Scientists Attack Report That Obstetrical Medications Endanger Children

But natural childbirth advocates rally to its defense

The press reports last fall were disturbing, to say the least. Yvonne Brackbill of the University of Florida and Sarah Broman of the National Institute of Mental Health (NIMH) announced that analgesics and anesthetics given to women during labor and delivery may have pervasive and long-lasting effects on their children's behavior and development. Since the vast majority of pregnant women receive these drugs, the consequences of Brackbill and Broman's reported findings could be of real importance.

But how solid are Brackbill and Broman's conclusions? One indication that they may be questionable is that their statistical consultant, John Bartko of NIMH, dissociates himself from their work because they would not follow his advice. Another indication is that their work was sharply criticized by statisticians, perinatologists, anesthesiologists, and obstetricians at a recent meeting of the Anesthetic and Life Support Advisory Committee of the Food and Drug Administration (FDA). The outcome of the meeting was the decision that there is as yet no evidence that there should be any new regulatory decisions pertaining to the use of these drugs. The FDA committee also decided to form a small subcommittee, under the guidance of anesthesiologist Athole Jacobi of the Medical College of Pennsylvania, to decide whether there is any good evidence that obstetrical medications have short-term effects on children.

In order to reach their conclusions about obstetrical medications, Brackbill and Broman, who are psychologists, analyzed data from the Collaborative Perinatal Project. This was a longitudinal study, sponsored by the National Institutes of Health, of over 50,000 pregnant women and their children. The study was conducted in the 1950's and the data include detailed medical histories of the women as well as periodic physical, neurological, and behavioral tests of the children through the age of 7 years.

Brackbill and Broman say they chose only the 3500 healthiest women with full-term babies and the most uncomplicated labors and deliveries for their analysis. This was to ensure that any effects they saw would be due to drugs and not to complications of pregnancy or birth. They claim that children whose mothers were given medications during labor and delivery were, on the average, retarded in their development of motor and cognitive skills. Moreover, they said these effects of drugs were dose-related: the greater the total dose of drugs or the stronger the drugs, the more likely that ill effects would occur.

Speakers at the FDA meeting decried the way Brackbill and Broman announced their results to the press before their paper was accepted for publication. In fact, their paper was rejected when they submitted it and they are still revising it prior to resubmission. At the time they were promoting their work, their paper had not even been released by NIMH, and it was not released until last January when the UPI put in a Freedom of Information Act request for it. (Research papers normally must be approved by supervisors in federal agencies before they are released.) But their conclusions were widely publicized by the media, including *Science* (17 November 1978, p. 732). The results were especially welcomed by prepared childbirth groups as well as by groups advocating home births and abhorring medical intervention in the "natural" process of labor and delivery. And, poignantly, the results were seized on by couples with developmentally and intellectually retarded children as a possible explanation of what went wrong. "This is an excellent example of how science can be perverted," says Milton Alper, an anesthesiologist at the Harvard Medical School and the Boston Hospital for Women.

Alper contended at the FDA meeting that Brackbill has exaggerated her findings when talking to the public even beyond what she and Broman say in their written report. For example, although IQ is nowhere mentioned in her written report, Brackbill said on the ABC television program "20-20" that obstetrical medications may cause an average loss of 4 IQ points per child. Richard Hughes, UPI's New York–New Jersey editor, later wrote a story saying that since there are 3.7 million births per year in this country, the use of obstetrical medications causes a loss of about 14 million IQ points. Although Brackbill claims no responsibility for Hughes' estimate, she alluded to a national loss of 14 million IQ points in a statement before the Senate Subcommittee on Health and Scientific Research in April of 1978. Hughes also quoted a government spokesman as saying that Brackbill and Broman's results mean children are being born "with less than a full deck." Brackbill's publicity campaign, Alpers says, was conducted in a way calculated to bring the greatest fear to patients.

The FDA sent Brackbill and Broman's written report to statistician Ralph d'Agostino of Boston University for his comments. Then, because the authors decided to reanalyze their data after that report was rejected for publication, the agency sent d'Agostino their reanalysis as well.

D'Agostino is a quiet, mild-mannered man who was careful to avoid the inflammatory language others used in discussing Brackbill and Broman's work. He said at the FDA meeting that there was "not enough material in the reports or enough analysis for an unequivocal acceptance of [the authors'] conclusions." He then went on to list problems with their data analysis and interpretations. (Bartko says he mentioned exactly these problems to the two investigators, but they ignored his advice.) In a conversation with *Science*, d'Agostino made it clear that he thought Brackbill and Broman's conclusions unwarranted on the basis of what he had seen of their work.

One of d'Agostino's criticisms, which was also raised by others at the meeting, was that Brackbill and Broman did not investigate whether the children who were developmentally retarded at one age were the same children who were retarded at another age. For example, it was unclear whether the children who could not stand alone at 12 months were the same children who later were retarded in learning to read. Yet the two researchers had said that the adverse effects of obstetrical medications persist for at least 7 years. As Norman Bergman of the University of Oregon Medical School pointed out, before you can say that children are forever tainted by obstetrical medications, you should be sure

0036-8075/79/0427-0391$00.50/0

that, if there are effects at all, they are not just transient effects expressed in different children at different times.

A much harsher critic than d'Agostino at the FDA meeting was Emanuel Friedman, a professor of obstetrics and gynecology at Harvard Medical School. Friedman, who has been associated with the Collaborative Perinatal Project since 1958, is furious with the way Brackbill and Broman publicized their findings and did not hesitate to say so. He said of their written report, "In tone, it is shrill and strident, leaving no doubt about the authors' preconceptions."

Friedman pointed to what he described as "a few glaring specifics" of the faults with Brackbill and Broman's work. He and his associate Raymond K. Neff, a statistician at Harvard School of Public Health, are also analyzing the collaborative Perinatal Project data, and they suspect that Brackbill and Broman's purported drug effects might in fact be effects of maternal hypertension or difficult deliveries. In either of these situations, women are more likely to be given medications and are likely to be given larger doses. For example, Friedman and Neff find that one-third of all stillbirths in the Collaborative Perinatal Project and an equivalent proportion of neurological and developmental defects in surviving children are associated with maternal hypertension; these effects are apparently independent of obstetrical medications. These women were not excluded from Brackbill and Broman's choice of what they say were the healthiest women with the most normal labors and deliveries.

Friedman says that Brackbill and Broman also did not exclude women who had midforceps deliveries. Forceps deliveries are classified as low, mid, and high, as indicators of how high in the mother the doctor has to reach to grasp the baby. The higher the doctor reaches, the more difficult and hazardous the delivery. Friedman and Neff find that midforceps deliveries, like maternal hypertension, are highly correlated with subsequent developmental defects, independently of the amount of drugs given the women. Although Broman insists that midforceps deliveries were excluded from their sample, Friedman says that they could not have excluded mid-forceps deliveries and still had so large a sample.

Brackbill's response to this harsh criticism was that her conclusions are confirmed by other, smaller studies. However, FDA statistician Mary Johnson reviewed the literature on long-term effects of obstetrical anesthetics and analgesics and concluded that the studies had severe methodological problems. She said that "the longer-term studies provide little information on whether medications affect behavior and neurological development."

A major concern of critics at the meeting was that women would hear of Brackbill and Broman's results and would then either refuse all medications, even to the detriment of their babies, or would forever feel guilty if they accepted them. Jacobi, for example, said that a long and difficult labor in which a woman refuses medical intervention can certainly damage a child whereas the adverse effects of obstetrical medications are as yet unproved.

There was also some question about whether analyses of the Collaborative Perinatal Project data are even applicable to medical practice today. Clinicians at the meeting said that there has been a dramatic change in obstetrical practices in the last 20 years. For example, Friedman says there is a trend away from midforceps deliveries and toward Cesarean sections instead. The kinds and doses of obstetrical medications have also changed. Alper showed data from a survey of 50 major training centers for obstetrical anesthesiologists and from his own hospital, Boston Hospital for Women. The data showed that general anesthesia is now virtually unheard of for routine vaginal deliveries. At the time of the Collaborative Perinatal Project, however, it was quite common. For example, Boston Hospital for Women reported that 20 percent of all vaginal deliveries in 1963 were done under general anesthesia. Alper says there is a trend reflected in his own hospital toward an increased use of minor forms of regional anesthesia, administered late in delivery by the obstetrician, or no anesthesia at all.

The critics at the FDA meeting emphasized that they are not trying to push drugs on women. They reiterated their support for the recommendations of the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics Committee on Drugs. These were to avoid the use of agents or dosages with known adverse effects, not to deny reasonable pain relief but to use minimum effective doses, and to discuss potential benefits and side effects of drugs with the mother before she goes into labor. The meeting participants expressed grave concern that obstetrical medications might in fact have long-term effects on children, but, as Friedman said, such a claim "is so important that the design of any study undertaken to provide the answers must be impeccable, the analysis of data unimpeachable, and the conclusions temperate and clearly warranted. It is therefore regrettable that none of these criteria had been fulfilled by the Brackbill-Broman report."

Brackbill and Broman did have sympathy at the FDA meeting from representatives of natural childbirth groups. These groups emphasized that nearly all women are given obstetrical medications although, they said, probably only a minority really need them. They also said that doctors generally fail to discuss the risks and benefits of these drugs with women.

As Alper points out, there were probably no converts won at the meeting. And clearly there is no way to undo the premature publicity given to Brackbill and Broman's findings.

The Brackbill-Broman episode is a particularly unfortunate example of premature publicity of research data. Brackbill, at least, seems to believe that she had to bypass the normal pathways of peer review and publication to avoid hostile reactions from obstetricians and anesthesiologists who did not want to hear what she had to say. Yet the result of her actions has been tragic. While gaining points with natural childbirth groups, she and Broman polarized the scientific community against them. Now, even if they are right about the effects of obstetrical medications, they will find that other scientists no longer have anything like open minds on the matter. What should have been a dispassionate study of important data has become an adversary proceeding with the familiar protagonists—the obstetricians and anesthesiologists against the natural childbirth advocates—reaching an impasse once again.—GINA BARI KOLATA

What should have been a dispassionate study of important data has become an adversary proceeding.