the birth of defective children, but it was not confirmed by a third report.

These studies cannot be considered at the moment to be more than tentative evidence, since the numbers of cases in all of the surveys of congenital heart disease associated with exposure to anti-obesity drugs are too small to be able to detect a three to four fold increase over the background level of congenital heart defects. The background incidence of congenital heart defects in humans is approximately 8 per 1000. To detect a teratogen which sufficiently raises this background level one would need a minimum of 18 cases of congenital heart disease occurring per 1000 exposed fetuses to demonstrate significant soft teratogenicity. However, I think the fact that these associations consistently turn up in a variety of studies makes the anti-obesity drugs a highly suspect drug for producing defects in humans at a low level.

We have been talking to this point about the teratogenicity of an agent which is only manifest as anatomic malformation recognizable at birth. I would like to raise the possibility that the anti-obesity drugs when administered in the critical period may be able to produce functional malformations not observable at birth but only at later stages. These so-called latent effects raise another hazard of prenatal drugs. Work published this year has shown that the administration of dexamphetamine sulphate to rats at the critical period in the same dosage as given to humans did not produce recognizable anatomic defects in the rat pups at birth. However, it was found that the experimental offspring showed a marked reduction in the ability to accommodate to new surroundings and this effect persisted for at least