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Effect of Morphine on Labor.*

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The occurrence of respiratory depression and failure at birth following the administration of morphine for relief of pain during labor has prompted numerous clinical investigations. Two chief questions arise regarding the mechanism by which administration of morphine to the mother may result in injury of the fetus. There is involved firstly, the effect of morphine upon the fetus directly; and secondly, the effect of morphine upon the labor mechanism. Evaluation of these factors in clinical studies has been difficult because of the complications present at the time of delivery which may result in injury to the child such as anesthesia, anoxemia and mechanical trauma. Accordingly, the present experiments have been undertaken in an attempt to control conditions of observation so that it could be determined whether or not the effect of morphine upon the fetus is of greater consequence than the effect of the narcotic upon the course of labor.

The effect of morphine on the fetus was first studied by direct observation of full-term rabbit fetuses within the unopened uterus according to a method previously described.[1] The change in rate of fetal respiratory movements afforded a sensitive indicator of the depressant effect of the narcotics. Results showed that rhythmical breathing of the fetuses persisted despite administration to the mother of more than 15 times the analgesic dose of morphine.[2]

Additional evidence regarding the state of narcosis of the fetus at various intervals following injection of morphine was obtained in a second series of animals in which the rabbits were not prepared for observation of intrauterine respiration. A dosage of 13 mg per kg of morphine was given by a single intravenous injection in rabbits about the time of the onset of labor, *i. e.*, at 31 or 32 days. This dosage resulted in well marked analgesia of the maternal animal but no loss of consciousness. In 8 litters containing 45 fetuses, all of

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1 Rosenfeld, M., and Snyder, F. F., *Am. J. Obs. and Gyn.*, 1939, **38**, 424.

2 Snyder, F. F., and Lim, K. T., *J. Pharm. and Exp. Therap.*, 1941, **72**, 39.

the fetuses except one were born alive and survived when delivery was carried out by hysterotomy at intervals varying from 12 minutes to 15 hours after injection. In litters delivered at 12 and 20 minutes after injection, fetal narcosis was marked, while in litters delivered at 12 and 15 hours after injection, the fetuses crawled about actively.

In order to determine the effect of morphine upon the labor mechanism the condition of the fetuses was observed following spontaneous birth. In striking contrast to delivery by hysterotomy, the incidence of stillbirths amounted to 70% when birth occurred spontaneously. In a consecutive series of 92 fetuses obtained from 17 litters, only 28 were born alive while 64 were dead at birth. Prolongation of labor was noted and gave evidence of impairment of the expulsion mechanism. In 13 animals, 13 mg per kg of morphine were given at 31 or 32 days just as in the preceding group delivered by hysterotomy. In the remaining 4 animals a second dose was given after 12 hours.

From the foregoing results it is evident that a reliable method of assay and comparison of drugs used for obstetrical analgesia involves the determination not only of the effect on the fetus but especially of the effect on labor. A sensitive indicator of the effect on the fetus is change in rate of intrauterine respiration. The incidence of stillbirth shows the effect on labor.

When morphine is administered for obstetrical analgesia the occurrence of asphyxia neonatorum has been commonly attributed to the effect upon the fetus of the narcotic. Experiment fails to confirm this. It reveals, on the contrary, that the chief damage of morphine is on the labor mechanism rather than directly on the fetus. In so far as the present experiments reveal the etiology of respiratory failure at birth following administration of morphine during labor, it is evident that injury of the fetus is largely a consequence of injury of the birth mechanism rather than of fetal narcosis.