ILPQC Mothers and Newborns Affected by Opioids (MNO) Workgroup

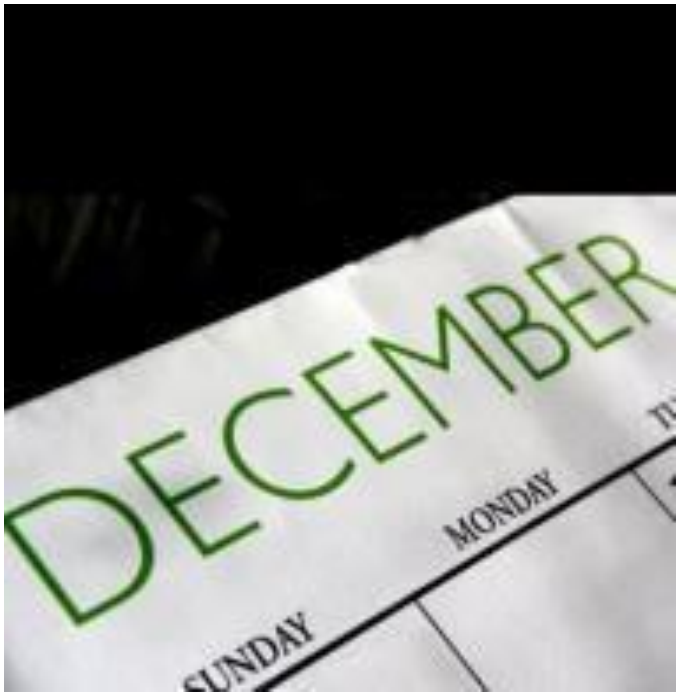
November 20th, 2017

1:00 – 2:00 pm

Overview

- Updates (5 min)
- MNO Survey (5 min)
- MNO AIM Statement (10 min)
- Literature Reviews
  - NAS Pharmacotherapy (12 min)
  - Discharge & Follow-up (12 min)
- Next Steps (5 min)

ILPQC 5th Annual Conference Save the Date!



Tuesday, December 19, 2017

Westin Lombard

REGISTRATION IS OPEN!

https://www.eventbrite.com/e/illinois-perinatal-quality-collaborative-5th-annual-conference-tickets-39493819076

Annual Conference Hotel Block Room Reservations Now Available

- https://www.starwoodmeeting.com/events/start.action?id=1710035949&key=21CC118E
- Group rate of $139 single/double available until Nov 27, 2017

NOW ACCEPTING Poster Session Abstracts for 5th AC

- We are asking **ALL ILPQC TEAMS** to submit an abstract sharing the great Severe Maternal HTN or Golden Hour QI they've done including plans for sustainability / ongoing work in 2018
- Teams are welcome to submit additional abstracts regarding mothers / newborns affected by opioids, IPLARC, and patient & family engagement or other QI projects teams want to share
- Submit abstracts by **TODAY** to qualify for awards of excellence.
- Late Breaking abstracts may be submitted through Nov 27th

Submit abstracts online: https://www.surveymonkey.com/r/ILPQC_5th_ACAbstractSubmission

2017 Annual Conference Agenda

8:00-8:45	Welcome – TBD & Year in review – Ann
8:45-9:30	Keynote - Matthew Grossman (MNO, Neonatal/Newborn)
9:30-9:45	Break
9:45-11:15	3 leaders from State PQCs (Carole Lannon- OH, Julie DeCesear-OH, Brenda Barker - TN)
11:15-12:00	Plenary- Tamela Milan (MNO, Patient & Family)
12:00-1:30	Lunch & Poster Session
1:30-2:15	Plenary- Melinda Campopiano (MNO, OB)
2:15-3:00	Plenary - Amy Crockett (IPLARC)
3:00-3:15	Break
3:15-5:00	Breakouts: OB, Neo, Patient & Family Engagement
5:00-5:15	Wrap-Up & Evaluation

GH Teams Survey

Due Monday, November 27th

https://www.surveymonkey.com/r/NeoTeamsSurvey2017

One GH Team member fills out per team

MOC Part IV Credits

Coming in 2018 for physicians participating in the MNO Initiative

Current MNO Processes Survey

- To understand resources available and used by hospitals
- To understand hospital team MNO processes
- Distribute survey to MNO teams in early 2018

- What is the State of Illinois Opioid Action Plan?
- What is the IDPH NAS Committee
- What is the ILPQC MNO Workgroup doing?

MNO Timeline

Tasks	Oct-17	Nov-17	Dec-17	Jan-18	Feb-18	Mar-18	Apr-18	May-18
Develop QI Initiative (AIMS, Measures, Data Form) & Identify Clinical Leads								
Recruit and Launch Wave 1: with OB & Neonatal Teams (test data process)								
Launch Wave 2 with all hospital teams								

Ongoing input from IDPH NAS Committee, OB Advisory Workgroup, AIM Maternal Opioid Collaborative

IDPH NAS Committee Definition

Neonatal Abstinence Syndrome refers to the collection of signs and symptoms that occur when a newborn prenatally exposed to prescribed, diverted, or illicit opiates experiences opioid withdrawal. This syndrome is primarily characterized by irritability, tremors, feeding problems, vomiting, diarrhea, sweating, and, in some cases, seizures.

MNO DRAFT AIM

To decrease the amount of pharmacologic therapy in substance exposed newborns

DRAFT

MNO DRAFT AIM Considerations

- Term/35+ weeks newborns?
- Infants admitted to NICU or Level II nursery for reasons outside of NAS

DRAFT

Literature Review

NAS Pharmacotherapy group

Venkata Majjiga,MD, Christine Emmons,RN
Facilitator-Perinatal outreach, Ann Downey, MD

Methadone

- Mechanism of action: A synthetic opioid that is primarily a mu-opioid agonist. It has actions and uses similar to those of morphine. With a half life of 24 to 36 hours

- Adverse Effects - Respiratory depression, Ileus and delayed gastric emptying

- Contraindicated in respiratory depression, suspected gastrointestinal obstruction, including paralytic ileus

- Dose: Initial dose**:** 0.05 to 0.1 mg/kg per dose orally every 6 to 24 hours, then follow a weaning protocol

- Black Box Warning

- Serious and fatal respiratory depression
- QT interval prolongation and serious arrhythmias, including torsades de pointes
- Concomitant use of CYP inhibitors or discontinuation of CYP inhibitors can cause a fatal methadone hydrochloride overdose

Breast-Feeding Considerations

- is excreted in breast milk; the dose to a nursing infant is 2% to 3% of the maternal dose and peak levels appear in breast milk 4 to 5 hours after an oral dose

Neofax May 2016

Morphine

- Mechanism of action: Opioid, acts on the mu-opioid receptors with half life or 2 to 4 hours
- Clinical Use: Opioid replacement therapy is the preferred first-line pharmacologic intervention (supported by the AAP)
- Dose: 0.06-0.24 mg/kg/day PO titrated to manage clinical signs of NAS in divided doses
- Contraindications: Respiratory depression/CNS depression. Cautious use in patients with renal or hepatic impairment
- Drug Interactions: Cautious use in patients receiving other CNS depressants
- Safety: Recommend use of smallest concentration of oral solution available to reduce risk of dosing errors (2 mg/ml)

Lexi comp Online ™, Pediatric & Neonatal Lexi-Drugs Online ™, Hudson, Ohio: Lexi-Comp, Inc.; 2017

Opiate treatment for opiate withdrawal in newborn infants

Opiates compared to supportive care

May reduce time to regain birth weight and duration of supportive care but increase duration of hospital stay

Methadone Compared with morphine:

- Median days of NAS treatment (21 versus 14 days) p=0.008 in a double-blind, randomized trial (n=78) (Brown 2015)
- Statistically significant decreases in length of hospital and NICU stay, length of treatment, maximum opioid requirements, and total cost were found when neonates treated for NAS with oral morphine (Young 2015)
- Newborns with NAS treated with morphine had significantly higher scores in Cognitive and Gross Motor domains (Burke 2015)

Methadone Compared with sublingual buprenorphine: (Hall 2015)

- Shorter duration of opioid treatment (9.4 vs 14 days)
- Shorter length of inpatient stay (16.3 vs 20.7 days)

Cochrane Database Syst Rev. 2010 Oct 6;(10):CD002059
Brown MS, *J Perinatol* 2015
Hall ES, *J Pediatr* Dec15, 2015

Phenobarbital (PB)

- Efficacy: Long-acting barbiturate that enhances the inhibitory neurotransmitter GABA causing CNS depression
- Can be effective for neurologic symptoms, does not improve GI symptoms.
- Safety Profile: Contains alcohol (10-15%), sedation. High treatment failure. CNS depression, impaired sucking reflex, has ½ life of 40 to 70 hrs.
- Dosing Frequency: Load 16mg/kg, maintenance 1-4mg/kg/dose Q12H. Levels of 20-30 mg/dL effective for NAS.
- Impact on Length of Stay: Studies show a longer duration of therapy, but can discharge home on PB wean. Need follow up visits.
- Summary of the Evidence: Drug of choice for non-narcotic withdrawal (AAP 2014) or polysubstance use.
- Combination Use: adjunct therapy With opioids. AAP and OPQC provides dosing regimen for adjunct therapy.

Sedatives for opiate withdrawal in newborn infants

Phenobarbitone vrs supportive care alone

- Did not reduce treatment failure or time to regain birthweight,
- Resulted in a significant reduction in duration of supportive care (1 study)

Opiate versus phenobarbitone

- no significant difference in treatment failure (4 studies)
- significant reduction in treatment failure in infants of mothers using only opiates (Finnegan 1984)
- a significant reduction in days treatment and admission to the nursery for infants receiving morphine (Jackson 2004)
- a reduction in seizures, of borderline statistical significance, with the use of opiate (Kandall 1983)
- Compared to diazepam, opiates reduce the incidence of treatment failure

Phenobarbitone vrs diazepam, meta-analysis of two studies

- Phenobarbitone resulted in a significant reduction in treatment failure (2 studies)

Phenobarbitone vrs chlorpromazine, no significant difference in treatment failure (1 study)

Cochrane review 2010

Clonidine (C)

- Efficacy: Centrally acting alpha 2 adrenergic receptor agonist used as adjunct therapy. Stimulates presynaptic adrenergic receptors→inhibits CNS sympathetic outflow and reducing norepinephrine. It ameliorated autonomic overactivity.

- Safety Profile: No sedation, well tolerated, no alcohol, long half-life (44-72H), need to monitor levels. May cause hypotension, metabolic acidosis. Abrupt discontinuation may cause rapid rise of BP, HR.

- Dosing Frequency: Load 0.5-1microgram/kg, Maintenance 0.5-1.25microgram/kg/dose Q4-6 hours.

- Impact on Length of Stay: Compared to PB as secondary agent, LOS may be increased. Though total drug exposure significantly decreased.

- Summary of the Evidence: No large scale studies have been published regarding clonidine and NAS.

- Combination Use: With opioids for combination use.

- Available Evidence Based Protocol: AAP provides dosing regimen for adjunct use.

Take Home Points on Phenobarbital and Clonidine

- Evidence is lacking for ALL secondary agents. Additional prospective studies are needed.

- AAP 2014: PB is the drug of choice for non-opiate NAS. Both medications are options for secondary agents. No global recommendation on which one. Data are lacking.

- OPQC: Consider PB if polysubstance use suspected/confirmed AND CNS symptoms predominate and morphine dose at “maximum” or unable to wean for 2 days. Can discharge with ongoing PB wean. Centers may opt for C due to lack of PB evidence. It is NOT recommended to discharge home on C.

- Systematic Review of Clonidine (*Annals of Pharmacotherapy* 2016): Limited data suggest that C in combination or as monotherapy may be as effective as standard opioids with minimal adverse effects and shorter treatment time.

- VON: No specific recommendations for pharmacologic therapy.

Chloral Hydrate

- Drug Class: Sedative hypnotic

- Clinical Use:
  - Combined with phenobarbital as first line agent in some European studies
  - Some literature cite the use of chloral hydrate as an adjunct agent to clonidine
  - AAP does not support its use as first line or adjunctive treatment

- Dose: 25 mg/kg/dose q 6-8 hours

- Contraindications: Hepatic impairment, renal impairment. Prolonged use is associated with elevated direct bilirubin

- Drug Interactions: may enhance the CNS depressant effects of opioid analgesics

- Safety: Some dosage forms contain Sodium Benzoate (metabolite of benzyl alcohol) which pose the risk of toxic levels (gasping syndrome, as evidenced by metabolic acidosis, respiratory distress, gasping respirations, and CNS dysfunction). This condition may be fatal.

Lexi comp Online ™, Pediatric & Neonatal Lexi-Drugs Online ™, Hudson, Ohio: Lexi-Comp, Inc.; 2017

Chloral Hydrate

Dabek, M.T., et al 2013

Citing surprisingly high cumulative doses of chloral hydrate, the authors reported a planned change in first line medication to morphine

Esmaeili et al 2010

Clonidine as first line and Chloral Hydrate as adjunct when compared to Morphine as first line with Phenobarbital as adjunct

- had lower length of stay (32 vs 44)
- lower days of treatment (14 vs 35 days)

While there were no adverse events related to the use of chloral hydrate in this Study, evidence in the literature doesn't cite a high safety profile for this agent

Dabek, M.T., et al *Klinische Padiatrie 2013; 225:252-256*
Esmaeili, A et al *Foundation Acta Paediatrica 2010 99, 209-214*

Pharmacotherapy in NAS

- No studies to date have compared the **use of different withdrawal score thresholds for initiating pharmacologic intervention** on short-term outcomes

- Withdrawal from opioids or sedative-hypnotic drugs may be **life-threatening**, but ultimately, **drug withdrawal** is a self-limited process

- Unnecessary pharmacologic treatment will **prolong drug exposure and the duration of hospitalization** to the possible **detriment of maternal-infant bonding**.

- The only clearly defined benefit of pharmacologic treatment is the **short-term amelioration of clinical signs**.

- Studies have not addressed whether pharmacologic management related to neonatal drug withdrawal is
  - decreased **long-term morbidity** of affected infants, or
  - augments the risk of neurobehavioral and other morbidities

- **May reinforce a maternal disposition to rely on drugs** for the treatment of infant discomfort or annoying behavior

Shifting the paradigm of treatment for NAS

Grossman et al a New Haven Study

Discontinued use of FNASS scores to guide pharmacologic management

- assessment focused on 3 simple parameters: If the infant was able
  - to breastfeed effectively or to take ≥1 oz from a bottle per feed,
  - to sleep undisturbed for ≥1 hour
  - if crying, to be consoled within 10 minutes

  then morphine was neither started nor increased regardless of other signs of withdrawal

If the infant did not meet these criteria, staff first attempted to maximize nonpharmacologic interventions; if these attempts were unsuccessful, morphine was initiated or increased

Before this study they used to reduce the initial dose of morphine by not >10% every 24 to 48 hours.

Rapid Morphine Weans

- To allow for decreases in the peak dose of morphine by 10% as often as 3 times a day
- If assessment criteria was met, no additional morphine given

Pediatrics. 2017;139(6):e20163360

Discharge and Follow-up: Important Part of the Continuum of NAS Care

Literature Review

Donna Lemmenes, Elyssa Galloway, Jennifer Gilpin, and Kenny Kronforst

11/14/2017

Discharge and Follow-up Outline

- Discharge criteria
  - Minimum criteria defined
  - Australian experience
  - Ontario experience

- Post-discharge care
  - Short term adverse outcomes
  - Empowering transition home
    - Kalamazoo County NAS Prevention and Treatment Project
    - CRADLE project
    - Local Community Resources
  - Long term adverse outcomes
    - Follow-up- key areas of focus

Elements of the Discharge Process

- Primary goals include
  - Promoting normal growth & development
  - Averting/minimizing negative outcomes

- Minimal criteria for discharge
  - No major signs of withdrawal
  - Maintaining scores with minimal medication support
  - Infant is sleeping well
  - Infant is feeding well and gaining weight

- Home environment needs to be safe and stable

Kocherlakota, P. Neonatal Abstinence Syndrome. Pediatrics 2014; 134;e547; DOI 10.1542/peds.2013-3524

Discharge Criteria- the Australian Experience

- Multidisciplinary team considers both mother and infant health status, any psychosocial issues and the future care-giving environment- if appropriate, proceeds with discharge planning
- Discharge planning includes pediatric assessment and follow-up, social work or child at risk assessment, drug health assessment, parental education including safe sleeping and other best health practices, storage of drugs in the home and referral to support services
- Formal transfer of responsibilities from the hospital to community services

Western Australian Centre for Evidence Based Nursing and Midwifery, January 2007

Infants **Not Eligible** for Discharge

- Infant clinical status
  - > 10% weight loss and younger than 5 days old
  - If continued assessments for withdrawal symptoms are required

- Concern for child welfare
  - Concern for continued maternal drug use
  - Suspected infant neglect or abuse
  - Suspected home violence
  - Court order preventing baby from being discharged home
  - Inadequate home support or acceptance of assistance from external agencies
  - Inadequate housing or material goods
  - Inadequate parenting skills (such as failure to consistently demonstrate the ability to feed and provide appropriate care for the infant during hospitalization)
  - Inability to participate in a required pediatric follow-up program

Western Australian Centre for Evidence Based Nursing and Midwifery, January 2007

Infants **Eligible** for Discharge

- Mother-baby pair has been stabilized/managed
- Infant is at least five days old
- Infant is feeding well and gaining weight
- Improvement/resolution of withdrawal symptoms- neonates typically discharged on morphine therapy
- Plan in place to address any child protection concerns
- Referrals to appropriate community support agencies have been made
- On-going methadone treatment has been arranged and confirmed

Western Australian Centre for Evidence Based Nursing and Midwifery, January 2007

Discharge Criteria- the Ontario Experience

- Recommendations
  - Infant primary care provider identified prior to discharge
  - Professional home visitor to continue to address factors and support once the baby is discharged home
  - Developmental follow-up in place for baby
  - Develop links between child protection services and the primary health care team as a case management tool
  - Ensure that the substance abusing mom is linked to all psychosocial, medical, addiction services and social services to make it safe for the baby to go home
  - Plan or prevent future pregnancies through education
  - Teach foster parents to recognize withdrawal symptoms in an asymptomatic infant at risk for NAS

Provincial Council for Maternal and Child Health, NAS Clinical Guidelines, 2012.

Post-discharge Care

- A multidisciplinary approach that includes parental participation is extremely helpful in the management of neonates with NAS
- Goal is to avoid short and long term adverse outcomes
  - Follow-up to include
    - neurodevelopmenal assessments to identify motor deficits, cognitive delays or relative microcephaly
    - psycho-behavioral assessments to identify hyperactivity, impulsivity and ADHD in preschool-aged children, as well as school absence, school failure and other behavioral problems
    - ophthalmologic assessment to identify nystagmus, strabismus, refractive errors, and other visual defects
    - growth and nutritional assessments
    - family support assessments

Kocherlakota, P. Neonatal Abstinence Syndrome. Pediatrics 2014; 134;e547; DOI 10.1542/peds.2013-3524

Adverse Post-discharge Outcomes

- Readmissions
  - 2.5 times as likely to be readmitted to the hospital within 30d of discharge compared with full-term infants born without complications
  - Most common indication- drug withdrawal
- Child abuse
  - Safety of the infant is paramount and often includes coordination with child welfare systems
- Neglect
- Important for families to be supported on the transition from hospital to home

Patrick et al. Risk of Hospital Readmission Among Infants with NAS. Hosp Pediatrics. 2015 October: 5(10): 513-519
Pryor et al. The opioid epidemic and neonatal abstinence syndrome in the USA: a review of the continuum of care. Arch Dis Child Fetal Neonatal Ed 2017; 102:F183-187. doi:10.1136/archchild-2015-310045

Empowering the Transition Home

- Study compared safety/efficacy of a traditional inpatient only approach with a combined inpatient/outpatient methadone program
  - Retrospective review (2007-2009)
- Included infants born to mothers maintained on methadone or buprenorphine in an antenatal substance abuse program
  - Traditional group = 75 pts
  - Combined group = 46 pts
  - All received methadone as inpatient

Backes, C.H., Backes C.R., Gardner, D., et al. (2012). Neonatal Abstinence Syndrome (NAS): Transitioning Methadone Treated Infants From An Inpatient to an Outpatient Setting. J Perinatol, 32(6): 425-430.

Empowering the Transition Home

- Findings
  - Hospital stay: traditional (25d) vs combined (13d), $p < 0.01$
  - Duration of treatment: traditional (21d) vs combined (37), $p < 0.01$
  - Cumulative methadone dose similar (3.6 vs 3.1 mg/kg)
- Combined group
  - all infants in combined group seen 72 hrs after d/c
  - breastfeeding was more common in combined group (24 vs 8%)
  - average hospital cost was $13,817 less than traditional group
  - no difference for short term adverse outcomes (hospital readmissions, ER visits)

Backes, C.H., Backes C.R., Gardner, D., et al. (2012). Neonatal Abstinence Syndrome (NAS): Transitioning Methadone Treated Infants From An Inpatient to an Outpatient Setting. J Perinatol, 32(6): 425-430.

Kalamazoo County NAS Prevention and Treatment Project

- Participants include area hospitals, physicians, mental health providers, substance abuse professionals, early childhood educators, social workers, toxicologists, and the court system.
  - "The period from age zero to 3 is when the brain is the most plastic it will ever be. So we're hoping to be able to make an impact by getting these babies hooked up more consistently with groups like Early On and occupational or physical therapy."

CRADLE Project: A Model Community Program

- Home intervention program created & delivered by NNPs for infants exposed prenatally to drugs/alcohol (1997-2001)
  - 447 moms (499 infants/children)
  - Services offered- curriculum-based parenting classes, mental health services, food, housing, transportation, day care, 7 recovery/relapse prevention & education programs
  - Multidisciplinary (SW, case managers, NNPs)
  - Weekly home visit during first month, followed by monthly visits for the first year
  - "red flags" identified
- Conclusions
  1. mothers most valued programs when professional nurses conducted the visits
  2. infants/children showed positive effects in long term cognitive function
  3. groups with highest psychosocial risk benefited most

Vasquez, E.P., Pitts, K. & Mejia, N.E. (2008). A Model Program: Neonatal Nurse Practitioners Providing Community Health Care for High-Risk Infants. Neonatal Network, 27(3): 163-69.

Local Community Resources

- The Women's Treatment Center
  - Parenting program- provides services to 300 moms and 400 children
    - Children may reside with mom while they receive rehabilitation services
  - Licensed infant/toddler daycare- provides assessments, referrals, developmentally appropriate curricula and individualized lesson plans for children 6 wks -3 year olds
- Other
  - Association House of Chicago
  - Project Safe
  - Safe Haven

Issues and Care Beyond the Neonatal Period

- Confounding sociodemographic, economic and environmental variables are common and make interpretation of outcomes difficult to fully attribute to prenatal substance exposure
  - Exposure to drugs produce transmissable epigenetic changes that result in profound alterations to infant physiology and future behavior, even in the absence of direct fetal exposure
- Known deficiencies
  - Lower scores using validated assessment tools
    - Hand-eye coordination
    - Personal skills
    - Social skills
  - At risk of relatively reduced cognitive functioning (adolescents)

Vassoler et al. The impact of exposure to addictive drugs of future generations: physiological and behavioral effects. Neuropharmacology. 2014 March; 76: 269-275.

Irner et al. Cognitive and social development in preschool children born to women using substances. J Addict Dis 2012; 31:29-44.

Summary

- Discharge process must be supported by a multidisciplinary team
- Need for population based research examining long term outcomes such as mental health, behavioral problems, maltreatment, visual disorders
- Medical/social services follow-up is absolutely necessary to promote safety & healthy development
    - Early Intervention
    - Reliable health care
    - Child protective services
- Studies have shown reduction/elimination of disparities if a child obtains appropriate and timely interventions

McQueen, K. & Murphy-Oikonen, J. (2016). Neonatal Abstinence Syndrome, N Eng
Med. 375: 2468-2479

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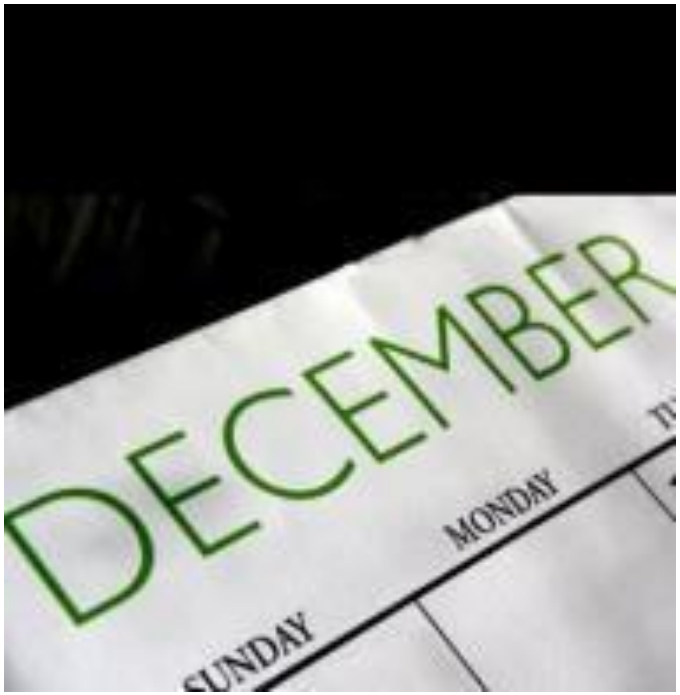

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