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Neonatal Abstinence Syndrome (NAS)

A Pharmacologic and Rehabilitation Program that Promotes Narcotic Weaning and Autonomic Regulation Necessary for Infant Development

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Objectives

- Define Neonatal Abstinence Syndrome
- Identify some of the signs and symptoms of withdrawal
- List the medical management for an opiate exposed infant
- Discuss the rational for therapeutic intervention for a drug exposed infant

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Setting the Stage for High Risk Newborns

- Infections
- Diabetes, Obesity
- IVF (superovulation) (10-15%)
- Pregnancy Induced Hypertension
- Maternal age: <17yrs and >35yrs
- Previous history of prematurity
- Uterine and Placental Indicators
- Illegal Drugs
- Prescription Medication
- Drinking, Smoking

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Epidemiology: Public Health Issue

- 2009: Rate of NAS in the United States – 3.9/1,000 (out of 4.1 million live births per year)

- > 41% of pregnant women report illicit drug use.
- > 71% of pregnant women report use of prescribed pain medications
- > 10% of pregnant women report use of prescribed psychoactive medications

- Withdrawal signs develop in 55-94% of exposed newborns.

*2009 – National Survey on Drug Use and Health. US Dept. of Health and Human Services.

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Prescription Drug Use Among the Next Generation of Mothers

- 8% of teens, ages 12-17 years, use prescription drugs.
  - Pain medication: Vicodin, Oxycontin
  - Antidepressant: Prozac, Zoloft
  - Anti-Anxiety: Xanax
  - Stimulants: Adderal, Converta

* 2010: National Institute on Drug Abuse

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Cost of Care

- National Aggregate: 2009
  - Mean Hospital Charges in 2009: $53,400 ($1,780/day)
  - 78% of cost covered by Medicaid*

* 2010: National Institute on Drug Abuse

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Definition: Neonatal Abstinence Syndrome

- Constellation of behavioral and physiological signs and symptoms that occur in the newborn after the abrupt cessation of substances, most notably, Opioids.
  - NAS due to prenatal maternal drug use that results in withdrawal symptoms in the newborn.
  - NAS due to discontinuation of medications, such as Fentanyl or Morphine, used for pain therapy in the newborn.

* Neonatal Drug Withdrawal, AAP 2012

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Drugs Frequently Associated with NAS / Withdrawal

- Opiates and Narcotics
  - Fentanyl, Morphine, Hydromorphone, Buprenorphine, Heroin, Methadone (Half-Life 24-72 Hours)
  - Codeine, Oxycodone, Pentazocine, Propoxyphene
- Other Drugs
  - Barbituates (Half-Life 36-96 Hours)
  - Cocaine, Amphetamines (Half-Life <24 Hours)
  - SSRI's, Antihistamines

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Pathophysiology

- Illicit drugs can cause addiction in mother and physical dependence in the newborn, with passage of drugs across placental and CNS barrier.

- Drugs such as opiates cross maternal to fetal circulation quite readily, where they quickly accumulate due to immature liver metabolism and renal excretion.

- Abrupt discontinuation of drug at birth results in withdrawal in the newborn mitigated by increased Adenylyl cyclase activity with an abrupt rise in norepinephrine and subsequent autonomic symptomatology.

- Withdraw al is a function of half life: the longer the half life, the later onset of withdrawal.

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Lab Studies

- Urine toxicity: Only provides maternal drug use history a few days prior to delivery up to 72 hours after birth.
- Meconium analysis: Can be used to detect maternal opioids and cocaine exposure after 1st trimester up to 72 hours after birth. (Collected before contamination with formula).
- Hair analysis: Can indicate maternal use in the last trimester and up to 3 months postnatal life (Research laboratories).
- Umbilical cord tissue (immunoassay): Easy and rapid collection may foster its use.

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Proposed Hypothesis for Expression of NAS Symptoms

- Methadone affects maternal vagal tone responsiveness.
- Fetal adaptation within the uterine environment to methadone induced changes in maternal vagal tone correlate with later newborn dysregulation of autonomic nervous system.
- Newborn autonomic instability may be moderated by both genetic and epigenetic factors. (Jansson, 2007)

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Clinical Presentation of Autonomic Dysregulation

- CNS
  - High pitched cry, restlessness, sleeps <1-3 hours.
  - Hyperactive reflexes, tremors, myoclonic jerks.
  - Hypertonia, convulsions, frequent sneezing, yawning.
- Vasomotor
  - Sweating, mottling, temperature instability, apnea, fever, excoriation of skin.
- GI Disturbances
  - Poor feeding, excessive sucking or rooting,

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Finnegan Scale

- Scale assesses 21 signs of withdrawal, based on the following domains:
  - CNS
  - Vasomotor
  - GI Disturbances
- Start pharmacotherapy for 3 scores of >8
- Wean medications for 3 scores of <4
- Score of 1 for least adverse effect.
- Score of 3 for most adverse effect.

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Pharmacotherapy

- No optimum, absolute treatment established. Treat with medications in same drug class causing withdrawal.

- Opiate related and polydrug withdrawal.
  - Morphine: full mu receptor agonist (0.03mg/kg q 4); shorter acting
  - Methadone -full mu receptor agonist, longer acting, less fluctuation in levels at less frequent intervals; 0.05mg/kg q 6)
  - (Buprenorphine - Buprenorphine-partial mu receptor agonist ;shorter duration of treatment but potential ceiling effect in patients that may require adjunct therapy .
  - Phenobarbital, -poly substance use; prolonged half life; adjunct therapy rather than primary treatment.
  - Benzodiazepines for alcohol withdrawal, adjunct for calming.
  - Clonidine as primary or adjunct therapy; reduces global sympathetic tone. less efficacious than opioids, 1 report SVT,3 Myocarditis,1 SIDS (Leikin Clinic Toxicol, 2009)
  - NOTE: Tincture of opiate (0.1ml / kg q 4) and paregoric no longer recommended (due to additives, camphor, ethanol - 46%; benzoic acid.

* AAP – Policy Statement: Neonatal Drug Withdrawal Pediatrics, 2012; 129

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Mortality and Morbidity

- Long term mortality rate is low.
- Increased risk of SIDS :
  - 3.7 fold increase risk in methadone exposed infants.
  - 2.3 fold increase in cocaine exposed infants.
- Seizures
  - 2-11% incidence of seizures in infants withdrawing from opioids. (Lacroix. Addiction, 2004)
  - Breastfeeding encouraged except with Buprenorphone (buprenorphine and

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Children's Specialized Hospital: Infant Rehabilitation Program for therapy based interventions for infant withdrawal.

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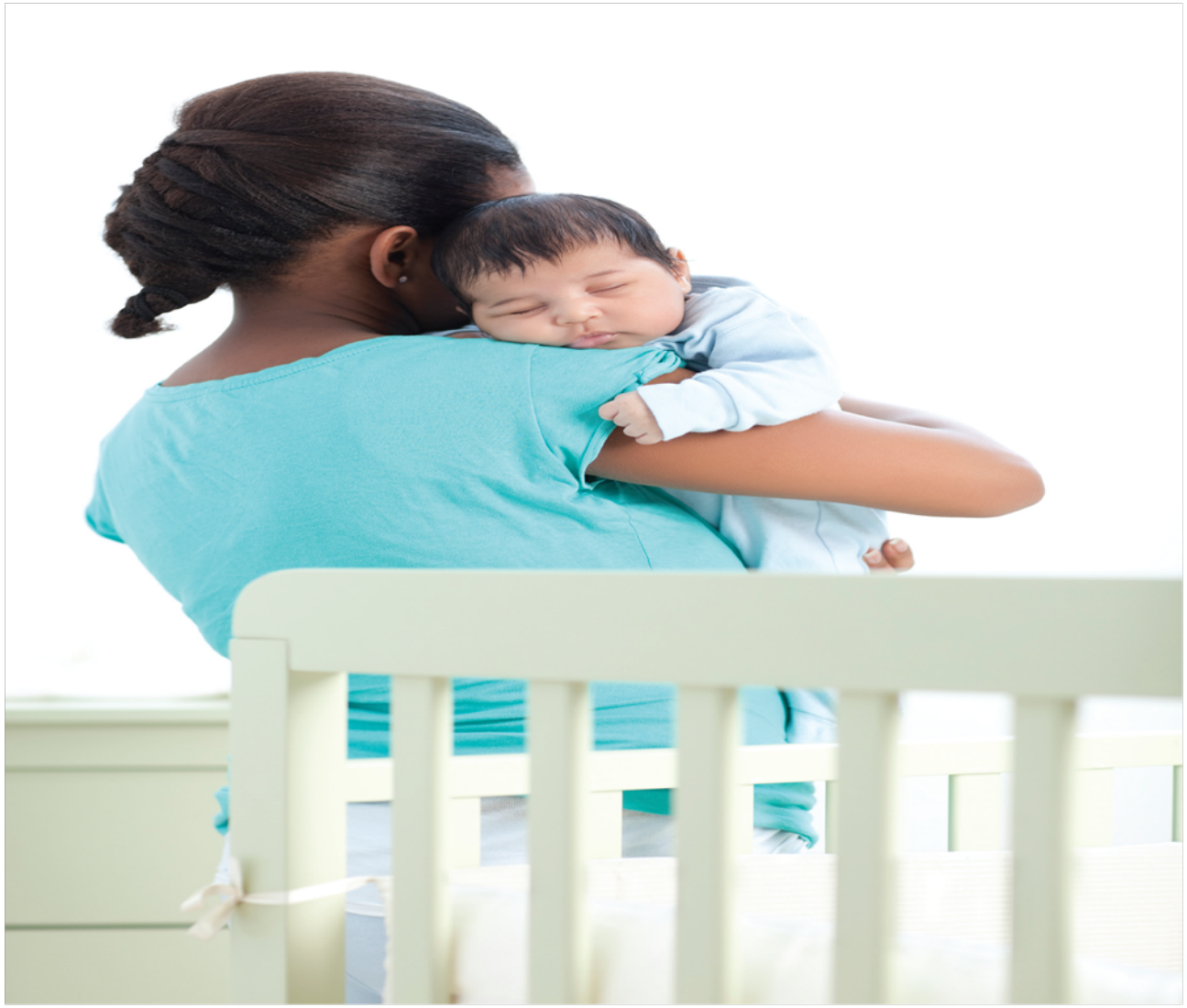
Neonatal Abstinence Syndrome (NAS) Program



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Behavioral Epigenetics: Impact on development

- Confounding variables such as withdrawal of opioids, genetic dysmorphisms (adult addiction) and environmental factors may all play a role in the pathogenesis of Neonatal Abstinence Syndrome and subsequent developmental issues.

- Fetal adaptation to unfavorable uterine environment may present as maladaptive or inappropriate physiologic and/or behavioral responses to extra uterine life. (Jansson)

- That is, vulnerable prenatal experiences may shape / moderate post natal autonomic and developmental outcome.

Lester, 2011

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Pathophysiology of Developing Systems: Rationale for Rehabilitation

- Developing Neuronal Systems, especially opioid exposed, need experienced assessment, stimulation and interventional therapy to positively impact on development of the newborn beyond the pharmacologic treatment.
  - Sensory recruitment of muscles
  - Motor patterns
  - Motor planning
  - Cognitive processing
  - Social interaction and integration
  - Guidelines for opioid addiction in adults recommend comprehensive modalities: pharmacotherapy, behavioral modifications and psychosocial therapy. (Amer Soc Addiction Medicine, 2001)

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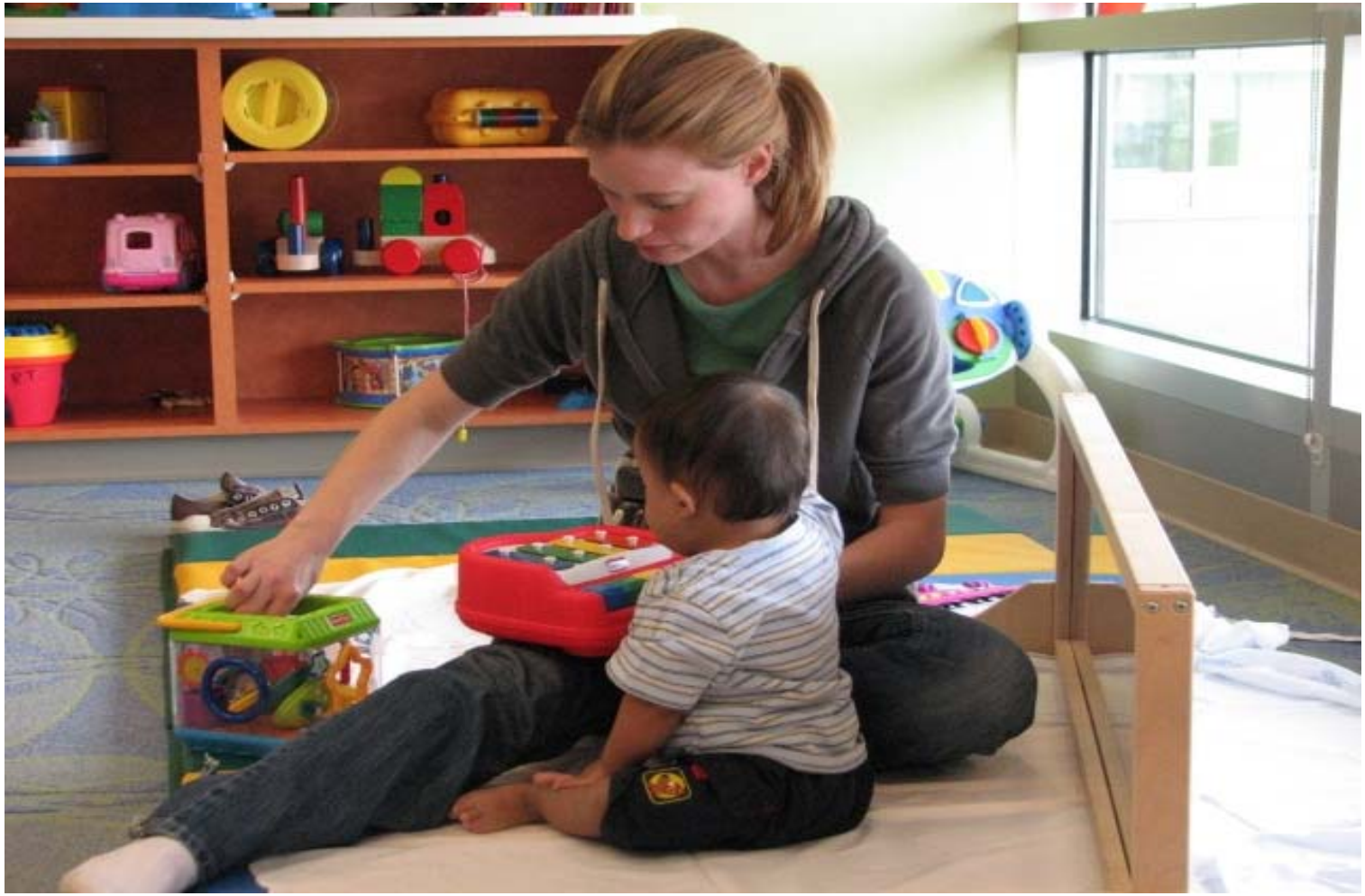
Healing – it comes from the heart



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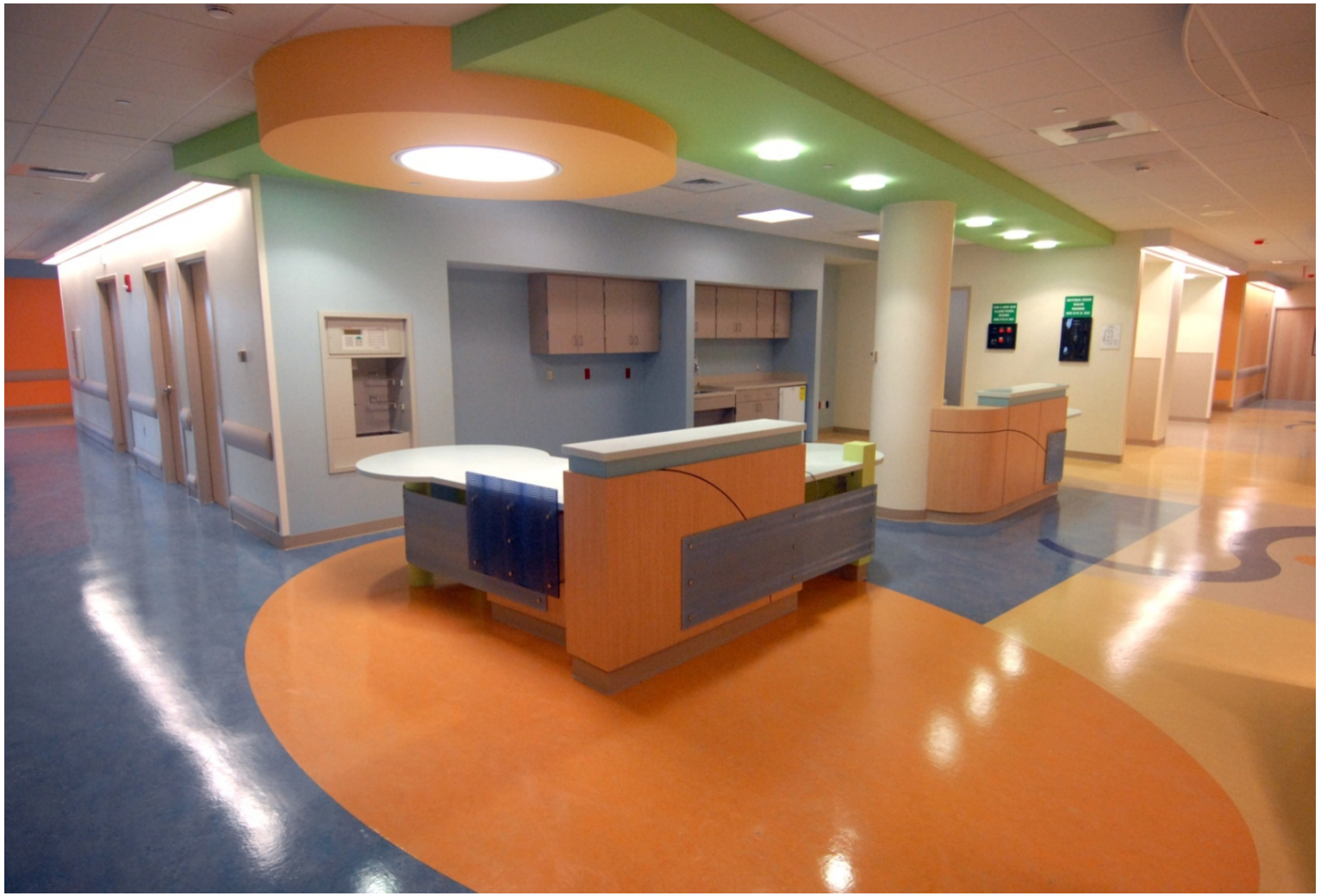
Healing Environment



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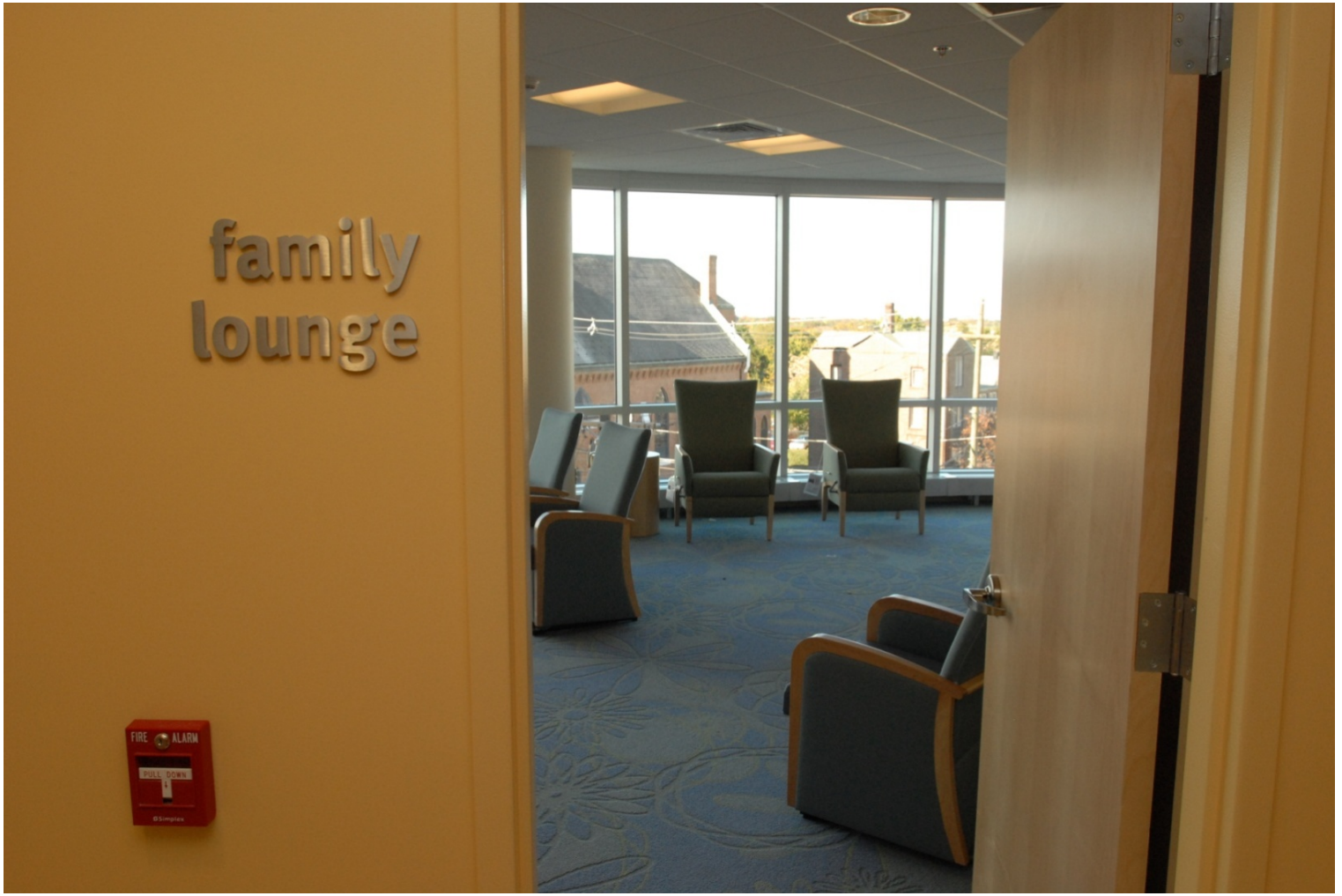
A Place Where Moms Can Relax



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Aquatics for Tots: Soothing sensory input for calming, tone management and awareness.

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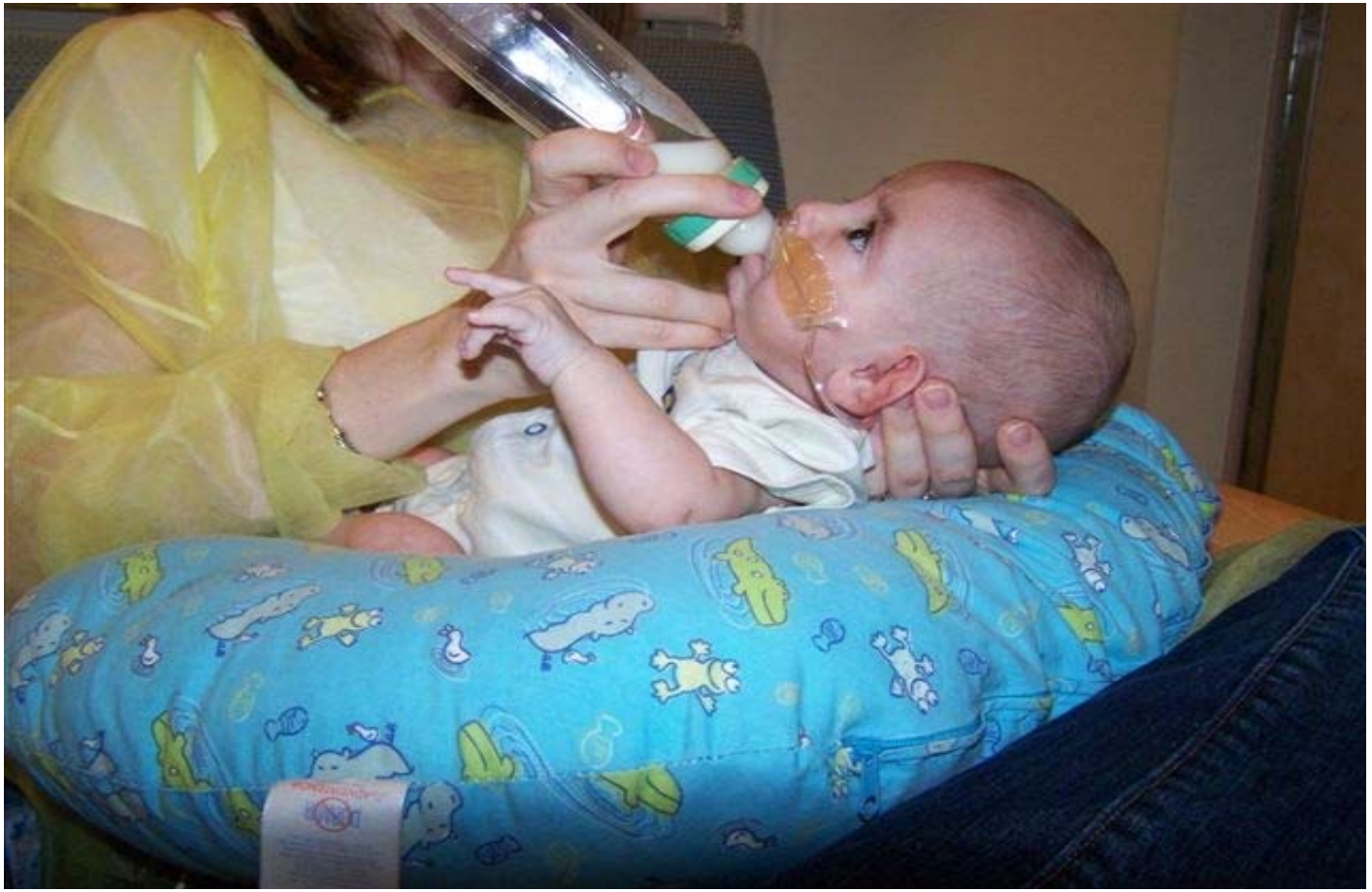
Motor Patterns: Vital Stimulation

- Program to enhance feeding outcomes in medically fragile infants.



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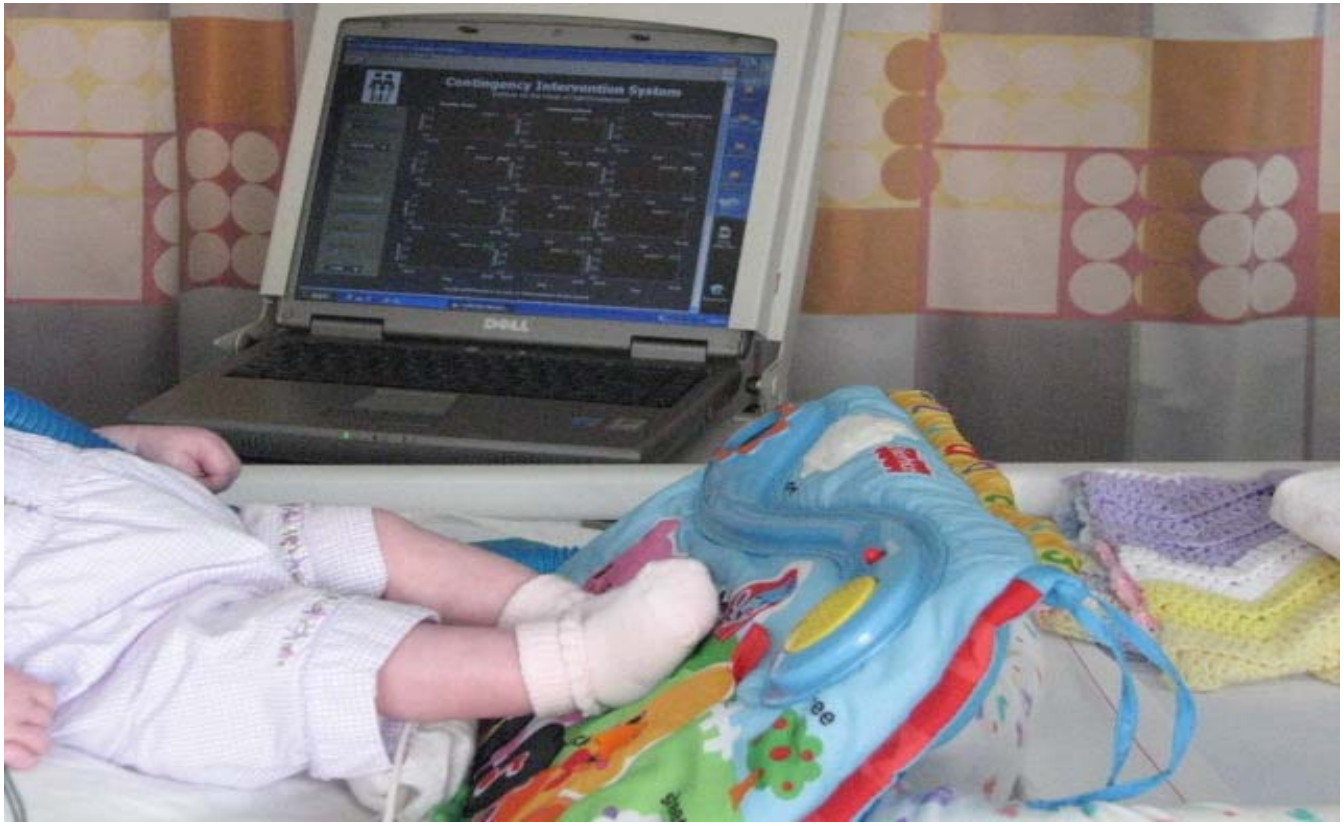
Motor Planning: Computer Mediated Learning

- Interactive modality stimulates infant motor response to sensory input.



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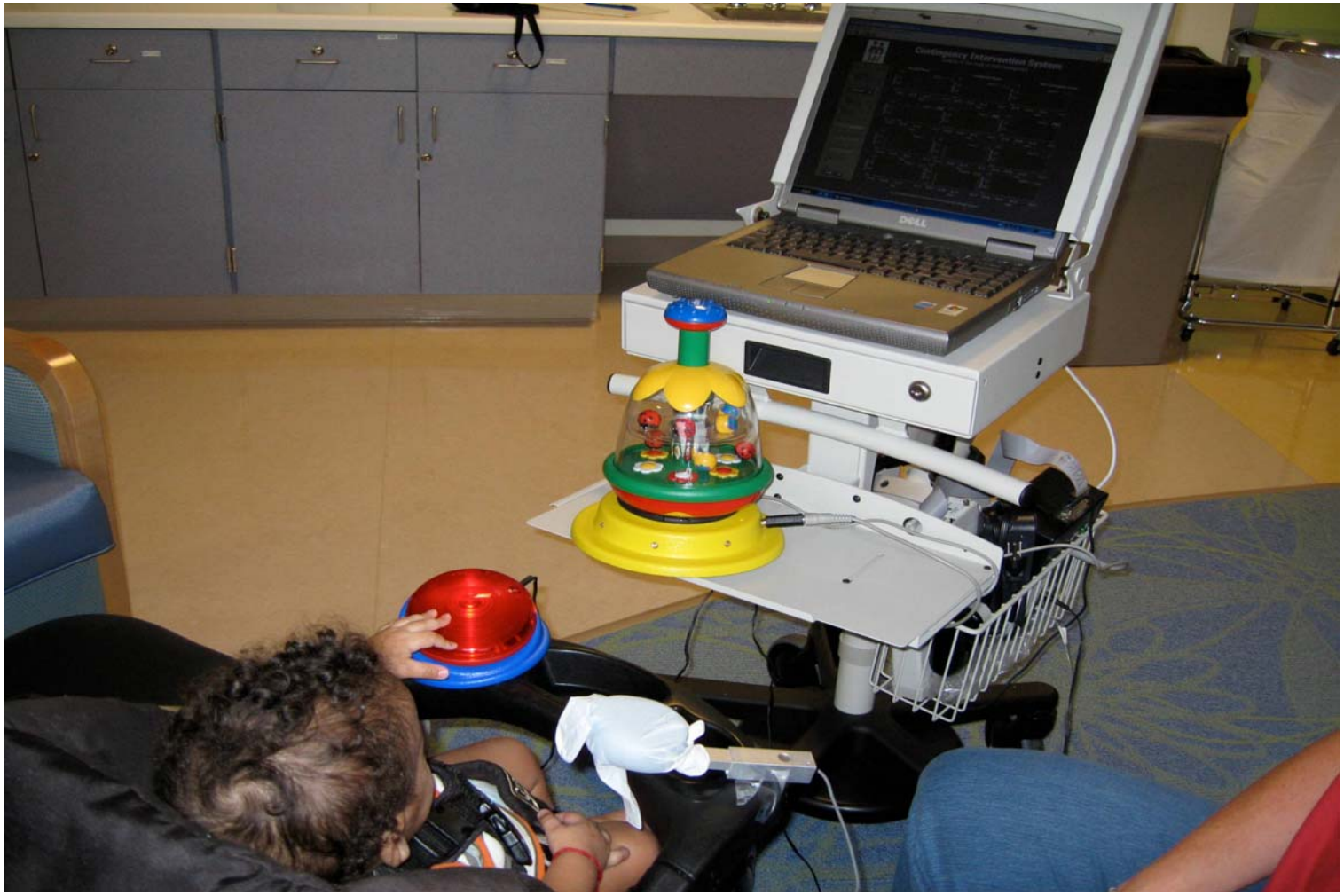
Cognitive re-enforcement: Computer Based Learning



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Sensory Recruitment of Muscles: Infant Massage

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Social Interaction and Integration: Group Therapy

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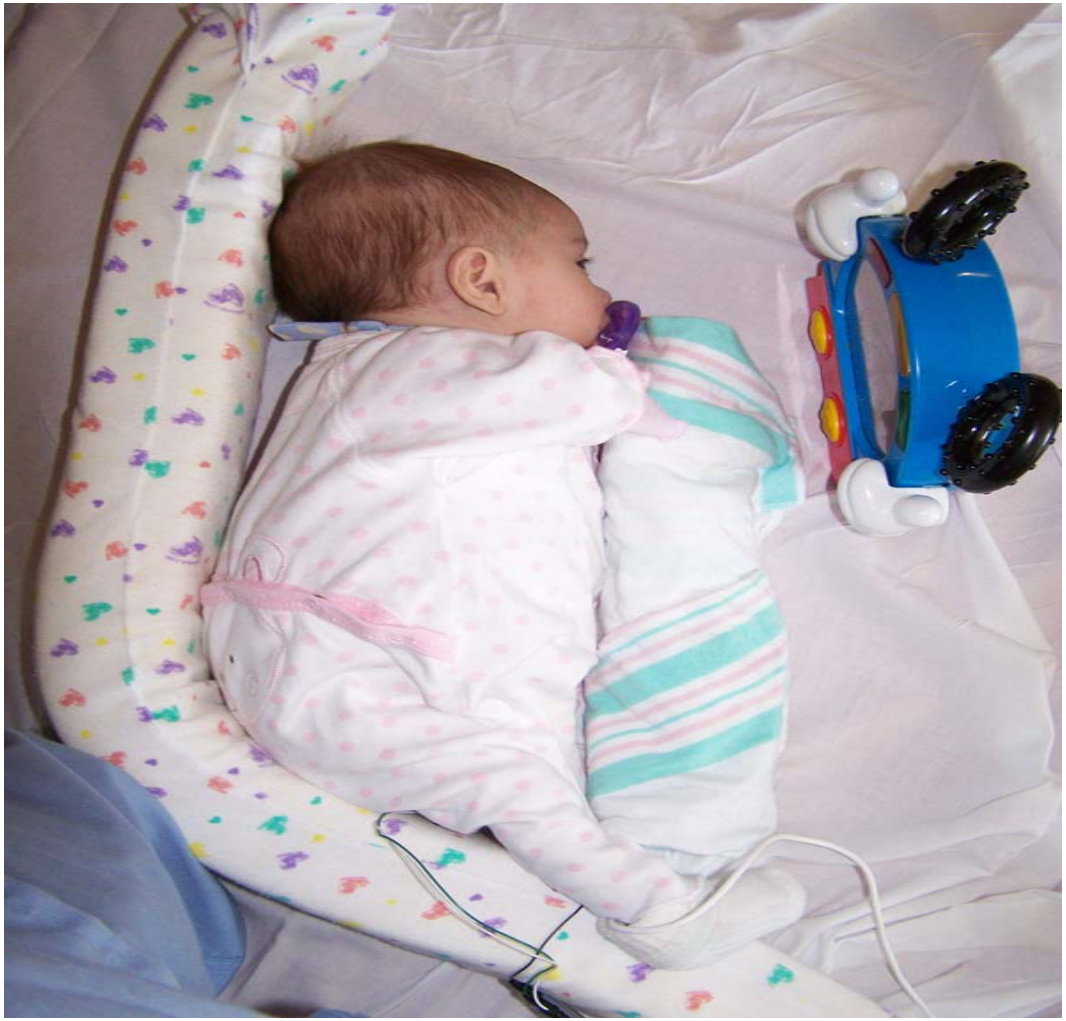
Self-calming strategies, music and positioning aids



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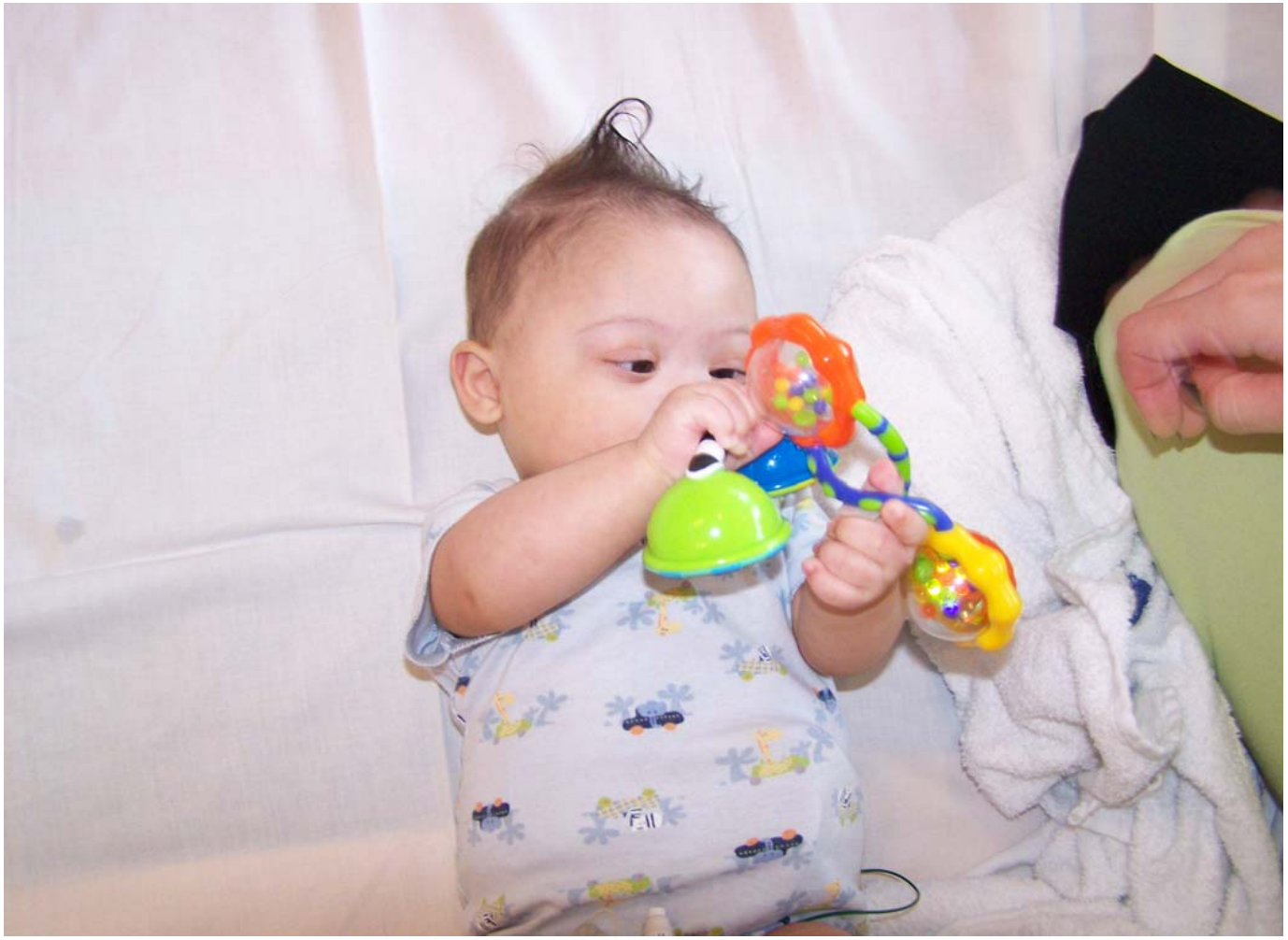
Sensory stimulation for cognitive processing



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Nutrition

- Small, frequent feedings to provide 150-220 kcal/kg
- Monitor growth velocity
- NAS exacerbates symptoms of GER
- Consider high calorie formulas when infant irritability or fatigue interferes with feeding
- Consider tube supplementation in infants with dysphasia
- Feeding specialist: When required
- WIC Program registration.
- **Breastfeeding is not contra-indicated in mothers on Methadone, but not recommended in mothers on Suboxone by the manufacturer.**

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Coordination of Home Services

- Physician services (PMD, Specialists, Apnea Testing)
- Nursing (CPR and Formula Training
- Home Nursing Services or Medical Day Car
- Medical or Positioning equipment
- Car seat safety check
- WIC referral and registration
- Provide medications prior to discharge

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NAS Program Outcomes: 2010 – 2012

- Infant Drug Screen: 32/33 97% Positive
  - Opiates: 14/33 42% of patients
  - Methadone: 17/33 52% of patients
  - Cocaine: 4/33 12% of patients
  - Benzodiazepine: 4/33 12% of patients
  - Polypharmacy including Subutex: 6/33 20% of

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Infant Medication: Admission and Discharge

Medication on Admission:	33/33	100%
• Methadone: patients	17/33	52% of
• Morphine: patients	7/33	21% of
• Morphine and Ativan: patients	7/33	21% of
• Ativan:	1/33	6% of patients
• Phenobarbitol: patients	1/33	3.4% of
•No Medication at Discharge:	32/33	97%

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•**Outpatient therapy programs have shorter hospital stay, but longer**

NAS Program Outcomes: 2010 - 2012

•Normal Pneumogram:	32/33	97%
•Age appropriate weight gain:	33/33	100%
•Calorie dense formula:	14/33	34%
•Discharge Disposition	ALOS	4-6 weeks *
• Home:	25/33	72%
• Foster:	5/33	17%
• Adoption:	1/33	3.4%
• Other facility:	1/33	3.4%

•Note- average duration of treatment in adult- 6 mos-2 years (Nicholls. 2010)

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Bayley Assessment

- Total Motor Composite: 20% low average – Refer to EIP
- Cognition: 15% low average range – Refer to EIP
- Language: 40% low average range – Refer to EIP
  10% significantly delayed – Refer to EIP
- Feeding: 5-7% refer to Outpatient Feeding Therapy

* Gestational age > 36 weeks

** Mean age: 55 days of life

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Outcomes: Program Services to Keep the Gains

- CSH Developmental Specialty Clinic and Follow-up
- Bayley Assessment at regular intervals
- EIP services for therapy
- 11 sites for OP therapy
- DCP&P to monitor family environment
- VNA - continued evaluation of patient
- CSH Pediatric Practice for patient and sibling
- CSH Medical Day Care

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Outcomes: Press Ganey Parent Satisfaction

- PT, OT, Speech and Recreational Therapies all scored higher than the **94th** percentile with respect to parent satisfaction, compared to other pediatric facilities.

- **100** percent of parents were confident with their training and could independently render their child's care.

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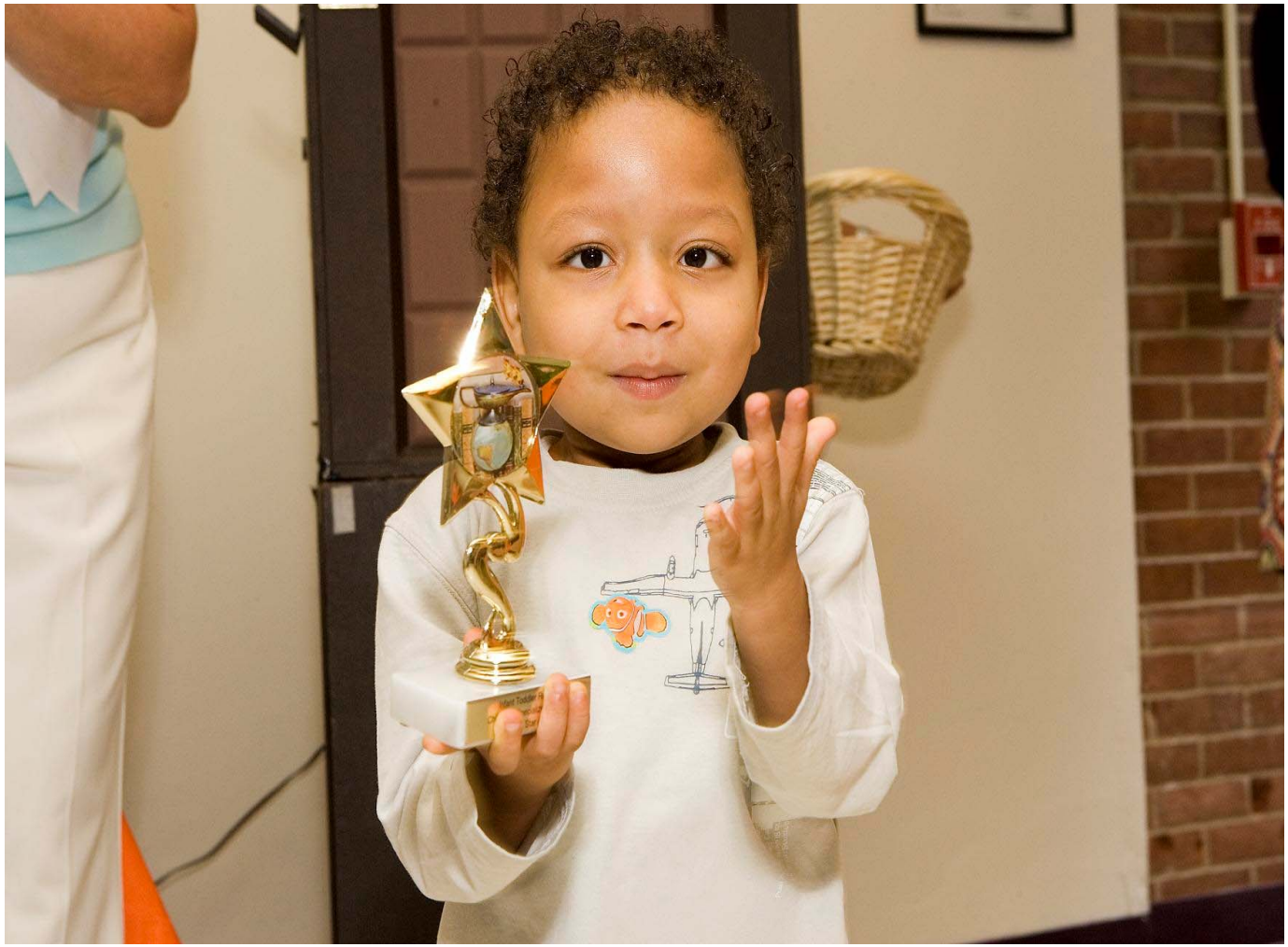
Children's Specialized Hospital: Extra Care. Extraordinary Results



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