INTRODUCTION

Certain chemicals, including energy-related pollutants such as polycyclic aromatic hydrocarbons (PAHs) are highly destructive to mouse female germ cells (Felton et al., 1980). Like ionizing radiation, these chemicals readily kill oocytes, and the gametic cell loss can be quantified to provide dose-response curves and in vivo measurements of chemical cytotoxicity.

Although twenty-five years have passed since it was recognized that chemicals can destroy oocytes in mice (Marchant, 1957; Mody, 1960; Kuwahara, 1967; Krarup, 1969), only recently has the oocyte system been used for detecting low-exposure effects and quantitatively evaluating hazards. Studies of exposures to tritium and gamma rays (Dobson and Cooper, 1974; Dobson and Kwan, 1976; Dobson et al., 1976; Dobson, 1976; Dobson and Kwan, 1977) were the model for our work on PAHs, in which differences in genetic control of PAH-metabolizing activity were shown to influence benzo(a)pyrene (B[a]P) and 3-methylcholanthrene (MC) killing of oocytes (Felton et al., 1978). Using MC as a representative test compound, it was found that chemical vulnerability of mouse oocytes varies systematically with the animal's age (Dobson et al., 1978a), and that the variation closely follows the pattern of sensitivity to radiation (Dobson et al., 1978b). While oocyte killing by PAHs in adult mice has been
reported to be correlated with induction of aryl hydrocarbon hydroxylase activity in the target ovary (Mattison and Thorgeirsson, 1977), more complicated relationships apparently operate in the maternal-fetal system where in utero exposure occurring transplacentally causes large oocyte depletion in the developing fetus (Felton et al., 1978).

Here we describe a "standard" toxicity assay based on the mouse oocyte system, and we show its application to toxicity determinations of complex mixtures as well as of pure compounds. For the standard assay we use the juvenile mouse because its oocytes are especially sensitive, and we use exposure via i.p. injection because this route allows ready control of dosage. To facilitate comparisons of oocytotoxicity among chemical agents, we have developed the Oocyte Toxicity Index (OTI), the ratio of whole-animal toxic dose to oocyte LD$_{50}$. Measured OTIs are found to range from less than 1 (for benzene) to almost 40 (for 7,12 dimethylbenz[a]anthracene [DMBA]), and even higher for certain compounds (e.g., more than 50 for ethyl nitrosourea).

In addition, this intact-mammal system has important versatility, allowing the evaluation of various other exposure routes, including ingestion and transplacental exposure. Transplacental exposure is of particular interest: PAHs administered orally to the pregnant animal have been found to cause even greater oocyte deficiency in offspring than in the mother (MS. in preparation).

MATERIALS AND METHODS

Chemicals

The chemicals used were of the highest purity readily available commercially and include the following (with their sources): bleomycin, mitomycin-C, and MC (Sigma); urethane, methylmethane sulfonate, and B(a)P (Aldrich); DMBA and dibromochloropropane (Chemical Procurement Laboratories); N-ethyl-N-nitrosourea (Fluka); procarbazine (Hoffman-LaRoche); and decarbamoyl mitomycin-C (kind gift of Dr. M. Sasaki).

Animals

All mice were of the C57BL/6 strain and were purchased from Simonsen Laboratory (Gilroy, CA). They were housed either 6 per cage or as single litters per cage and allowed free access to food and water. A 12-h light-dark cycle was maintained.