PREGNANCY PLUS

Pregnancy and injecting drug use

James Bell,^{1,2} Lucy Harvey-Dodds²

¹National Addiction Centre, Institute of Psychiatry, London SE5 8RS

²The Langton Centre, Sydney, NSW 2011, Australia

Correspondence to: J Bell
james.bell@sesiahs.health.nsw.gov.au

BMJ 2008;336:1303-5
doi:10.1136/bmj.39514.554375.AE

Injecting drug use has adverse effects on pregnancy and perinatal outcomes. Methadone treatment improves birth rate but carries a risk of neonatal abstinence syndrome; withdrawal of methadone during pregnancy is not recommended

The case described in the Scenario box highlights some of the problems of managing a pregnant injecting drug user. Such patients often present late and have chaotic lifestyles, including poor care for themselves and compromised capacity to care for infants and children.

How common is injecting drug use in pregnancy?

Accurate figures on numbers of pregnant women who misuse drugs are difficult to obtain. Health professionals do not always ask specifically about drug misuse, and when they do pregnant women often fail to disclose it. In a large US study in a sample of pregnant women, meconium testing for opioids, cocaine, or both was positive in 10.5% of cases; 38% of the mothers who tested positive had denied drug misuse.¹ Data from the United Kingdom are lacking, but a recent study from Northumberland in 150 pregnant women reported that 16 (10.7%) of them had positive urine tests for drugs of misuse; all 16 had denied any illicit drug use.² Although the incidence of drug misuse among pregnant women is difficult to obtain, a survey of consumers in treatment suggested the existence of between 250 000 and 350 000 children of problem drug misusers in the UK.³ Most clinical experience and published reports on pregnancy and injecting drug use relate to women who are dependent on opioids, and this group will be the focus of this article.

What is the impact of pregnancy on the course of opioid dependence?

Pregnancy produces a polarised response. Many women stop using alcohol or other drugs once they know they are pregnant. Survey data from Australia indicate that the proportion of women using any illicit drug decreased from 17% when non-pregnant to 6% while pregnant. Women were less likely to reduce their consumption of tobacco than that of other drugs or

alcohol; 22% smoked when not pregnant, and 20% continued to smoke during pregnancy.⁴ Although few data relating specifically to pregnancy are available, substantial evidence has accumulated to show that dependent opioid users, like smokers, have great difficulty maintaining abstinence.⁵ Indeed, clinical experience is that for some injecting drug users, the stress of pregnancy and parenthood is associated with continued or escalating drug use.

The polarised response extends to the seeking of antenatal care. For women who misuse substances, and for their partners, concern for children and fear of their removal by child protection services is a motivating factor in seeking both medical treatment and drug treatment and, conversely, in not approaching services.⁶

How does opioid dependency affect pregnancy progression and outcome?

As in the case discussed above, menstrual irregularity related to opioid use often means that women who misuse drugs are unaware that they are pregnant. Almost three quarters of the women in a British sample of women who misused substances (n=50) reported unplanned pregnancy.⁷

Injecting drug use has adverse effects on pregnancy and perinatal outcomes. Analysis of data from an obstetric outcome database on 89 080 confinements identified 0.8% of women who reported drug misuse during pregnancy⁸; the most commonly reported drugs were opioids, stimulants, and cannabis. Substance misuse was associated with an increased risk of placental abruption (odds ratio 2.5, 95% confidence interval 1.6 to 4.1) and other causes of antenatal haemorrhage. Women who misused substances had an increased risk of stillbirth (odds ratio 2.5, 1.5 to 4.2) and of neonatal death (2.9, 1.4 to 6.0). Exposed babies were more likely to be premature (odds ratio 2.6, 2.2 to 3.3) or small for gestational age (1.8, 1.5 to 2.2) and to need to stay in a nursery for more than seven days (4.1, 3.4 to 4.9). These adverse outcomes have previously been identified in several small studies and case series of injecting drug users.

Many factors contribute to poor outcomes of pregnancy. The South Australian study confirmed that women who misuse drugs tend to have social

SCENARIO

A 23 year old woman presented, stating she was pregnant and requesting methadone treatment. She reported having used heroin since the age of 13. She had been on buprenorphine for six months but had dropped out two months earlier. She was started on methadone and confirmed to be 20 weeks pregnant. In addition to heroin, she reported smoking cigarettes and cannabis.

She lived with her partner of five months, who was also on methadone. Medically, she had asthma and was hepatitis C positive. She rarely accessed health care. This was her second pregnancy. Her first child had been born one year earlier. During that pregnancy she was homeless and using heroin regularly. Her daughter was born at 36 weeks and weighed 2800 g. The child was removed at birth and remains in care.

Treatment comprised daily supervised methadone, weekly review by a nurse and medical practitioner, drug testing of urine, and assistance to attend antenatal care. Her methadone dose was increased to 50 mg/day by the time of delivery. Urine tests showed only methadone.

A baby weighing 3100 g was delivered at full term and did not need treatment for neonatal abstinence syndrome. After discharge, mother and baby continued to receive support and supervision from multiple services.

disadvantage and multiple risk factors. Substance misusers were more likely to also smoke tobacco (odds ratio 9.8, 7.5 to 11.7), to be unemployed (5.6, 3.3 to 9.4), to live in a metropolitan area rather than a rural one (3.3, 2.7 to 4.2), to be single (2.8, 2.3 to 3.3), and to have a psychiatric condition (2.9, 2.2 to 3.8).⁸

How should opioid dependence be managed in pregnancy?

Methadone treatment in pregnancy improves birth weight, and this has been the basis of recommendations that it is the treatment of choice for pregnant opioid dependent women. Not all studies have been consistent, but a meta-analysis of 18 studies found that heroin use during pregnancy was associated with a mean reduction in birth weight of 489 g, whereas methadone treatment was associated with a significantly smaller decrease of 279 g. Compared with non-drug using mothers, the relative risk of low birthweight infants for maternal heroin use was 4.61 (95% confidence interval 2.78 to 7.65); for women on methadone treatment, the relative risk was 1.36 (0.83 to 2.22).⁹

Several case reports of risks associated with withdrawal of methadone in the third trimester have been published. Most of these are old, reflecting the fact that withdrawal in the third trimester is now seldom done. Clinicians running a withdrawal programme for pregnant opioid addicts reported meconium staining in 33% of pregnancies in women using heroin; they hypothesised that meconium was passed during periods when the mother (and fetus) were having opiates withdrawn.¹⁰ They also observed that very few of their patients remained drug free after withdrawal. This, and similar reports, led to US guidelines recommending that opioid withdrawal should not be attempted after 32 weeks' gestation.¹¹

In addition to the above risks, concern exists that withdrawal of methadone during pregnancy is often associated with relapse to use of heroin. The very

limited published data support this poor prognosis. One UK study of 101 pregnant women admitted for opioid withdrawal reported that only 42 completed withdrawal. Only 24 women were successfully followed up after discharge, of whom only one remained abstinent from opioids at the time of delivery.¹² On the basis of the risks and poor outcomes of withdrawal, maintenance on methadone throughout pregnancy has been recommended by consensus meetings in the United States and Australia.^{11 13}

Multiple mechanisms probably exist by which methadone treatment improves outcomes of pregnancy. It attracts and engages patients. Specialist drugs in pregnancy services assist women in stabilising their social circumstances through liaison with social services and facilitate attendance at antenatal obstetric care. Methadone also produces pharmacological stability. Heroin is a short acting drug. Taken intravenously, it produces rapid intoxication, followed about eight hours later by the onset of withdrawal. Methadone is slowly absorbed and long acting, producing stable blood concentrations and abolishing most symptoms of intoxication and withdrawal—states that have been shown to have an adverse effect on the fetus.^{14 15}

Is methadone safe in pregnancy?

The downside of these benefits is that methadone treatment, except at doses that are subtherapeutic for most pregnant women, is associated with an increased risk of neonatal abstinence syndrome. Between 55% and 94% of infants born to opioid dependent women show signs of neonatal abstinence syndrome of varying severity. The symptoms include irritability, hyper-reflexia, hyperactivity, abnormal cry, diarrhoea, fever, vomiting, tachypnoea, convulsions or seizures, and coma. Maintenance doses of less than 20 mg/day during pregnancy convey a lower risk of neonatal abstinence syndrome,¹⁶ but such doses are subtherapeutic and risk relapse to heroin use. However, at therapeutic doses, no relation exists between dose of methadone and risk of neonatal abstinence syndrome.^{17 18}

Few long term studies of children born to methadone maintained mothers exist, and they are old. After adjustment for social disadvantage, the weight of evidence suggests that methadone treatment throughout pregnancy does not have adverse effects on postnatal development.¹⁹ In one follow-up study of children of drug affected mothers, children who were removed had better developmental outcomes than those who remained with their parent, suggesting that environmental factors are more important than drug exposure in utero.²⁰

Pregnancy planning

Dependence on heroin can produce amenorrhoea and impaired fertility, something that clinical experience suggests is reversed by treatment with methadone or buprenorphine. As in the case outlined in the Scenario

box, women may become pregnant after a brief period in treatment, and advising women entering treatment of the risks of becoming pregnant is judicious. Women stabilised on treatment (stopped injecting drug use; stable lifestyle) who wish to become pregnant should be informed of the risks—that withdrawing from treatment before becoming pregnant carries a risk of relapse and that pregnancy while remaining on methadone carries a risk of neonatal abstinence syndrome for the baby.

Clinical management at different stages of pregnancy

The box lists the initial tasks on diagnosis of pregnancy. In the second trimester, withdrawal from methadone may be attempted if it is strongly desired by the patient. Withdrawal is associated with a high risk of relapse to heroin use, and clinicians must be careful not to set patients up to fail by pushing for withdrawal. The best prospects for successful withdrawal are in women with good social and psychological functioning, who are not using other drugs in addition to methadone. Tapering methadone seems to be the method of choice. If it is to be done after 24 weeks, withdrawal should involve fetal monitoring.

Metabolism of methadone is enhanced in the third trimester, and most women need increases in dose. Dose reduction is contraindicated, to minimise withdrawal stress. Clinical experience suggests that split dosing (administering methadone twice daily rather than as a single dose, in order to reduce peak-trough differences in blood concentrations) is useful to minimise intoxication and withdrawal.¹⁴

Breast feeding has not been found to affect the concentrations of methadone in the blood of the neonate.²¹ A recent clinical consensus group recommended that the benefits of breast feeding outweigh possible risks in women on methadone.¹³

Do any alternatives to methadone exist?

Buprenorphine, an alternative maintenance drug (in the treatment of heroin addiction), has been used extensively in practice in France, and outcomes suggest that it is safe in pregnancy.²² The effectiveness of buprenorphine in pregnancy has been shown in a recent randomised controlled trial.²³ The use of morphine as a maintenance drug in pregnancy has been reported,²⁴ although less clinical experience and accumulated safety data exist for opioids other than methadone and buprenorphine.

Conclusion

In the case described in the Scenario box, the outcomes of the pregnancy were positive, but concluding that this is a good outcome would be premature. The patient and her child are currently doing well, but strong evidence shows that parents who misuse drugs often have difficulties in providing a safe and nurturing home for children. A recent UK review details the extensive evidence that parental drug misuse may cause serious harm to children at every age from conception to adulthood.³ Ensuring a good outcome from pregnancy

is only the first step in a long process of monitoring, support, and intervention.

Contributors: JB wrote the first draft and revisions of the paper. LH-D wrote the case history and commented on the initial draft.

Competing interests: JB has received research support, consulting fees, and support to present results of studies at conferences from ReckittBenckiser P/L, manufacturers of buprenorphine.

Provenance and peer review: Commissioned; externally peer reviewed.

- 1 Lester BM, ElSohly M, Wright LL, Smeriglio VL, Verter J, Bauer CR, et al. The maternal lifestyle study: drug use by meconium toxicology and maternal self-report. *Pediatrics* 2001;107:309-17.
- 2 Sanaullah F, Gillian M, Lavin T. Screening of substance misuse during early pregnancy in Blyth: an anonymous unlinked study. *J Obstet Gynaecol* 2006;26:187-90.
- 3 Advisory Council on the Misuse of Drugs. *Hidden harm: responding to the needs of children of problem drug users*. London: Home Office, 2003.
- 4 Australian Institute of Health and Welfare. *Statistics on drug use in Australia 2004*. Canberra: AIHW, 2005.
- 5 Maddux JF, Desmond DP. Methadone maintenance and recovery from opioid dependence. *Am J Drug Alcohol Abuse* 1992;18:63-74.
- 6 Klee H. Drug-using parents: analysing the stereotypes. *Int J Drug Policy* 1998;9:437-48.
- 7 Klee H, Lewis S. Preparing for motherhood. In: Klee H, Jackson M, Lewis S, eds. *Drug misuse and motherhood*. London: Routledge, 2002.
- 8 Kennare R, Heard A, Chan A. Substance use during pregnancy: risk factors and obstetric and perinatal outcomes in South Australia. *Aust N Z J Obstet Gynaecol* 2005;45:220-5.
- 9 Hulse G, Milne E, English D, Holman C. The relationship between maternal use of heroin and methadone and infant birth weight. *Addiction* 1997;92:1571-9.
- 10 Blinick G, Wallach R, Jerez E. Pregnancy in narcotic addicts treated by medical withdrawal. *Am J Obstet Gynecol* 1969;105:997-1003.
- 11 Finnegan L, Kandall S. Maternal and neonatal effects of drugs. In: Lowinson JH, Ruiz P, Millman RB, Langrod JG, eds. *Substance abuse: a comprehensive textbook*. Baltimore, MD: Williams & Wilkins, 1997.
- 12 Luty J, Nikolau V, Beam J. Is opiate detoxification unsafe in pregnancy? *J Subst Abuse Treat* 2003;24:363-7.
- 13 Bell J, National Working Group. *National clinical guidelines for the management of drug use during pregnancy, birth and the early development years of the newborn*. Canberra: Inter Governmental Committee on Illicit Drugs, 2006.
- 14 Wittman B, Segal S. A comparison of the effects of single and split-dose methadone administration on the foetus: ultrasound examination. *Int J Addict* 1991;26:213-8.
- 15 Jansson L, Dipietro J, Elko A. Fetal response to maternal methadone administration. *Am J Obstet Gynecol* 2005;193:611-7.
- 16 Dashe JS, Sheffield JS, Olscher DA, Todd SJ, Jackson GL, Wendel GD. Relationship between maternal methadone dosage and neonatal withdrawal. *Obstet Gynecol* 2002;100:1244-9.
- 17 Berghella V, Lim PJ, Hill MK, Cherpes J, Chennat J, Kaltenbach K. Maternal methadone dose and neonatal withdrawal. *Am J Obstet Gynecol* 2003;189:312-7.
- 18 McCarthy JJ, Leamon MH, Parr MS, Anania B. High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes. *Am J Obstet Gynecol* 2005;193:606-10.
- 19 Kaltenbach K, Finnegan L. Perinatal and developmental outcome of infants exposed to methadone in-utero. *Neurotoxicol Teratol* 1987;9:311-3.
- 20 Omoy A, Michailovskaya V, Lukashov I, Bar-Hamburger R, Harel S. The developmental outcome of children born to heroin-dependent mothers, raised at home or adopted. *Child Abuse Negl* 1996;20:385-96.
- 21 Wojnar-Horton RE, Kristensen JH, Yapp P, Ilett KF, Dusci LJ, Hackett LP. Methadone distribution and excretion into breast milk of clients in a methadone maintenance programme. *Br J Clin Pharmacol* 1997;44:543-7.
- 22 Lejeune C, Aubisson S, Simmat-Durand L, Cneude F, Piquet M, Gourarier L, et al. Withdrawal syndromes of newborns of pregnant drug abusers maintained under methadone or high-dose buprenorphine: 246 cases. *Ann Med Interne (Paris)* 2001;152(suppl 7):21-7.
- 23 Fischer G, Ortner R, Rohrmeister K, Jagsch R, Baewert A, Langer M, et al. Methadone versus buprenorphine in pregnant addicts: a double-blind, double-dummy comparison study. *Addiction* 2006;101:275-81.
- 24 Fischer G, Jagsch R, Eder H, Gombas W, Etzersdorfer P, Schmidl-Mohl K, et al. Comparison of methadone and slow-release morphine maintenance in pregnant addicts. *Addiction* 1999;94:231-9.

Initial tasks on diagnosis of pregnancy in an opioid dependent woman

- Explain risks and benefits of treatment, including risks of neonatal abstinence syndrome
- Stabilise patient (and, where appropriate, her partner) in treatment
- Counsel regarding continuation of pregnancy
- Refer patients with complex needs to a specialist drugs in pregnancy service
- Advise to sip doses slowly if nausea and vomiting are a problem; if the problem persists, methadone tablets may be better tolerated
- Establish structured treatment with close monitoring and comprehensive assessment of needs
- Facilitate attendance for obstetric antenatal care