

Assessment of Infants with Neonatal Abstinence Syndrome

by
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Faculty Disclosure

- I am the developer of the inter-observer reliability program for the Finnegan Scoring Tool.

Objectives

- 1) Describe the drugs that may cause NAS.
- 2) Identify screening methods used to diagnose neonatal drug exposure.
- 3) Describe the signs of NAS.
- 4) Describe the Finnegan Scoring Tool and how it is used in the management of NAS.

Case Study

- Baby boy A is a 36 week infant admitted to the NICU at 12 hours of age for tachypnea, tremors, vomiting, high pitched cry and hypertonicity. The mother had no prenatal care. What is going on with this baby?



Differential Diagnosis

- Hypoglycemia – glucose is 96
- Hypocalcemia - calcium is 9
- Hypomagnesemia – magnesium is 1.58
- Hyponatremia – Na is 140
- CNS insult – Apgars 8 & 9
- All must be considered and evaluated



Hamdan, et., al, 2012

Case Study

- Check further in the history and you find:
 - Mother's urine toxicology is positive for opiates, marijuana and cocaine.
 - Check with the labor & delivery room nurse and find the mother was in a methadone treatment program during the latter part of her pregnancy.
 - Mother has had her three other children taken away from her due to her drug use.

Final Diagnosis

- Neonatal Abstinence Syndrome
- Generalized disorder
- Licit & illicit drugs
- Poly drug use



What is Addiction?

- A chronic, relapsing, disease involving drug-seeking and abuse by long-lasting chemical changes in the brain
- Uncontrollable craving, seeking, and use of a substance such as a drug or alcohol

Fenton, Aivady & Hasin, 2013;
American Society of Addiction
Medicine, 2011.

NO?? ??? NO?? YES??
 YES?? YES?? NO?? YES??

NO?? **ARE INFANTS BORN
ADDICTED TO DRUGS?** YES??
 YES?? NO?? ???

YES?? NO?? NO??
 ??? YES?? ??? YES??



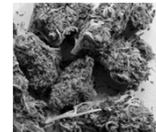
Drugs Associated with NAS

- Opioids:
 - Illicit
 - Heroin
 - Methadone
 - Buprenorphine
 - Prescription
 - Oxycodone
 - Percodan
 - Percocet
 - Oxycotin
 - Hydrocodone
 - Dilaudid
 - Vicodin
 - Lortab
- Non-opioid CNS Depressants
 - Benzodiazepines
 - Valium
 - Librium
 - Xanax
 - SSRI's
 - Celexa
 - Paxil
 - Zoloft
 - Barbiturates
 - Nembutol
 - Tuinal
 - Anticonvulsants
 - Antipsychotics
 - Alcohol



Drugs Associated with NAS

- Hallucinogens
 - PCP
 - Marijuana
- Stimulants
 - Cocaine
 - Methamphetamine
 - Ecstasy



Properties of Opioids

- Opiates are constituents or derivatives of constituents found in opium, which is processed from the latex sap of the opium poppy plant
- Semi-synthetic opioids such as heroin, oxycodone, and hydrocodone are derived from these substances

Action of Opioids

- Binds opioid receptors found principally in the CNS and the GI system
- Cough suppressant
- Analgesic effect by decreasing perception of pain, reaction to pain and increases the tolerance to pain

Types of Opioids

- Natural
 - Morphine & Codeine
- Semi-Synthetic
 - Hydrocodone, Oxycodone, Heroin, Buprenorphine
- Fully Synthetic
 - Methadone, Fentanyl, Tramadol

Properties

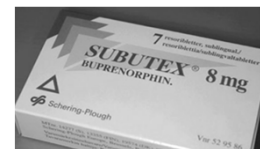
- Heroin
 - 20-25 times stronger than morphine
 - Very addictive
 - Fetal tissue within 1 hour
- Methadone
 - Substitute for heroin
 - Detected in fetal brain: 1-2 hrs
 - Metabolite present in urine up to 5 days

Buprenorphine

- Buprenorphine
 - Similar to methadone
 - Better outcomes/less relapse
 - Easily tapered for detox
 - Less withdrawal
 - Approved for use with non-pregnant women
 - Preliminary studies

Types of Buprenorphine

- Subutex
 - Buprenorphine
 - Sublingual tablet
- Suboxone
 - Buprenorphine + Naloxone
 - Naloxone
 - Keep people from abusing buprenorphine
 - Severe withdrawal if injected (IV, IM, Snorting)



Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D.

New England Journal of Medicine, December 9, 2010

Funded by NIDA

Findings

- 131 babies (58 buprenorphine; 73 methadone)
- % of neonates needing treatment was not significantly different (p=0.26)
- No difference in peak NAS scores (p=0.04)

Findings

- Significant differences
 - Buprenorphine vs Methadone:
 - 89% less treatment with morphine - mean total dose 1.1 mg vs 10.4 mg (p=0.0091)
 - 43% less time in the hospital - 10 days vs 17.5 days (p=0.0091)

Signs of Withdrawal in Neonate

Physiologic	Heroin	Methadone	Buprenorphine
Sneezing		X	X
Stuffy nose	X	X	X
Spitting/Drooling		X	X
Diarrhea	X	X	X
Vomiting	X	X	X
Poor feeding	X	X	X
Sweating	X	X	X
Tachypnea	X	X	X
Tachycardia			

Signs of Withdrawal in Neonates

Neurobehavioral	Heroin	Methadone	Buprenorphine
Fist sucking		X	
Irritability	X	X	
Restlessness	X	X	
Tremors	X	X	X
High-Pitched Cry	X	X	
Seizures		X	X
Yawning		X	
Disturbed sleep	X	X	
Increased crying		X	X
Hyper tonicity	X	X	X
Drowsiness			
Increased sleep			

Barbiturates/Alcohol

Commonalities

- depressants
- cross placenta readily
- addictive
- produce withdrawal



Alcohol Use During Pregnancy

Status	Age	Current	Binge	Heavy	Year
Pregnant	15-44	9.4%	2.3%	0.4%	2012 & 2013
Non-Pregnant	15-44	52.2%	22.9%	6.3%	2012 & 2013

Note: These data were averaged over 2 years

SAMSA (Substance Abuse and Mental Health Services Administration), 2013

Fetal Alcohol Spectrum Disorder

- Spectrum of deformities
- Criteria are ranked from 1 (normal) to 4 (significant of FAS)
- Elimination of the FAE term
- Includes dysmorphology scoring system
- More objective diagnosis

FASD

Definition of FASD	
Fetal alcohol syndrome (FAS)	<ul style="list-style-type: none"> • Abnormal facial features (smooth philtrum, thick upper lip, short palpebral fissure length) • Growth problems • CNS problems • Learning, memory, attention span, communication, vision or hearing
Alcohol related neurodevelopmental disorder (ARND)	<ul style="list-style-type: none"> • Intellectual disabilities • Problems with behavior and learning
Alcohol related birth defects (ARBD)	Problems with heart, kidneys, bones or hearing

Fetal Alcohol Spectrum Disorders Center for Excellence, 2013

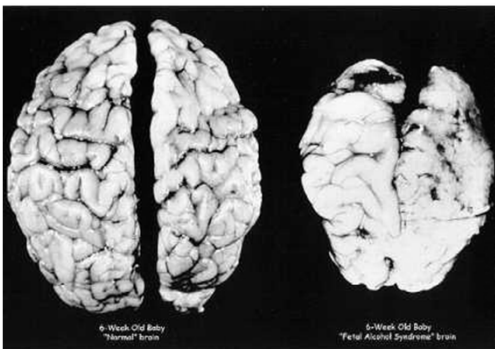
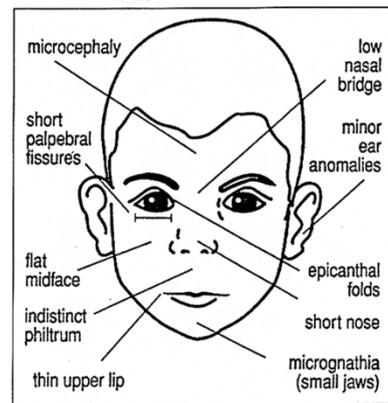
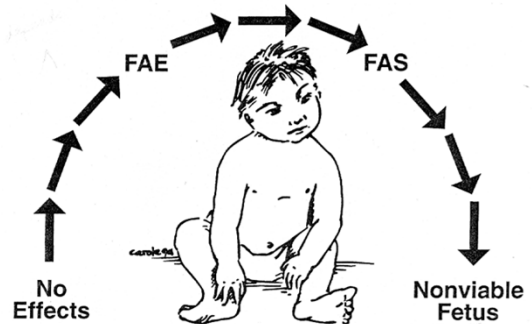


Figure 1. Continuum of Pregnancy Outcome of Women Who Drink Alcohol



Marijuana



- 1) Cannabis plant
- 2) Delta 9 Tetrahydrocannabinol (THC)
- 3) Crosses placenta
- 4) Detected in infant's urine 1st day & stool for up to 3 days



Nicotine

- Tobacco is the only source of nicotine
- Active ingredient in tobacco
- Stimulant & relaxant
- Causes relaxation, calmness, alertness, decreases appetite and increases metabolism through release of chemicals

Nicotine

- Release of:
 - Acetylcholine - ↑ concentration, memory
 - Norepinephrine - ↑ arousal
 - Acetylcholine & Beta-Endorphin - ↓ pain
 - Beta-Endorphin - ↓ anxiety
 - Dopamine - ↑ arousal and reward

<http://en.wikipedia.org/wiki/Nicotine>

Signs of Withdrawal in Neonates

Physiologic	Alcohol	Marijuana	Barbiturates	Nicotine
Sneezing			X	
Stuffy nose				
Spitting/ Drooling				
Diarrhea	X			
Vomiting	X			
Poor feeding	X			X
Sweating	X			
Tachypnea	X			
Tachycardia				

Signs of Withdrawal in Neonates

Neurobehavioral	Alcohol	Marijuana	Barbiturates	Nicotine
Fist sucking				
Irritability	X	X	X	X
Restlessness			X	X
Tremors	X			
High-Pitched Cry	X			
Seizures	X		X	
Yawning				
Disturbed sleep		X	X	
Increased crying			X	
Hyper tonicity				X
Drowsiness				
Increased sleep				

Phencyclidine (PCP)

- Psychoactive Drug
- Used as anesthetic before 1965
- Low doses: numbness in extremities & intoxication (staggering, slurred speech)
- Mod doses: analgesia & anesthesia
- High doses: convulsions

<http://en.wikipedia.org/wiki/Phencyclidine>

Phencyclidine (PCP)

- Psychological effects – out of body experiences, paranoia, hallucinations, euphoria, suicidal impulses
- Infant: metabolites found in urine for 1-7 days after mother stopped using 3 months before delivery

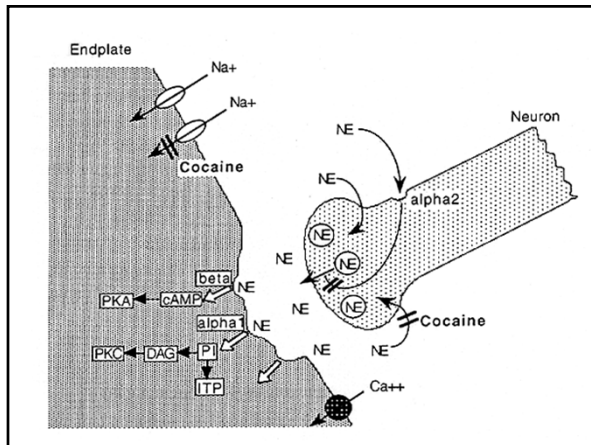
<http://en.wikipedia.org/wiki/Phencyclidine>

Crack/Cocaine



- Powerful CNS stimulant
- Crosses placenta
- Metabolite present in urine & stool (urine 1-2 days; meconium > 7 days)
- $t_{1/2} \sim 60 \pm 30$ min in adult; 6-8 hr in infant
- Powerful vasoconstrictor

Askin & Diehl-Jones, 2001



Methamphetamine

- 1) Highly addictive form of amphetamine
- 2) Stimulant like cocaine
- 3) man-made where cocaine is plant-derived
- 4) Damages neurons that produce serotonin & dopamine



NIDA Notes, September 2000; April 2002

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Increases the availability of serotonin
- Weak affinity for acetylcholine and dopamine
- Uses:
 - Depression
 - General anxiety disorder
 - Obsessive compulsive disorder
 - Eating disorders

http://en.wikipedia.org/wiki/Selective_serotonin_reuptake_inhibitor

Signs of Withdrawal in Neonates

Physiologic	PCP	Cocaine/ Crack	Methamphetamine	SSRI
Sneezing	X			
Stuffy nose				
Spitting/ Drooling				
Diarrhea	X			
Vomiting	X			
Poor feeding	X	X		X
Sweating				
Tachypnea				X
Tachycardia				

Signs of Withdrawal in Neonates

Neurobehavioral	PCP	Cocaine/ Crack	Methamphetamine	SSRI
Fist sucking	X			
Irritability	X			X
Restlessness				
Tremors				
High-Pitched Cry				
Seizures				X
Yawning				
Disturbed sleep				X
Increased crying	X			X
Hyper tonicity				X
Drowsiness		X	X	
Increased sleep		X	X	

Frequency of NAS

- 50-80% of heroin exposed infants develop NAS
- 60-90% of methadone and buprenorphine exposed infants develop NAS
- 60-80% of infants with NAS will require pharmacologic management



Handan, 2014; Farid, et al, 2008;
Sarkar & Dunn, 2006

Onset of Signs

- Depends upon:
 - Type of drug
 - Additional Substances
 - Timing of maternal dose
 - Infant metabolism
 - Gestational age and birth weight
 - Genetics????



Hudak & Tan, 2012;
Ashraf et al, 2014

Onset of Signs

- Alcohol – 3-12 hours
- Barbiturates - 1-14 days
- Caffeine – At birth
- SSRI – Hours to days
- Heroin (opioids with short t1/2) – 12-24/peak 72 hrs
- Methadone – 48 hours to as long as 7-14 days

Hamdan et al, 2012; Sanz, et al, 2005;
Pierog, et al, 1977; Tierney, 2013

Onset of Signs

- Cocaine/Methamphetamine
 - After the first week of life
 - First week: signs are drug effect
 - Irritability
 - Hyperactivity
 - Tremors
 - Increased crying
 - Increased sucking

Oro & Dixon, 1987

Premature Infant

- Lower risk of having signs of NAS
 - < 35 weeks More immature CNS
 - Less fat stores
 - Differences in total drug exposure



Doberczak, et al, 1991; Liu Aj, 2010;
Hudak & Tan, 2012

Genetics



- **Genes in adults (SNPs)**
 - Mu-opioid receptor (OPRM1)
 - Multidrug resistance (ABCB1)
 - Catechol-0-methyltransferase (COMT)
- **Study in Infants**
 - 5 hospitals in Mass & Maine
 - DNA samples were genotyped for SNPs, and then NAS outcomes were correlated with genotype.

Wachman, et al, 2013

Genetics



- **86 mother/infant dyads**
- **36wks or greater; exposed to methadone or buprenorphine**
- **Collected cord blood, maternal peripheral blood, or a saliva sample**
- **Outcome**
 - Variants in the OPRM1 and COMT genes were associated with a shorter length of hospital stay and less need for treatment.

Detection and Screening

Testing for drug exposure:

- Urine
 - Obtain as soon as possible after birth
 - High false-negative (up to 60%) rate because only reports recent drug exposure
- Meconium
 - Better than urine
 - Drug exposure from 16 weeks GA

Ostrea, 2001

Screening

- **Umbilical Cord**
 - 10 cm section of cord at delivery
 - Rise with sterile saline
 - Place in sterile container
 - ELISA based test
 - Information: www.usdtl.com



Montgomery et al, 2008

Compared to Meconium

Drug	UC
Amphetamine	Agreement – 96.6% Specificity – 97% Sensitivity – 95%
Opiates	Agreement – 95% Specificity – 96% Sensitivity - 78%

Montgomery, et al, 2005

Compared to Meconium

Drug	UC
Cocaine	Agreement – 99% Specificity – 100% Sensitivity – 75%
Cannabinoids	Agreement – 91% Specificity – 91% Sensitivity – 89%

Montgomery, et al, 2005

Detection and Screening

- **Hair Analysis:**
 - Radio immunoassay
 - Grows 1 cm/month
 - Metabolite present for life of hair
 - Tells you drug use for months
 - Gets into microfibrils
 - Can use neonatal hair



Ostrea, 2001

Neonatal Abstinence Scoring Tools

- Lipsit
- Neonatal Withdrawal Inventory
- Neonatal Narcotic Withdrawal Index
- Finnegan Neonatal Abstinence Scoring Tool

Lipsit, 1975; Green & Suffet, 1981; Zahorodny, 1998; Finnegan, 1975

Multiple Drug Use



Accurate in Assessing Infants for Signs of NAS

Assessment tool recommended to examine infants for signs of NAS is the Finnegan Scoring Tool

Finnegan Neonatal Abstinence Scoring Tool (FNAST)						
Patient ID:	Name:	Today's Weight:	DOB:	Date:	Comments	
Signs & Symptoms	Time	AM	PM	Score		
Central Nervous System Disturbances						
Crying: Excessive High Pitched						
Crying: Cont. High Pitched						
Sleeps < 1 Hr After Feeding						
Sleeps < 2 Hr After Feeding						
Sleeps < 3 Hr After Feeding						
Hyperactive Moro Reflex						
Markedly Hyperactive Moro Reflex						
Mild Tremors: Disturbed						
Mod-Severe Tremors: Disturbed						
Mild Tremors: Undisturbed						
Mod-Severe Tremors Undisturbed						
Increased Muscle Tone						
Excoriation (Specific Area)						
Myoclonic Jerk						
Generalized Convulsions						
Metabolic, Vasomotor And Respiratory Disturbance						
Sweating						
Fever < 101 (37.2-38.3c)						
Fever > 101 (38.4c)						
Frequent Yawning (> 3)						
Mottling						
Nasal Stuffiness						
Sneezing (>3)						
Nasal Flaring						
Respiratory Rate (> 60/Min)						
Respiratory Rate (>60/Min With Retractions)						
Gastrointestinal Disturbances						
Excessive Sucking						
Poor Feeding						
Regurgitation						
Score						
Total Score						
Adjusted Body Score						
Mean Observation Probability %						
Global Of Score 1						
Global Of Score 2						

Finnegan Neonatal Abstinence Scoring						
Patient ID:	Name:	Today's Weight:	AM	PM	Score	
Signs & Symptoms	Time	AM	PM	Score		
Central Nervous System Disturbances						
Crying: Excessive High Pitched						
Crying: Cont. High Pitched						
Sleeps < 1 Hr After Feeding						
Sleeps < 2 Hr After Feeding						
Sleeps < 3 Hr After Feeding						
Hyperactive Moro Reflex						
Markedly Hyperactive Moro Reflex						
Mild Tremors: Disturbed						
Mod-Severe Tremors: Disturbed						
Mild Tremors: Undisturbed						
Mod-Severe Tremors Undisturbed						
Increased Muscle Tone						
Excoriation (Specific Area)						
Myoclonic Jerk						
Generalized Convulsions						
Metabolic, Vasomotor And Respiratory Disturbance						

Myoclonic Jerk	3					
Generalized Convulsions	5					
Metabolic, Vasomotor And Respiratory Disturbance						
Sweating						
Fever < 101 (37.2-38.3c)	1					
Fever > 101 (38.4c)	2					
Frequent Yawning (> 3)	1					
Mottling						
Nasal Stuffiness						
Sneezing (>3)						
Nasal Flaring						
Respiratory Rate (> 60/Min)						
Respiratory Rate (>60/Min With Retractions)						
Gastrointestinal Disturbances						
Excessive Sucking						
Poor Feeding						
Regurgitation						

Remedy

- Developed item definitions
- Inter-Observer reliability program



Scoring Frequency

- Initially after transition (2-4 hours after birth)
- Then, Q 3-4 hours
- Treatment begins when score is 8 or greater



Scoring Frequency

- If no treatment required by 72 hrs scoring can be discontinued & discharged after 24 hrs



Important Points

- Scoring is dynamic and not static
- Signs of withdrawal present within the 3-4 hour scoring interval need to be scored



Techniques

- Check tone:
 - Pull-to-Sit method



D'Apolito & Finnegan, 2010

Techniques


- Check tone:
 - Upright Suspension method



D'Apolito & Finnegan, 2010

Techniques

Check tone:
• Flexion/Extension method



D'Apolito & Finnegan, 2010

Techniques

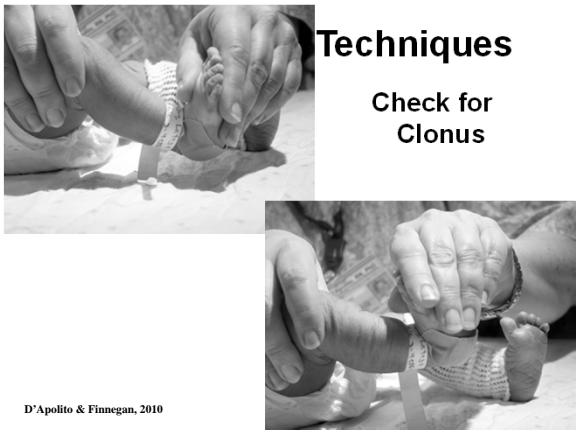
Moro Reflex



D'Apolito & Finnegan, 2010

Techniques


Check for Clonus



D'Apolito & Finnegan, 2010

Crying


- Score 2 if excessive high pitched and unable to self console in 15 sec or continuous up to 5 minutes despite intervention.
- Score 3 if unable to self console in 15 sec or continuous >5 min despite intervention.



D'Apolito & Finnegan, 2010

Sleep


- Based on longest period of sleep light or deep after feeding.
- Score 3 if <1 hour
- Score 2 if <2 hours
- Score 1 if <3 hours



D'Apolito & Finnegan, 2010

Moro Reflex

- *Hyperactive*: elicit from quiet infant.
- Score 2 for hyperactive-jitteriness that is rhythmic, symmetrical, and involuntary.
- Markedly Hyperactive:
- Score 3 for jitteriness as above with clonus of hands/arms. May test at hands or feet if unclear (more than 8 to 10 beats).



D'Apolito & Finnegan, 2010

Tremors Disturbed

- *Tremors are* involuntary, rhythmical muscle contraction and release involving to and from movements
 - Disturbed:
- Score 1 for mild/disturbed- of hands or feet while being handled.
- Score 2 for moderate/severe disturbed - of arms or legs while being handled.

D'Apolito & Finnegan, 2010

Tremors Undisturbed

- **NOT** touching baby after the infant has been handled (wait 15-30 seconds)
- Score 3 for mild undisturbed - Tremors of hands or feet when not handled.
- Score 4 for moderate/severe undisturbed - Tremors of arms and/ or legs or both when not handled.

D'Apolito & Finnegan, 2010

Increased Muscle Tone

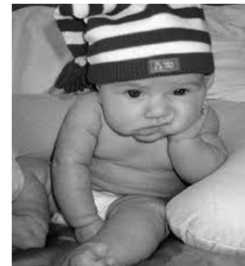
- *To test:* perform pull to sit maneuver.
- Score 2- no head lag with total body rigidity. Do not test while asleep or crying. Other maneuvers may be used.



D'Apolito & Finnegan, 2010

Excoriation

- Score 1 if present at nose, chin, cheeks, elbows, knees, or toes.
- Do not score for diaper area. This is related to loose or watery frequent stools.



D'Apolito & Finnegan, 2010

Myoclonic Jerks

- Involuntary twitching of muscle.
- Score 3 for twitching at face/ extremities or jerking at extremities (more pronounced than jitteriness of tremors).



D'Apolito & Finnegan, 2010

Generalized Seizures

- Score 5 for tonic seizures with extension or flexion of limb(s). Does not stop with containment. May include few clonic beats and/or apnea



D'Apolito & Finnegan, 2010

Sweating

- Score 1 for wetness at forehead, upper lip, or back of neck
- Do not score related to the environment (be consistent with linen)



D'Apolito & Finnegan, 2010

Fever/Frequent Yawning/Mottling

- Fever
- Score 1 if 37.2-38.3 C (101F or <).
- Score 2 if 38.4 C (>101F)
- Frequent Yawning
- Score 1 if >3 within interval.
- Mottling (marbled appearance (pink & white))
- Score 1 if present at chest, trunk, arms, or legs.



D'Apolito & Finnegan, 2010

Nasal Stuffiness/Sneezing

- Nasal Stuffiness - nares partially blocked from drainage with noisy respiration.
- Score 1 if present with/without runny nose
- Sneezing - individual or serial
- Score 1 for >3 during scoring interval



D'Apolito & Finnegan, 2010



Nasal Flaring

- Nasal Flaring - nostrils flared out during respirations.
- Score 2 if present



D'Apolito & Finnegan, 2010

Respiratory Rate

- Respiratory Rate - tachypnea >60 with/without retractions.
- Score 1 for rate >60 without retractions
- Score 2 for rate >60 with retractions
- Count for one full minute



D'Apolito & Finnegan, 2010

Excessive Sucking

- Rooting with attempts to suck fist, hand, or pacifier before or after feeding.
- Score 1 for >3 attempts noted.



D'Apolito & Finnegan, 2010

Poor Feeding

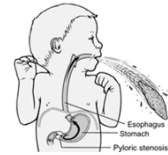
- Excessive sucking - (as described previously) but infrequent or uncoordinated with feeding. Gulping with frequent rest periods to breath.
- Score 2 if present



D'Apolito & Finnegan, 2010

Regurgitation/Projectile Vomiting

- Regurgitation - effortless (not associated with burp).
- Score 2 for 2 or more episodes
- Projectile Vomiting - forceful during or after feed.
- Score 2 for 1 or > episodes



D'Apolito & Finnegan, 2010

Loose/Watery Stools

- Loose stool - Loose, curdy, seedy, or liquid without water ring
- Score 2 if present
- Watery stool - Soft, liquid or hard with water ring
- Score 3 if present

D'Apolito & Finnegan, 2010

Optimal Scoring

- Important to know the item definitions
- Important to establish an inter-observer reliability strategy to assure accurate scoring
- Scoring is dynamic and not static



D'Apolito & Finnegan, 2010

Inter-observer Reliability

- The two nurses compare their scores
- Determine their percent agreement
- Goal: Achieve 90% agreement or greater

D'Apolito & Finnegan, 2010

Total Number of Items of Agreement	Total Number of Items of Disagreement	Percentage Score
21	0	100%
20	1	95%
19	2	90%
18	3	85%
17	4	80%

Reliability Testing

- Initial
- Each new staff member caring for the baby
- Two staff score at same time
- Determine a protocol – reliability assessment every 9, 10 or 11th score



Demonstration Video

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