

NEONATAL NARCOTIC DRUG WITHDRAWAL SYNDROME

B. H. Khoo

F.A.A.P. (U.S.A.), M.R.C.P.(U.K.)
M.Sc. (Lond.), D.T.M.H. D.C.H.

Lecturer in Paediatrics
University of Malaya
Kuala Lumpur

INTRODUCTION

IN RECENT YEARS, narcotic addiction to heroin among adolescents and young adults has become a major medical and social problem in Malaysia. E. Tan, 1972; Navaratnam, 1976; Deva, 1978). Navaratnam (1976) reported that out of 372 drug addicts seen at the Penang General Hospital, 85% were below 30 years of age and that heroin was the most commonly abused drug followed by marihuana ("ganja"), opium and morphine. He also found multiple drugs abuse to be frequent as 65% of the drug addicts had used 3 or more different drugs and 41% had used 5 or more different drug types. Although the full extent of the problem is not known because of the illicit nature of the drug traffic, it is estimated that there are about 200,000 heroin addicts in this country, seventy per cent of whom were below 25 years old (Datuk Musa Hitam, 1978). Although there are not many female addicts, recent trend shows an increase in their numbers. Since the majority of the female drug addicts are in the child bearing age (15 to 40 years) one would expect an increase in the number of infants born of addicted mothers. It is most important for doctors, nurses and social workers to recognise such infants undergoing narcotic withdrawal not only from the point of obviating unnecessary investigations but also prompt treatment does significantly reduce the mortality rate (Goodfriend *et al.*, 1956). Prior to September 1977, we did not encounter any infant of addicted mothers at the special care nursery at the University Hospital; but since then we have had 3 such infants. It is the purpose of this paper to report on one of the cases and to discuss the early

recognition and management of such infants and the effects of narcotic drugs on the foetus.

REPORT OF A CASE

Baby S, a full term 2550 gram. boy, was born on 14th September, 1977 to a 17 years old unmarried primigravida Indian Muslim who had no antenatal care. The baby was delivered in the car on the way to the hospital. The physical examination was unremarkable. At 6 hours of age the neonate was noted to be hyperirritable and vomited his first feed. A few hours later, he showed continuous tremors of all extremities (jitteriness), a high-pitched cry and poor feeding with frequent vomiting. Neonatal narcotic drug withdrawal syndrome was suspected and on direct questioning the mother admitted that she had been smoking heroin (locally called 'chasing the dragon') for 3 years and consumed approximately \$20 of heroin daily. The last dose was 12 hours prior to delivery. The child was treated with oral phenobarbitone (10 mg/Kg/day divided into 4 doses) and the symptoms subsided, feeding improved and he was asymptomatic by the 7th hospital day. The phenobarbitone was gradually reduced over the next 3 weeks. Blood glucose, calcium and magnesium levels were normal and VDRL was negative. The patient developed right gonococcal ophthalmitis on the 3rd hospital day which was successfully treated with a 10 days course of parenteral penicillin and penicillin eye drops. Follow up at 4 months revealed a normal child.

Comments: Most often, addicted mothers do not volunteer any information about their drug habits.

It is important to question them closely about narcotic drug addiction whenever one suspects narcotic drug withdrawal syndrome in the newborn. Besides, syphilis and gonococcal infection are more prevalent in both the neonate and the addicted mother as she frequently has to support her drug habit by prostitution. Purulent eye discharge in such newborn had to be treated aggressively as gonococcal ophthalmitis unless proven otherwise.

EFFECTS OF NARCOTIC DRUGS ON THE FOETUS

Heroin (diacetylmorphine) is the most commonly abused narcotic drug and can be obtained by illegal means only. The heroin addict usually starts with smoking the heroin in cigarettes, then moved on to "chasing the dragon", and many subsequently used the intravenous route. (Chasing the dragon consists of heating the heroin and following the resulting curl of smoke – the dragon's tail – with a straw or empty match box through which the smoke is inhaled). Heroin is hydrolysed in the body to morphine and is excreted in the urine largely as free and conjugated morphine. Babies born to heroin addicts tend to be small for gestational age and often weighing less than 2500 gm (Naeye *et al.*, 1973; Kandall *et al.*, 1975). The low birth weight is due partly to poor maternal nutrition and health and also to heroin which had been shown experimentally to retard growth. (Taeusch *et al.*, 1971). However, these neonates have a lower incidence of neonatal jaundice due to its inductive effects on glucuronyl transferase enzyme activity in liver (Zelson *et al.*, 1971). Heroin also accelerates the lung maturation process and neonates of heroin addicts have a higher lecithin to spingomyelin ratio in the amniotic fluid and the incidence of hyaline membrane disease is lower (Gluck and Kulovich, 1973). Various types of congenital defects are found but the incidence of these defects does not seem to be any higher than in the general population. The withdrawal symptoms occur early, usually within the first 24 to 48 hours and rarely after the fourth day and relatively easy to control. Respiratory alkalosis and hyperventilation are frequently associated with the withdrawal.

Methadone differs greatly from morphine and its derivatives in both structure and detoxication. It is demethylated in the liver and excreted in the urine and bile. Methadone, when initially used to treat narcotic addicted mothers, was thought to produce little or no withdrawal effects in infants. (Wallach *et al.*, 1969). However, it was subsequently shown that 91% of exposed babies not only become symptomatic, but have more severe signs of withdrawal which were more difficult to control. These

babies were usually appropriate for gestational age, had an higher incidence of hyperbilirubinaemia and convulsions (Reddy *et al.*, 1971). The withdrawal symptoms may appear late (7 to 10 days). Kandall and Gartner (1974) reported seven cases of neonatal methadone withdrawal in which severe symptoms developed between 2 and 4 weeks of age. Fortunately methadone is not commonly used in this country in the treatment of the heroin addict.

Barbiturate can give rise to withdrawal syndrome in the newborn. This may be due either to drug abuse (most often involving intermediate acting barbiturates such as secobarbital or amobarbital) or for medical reasons. Long term phenobarbital is often prescribed for seizure disorders, preeclamptic toxemia and sedation during pregnancy. The withdrawal symptoms from barbiturates are usually more prolonged and appear late (7 days median; often seen up to 14 days) with predominance of central nervous system symptoms such as jitteriness and marked irritability (Desmond *et al.*, 1972).

RECOGNITION AND DIAGNOSIS OF NEONATAL NARCOTIC WITHDRAWAL SYNDROME

During intrauterine life the foetus has been exposed repeatedly to narcotics which is suddenly cut off at the time of delivery. If he has developed a physiological dependence to these drugs, withdrawal symptoms may be expected to follow. Unless the mother has abstained from drugs for at least 4-6 weeks prior to delivery, it is likely that at least some symptoms will occur. It has been estimated that 67-85% of infants born to mothers addicted to narcotic drugs manifest signs of withdrawal (Zelson *et al.*, 1971; Reddy *et al.*, 1971). Why some of these infants do not manifest signs of withdrawal is not known. However, the sleep pattern of every infant born to the drug addicted mother is abnormal, particularly so in the rapid-eye-movement (REM) aspect of sleep, even though some of these infants show no clinical evidence of withdrawal (Schulman, 1969).

The onset of withdrawal can occur at any time from birth to 3 or 4 days after birth. This interval depends to a degree on the mother's dosage, the type of narcotic used, the duration of addiction and the time of the last dose taken before delivery. However, it is said that withdrawal symptoms are only detectable if the mother had been taking 10-15 mg of heroin a day regularly, but histories of drug use in terms of dosage and frequency are so unreliable that it is not possible to base treatment on such data.

The diagnosis is often difficult due to lack of information from the mother who may conceal the

fact that she was using drugs illegally or due to the failure of the physician to consider the diagnosis. The importance of early recognition of newborn undergoing withdrawal symptoms cannot be over emphasized, since undiagnosed and untreated early, the infant may die or may have significant effects on growth, development and neurological status later in life. The signs and symptoms may be vague and non-specific, but the physician with a high index of suspicion may elicit a maternal and social history that corroborated with laboratory data and allow treatment of the infant and subsequent help to the mother.

Table I: Signs and symptoms of neonatal narcotic withdrawal syndrome

1. Central nervous system:	Restlessness, irritability, high pitched cry, tremors or jitteriness are most frequently encountered; and rarely convulsions.
2. Gastrointestinal:	Poor feeding, vomiting and frantic sucking activity frequently occur, and at times diarrhoea.
3. Respiratory:	Depressed respiration or respiratory distress are infrequent but occasionally do occur.
4. Others:	Fever, skin abrasions, excessive yawning, sweating, blanching and flushing of skin, nasal discharge, hiccups and poor weight gain.

The most common symptoms of withdrawal are generalised hyperactivity, coarse tremors or jitteriness and irritability. The infant develops skin abrasions on the knee, chin and elbow because of excessive movement and has an increased muscle tone. He cries fretfully most of the time especially when disturbed. He appears hungry and sucks frantically at his fists with a voracious appetite but relatively little milk goes into the stomach because of the ineffective sucking activity (Kron *et al.*, 1974). The other symptoms include sneezing, yawning, nasal congestion, sweating, loose stools, vomiting and occasionally hyperthermia. With excessive motor activity and poor caloric intake the infant may lose weight. Sleep disturbances have been reported even after the acute symptoms of withdrawal had diminished as well as an increased level of response to auditory stimuli (Sisson *et al.*, 1974). Occasionally these infants developed hypocalcaemia and its symptoms because of a respiratory alkalosis resulting from tachypnoea and hyperventilation. (Glass *et al.*, 1972).

TREATMENT

Once the diagnosis of narcotic withdrawal syndrome is made, treatment must be considered. Drug addiction in the adult is characterised by tolerance, physical and psychological dependence and in treatment these 3 factors need to be considered. However, in neonates only physical dependence to the narcotic drugs is present and treatment is much easier compared to adults. All neonates of addicted mothers should be admitted to hospital or the special care nursery for careful observation for signs of withdrawal. If signs of withdrawal occur they should be evaluated every 1 to 2 hours and treatment to be considered. Blood should be sent for blood gases, electrolytes, glucose, calcium and magnesium levels, to rule out metabolic disorders. Whenever indicated a blood culture and a lumbar puncture should be done to exclude neonatal sepsis and meningitis.

During the hospitalisation of the addicted infant, the parents should be encouraged to be with the infant as often as possible to facilitate parent-infant interaction. Supportive counselling is maximised during this period since many parents may feel guilty and depress. The nature of the infant's withdrawal should be explained to the parent and they be kept informed of the clinical condition and progress of treatment. They should be given the opportunity to express their fears and feelings concerning the withdrawal and other problems that they have. The assistance of other persons, e.g. grandparents, who might provide needed help during the crisis, should be sought.

Approximately 30% of the infants who manifest signs of withdrawal show only mild signs and will recover spontaneously within a short period of time. These infants do not require treatment. A quiet, warm and darkened environment, gentle handling, swaddling a pacifier and frequent small feeds are all that is required.

However, infants who cry continuously, have feeding difficulty, diarrhoea, marked irritability and jitteriness, should receive some form of sedation to relieve their discomfort and to prevent the condition from deteriorating further. Various treatment regimens have been used successfully in controlling the signs of withdrawal. Evaluation of these different regimens are difficult. Various scoring systems based on the signs and symptoms of withdrawal have been used. (Lipsitz, 1975; Finnegan *et al.*, 1975). However, it is important to provide adequate fluid and caloric intake as the major cause of death in drug addicted infants is dehydration which has not been diagnosed and/or

improperly treated. The dehydration may be severe and of sudden onset in those infants who develop diarrhoea and vomiting. Thus daily intake and output and weight gain or loss, is an essential part of the management. The most frequently used drugs are chlorpromazine, phenobarbitone and diazepam. Paragoric is used only occasionally for severe gastrointestinal symptoms.

Table II: Drugs used in the treatment of neonatal narcotic withdrawal syndrome

Phenobarbital:	8.0–10.0 mg/Kg/day in divided doses every 6 to 8 hourly. IM or orally (initial doses should be IM), decrease dose to 5 mg/Kg/day after 48 hours.
Chlorpromazine:	2.0–3.0 mg/Kg/day in divided doses every 6 hours, IM or orally (initial 2 doses should be IM).
Diazepam:	1.0–2.0 mg/Kg/day in divided doses every 8 hours, orally, halved the dose once symptoms are controlled.
Paragoric U.S.P. (camphorated tincture of opium)	1–2 drops/Kg q. 4 hourly, increased if necessary by 2 drops every 4 hourly to stabilizing dose.

Phenobarbitone is an effective and relatively safe drug and provide adequate control of symptoms for most infants (Kahn *et al.*, 1969). The starting is 8–10 mg/Kg/day in 3 to 4 divided doses. The initial 2 to 3 doses are administered intramuscularly and subsequent doses orally. After 48 hours, the dose is reduced to 5 mg/Kg/day, and according to the clinical condition the infant is slowly weaned off the drug. Although phenobarbitone provides good control of CNS symptoms, it affords poor control of gastrointestinal symptoms like vomiting and diarrhoea (Cobrinik *et al.*, 1959). Besides it also has a depressing affect on the respiratory center.

Chlorpromazine had been widely used in the treatment of neonatal narcotic withdrawal syndrome and considered the drug of choice by Zelson (1971). It provides good and rapid control of both the central nervous system and gastrointestinal symptoms. The initial dose is 2.0 to 3.0 mg/Kg/day in 4 divided doses. The initial 2 doses are given intramuscularly and subsequent doses orally. The dose is maintained for 2 to 4 days and then gradually tapered. In general, 25% of infants require treatment for less than 10 days, 50% for 10 to 20 days and 25% for up to 40 days. (Zelson *et al.*, 1971). However the disadvantage of this drug is that it may cause extrapyramidal symptoms (Kahn *et al.*, 1969) and its long term effects on the developing cardiovascular, endocrine, central nervous systems are incompletely understood (Jarvik, 1970).

Diazepam had only been recently used to treat neonatal narcotic withdrawal (Nathenson *et al.*, 1971, Bauer, 1973). It provides good control of the CNS and gastrointestinal symptoms but does not seem to offer any particular advantage over phenobarbital or chlorpromazine. The initial oral dose is 1.0 to 2.0 mg/Kg/day in 3 divided doses. Once the symptoms are controlled the dose is halved and the dose interval is lengthened to 12 hours. The drug is discontinued once the dose of 0.5 mg is reached, only a short course of therapy is needed because of the extremely long half life of the drug in the newborn. The other theoretical risk of diazepam is the presence of 5% sodium benzoate used as a buffer; this is a potent competitor for bilirubin binding sites in albumin and thus not recommended in jaundiced neonates. (Cohen and Fern, 1972).

Paragoric (Camphorated tincture of opium U.S.P.) is not recommended except when diarrhoea is part of the withdrawal syndrome. The main objection to the use of paragoric is that the newborn after another narcotic drug. Besides causing constipation and lethargy, large doses must be given to control symptoms and durations of treatment is prolonged.

Once the withdrawal symptoms are under-control the same dosage of the above drugs is maintained for 1 to 3 days before gradually tapering off. The indications of adequate treatment are, decrease or complete control of clinical signs, able to sleep and feed well with no vomiting or diarrhoea and show no untoward reaction to the drugs used. (Zelson, 1975).

FUTURE CARE OF THE INFANT

The future care of the infant of the addicted mother poses a greater challenge than the acute management of the withdrawal symptoms as many of the addicted mothers are unmarried and have emotional and psychological problems of their own. Even though they express the desire to keep the baby, they may not be able to satisfy the emotional and physical needs of the child.

There is a higher incidence of child abuse and sudden infant death in these children. It is important for the physician to establish a positive relationship with the parents and provide them with guidance and emotional support. A lot of effort must go into the treatment of the addicted mother, she must be provided with medical support and treatment, psychological help and complete and honest information as to the effect of her addiction on herself and her baby. She needs to be handled with patience

and consideration. Many different factors need to be considered before discharging these infants from the hospital, that is, the home environment, the mother's drug habit and motivation of seeking treatment, the family dynamics and home help, the desire to keep the child and other social problems. The physician needs to work closely with the medical social worker and the public health nurse in following up these infants and also to provide supportive and other help to the mother.

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