DRUGS IN PREGNANCY

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Since the thalidomide tragedy of 1960 to 1962, pregnant women have been in a quandry about taking common medications on their own initiative, and physicians have been troubled about prescribing drugs for them. Peckham and King have shown recently that 92 percent of women have at least one drug prescribed by their physicians during pregnancy, and 3.9 percent are given 10 or more (1). There is no count of babies who have survived because of drugs administered during pregnancy, infants who escaped birth defects because their mothers were given certain drugs, or full-term babies who might have been born prematurely without drugs. Both physicians and patients rightly demand to know what information is available about drugs and human pregnancy.

Very little is known that can actually be applied to all pregnancies. According to Lenz, 80 percent of the mothers who took thalidomide during the period of fetal sensitivity had normal infants (2). What was it in the genetic background of the mother or the father that caused the serious anomalies that occurred in 20 percent of the infants? What environmental associations were related? The answers to these questions are a long way off.

This past year, two useful reviews appeared, by Cohlan and Lucey, about the effect of medication administered during pregnancy on the fetus and newborn infant, from which these comments are largely drawn (3,4). Two other reviews, which discuss in detail the problems of human teratogenesis, were written by Warkany and Kalter and by Fraser. All are highly recommended (5,6).

The table lists some relationships observed between maternal medication and fetal or neonatal changes. Only a few are proved beyond a shadow of doubt, but until further data are collected, caution should be exercised in administering these substances to pregnant women.

The best way to determine a *post hoc ergo propter hoc* relationship between maternal medication and changes in the fetus and newborn infant is to conduct a prospective study in a population of women who enter the study by the eighth week of pregnancy. They should be frequently observed and interrogated by only one, two, or three astute clinicians, and the data should be entered and analyzed within a few hours' time. Such a study, a continuation of the Fetal Life Study of McIntosh and Merritt begun in 1947, is being conducted by Mellin (8). Routine questioning about the intake of certain drugs formed the basis of their report that meclizine hydrochloride (Bonadettes, Bonine Hydrochloride) was not under suspicion as a teratogenic agent (9). Other prospective studies, such as that of the Kaiser Permanente group, and the Collaborative Study of the National Institute of Neurological Disease and Blindness can be expected to show certain relationships between medication administered during pregnancy and fetal and neonatal changes. But these studies lack the accuracy achieved by a small, closely controlled group of pregnant women, observed by the same professional team.

The greatest danger of inducing malformations is in the first trimester of pregnancy. Since this includes the period before a woman may be aware that she is pregnant, and since we know very little about the effects of drugs on the fetus, physicians are urged to exercise great restraint in prescribing medications for women of childbearing age, and self-medication by patients in this group should be strongly discouraged.

Dr. Ernest Page's doublet, "Don't make mirth of the afterbirth," is certainly true; the placental "barrier" is mythical. Every drug given to the mother by any route, can be expected to be found in the fetus as soon as placentation is established. However, as Cohlan suggests, "placental panic" need not replace "placental pride," for in about 92 percent of all pregnancies that terminate in a viable baby, the placenta has performed admirably.

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MEDICATION AND CHANGES PRODUCED

MATERNAL MEDICATION	FETAL OR NEONATAL EFFECT
Oral progestogens	Masculinization and advanced bone age
Androgens	
Estrogens	
Cortisone Acetate (Cortogen Acetate, Cortone Acetate)	Anomalies: cleft palate (?)
Potassium iodide	Goiter and mental retardation
Propylthiouracil	
Methimazole (Tapazole)	
Iophenoxic acid (Teridax)	Elevation of P.B.I.
Sodium aminopterin	Anomalies and abortion
Methotrexate (Amethopterin)	
Chlorambucil (Leukeran)	
Bishydroxycoumarin (Dicumarol)	Fetal death; hemorrhage
Ethyl bicoumacetate (Tromexan Ethyl Acetate)	
Sodium warfarin (Coumadin Sodium, Panwarfin, Prothromadin)	
Salicylates (large amounts)	Neonatal bleeding
Streptomycin	Possible 8th nerve deafness
Sulfonamides	Kernicterus
Chloramphenicol (Chloromycetin)	"Grey" syndrome; death
Sodium novobiocin (Albamycin Sodium, Cathomycin Sodium)	Hyperbilirubinemia
Erythromycin (Ilosone)	Liver damage (?)
Nitrofurantoin (Furadantin)	Hemolysis
Tetracyclines	Inhibition of bone growth Discoloration of teeth
Vitamin K Analogues (in excess)	Hyperbilirubinemia
Ammonium chloride	Acidosis
Intravenous fluids (in excess)	Electrolyte Abnormalities
Reserpine (Rauloydin, Raurine, Rau-Sed, Reserpoid, Sandril, Serfin, Serpasil, Serpate, Vio-Serpine)	Stuffy nose; respiratory obstruction
Hexamethonium bromide (Bistrium Bromide)	Neonatal ileus
Heroin and morphine	Neonatal death
Phenobarbital (in excess)	Neonatal bleeding; death
Smoking	Birth of small babies
Sulphonylurea derivatives	Anomalies (?)
Phenformin hydrochloride (DBI)	Lactic acidosis (?)
Phenothiazines	Hyperbilirubinemia (?)
Meprobamate (Equanil, Wyseals, Meprospan, Meprotabs, Miltown)	Retarded development (?)
Chloroquine phosphate (Aralen Phosphate)	Retinal damage or death (?)
Quinine	Thrombocytopenia
Thalidomide	Phocomelia; death; hearing loss
Vaccination, smallpox	Fetal vaccinia
Vaccination, influenza	Increased anti-A and B titers in mothers
Antihistamines	Anomalies (?); infertility (?)
Thiazide diuretics	Thrombocytopenia (?)