This is a text version of the PedsCases podcast "**Managing infants born to mothers who have used opioids during pregnancy – CPS Podast**." These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedcases.com/podcasts.

Managing infants born to mothers who have used opioids during pregnancy – CPS Podcast

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Hello everyone, my name is Maya Dahan and I am a second-year Paediatrics Resident at SickKids Hospital and the University of Toronto. This podcast was made in conjunction with PedsCases and the Canadian Paediatrics Society (CPS). We will summarize the recently published 2017 CPS Guideline for managing infants born to mothers who have used opioids during pregnancy. The podcast was developed with Dr. Thierry Lacaze, staff Neonatologist and Section Chief for the Department of Neonatology at the University of Calgary. He is the lead author of the CPS statement that we will be reviewing today. For additional information and to view the complete CPS Practice Point, please visit www.cps.ca. The script for this podcast can be viewed at www.pedscases.com.

Objectives:

The goal of this podcast is to review the recently published CPS guidelines on caring for an infant born to a mother who used opioids during pregnancy. Using a case-based approach we will discuss:

1. The presentation of Neonatal Abstinence Syndrome (NAS) and its differential
2. The assessment of an infant with NAS
3. The treatment and discharge planning of an infant and their family

Let us start with the case.

Case

A 32-year-old primiparous caucasian mother with protective serologies gives birth by SVD to a 39+1 weeks gestation, baby girl, BW 2.72kg (15th percentile). Pregnancy reported as unremarkable but the mother was followed closely due to her known opioid addiction following a back injury and surgery. Delivery uncomplicated, GBS negative, Apgars 9,9. You are called to the mother's room to assess the baby 18 hours after birth for tachycardia, inability to settle and poor feeding. The baby had been getting frequent nursing assessments due to the maternal opioid history. Nothing had been reported on

the previous shift but the mother says the symptoms have been progressing over the night.
The nurse gives you the following vitals: Her temperature is 38.1 degrees Celsius rectally, her heart rate is 169bpm, respiratory rate 63bpm, oxygen saturation is 100% on room air, and blood pressure 74/51mmHg.
She is very alert, extremely irritable, has a very loud agonizing cry and no one is able to settle her. Her fists are clenched, her limbs are flexed, and her tone is increased. She is hyper-reflexic. Her fontanelle is soft and flat. She is pink but slightly diaphoretic. She is non-dysmorphic but as you look at her nose, you see some clear fluid dripping from it. As you unbundle her, you note jittering. Her cardiac sounds are normal, no murmurs, she is warm and well perfused with strong and equal brachial and femoral pulses. Her capillary refill is 2 seconds. She has good air entry bilaterally, no adventitious sounds. She has mild tachypnea with some nasal flaring but no other work of breathing. Her abdomen is soft, non-tender, with no palpable masses or hepatosplenomegaly. Her skin is unremarkable. Genital and rectal exam are unremarkable.

You stop and think of your differential:

- Hypoglycemia
- Hypocalcemia
- Hyperthyroidism
- And… Neonatal abstinence syndrome. Don't forget that NAS can present like metabolic abnormalities!

Keep the case in mind and we will get back to in shortly.

Background:
In 2015, just under 2000 Canadian infants developed neonatal abstinence syndrome. This is more than a fivefold increase in the last decade. The average hospitalization for these infants is 15 days, creating a significant stress on families and a very large financial burden for hospitals.

Opioid use in pregnancy has been associated with spontaneous abortions, IUGR/low birth weight, prematurity, sudden infant death syndrome and infant neurobehavioral abnormalities. NAS is the most common short term complication of maternal opioid use.

There exists a huge window of opportunity for us to support mothers who are dependent on opioids throughout their pregnancy and minimize risk to the infant/child. Improving prenatal care for these women allows for monitoring of IUGR, infectious risk factors and maternal malnutrition, all of which can have compounded detrimental effects on the fetus. This is also an opportunity to provide guidance and enrol the mother into a methadone maintenance program. Through education, counselling and social support, a trusting bond with the care team can lead to better outcomes.

Unfortunately, as pediatricians we rarely get the opportunity to provide prenatal support to the families of our patients. We must have a high index of suspicion for neonatal abstinence syndrome to be able to diagnose it in our patients.

Presentation:
NAS can be very variable in presentation, both in the way it presents and the timing of the presentation. This wide spectrum is attributable to both maternal factors and infant factors. Maternal factors include the type of opioid consumed, the frequency and dose of consumption, maternal metabolic rate and the timing of the last use. For example, some studies suggest later presentation of NAS in the infant if the mother was using methadone or buprenorphine, as they both have longer half-lives. Infant factors are mainly related to gestational age and infant metabolic rate. Preterm infants appear to be less at risk than their term counterparts; they have a lower capacity to express these symptoms as their brains are still too immature.

So how do these infants present?

To understand withdrawal presentation, let us start by talking about opioids. Opioids are CNS depressants. Someone overdosed on opioids will have depressed vital signs, myosis, poor reflexes, and will be sedated. Withdrawal symptoms present as the opposite. The body, used to compensating for a depressed CNS state, goes into overdrive with an over activation of the sympathetic system.

NAS will affect three major systems: the central nervous system, metabolic and gastrointestinal systems. Let's talk about one system at a time.

1. From a CNS perspective, infants suffering from NAS can present as extremely irritable and inconsolable, have high pitched crying and are unable to sleep. On exam, they can have hyperactive reflexes, hypertonia, jitteriness or tremors, myoclonic jerks or even seizures.
2. Metabolic derangements in NAS present in the vital signs changes such as fever and tachypnea. On exam you can see sweating, mottling and nasal flaring. Always be cautious of infants that have frequent yawning, sneezing or nasal stuffiness as those can all be signs of opioid withdrawal in the infant.
3. From a GI standpoint, infants appear excessively hungry with rooting and sucking but have poorly coordinated feeding, excessive disorganized sucking and are unable to self sooth or satisfy. They also can have vomiting and loose, watery stools.

The majority of symptoms will present within the first 48-72hrs of life. The initial acute symptoms can persist up to 10-30 days but the milder, subacute symptoms such as feeding difficulties, irritability and sleep dysregulation can persist for up to 6 months.

Let's return to the case and our patient. How many of these symptoms did she display? Irritability, tachycardia, tachypnea, febrile, tremors, diaphoresis, clear rhinorrhea, poor feeding, loose stools. So what does that mean?

Assessment
To quantify the severity of withdrawal symptoms, we use the Modified Finnigan Scoring Tool. This Withdrawal Assessment Tool, (WAT), gives you a score based on behaviours associated with withdrawal.

When maternal opioid is known prenatally or at delivery, WAT scores should be obtained within 1-2 hours of life and then repeated every 3-4hours in conjunction with other nursing assessments for a minimum of 72hrs to 120hrs of life if the mother is known to be on a long acting opioid such as methadone or buprenorphine. This does imply that these mothers and infants require a longer minimum length of stay. The scoring system can also be used to monitor the improvement of symptoms once treatment is initiated.

Remember how we divided the signs and symptoms of opioid withdrawal into three systems before? The Modified Finnigan score is divided into the same three categories as per the main systems affected by withdrawal; the CNS disturbances, metabolic/vasomotor/respiratory disturbances, and the gastro-intestinal disturbances. This scale is used to grade the NAS severity and guide the treatment. Accurate scoring is crucial for appropriate care.

By knowing the scoring system, you will know the signs and symptoms of neonatal abstinence syndrome. Let us go through it one more time, this time with the amount of points attributed to each category.

1. CNS disturbances can account for a maximum of 20 points. High pitch crying is divided into continuous crying less than 5 minutes or more than five minutes at a time. Sleeping for less than one hour after feeding get you more points than sleeping for two or three consecutive hours. The Moro reflex is assessed and the more hyperactive it is, the more points are given. Tremors are graded on severity. Increased muscle tone, myotonic jerks and generalized convulsions all give you an increasing amount of points.
2. Metabolic and vital sign derangements can give you a maximum score of 11. Look for fever, tachypnea, sweating, mottling, nasal flaring, yawning, nasal stuffiness and sneezing. Each of these give you one or two points depending on severity.
3. From a GI standpoint, infants can get a maximum of 9 points. Poor feeding, excessive sucking, vomiting, and loose stool, each get 1 to 3 points depending on degree.

Consistent scores of 8 and over on three consecutive occasions or WAT scores of 12 and over on two subsequent evaluations are considered elevated and warrant pharmacological interventions.

Management

This brings us to management of these infants. Goals for treatment are preventing further complications associated with opioid withdrawal in addition to restoring normal newborn activities, such as feeding with appropriate weight gain, sleeping and adapting to their new environment.
There are two phases of interventions, non pharmacological and pharmacological.

Initial treatment should always begin with non-pharmacological as medications can prolong hospital stay and disrupt maternal-infant bonding. In known opioid users,

postpartum preparation, breastfeeding and NAS education for the mother can begin prenatally.
Separating infant and mother are known to be detrimental to early attachment, decrease breastfeeding initiation, and increase hospital stay. If possible, it is best to have the infant 'room-in' with the mother. Early initiation of breastfeeding should be encouraged as it may decrease NAS symptoms and the potential need for medications. Early initiation of other non-pharmacological interventions such as skin-to-skin, safe swaddling, gentle waking, quiet environment, minimal stimulation, lower lighting, developmental positioning, music or massage therapy have been shown to decrease the severity of NAS symptoms.
Given the GI symptoms of NAS it is important to monitor closely the infants' growth and supplement calories for those who are not gaining weight adequately.

Second line therapy is medications. Indications to progress to this second line are:
1. Infants whose withdrawal signs are increasingly severe with WAT scores of 8 and over for three consecutive evaluations or 12 and over for two consecutive evaluations or
2. Infants whose concurrent NAS scores climb despite supportive measures to reduce and manage symptoms.

Usually these infants need to be admitted to the NICU for cardiorespiratory monitoring if initial medication management becomes escalated. Once stabilized, the infant may be transferred back to rooming in with their parents. Consistent and strong support from the medical team is crucial for these families on the mother baby unit as well as in the NICU; they require lots of support and resources to ensure successful parenting skills acquisition and subsequent transition to home. It is important to highlight that pre-birth knowledge of the maternal history is essential to be able to intervene early and decrease neonatal need for medications and admissions.

Since maternal infant bonding and breastfeeding has been shown to decrease the need for medications, it is important to accommodate for the non-pharmacological methods as much as possible even when the infant is in the NICU. NICUs can be a difficult environment to provide non-pharmacological support; single rooms units are quiet but when parents aren't there, due to staffing limitations, it is difficult to give these patients the attention they need. In rooms with multiple beds, it is often loud with limited space for parents to come visit. Caregivers require special education on how to best support these families. As physicians, it is important for us to be aware of our unit's limitations in order to best adapt and personalize care for our patients. There are a few nurseries in Canada built to support these mothers and their children in Edmonton and Vancouver. However, this requires provincial or regional organization.

Although there is little evidence as there are very few studies, first line treatment tends to be morphine and methadone. There is one exception, mothers on methadone; A recent study compared buprenorphine to morphine as a treatment option, and showed that buprenorphine decreases length of stay by 42% in children of mothers on methadone.

There are published guidelines for starting doses, dosing increments, initiating additional treatments and weaning, and to assist in a consistent approach to management.

Let's talk about the different pharmacological options:

1. Morphine is the most common first line agent in Canada. It is started when WAT scores are above 8 on three consecutive evaluations. One of its advantages is that it does not contain any alcohol and has a short half-life of 9 hours. Once the infant is stable, the dose can be weaned by about 10% every 48-72 hours while keeping a close eye on the WAT scores.
2. Methadone is commonly used in other countries as first line treatment. Formulations are now available without special access prescriptions. It is a synthetic compound that acts on the same receptor as morphine. Contrary to morphine, it has a long 26 hour half-life.
3. Buprenorphine is a semi-synthetic agent that has an even longer half life than methadone, lasting up to 60 hours. It is administered sublingually, which can be challenge in infants. But its biggest downfall is that it contains 30% alcohol, the most of the three compounds.
4. Phenobarbital and clonidine act on different receptors and can be rarely used as adjuncts.

Let's get back again to our case:
By adding up points for all of her symptoms, she gets a WAT score of 14. This mother should have already been encouraged to breastfeed, do kangaroo care, dim the lights, and staff should be minimizing disturbances.
Despite this, the WAT scores have been climbing. With the infant this sick, you opt to admit her to the NICU and start her on oral morphine every 4 hours. Her WAT scores stabilize over the first few days as her temperature and tachypnea settle and her tremors disappear. But she continues to be difficult to settle, she is still not feeding well and continues to lose weight, and she has now developed loose stool and a subsequent diaper rash. Since her WAT scores have dropped below eight consistently, you can now wean her morphine down by ten percent. You may consider supplementing her feeds if weight loss continues.
But, if her WAT scores had instead increased and didn't stabilize despite non-pharmacological treatment, you would increase her morphine dose (as per protocol to a maximum).
All the while, the parents are spending much of their day with their daughter in the NICU, and mother is breastfeeding. You should be using this opportunity to screen for parental skills, to guide, teach and reinforce positive parenting.

Follow-up/discharge

Infants of mothers who used opioids during pregnancy should stay in hospital for observation for a minimum of 72 hours. If the infant never reaches a point requiring medical treatment, the child is eligible for discharge. It is essential to ensure that adequate follow up is organized with a primary health care provider and social services

in the community. Discharge planning should begin early as not to delay discharge from hospital.

Take home messages

So let us recap the 4 clinical pearls discussed in this podcast:

1. Use the Finnigan scoring system (or equivalent scoring system) to quantify the NAS symptoms and guide your treatment plan.
2. Always include non-pharmacological treatment in your treatment plan of infants presenting with NAS. Remember that it will decrease their need for medication and their length of stay!
3. If medications are required, monitor carefully and frequently to ensure that you are using the minimum amount of medication required and that you are tapering slowly to not worsen the withdrawal effects.
4. Start planning discharge and follow up in the community early on!

Thank you very much for listening to this podcast about the CPS statement on Neonatal Abstinence Syndrome. If you have questions or comments please contact Dr Thierry Lacaze or myself and we would be happy to answer them!