PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES

Care of the Neonate with Neonatal Abstinence Syndrome (NAS)

Clinical Practice Guideline: Care of the Neonate with Neonatal Abstinence Syndrome

Points of emphasis/Primary changes in practice:

1. If possible, mothers should be identified antenatally and referred to the Neonatology Antenatal Consultation Service to begin education and encourage collaborative care.

2. Modifications to the environment and non-pharmacologic comfort measure will be optimized prior to medication initiation and throughout medication titration.

3. Depending on the exposure, neonate will initially receive morphine **and** clonidine or morphine **and** phenobarbital to encourage rapid stabilization and efficient weaning.

Rationale for change:

To optimize and standardize parental involvement, comfort care, and pharmacologic management of neonates with NAS.

Questions? Please contact: Pharmacy Department

Clinical Guideline Name	Care of the Neonate with Neonatal Abstinence Syndrome (NAS)
Implementation Date	March 3, 2015 (updated 10/24/2018) (MSO4 concentration updated April 2020)
Due for CPC Review	In process
Contact Person	NICU Clinical Pharmacist
Approved By	Department of Pediatric Newborn Medicine 2/15/15 Clinical Practice Council 2/15/15 CWN PPG 2/11/15 BWH SPP Steering 2/18/15 Nurse Executive Board/CNO 10/26/15

This is a clinical practice guideline. While the guideline is useful in approaching the care of the neonate with Neonatal Abstinence Syndrome, clinical judgment and / or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

I. Purpose

The purpose of this clinical practice guideline is to address the care and medical management of the neonate experiencing neonatal abstinence syndrome (NAS). The scope of this guideline includes the following aspects of care and medical management:

(i) Maternal and newborn screening for exposure to opioids, such as methadone and buprenorphine (Subutex), or SSRIs during pregnancy
(ii) non-pharmacologic aspects of care including the environment of care, other comfort measures, and nutrition
(iii) Pharmacotherapy
(iv) Continuity of care
(v) Discharge or transfer planning

II. All CPGs will relay on the NICU Nursing Standards of Care. All relevant nursing PPGs are listed below.

WNH S.5 Identification and Referrals of Patients and/or Infant's Family to Social Work
WNH B.9 Infant Feeding
WNH S.1 Skin to Skin Care
WNH M.1 Administration of Medications to Infants

III. Scope

Inclusion criteria:	Neonates ≥ 35 weeks gestation with development of moderate to severe NAS, defined as 2 consecutive abstinence scores of ≥ 8 or one score > 12
	Neonates who experienced intrauterine exposure to opioids, such as methadone and buprenorphine (Subutex), and/or other clinically relevant substances during the prenatal period as demonstrated through maternal history and positive urine toxicology screening.
Exclusion criteria:	Gestational age < 35 weeks
	Known neurologic abnormalities

IV. Maternal and Neonatal Screening

All pregnant women should be screened by their obstetrician at the initial prenatal visit, at 28 weeks gestation, and upon admission to Labor and Delivery using a standardized screening tool (Appendix 1).[1]

WNH S.5 Identification and Referrals of Patients and/or Infant's Family to Social Work

All pregnant women who screen positive at any time during their pregnancy or at birth will be referred to the Neonatology Antenatal Consultation Service. At their consultation, mothers will be educated regarding Neonatal Abstinence Syndrome by the physician and given an informational brochure. The State Protection and Care of Children Act (51A) is described in the informational brochure and will be discussed at the antenatal consultation. The Neonatology Antenatal Consultation Service will ensure that social work is involved prenatally. The Neonatology Antenatal Consultation Service will collaborate with a clinical pharmacist for questions regarding specific medications in relation to expected course of neonatal abstinence or breastfeeding. Breastfeeding recommendations will be reviewed on a case by case basis and discussed with the mother during the prenatal visit. Antenatal discussions will be documented in the consult note.

All pregnant women who screen positive or those deemed to be at risk (less than 5 prenatal visits, known substance abuse or positive urine drug screen during this or previous pregnancy, any history of narcotic abuse, history of drug abuse within the last 3 years, any DCF involvement, and/or pertinent mental health history) will have urine toxicology sent upon admission to Labor and Delivery prior to the use of pain medications during labor. These pregnant women will also be referred to social work upon admission. If urine toxicology is positive, social work will file the State Protection and Care of Children Act (51A).

Infants born to women who screen positive or those deemed to be at risk should have urine and meconium specimens obtained as soon after birth as possible for neonatal screening procedures.

Urine and meconium testing should also occur at the discretion of the medical care team for infants with symptoms consistent with neonatal abstinence, severe intrauterine growth restriction (birth weight < 3rd percentile) without other identified etiology, symptoms consistent with intracranial hemorrhage, and/or placental abruption.

Mothers will be made aware of this screening by the attending pediatrician or his/her designee. Documentation of this discussion should be made in the infant's medical record. Specific consent is not required. In the event that the parents, when informed, object to the performance of the toxicology screen, the legal office should be contacted for consultation.

If urine and/or meconium specimens are positive, social work will file the State Protection and Care of Children Act (commonly known as 51A). See Physician Guidelines: Neonates Exposed to Controlled Substances (policy number 1.11.5) for detailed information on this aspect of NAS care.

V. Non-pharmacologic Aspects of Care

Non-pharmacologic care will be optimized at all times during the assessment and treatment of NAS.

Environment

The literature suggests that optimal nursing care provided to infants experiencing NAS and their families is often provided by cohorts of nurses who develop specific expertise relative to the needs of the NAS infant.[2] This allows the nurse to further develop their assessment skills, establish the highest levels of interrater reliability in the withdrawal assessment scale, and establish a depth of expertise in working with parents who have specific educational and care needs that are unique to the NAS infant. For this reason, neonates in the NICU at BWH with NAS should be preferentially admitted to the Growth and Development Unit. Additionally, under optimal circumstances, infants with NAS will be cared for by a nurse with no more than a 2:1 staffing ratio.

Further measures will be implemented to optimize the environment of care for the infant with NAS and their family as outlined below.

Comfort Measures

The goals of nonpharmacologic interventions are to facilitate supportive parenting behaviors and decrease external stimuli that tend to exacerbate withdrawal signs. Non-pharmacologic care has been defined as modification of the environment and social interactions that support neurodevelopmental and physiologic stability[3]. Ideally, comfort measures will be the first

approach to care for infants with NAS. When comfort measures do not adequately capture an infant's symptoms associated with NAS, they will be used in combination with pharmacotherapy.

Neonates with NAS will ideally have an NAS Passport completed collaboratively by the bedside nurse and parent(s) (Appendix 3). This educational guide will emphasize that parents are one of the most important aspects of their infant's care. The use of the NAS Passport will provide specific information and anticipatory guidance about what to expect during the different stages of withdrawal.

Specific non-pharmacologic interventions relative to care of NAS infant[2,3]:

Intervention	**Purpose/use**
Decrease External Stimulation	
• Dim lights/cover isolette or crib if appropriate. Ideally, crib canopy will be used when infants are in an open crib. • Decrease noise/ensure a quiet and soothing environment • Use slow infant handling • Avoid circumcision until NAS resolves	Room should be as quiet as possible, dimly lit, and movements slow so as to minimize environmental stimulation that can be especially noxious during withdrawal.
Promotion of infant self-regulation	
• Nonnutritive sucking • Pacifier use • Swaddling/modified swaddling with sleep sac when appropriate to prevent infant from overheating • Prone/therapeutic sleep positioning [4]	NNS helps organize a dysregulated infant and prevents disorganization. Swaddling may help infant with motor or tone dysregulation. Infants who have poor motor control (thrashing or exaggerated rooting) respond to gentle head/limb restraint by helping them regulate.
Supplemental comfort care measures • Holding (skin to skin with parent is optimal) • Rocking • Rubbing • Containment • Movement (i.e. use of swing and/or stroller) • Use of warm blanket • Soothing music	Gentle containment or pressure supports motor and tone control. Rubbing is often better than patting when burping during feedings to avoid triggering the Moro reflex. Rocking helps to facilitate relaxation and eye contact. When rocking is vertical, it is thought to be more soothing than "regular" rocking or side to side rocking. Soothing music may be effective in individual infants.

Nutrition

Misuse of non-prescribed drugs is a contraindication to breast feeding or providing breast milk, however mothers will receive counseling from the medical team and lactation consultants to encourage treatment/cessation from use of non-prescribed drugs. Known HIV is a contraindication and in these cases, breastfeeding or providing breast milk nutrition will be discouraged

Breastfeeding will be encouraged for mothers in treatment programs or on medications prescribed by a physician. Questions regarding the safety of specific medications in breast milk will be addressed and documented in the note by the Neonatology Antenatal Consultation Service (in consultation with pharmacy) prior to delivery. For mothers not counseled prior to delivery, the safety of specific medications in breast milk will be discussed by the

multidisciplinary team (including attending physician, fellow/NP, pharmacist, lactation consultant, and primary nurses) prior to communicating the recommendation to the family.

Frequent small volumes of human milk, unless contraindicated, or formula should be provided to minimize hunger and allow for adequate growth. In acute withdrawal that results in weight loss, consider increased calories to replace caloric expenditure caused by increased activity, crying, and decreased sleep and calories lost by regurgitation and diarrhea. Neonate will be assessed for nutritional risk by Neonatal Dietitian within 72 hours of NICU admission per standard practice and reassessed at regular intervals throughout the infant's hospitalization. Consult dietitian for questions or concerns regarding infant feeding and growth.

There are inconsistent data on value of formulas with reduced lactose. The best evidence seems to suggest that lactose-free formula be reserved for infants with persistent diarrhea uncontrolled by adequate pharmacotherapy for NAS.
WNH B.9 Infant Feeding

VI. Initial Assessment of Neonates at risk for NAS

Scoring of babies deemed to be at risk of neonatal abstinence syndrome will begin after arrival to the nursery and occur every 3-4 hours utilizing the Modified Finnegan Neonatal Abstinence Scoring Tool (Appendix 2). Scores should reflect the entire 3-4 hour period considering the normal infant sleep-wake cycle.

Scores should be reviewed daily by the attending pediatrician and discussed with the bedside nurse. A Finnegan score > 12 should be verified by a second nurse and the attending pediatrician should be contacted. Two Finnegan scores > 8 with the second score verified by a second nurse or significant nursing concerns also warrant contacting the attending pediatrician. The attending pediatrician will discuss clinical course and indications for NICU evaluation.

Asymptomatic neonates with known antenatal exposure to opioids and/or benzodiazepines will be observed in the regular nursery for 3 to 7 days. An infant born to a mother on a low-dose prescription opiate with a short half-life (e.g., hydrocodone) may be safely discharged if there are no signs of withdrawal by 3 days of age. An infant born to a mother on an opiate with a prolonged half-life (e.g., methadone) should be observed for a minimum of 5 to 7 days. After discharge, outpatient follow-up should occur early and include reinforcement of the education of the caregiver about the risk of late withdrawal signs.

If possible, delay circumcision until NAS symptoms are resolving and infant is near discharge.

VII. Pharmacotherapy

The decision to initiate or adjust medications will be made collaboratively by the medical care team. All Finnegan scores > 8 will be verified and signed by a second nurse or a prescriber. All confirmed Finnegan scores > 8 will be assessed by a prescriber to determine the necessity of medication adjustment. Significant nursing concerns also warrant contact of the prescriber, regardless of Finnegan scores.

Modifications to the environment of care and non-pharmacologic comfort measures will be optimized prior to medication initiation and throughout medication titration.

Concomitant SSRI and long-acting opioid (methadone or buprenorphine) exposure is common. SSRI intoxication presents early after birth with primarily neurologic symptoms. This syndrome does not respond to pharmacologic therapy. Prescribers should attempt to distinguish this early symptomatology from the later onset, multifocal presentation (including vasomotor and gastrointestinal disturbances) of long-acting opioid withdrawal. (Appendix 2)

Protocol below is derived from the randomized controlled trial of Surran and colleagues[5]. Weaning morphine by 10% of maximum dose per Brown and colleagues, Surran and colleagues and Lainwala and colleagues[14,5,13]. Discontinuation of morphine at 10% of maximum dose per Lainwala and colleagues[13]. Combination therapies are superior to opioid replacement alone[6 7]. Clonidine is the preferred adjunctive therapy compared to phenobarbital for NAS secondary to opioid exposure, due to the adverse neurodevelopmental and behavioral consequences of prolonged exposure to phenobarbital[8 9 10 11]. Notably, phenobarbital is the preferred adjunct for NAS with significant benzodiazepine or barbiturate exposure[12].

Management of newborns with NAS primarily due to opioid-exposure

Starting doses of concomitant medications:

For NAS score	Oral morphine dose	**AND**	Oral clonidine dose
8-10	0.05 mg/kg/dose q6h	+	1.5 mcg/kg/dose q6h
11-13	0.1 mg/kg/dose q6h	+	2 mcg/kg/dose q6h
14-16	0.15 mg/kg/dose q6h	+	2.5 mcg/kg/dose q6h
≥17	0.2 mg/kg/dose q6h	+	3 mcg/kg/dose q6h

Adjustment:

For NAS score	Oral morphine	Oral clonidine
> 12	Increase dose by 10% (rounded in increments of 0.02 mg) or decrease interval to q3h or q4h to correlate with feedings	Increase dose by 1 mcg/kg/dose to a maximum of 6 mcg/kg/dose
8-12	No change unless clonidine dose is maximized	Increase dose by 1 mcg/kg/dose to a maximum of 6 mcg/kg/dose
< 8 x ≥ 24 hours See Appendix 4	-Wean by 10% of the maximum daily dose (rounded in increments of 0.02 mg) -When oral morphine dose is 10% of the maximum daily dose (or has reached a minimum measurable dose) discontinue -If infant has been weaned too quickly, go back to last effective dose	No change When morphine off x 24 hours, wean clonidine by 1 mcg/kg/dose every 24 hours until off. If infant has been weaned too quickly, go back to last effective dose.

Note: The threshold for weaning should be increased by 2 when the infant exceeds 21 days old to account for infant maturation.

Note: Rounding increment and minimum dose in Epic is 0.02 mg.

-Monitor blood pressure q6h x 24 hours after initiation or adjustment of clonidine.

-Infant may be discharged on clonidine without blood pressure monitoring at the discretion of the medical care team. Wean outpatient clonidine 1 mcg/kg/dose ~weekly.

-**Effective March 2020, oral morphine concentration of 0.4 mg/ml is available for use.**


BWH

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Management of newborns with NAS primarily due to benzodiazepine or barbiturate exposure

Starting dose

For NAS score	Oral phenobarbital dose
8-10	10 mg/kg PO x 1, followed by 5 mg/kg daily
11-13	10 mg/kg PO x 1, followed by 5 mg/kg daily
14-16	15 mg/kg PO x 1, followed by 5 mg/kg daily
≥17	20 mg/kg PO x 1, followed by 5 mg/kg daily

Adjustment

For NAS score	Oral phenobarbital
> 12	10 mg/kg PO x 1 to a maximum level of 40 mcg/mL Consider increasing maintenance dose by 2 mg/kg/day if scores persistently elevated
8-12	10 mg/kg PO x 1 to a maximum level of 40 mcg/mL
< 8 x ≥ 24 hours See Appendix 4	Wean by 10% once weekly If infant has been weaned too quickly, go back to last effective dose.

Note: Consider administering daily phenobarbital dose in the evening to promote quiet sleep over night.

Note: The threshold for weaning should be increased by 2 when the infant exceeds 21 days old to account for infant maturation.

Management of newborns with NAS due to opioid and benzodiazepine/barbiturate exposure

Starting doses of concomitant medications:

For NAS score	Oral morphine dose	**AND**	Oral phenobarbital dose
8-10	0.05 mg/kg/dose q6h	+	10 mg/kg PO x 1, followed by 5 mg/kg daily
11-13	0.1 mg/kg/dose q6h	+	10 mg/kg PO x 1, followed by 5 mg/kg daily
14-16	0.15 mg/kg/dose q6h	+	15 mg/kg PO x 1, followed by 5 mg/kg daily
≥17	0.2 mg/kg/dose q6h	+	20 mg/kg PO x 1, followed by 5 mg/kg daily

Adjustment:

For NAS score	Oral morphine	Oral phenobarbital
> 12	Increase dose by 10% (rounded in increments of 0.02 mg) or decrease interval to q3h or q4h to correlate with feedings	10 mg/kg PO x 1 to a maximum level of 40 mcg/mL Consider increasing maintenance dose by 2 mg/kg/day if scores persistently elevated
8-12	No change unless phenobarbital is maximized	10 mg/kg PO x 1 to a maximum level of 40 mcg/mL
< 8 x ≥ 24 hours See Appendix 4	-Wean by 10% of the maximum daily dose (rounded in increments of 0.02 mg) -When oral morphine dose is 10% of the maximum daily dose (or has reached a minimum measurable dose) discontinue -If infant has been weaned too quickly, go back to last effective dose	No change When morphine off x 24 hours, wean by 10-20% once weekly. If infant has been weaned too quickly, go back to last effective dose.

Note: **Consider administering daily phenobarbital dose in the evening to promote quiet sleep over night.**

Note: **The threshold for weaning should be increased by 2 when the infant exceeds 21 days old to account for infant maturation.**

Note: Rounding increment and minimum dose in Epic is 0.02 mg.

VII. Continuity of Care

A multidisciplinary plan of care based on the guideline outlined above will be tailored to the individual infant and family's needs on the day of admission to the Neonatal ICU. Any deviation from the established plan will be discussed by available members of the multidisciplinary team when progression of the infant's course requires reassessment.

Neonates with NAS should be assigned a team of primary nurses covering day and night shifts as early as possible in their course in order to facilitate optimal continuity of care. This team will ensure that the infant and family are cared for by a dedicated core group of caregivers during their NICU stay.

VIII. Discharge or Transfer Planning

Parental desire to transfer infant for social reasons should be identified as early as possible in the infant's course. Plan of care will be tailored to facilitate rapid stabilization and transfer.

Discharge planning should be established early in the infant's course considering the needs of the infant and resources available to the family. An infant may be discharged on clonidine or phenobarbital considering the risks and benefits to the infant and family, and in collaboration with the outpatient pediatrician.

Discharge education will include healthy newborn care and also focus on comfort care, medication adherence, and/or symptom assessment. The parent passport will be utilized to assess discharge readiness and ensure appropriate parent education throughout the duration of care and especially at the time of discharge.

An Early Intervention referral will occur for all neonates with NAS requiring treatment with medications.

Appendix 1 – Screening tools

5 P's Screen for Alcohol/Substance Use: Prenatal and Postpartum visits

PARENTS: Did any of your parents have a problem with alcohol or drug use? Yes No

PEERS: Do any of your friends have a problem with alcohol or drug use? Yes No

PARTNER: Does your partner have a problem with alcohol or drug use? Yes No

PAST: In the past, have you had difficulties in your life due to alcohol or other drugs, including prescription medications?
Yes No

PRESENT: In the past month, did you drink any alcohol or use other drugs? Yes No

1. How many days per month do you drink? _____
2. How many drinks on any given day? _____
3. How often did you have 4 or more drinks per day in the last month? _____

Questions may also be more specific, for example:

1. What kind of alcohol (beer, wine, liquor)/drugs (heroin, cocaine, prescription drugs, methamphetamines, marijuana) do you use?
2. During the month before you were pregnant, how many times a week did you drink____(alcohol)/ use____(drugs)?
3. How many bottles/cans/shots/glasses of_____(alcohol) /how much____(name the drug) did you use each time you drank/used drugs during the month before you were pregnant?

CRAFFT Substance Abuse Screen for Adolescents and Young Adults

During the past 12 months, did you:

1. Drink any alcohol (more than a few sips)?
2. Smoke any marijuana or hashish?
3. Use anything else to get high?

If "no" to all three questions, ask only the first question below. If "yes" to any question, ask all questions below. Two or more positive responses to the following questions indicate the need for further assessment:

C - Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs?

R - Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?

A - Do you ever use alcohol/drugs while you are by yourself, ALONE?

F - Do you ever FORGET things you did while using alcohol or drugs?

F - Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?

T - Have you gotten into TROUBLE while you were using alcohol or drugs?

Appendix 2 – Finnegan Scoring Tool

Finnegan Scoring System

System	Symptoms	Points	Score		
Central Nervous System	Excessive high pitched (or other) cry (< 5 min) Continuous high pitched (or other) cry (> 5 min)	2 3			
	Sleep < 1 hour after feeding Sleep < 2 hours after feeding Sleep < 3 hours after feeding	3 2 1			
	Hyperactive Moro reflex Moderately hyperactive Moro reflex	2 3			
	Mild tremors when disturbed Moderate-severe tremors when disturbed	1 2			
	Mild tremors when undisturbed Moderate-severe tremors when undisturbed	3 4			
	Increased muscle tone	1			
	Excoriation (eg. Chin, knees, elbows, toes, nose)	1			
	Myclonic jerks (twitching/jerking of limbs)	3			
	Generalized convulsions	5			
Metabolism Vasomotor Respiratory	Sweating	1			
	Hyperthermia (37.2 – 38.2°C) Hyperthermia (≥ 38.4°C)	1 2			
	Frequent yawning (>3-4/interval)	1			
	Molting	1			
	Nasal stuffiness	1			
	Frequent sneezing (> 3-4/interval)	1			
	Nasal flaring	2			
	Respiratory rate > 60/min Respiratory rate > 60/min with retractions	1 2			
Gastro-intestinal	Excessive sucking	1			
	Poor feeding (infrequent/uncoordinated suck)	2			
	Regurgitation (≥2 times during/past feed) Projectile vomiting	2 3			
	Loose stool Watery stool	2 3			
	TOTAL SCORE				

Appendix 3 – NAS Passport

NAS Care Plan-Acute Phase

Here are a few ways to help comfort and settle me during the beginning of my stay.

- If I am sleeping, please do not wake me up.
- Keep the lights around me dimmed.
- Used hushed/quiet tones when talking to me.
- Swaddle me in a sleep sac with my hands close together near my face.
- Help me find my fingers to suck on or offer me a pacifier.
- Gently place your hands on my head and stomach.
- Quietly snuggle me or gently rock me.
- Move slowly with me, I can only do one thing at a time.

You can tell I am happy & Comfortable when:

- I am sleeping.
- My face and hands are relaxed.
- My body is quiet .
- I am cooing.
- I am smiling.

You can tell I am stressed when:

- I cry, hiccup, or yawn.
- I breathe fast.
- I wave my arms around.
- My color gets pale or mottled (marble-like).
- I sneeze.
- I stretch and stiffen my legs.
- I hold out my hands in a "stop" signal.
- I close my eyes or look away.

NAS Care Plan- Tapering Phase

Now that I am tapering off my medication, here are a few more ways to help comfort and settle me.

- Let me have quiet time in my crib or chair. I like to look around; hang a mobile or mirror for me to look at.
- Softly sing me a song
- If my nurse or doctor says it's okay, let me have some tummy time while you watch. Please make sure to put me on my back when it is time for you to leave.
- Bring in a bouncy seat for me.
- Play soft music for me.
- Quietly talk to me. Read me a book.
- If I am sleeping, please do not wake me up.
- Keep the lights around me dimmed.
- Used hushed/quiet tones when talking to me.
- Swaddle me in a sleep sac with my hands close together near my face.
- Help me find my fingers to suck on or offer me a pacifier.
- Gently place your hands on my head and stomach.
- Quietly snuggle me or gently rock me.
- Move slowly with me, I can only do one thing at a time.

You can tell I am happy & Comfortable when:

- I am sleeping.
- My face and hands are relaxed.
- My body is quiet.
- I am cooing.
- I am smiling.

You can tell I am stressed when:

- I cry, hiccup, or yawn.
- I breathe fast.
- I wave my arms around.
- My color gets pale or mottled (marble-like).
- I sneeze.
- I stretch and stiffen my legs.
- I hold out my hands in a "stop" signal.
- I close my eyes or look away.

Appendix 4 - Expected duration of withdrawal

The frequency of weaning in NAS should be determined considering maternal drug exposure and the expected duration of withdrawal. A tentative weaning plan should be established for individual infants by the medical care team after initial stabilization. Please use the table below for guidance and consult clinical pharmacist.

Exposure	**Expected duration of withdrawal**
Cocaine	Hours to days
Methamphetamine	Hours to days
Heroine	1-2 weeks
SSRI*	1-4 weeks
Methadone/buprenorphine	1-4 weeks
Benzodiazepines	1-6 months
Barbiturates	4-6 months
Alcohol	1-2 years

*In utero exposure to SSRIs is common. Most infants experience a hyperserotonergic state, similar to serotonin syndrome in adults, caused by an increased concentration of serotonin in the intersynaptic cleft. Clinical signs and symptoms in infants may include crying, irritability, tremors, poor suck, feeding difficulty, hypertonia, tachypnea, sleep disturbances, hypoglycemia, and seizures. This "serotonin discontinuation syndrome" should be differentiated from a withdrawal state. Currently, treatment of serotonin discontinuation syndrome with pharmacologic agents is not recommended. Most cases have reported a gradual resolution of the hyperserotonergic state rather than evolution to a hyposerotonergic (withdrawal) state. Reviews have failed to identify any adverse neurodevelopmental outcomes from infants exposed to SSRIs.

IX. References

1. Chang G, Orav EJ, Jones JA, Buynitsky T, Gonzalez S, Wilkins-Haug L. Self-reported alcohol and drug use in pregnant young women: a pilot study of associated factors and identification. Journal of addiction medicine 2011;5:221-6.

2. Maguire D. Care of the infant with neonatal abstinence syndrome: strength of the evidence. The Journal of perinatal & neonatal nursing 2014;28:204-11; quiz E3-4.

3. Velez M, Jansson LM. The Opioid dependent mother and newborn dyad: non-pharmacologic care. Journal of addiction medicine 2008;2:113-20.

4. Maichuk GT, Zahorodny W, Marshall R. Use of positioning to reduce the severity of neonatal narcotic withdrawal syndrome. Journal of perinatology : official journal of the California Perinatal Association 1999;19:510-3.

5. Surran B, Visintainer P, Chamberlain S, Kopcza K, Shah B, Singh R. Efficacy of clonidine versus phenobarbital in reducing neonatal morphine sulfate therapy days for neonatal abstinence syndrome. A prospective randomized clinical trial. Journal of perinatology : official journal of the California Perinatal Association 2013;33:954-9.

6. Coyle MG, Ferguson A, Lagasse L, Oh W, Lester B. Diluted tincture of opium (DTO) and phenobarbital versus DTO alone for neonatal opiate withdrawal in term infants. J Pediatr 2002;140:561-4.

7. Agthe AG, Kim GR, Mathias KB, et al. Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized, controlled trial. Pediatrics 2009;123:e849-56.

8. Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for febrile seizures--effects on intelligence and on seizure recurrence. N Engl J Med 1990;322:364-9.

9. Stefovska VG, Uckermann O, Czuczwar M, et al. Sedative and anticonvulsant drugs suppress postnatal neurogenesis. Annals of neurology 2008;64:434-45.

10. Chen J, Cai F, Cao J, Zhang X, Li S. Long-term antiepileptic drug administration during early life inhibits hippocampal neurogenesis in the developing brain. Journal of neuroscience research 2009;87:2898-907.

11. Forcelli PA, Janssen MJ, Stamps LA, Sweeney C, Vicini S, Gale K. Therapeutic strategies to avoid long-term adverse outcomes of neonatal antiepileptic drug exposure. Epilepsia 2010;51 Suppl 3:18-23.

12. Ebner N, Rohrmeister K, Winklbaur B, et al. Management of neonatal abstinence syndrome in neonates born to opioid maintained women. Drug and alcohol dependence 2007;87:131-8.

13. Lainwala S, Brown ER, Weinschenk NP, Blackwell MT, Hagadorn JI. A retrospective study of length of hospital stay in infants treated for neonatal abstinence syndrome with methadone versus oral morphine preparations. Adv Neonatal Care 2005;5(5):265-272.

14. Brown MS, Hayes MJ, Thornton LM. Methadone versus morphine for threatment of neonatal abstinence syndrome: A prospective randomized clinical trial. J Perinatol 2015;35:278-283.