What percentage of term cerebral palsy cases have a normal head MRI?

1. <10%
2. 25%
3. 33%
4. 50%

Cerebral Palsy: Definition

• Symptom complex, not a disease
• Consensus definition (1990)
  “a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development”
• International Workshop on Definition and Classification of CP (2004)
  – A group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain.
Definition

- The term cerebral palsy refers to any one of a number of neurological disorders that appear in infancy or early childhood and permanently affect body movement and muscle coordination but don’t worsen over time.
  - NIH website

Location of CP

- Diplegia
- Hemiplegia
- Quadriplegia

Etiology

- Largely unknown
- Rate of CP unchanged despite FHR monitoring
- Prematurity
- Birth asphyxia, or pre-natal HI brain injury
- Peri- or prenatal stroke, brain hemorrhage
- Brain injury in the premature brain
- Kernicterus
**Etiology**

- Brain malformation
- Infection
- Genetic/metabolic disorder
- Spinal cord disorder
- Neuromuscular disorder
- Neuodegenerative disorder
- Plaintiff attorneys – Vast majority due to preventable birth injury

**CP: Associated Disabilities**

- Mental retardation (50-60%)
- Speech and language deficits (40%)
- Epilepsy (mean 40%, range 34-94%)
- Visual (28%) and hearing (12%) impairment
- Disturbed GI function, oral motor deficits
- Growth retardation
- Orthopedic: hip dislocation/subluxation, scoliosis

**Gestational age**

- Preterm
  - Strong correlation with CP
- Term
  - Majority of cases
- Post term
  - Meconium
**Prematurity**

- Thorngren-Jerneck and Herbst (2006)
- Case Control Swedish study
- 2,303 infants 1984-1998
- 35% preterm

- Gestational age 23-27 weeks
  - OR 34 (95% CI 29-39)
- Gestational age 28-29 weeks
  - OR 37 (95% CI 32-42)
- Gestational age 30-31 weeks
  - OR 26 (95% CI 23-30)
- Gestational age 32-36 weeks
  - OR 3.9 (95% CI 3.4-4.4)

**Prematurity**

- Thorngren-Jerneck and Herbst (2006)
- Term infants
  - Apgar score of 6 @ 5 min OR 62 (52, 74)
  - Apgar score of 3 @ 5 min OR 498 (458, 542)
- Conclusion:
  - Preterm birth entails a high risk for CP
  - 65% of CP cases are born at term
  - Certain obstetrical factors and low Apgars are associated with CP

**Term gestation**

- Majority of patients
- Related to birth trauma
- Increased risk with infection
Head MRI in 273 Term Infants with CP

- Arterial infarction: 24%
- Brain malformation: 18%
- Periventricular white matter abnormality: 13%
- HI injury/globally atrophy: 13%
- Intracranial hemorrhage: 5%
- Delayed myelination: 2%
- Other abnormality: 6%
- Normal scan: 25%

Wu YW et al., Pediatrics 2006

Chorioamnionitis and CP

Full term infants

1) Nelson and Ellenberg 1985
   Clinical chorioamnionitis: OR 2.6 (95% CI 1.0-6.8)

2) Grether et al. 1998:
   Clinical/histologic chorioamnionitis: OR 12.0 (95% CI 3.6-39)

3) Walstab 2002
   Clinical/hist. chorioamnionitis: OR 12.5 (95% CI 1.4-112)

What percentage of cerebral palsy cases have adverse birth related events?

1. <10%
2. 25%
3. 33%
4. 50%

ACOG 2003 Publication Executive Summary

- ACOG and AAP publish in 2003
- Neonatal Encephalopathy and Cerebral Palsy: Defining the Pathogenesis and Pathophysiology
- Large Panel of experts
- Examine the available data
- Came up with recommendations and requirements
Neonatal encephalopathy (NE) is defined clinically:
- Constellation of findings to include abnormal consciousness, tone and reflexes, feeding, respiration, or seizures
- Caused by a myriad of conditions
- May or may not cause long term handicaps
- Intrapartum hypoxic-ischemic injury which ends in CP MUST progress through NE

Hypoxic ischemic encephalopathy (HIE) is one subset of NE

Epidemiologic studies of NE:
- 69% cause by antenatal events
- 25% by ante and intrapartum events
- 4% by intrapartum hypoxic events (1.6 per 10,000)
- 2% no identified factors

Requirements for intrapartum events causing CP. Criteria which suggest intrapartum:
- Sentinel hypoxic event before or during labor
- Sudden sustained bradycardia, or absence of variability with persistent variable or late decels
- Apgar scores 0-3 at or after 5 minutes
- Onset of multisystem involvement < 72 hours
- Early imaging showing acute non-focal cerebral abnormality
Korst et al 1999

- 47 cases of prolonged FHR decels
- Resulted in permanent brain injuries
- 56% of cases had arterial pH < 7.0
- 55% of cases had Apgars at 5 min ≤ 3
- 70% had multi-organ system dysfunction
- Conclusion: …currently used indicators to define permanent fetal brain injury are not valid.

California Delivery database.

- Close to 500,000 deliveries each year
- Three administrative databases
  - OSHPD maternal delivery record
  - OSHPD newborn delivery record
  - Birth certificate
- Medical payment database
  - Children with CP, autism, etc

California 1991-2001

- 6,145,357 deliveries
- Snap shot as of November 2006
- 8946 with CP
- 7242 with Spastic Quadriplegic or dyskinetic type
- 59% term gestation

California 1991-2001

- Examined multiple factors:
  - Demographic: Age, parity, education, race, level of prenatal care, payer source
  - Six adverse outcomes
    - Abruptio, Uterine rupture in labor, Fetal distress,
      Birth trauma, Cord prolapse, Asphyxia
- Compared term v. preterm
California 1991-2001

- Demographic results:
  - Maternal age (compared to 20-25 y.o.):
    - Preterm > 40 y.o. OR 1.3 (1.0, 1.7)
    - Term 35-40 y.o. OR 1.2 (1.02, 1.4)
  - Parity (compared to G0):
    - Preterm > CP with Para 0 OR 1.2 (1.02, 1.3)
    - Term < CP with Para 1+2 OR 0.9 (0.8, 0.97)
  - Race:
    - Preterm White > CP than other
    - Term - No differences

Findings

- Almost one third of children with CP had 1 or more adverse birth related events
- Preterm delivered children with CP had higher risks of adverse birth related events suggesting a greater possible role than just prematurity.
**Prevention of CP**

- Not allowing to go past 42 weeks of gestation
- Prevention of early onset GBS infection
- New evidence that head or body cooling could prevent CP
- Intrapartum magnesium sulfate for neuroprotection

**Hypothermia for treatment of HIE**

- Evidence that hypothermia of 34-35 °C in HIE may improve outcome.
- Different treatment modalities
  - Head cooling - New Zealand study
  - Whole body cooling – US study

**Gluckman et al published multicenter trial**

- 234 infants with mod to severe NE and abnormal aEEG randomized to control or treatment groups
- < 6 hrs of age, treated for 72 hours, temp 34-35 °C
- Analysis was intention to treat
- Primary outcome death or severe disability at 18 months of age
- Predefined subgroups Severe vs mod aEEG

**Results**

- All newborns
- Death or severe disability at 18 months
  - 59/108 (55%) vs 73/110 (66%)
  - OR 0.61 (0.34, 1.09) p= 0.1
- Death alone, OR 0.81 (0.47, 1.41) p=0.48
- Severe disability, OR 0.54 (0.25, 1.17) p=0.12
**Hypothermia for treatment of HIE**

- Intermediate aEEG
- Death or severe disability at 18 months
  - 40 (48%) vs 58 (66%) p=0.02
- Death alone, 24 (29%) vs 34 (39%) p=0.20
- Severe disability, 7 (12%) vs 15 (28%) p=0.03

**Gluckman et al. Lancet 2005**

- Conclusion
  - Induced head cooling is not protective in all cases
  - Appears to be beneficial in less severe aEEG cases

**Shankaran et al. 2005**

- Whole body hypothermia to 33.5°C
- 208 HIE randomized to cooling vs control
- >38 weeks, < 6 hrs of age with either
  - Cord pH < 7.0 or BD > 16 mEq/l or
  - Perinatal event and need for resuscitation AND moderate or severe HIE by exam.
- Primary outcomes: death or disability at 18 months

**Shankaran et al.**

- At 18 months
  - Death or mod/severe disability
    - Hypo (44%) vs Normal (62%) RR 0.72 (0.55, 0.93)
    - Death alone - hypo (24%) vs Normal (37%)
      - RR 0.66 (0.43, 1.01)
  - No worse adverse outcomes in either group
- CP – 19% v. 30% OR 0.68 (0.4, 1.22)
**Shankaran et al.**

- Conclusion
  - Whole-Body hypothermia reduces the risk of death or disability in Mod/Severe HIE
  - Demonstrated the effectiveness and safety of whole body cooling

**Intrapartum Mg SO4 for Neuro Protection**

- Not effective for preterm labor.
- Rouse et al. 2008 NEJM
  - RCT
  - 24-31 weeks with eminent delivery
    - > 3 cms dilation, ROM in labor
    - 6 gm load then 2 gm/hr
  - Outcomes Stillbirth + Infant death, Mod or severe CP > 2 years of age
  - 2241 randomized

**Magnesium Sulfate for Neuro Protection**

- Primary outcome NS, 11.3% v. 11.7%
- Mod/severe CP 1.9% v. 3.5%
  - OR 0.55  95%CI(0.32, 0.95)
- Conclusion: ...MgSO4...did not decrease the combined risk of death or Mod/severe CP but did decrease CP in survivors

**Take home messages**

- 1. CP is rare but not decreasing in frequency
- 2. Adverse birth related events represent a greater cause of CP than previously thought
- 3. New modalities for the prevention of CP are available MgSO4 and body cooling