criticised the green paper for not going far

enough are overlooking the effect of having an explicit document from which there can be no going back. The policies listed in the future election manifestos of all the political parties will be judged by their likely success at solving the problems acknowledged in *The Health of the Nation*.

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The daughters of stilboestrol

Grown up now but still at risk

Stilboestrol (diethylstilbestrol, DES) is a synthetic non-steroidal oestrogen, first described in 1938¹ and promoted in the late 1940s for preventing miscarriages and preterm births.² In 1971 an association was reported between in utero exposure to stilboestrol and the subsequent development of clear cell adenocarcinoma of the vagina in young women.^{3,4} The use of stilboestrol in pregnancy was prohibited in the United States that year. In 1973 the Committee on Safety of Medicines in the United Kingdom advised against the use of stilboestrol in pregnancy. An estimated two to three million American women received stilboestrol during pregnancy.⁵ A postal survey in 1974 suggested that 7500 women had received the drug in Britain, mostly during the 1950s.⁶

Further study of the daughters of women who received the drug in pregnancy led to the recognition of various teratogenic effects of in utero exposure. Stilboestrol affects the Müllerian duct system, leading to abnormalities of the uterus, cervix, and upper vagina. Benign structural anomalies of the cervix and vagina (collars, rims, cockscomb cervix, and pseudopolyps) are found in 25-40% of women exposed to stilboestrol.^{7,8} Colposcopy shows epithelial changes in the vagina and cervix in 65-90%,⁹ with vaginal adenosis (the presence of glandular epithelium in the vagina) being present in 30-75%.¹⁰ With time this glandular epithelium is replaced by squamous epithelium by a process of squamous metaplasia. As in the non-exposed population, this process may become abnormal, resulting in cervical and vaginal intraepithelial neoplasia. Reported rates of cervical and vaginal intraepithelial neoplasia in women exposed to stilboestrol vary widely.^{9,10} A multicentre study in 1984 found a twofold increase in the incidence of cervical intraepithelial neoplasia among these women.¹¹ Currently there is no evidence of an increased incidence of invasive squamous carcinoma in women exposed to stilboestrol.

The risk of clear cell adenocarcinoma of the vagina is low, being about one per 1000 women exposed in utero. Of 519 patients with this carcinoma registered in the United States up to 1985, 60% had documented proof of exposure to

stilboestrol, of whom 91% were 15 to 27 years old.¹² Though most cases present with vaginal bleeding or discharge, cases diagnosed by screening asymptomatic exposed women have been reported.^{13,14} Prognosis is related to the stage of disease at diagnosis.¹⁵ Three cases of vaginal clear cell adenocarcinoma have been reported in Britain in women exposed to stilboestrol.¹⁶⁻¹⁸

In 1977 abnormalities of the upper genital tract (most frequently a T shaped uterus) were described in 40 of 60 women exposed to the drug.¹⁹ Although no conclusive evidence exists of increased primary infertility in exposed women,^{20,21} rates of spontaneous abortion are higher and the risks of ectopic pregnancy and premature labour are increased, and women should be counselled about these risks.^{21,22} Hysterosalpingography is unhelpful in predicting the outcome of pregnancy, and the role of cervical cerclage is disputed.^{23,24} Despite these problems about four out of five women exposed to stilboestrol who conceive will have at least one live full term birth.²¹

Though most reports are devoted to women exposed to stilboestrol in utero, those for whom the drug was prescribed during pregnancy and their sons were also exposed to the drug. To date, the only significant untoward effect among mothers has been a small increase in the incidence of breast cancer, the relative risk being 1.4 (95% confidence interval 1.1 to 1.9) 20 years after exposure.²⁵ The incidence of benign abnormalities of the genital tract (epididymal cysts, hypoplastic testes, and cryptorchidism) in men exposed to stilboestrol in utero is more than three times that in unexposed men.²⁶ There have been unconfirmed reports of impaired fertility in men exposed to stilboestrol²⁶ but no evidence of an increased risk of cancer.

How should those who have been exposed to stilboestrol be managed? Young women presenting with abnormal vaginal bleeding or excessive vaginal discharge should be examined under anaesthesia. Screening for neoplasia of the genital tract should include inspection, palpation, and cytological and colposcopic examination of the cervix and vagina. Colposcopy

may be difficult as most women exposed to stilboestrol show some atypical features.¹⁰ Consequently, unless the colposcopist is familiar with the problems of exposure there is a tendency to overtreat these women. Caution is recommended in applying locally destructive measures for cervical intraepithelial neoplasia as up to three quarters of affected women will develop cervical stenosis.²⁷ Most women require annual colposcopy, with more frequent examination required in the presence of dysplastic change. No studies have been published concerning contraception in women exposed to stilboestrol. Lacking definite data, some physicians prefer not to prescribe hormonal contraceptives,²⁸ and as these women are already at risk of an impaired outcome of pregnancy avoiding using intrauterine contraceptive devices seems prudent.

In Britain stilboestrol was probably last prescribed in pregnancy in 1973. How relevant is this topic today? Many of those who were exposed in utero are now aged between 20 and 35. They have reached the reproductive phase of their lives and also the time when they are at most risk of cervical intraepithelial neoplasia. Whether in utero exposure to stilboestrol has any consequences for women entering the menopause and postmenopausal years is not yet known.

More generally, the stilboestrol story has important implications for clinical pharmacology and, in particular, for the use of drugs in pregnancy. It shows, if any further demonstration were needed, the absolute necessity for properly performed clinical trials—assessing both efficacy and long term side effects—before the introduction of any new treatment.

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Eye injuries in racquet sports

Proper protection needed

The causes of serious eye injury (requiring admission to hospital) have changed dramatically over the past 70 years.¹ In the 1920s occupational injuries predominated; by the 1970s road traffic accidents were becoming more important. Protective measures, including the Factories Act 1961, the Protection of Eyes Regulations 1974, seatbelt legislation, and the adoption of laminated windscreens reduced the incidence of eye injuries from these causes. Severe eye injuries from road traffic accidents are now uncommon,^{3,5} and work related eye injuries are rarely serious.⁵

The pattern of trauma continues to change. In the 1980s more participation in sport resulted in a predictable increase in the numbers of injuries. Only 0.7% of severe eye injuries were sustained at sport in 1909-13.¹ By 1967-76 the figure had risen to 4.1%,² by 1987 it was 25.1%,⁶ and by 1989, 42.2%.⁵ Sport is now indisputably the commonest cause of a serious eye injury in Britain, which seems to be rising in incidence. In addition, patients presenting with eye injuries associated with sports are more likely to have sustained sight threatening trauma than those with any other cause of injury,⁵ and almost half of those requiring admission to hospital suffer some permanent reduction in visual performance.⁶

Penetrating injury is seen only rarely in sport and is usually

associated with the inappropriate use of glass spectacles. More typical is a severe blunt injury caused by a blow from a ball, racquet, fist, or elbow. Mostly this results in intraocular haemorrhage. Many patients will have permanently damaged pupils and may later develop chronic glaucoma. The lens may be damaged, either by opacification or dislocation. Retinal breaks and detachment are sometimes seen, as are ruptures of the choroid and haemorrhagic oedema (commotio) of the macula. Any injury to the retina or choroid is potentially blinding. Blowout fractures of the floor or medial wall of the orbit are not uncommon and may result in diplopia or cosmetic problems. Fortunately, rupture of the globe from a high energy blow is rare; loss of the eye usually follows.

The immediate management of a severe blunt eye injury is conservative. An attending doctor without specialised equipment should simply exclude or confirm serious eye injury and transfer the patient to an accident and emergency department safely and quickly, with the eye padded. The patient may be shocked and may vomit, and the possibility of an associated head injury should be borne in mind. Attempting ocular examination within a few minutes of the injury is probably unwise. The eyelids should not be forced open. When possible an estimate of vision should be obtained. Using good