The steep increase in the number of opioid prescriptions dispensed in the United States has been associated with a parallel rise in their misuse, fatal overdoses, and heroin use. More recently, attention has been focused on the large increase in the number of infants born with neonatal abstinence syndrome (NAS). In the US, between 2000 and 2009, the incidence of NAS increased from 1.20 to 3.39 per 1000 live births,1 and between 2004 and 2013 the total percentage of days spent in intensive care because of NAS increased from 0.6% to 4.0%.2 The rise in NAS is also likely to be a consequence of increased opioid prescriptions—estimates indicate that 14-22% of pregnant women in the US receive an opioid prescription during their pregnancy3—as well as an increase in the prevalence of opioid use disorders among pregnant women.4

NAS results from the abrupt discontinuation of opioids at birth after a fetus has become physically dependent through exposure in the womb. The risk of NAS is greater if opioids are taken closer to the delivery day or for longer periods and if the drugs have short breakdown times.5 Opioid induced physical dependence wanes after discontinuation, which explains why NAS is observed predominantly when opioids are used in the last trimester of pregnancy. Similarly, the rate of opioid clearance influences severity, such that opioid drugs with slow clearance rates (such as buprenorphine) result in less severe withdrawal than drugs with intermediate (such as methadone) or fast (morphine) clearance rates. One study of pregnant women with opioid dependence reported that neonates exposed in utero to buprenorphine required significantly less morphine and shorter hospital stays for the management of NAS than neonates exposed to methadone.6

Other factors associated with increased risk of NAS include a maternal history of opioid or other drug misuse, exposure to other psychotropic medications, and smoking.7 These associations suggest that women with babies affected by NAS could have been taking additional opioid medications or other drugs that produce physical dependence and withdrawal, such as alcohol, benzodiazepines, or barbiturates. Nicotine enhances the release of endogenous opioids, which might explain how smoking could increase risk of NAS.8

The potential effects of opioid exposure on the developing infant brain are unknown. Preclinical studies in rodents have linked opioid exposure in utero to congenital defects in the central nervous system,9 while human epidemiological studies have reported an association between opioid use during pregnancy and an increased risk of neural tube defects and other birth defects.10 11 The opioid system is implicated in bonding between mother and infant12—for example, mice that lack the gene coding for the mu opioid receptor, the main target of opioid analgesics and heroin, show deficits in attachment toward their mothers.13 Opioid use during pregnancy could theoretically disrupt attachment between women and their babies. Cognitive impairments have also been reported in children and young people born to women who misused opioids during pregnancy, although the relative contributions of other drugs or lifestyle factors to such deficits are unclear.14

The lack of scientific information on the effects of opioids on fetal brain development, combined with their known association with NAS, indicates that opioids should be reserved for pregnant women with severe pain that cannot be controlled through more benign means, and ideally limited to a short term use. If long term use is unavoidable, such as for women in need of buprenorphine or methadone maintenance therapy for heroin addiction, then careful assessment and monitoring should be undertaken to minimise the risk of overdoses, NAS, and misuse.

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