

## Gonadal hormones and behavior

Two new reports indicate that prenatal exposure to pharmacological doses of gonadal hormones can masculinize or feminize the behavior of young rhesus monkeys. The papers were delivered to the symposium on primate reproductive biology at the Oregon Regional Primate Research Center in Beaverton. Robert Goy, director of the Wisconsin Regional Primate Research Center, and Anke Ehrhardt of Columbia University's College of Physicians and Surgeons discussed sex dimorphic behavior in monkeys and children whose mothers received hormones during pregnancy.

Ehrhardt described the results of a double-blind study in which she and Heino Meyer-Bahlburg, co-director of Columbia's psychoendocrinology program, observed 150 children. Half of their mothers had taken nonmasculinizing progesterones or estrogens, or both, during pregnancy. The children were closely matched in age and social class. "Mothers had been followed very closely from before pregnancy," says Ehrhardt, "so we had good records and early childhood data on these children. Our study was a developmental checkup." Data come from intensive day-long interviews with parents and children. They show that boys whose mothers were treated were slightly less aggressive and more nurturant than boys in the control group. Differences were on the 0.05 level, or between 0.05 and 0.1.

Ehrhardt admits that it is very difficult to characterize specific human behaviors as male or female. Nevertheless, she points out that some studies have linked the tendency to rough and tumble play and aggression to boys, while interest in infants and doll play are generally higher among girls. She further qualified her arguments by saying that since hormones were given to the mothers it is impossible to know how much of a given hormone crossed the placenta and reached the fetus. Nevertheless, this study is suggestive, and might point the way for work with nonhuman primates.

Goy plans to do such research. He has already shown that prenatal androgens can have a powerful effect on the behavior of female rhesus monkeys. Working at the Wisconsin Regional Primate Research Center Goy injected pregnant females with testosterone propionate (T) and dihydrotestosterone propionate (dhT). Of the offspring, 7 females were spayed during their first 3 postnatal months; 16 males were castrated in their first 3 months. There were 17 males whose mothers had been injected with one of the testosterone, 9 females virilized by prenatal dhT and 27 virilized by prenatal T. The control group included 87 intact females and 61 intact males.

After birth mothers and infants were placed in social groups of four to six. Each group contained at least one control male and one control female. All infants had been born within 6 weeks of one another.

Observations began when the infants averaged 3 months of age and ended around their first birthday. Researchers found virilized females exhibiting a behavior that is fairly rare among rhesus females: mounting peers. While control females mounted their peers an average of five times each, T-virilized females did so a little over 40 times and dhT-virilized females performed the behavior more than 50 times. Each control male performed the behavior about 110 times.

Mounting their mothers is also rare among rhesus females, but those prenatally virilized did so more than any other sex types. T females mounted their mothers an average of 15 times, dhT

females 17 times. Control males performed the behavior an average of 11 times, while control and spayed females did so less than once each.

Males of all sex types exceeded females in rough play. Frequency for the male control was 90 times; for androgenized males and castrated males 95 times. T-virilized females engaged in rough play 61 times, dhT females 55 times. Control and spayed females did so 25 and 14 times.

Goy began showing the power of hormones on the psychological development of rhesus monkeys in the 1970s. His current work doubles the earlier experimental populations, allowing more accurate comparisons of various sex types. He soon plans to begin using estrogens on male rhesus fetuses. The result, he hopes, will be a primate model that will show whether hormones can feminize behavior as well as they can masculinize it. □

## Good news for epileptic youngsters

Of the 300,000 children with epilepsy in the United States, a large number take anticonvulsant drugs indefinitely because their physicians assume that the risk of recurrent seizures outweighs the risk of adverse effects from the drugs. Now good news for many of these youngsters is reported in the May 7 *NEW ENGLAND JOURNAL OF MEDICINE* by Ronald Emerson and colleagues at Johns Hopkins University School of Medicine in Baltimore. A study conducted by Emerson and his team of epilepsy researchers suggests that these young people can safely discontinue their anticonvulsant medication if they have been free of seizures for four years while taking the medication.

Between 1973 and 1979 anticonvulsants were discontinued in 68 patients between the ages of six and 22 years who had had two or more seizures in the past but who had been seizure-free for four or more years while on anticonvulsants. Patients were followed for six months to six years after the start of drug withdrawal (with the mean 2.7 years). Because the length of a follow-up period after anticonvulsant withdrawal was thought likely to influence the probability of observing a recurrent seizure, statistics were also used to determine the probability of remaining free of seizures after actual follow-up. Clinical records from the patients were also analyzed retrospectively to see which factors were associated with recurrent seizures.

As Emerson and his co-workers report, of the 68 patients in the study, 50 (74 percent) were actually observed to remain free of seizures after drug withdrawal, and the overall probability for the 68 patients of remaining seizure-free was 79 percent after one year, 72 percent after two years and 69 percent after four years. These findings, the investigators conclude, "indicate that a child with epilepsy who has had no seizures for several years while taking an-

tic convulsants has about a 70 percent chance of remaining free of seizures when drugs are withdrawn."

However, the probability of avoiding seizures after discontinuing drug use was influenced by certain factors. A youngster who had abnormal electroencephalograms while on anticonvulsants or a history of numerous seizures before anticonvulsants brought the seizures under control was much more likely to relapse than was a youngster with normal EEG's on anticonvulsants or with few seizures before receiving anticonvulsant therapy. Another condition that was somewhat less likely to prompt a seizure relapse after discontinuation of drug therapy was mental retardation, suggesting a brain damage cause for the epilepsy as opposed to some other cause.

Thus, an epileptic youngster who has been without seizures for four years while taking anticonvulsants, has normal EEG's while on the drugs, had few seizures before going on the drugs and is of normal intelligence should probably be taken off anticonvulsants, Emerson and his team conclude. "Giving a child a target of four seizure-free years," they declare, "implies that he or she will become 'well' at some point and will no longer carry the stigma of epilepsy." Also, they add, if epileptic youngsters are taken off anticonvulsants it can spare them drug costs, doctor visits and costs and possibly detrimental learning and behavior effects from the drugs.

In fact, even as far as high-risk children who have been free of seizures for four years while on anticonvulsants are concerned, one can question whether the risk of seizure recurrence would necessitate lifelong continuation of anticonvulsants, Emerson and his colleagues point out. If such youngsters relapse, they would do so soon after stopping their drugs and could begin drug therapy again. □