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CARE PATHWAYS

EARLY DIAGNOSIS

Early Detection of Cerebral Palsy

Authors (AACPDM Early Detection of Cerebral Palsy Care Pathway Team): I Novak (team lead), C Morgan (team lead), L Adde, N Badawi, J Blackman, R N Boyd, J Brunstrom-Hernandez, G Cioni, D Damiano, J Darrah, A-C Eliasson, L de Vries, C Einspieler, M Fahey, D Fehlings, D Ferriero, L Fetters, S Fiori, H Forssberg, A Gordon, S Greaves, A Guzzetta, M Hadders-Algra, R Harbourne, A Kakooza-Mwesige, P Karlsson, L Krumlinde-Sundholm, B Latal, A Loughran-Fowlds, N Maitre, S McIntyre, G Noritz, L Pennington, D M Romeo, R Shepherd, A Spittle, M Thornton, J Valentine, K Walker, R White

https://www.aacpdm.org/publications/care-pathways/early-detection

SECTION I: EVIDENCE SUMMARY

DEFINITIONS

Cerebral palsy has traditionally been diagnosed between 12-24 months of age because there is no laboratory biomarker for cerebral palsy. Cerebral palsy is a clinical diagnosis, diagnosed based on a combination of clinical signs, neurological symptoms and physical limitations.

Late diagnosis means some infants do not receive early intervention when they would benefit most.

Cerebral palsy or high-risk of cerebral palsy can now be detected accurately and early using a combination of standardized assessment tools. Early detection enables timely early intervention when the greatest gains are possible from neuroplasticity.

WHY IS EARLY DETECTION IMPORTANT?

Cerebral palsy should be detected as soon as possible because:

1. Cerebral palsy specific early intervention using intense, motor learning task-specific approaches plus environmental enrichment optimizes natural plasticity and improves children's motor and cognitive outcomes.
2. Early, regular monitoring and treatment for the known musculoskeletal complications of cerebral palsy can prevent the onset of hip dislocation, scoliosis and contracture.
3. Parents experience more depression and stress when they are dissatisfied with the diagnostic process. Families prefer early diagnosis, followed by early intervention and parent-to-parent support.

It is not good practice to offer conservative "wait and see" monitoring, when clear clinical diagnostic indicators exist, especially in contexts where the absence of a diagnostic label precludes the infant from accessing the recommended early intervention. There is evidence that delayed diagnosis worsens parental mental health (Baird et al, 2000) and clinical trial evidence is emerging that the lack of intense early intervention may restrict the infant's motor and cognitive gains (Morgan et al, 2016). Neuroscience evidence indicates that brain development and refinement of the motor system continues in the postnatal period, driven by activity in the motor cortex (Eyre et al, 2014; Martin et al, 2011). Early active movement and intervention is essential because infants not actively using their motor cortex risk losing cortical connections and dedicated function (Eyre et al, 2014; Martin et al, 2011). Furthermore, there is increasing evidence that the infant's motor behavior, through discovery and interaction with the environment, controls and generates the growth and development of muscle, ligament, and bone, as well as driving the ongoing development of the neuromotor system. These recent discoveries about brain and muscle plasticity support the earliest possible intervention to: (a) exercise muscles through their functional length (as muscles grow throughout development in response to the infant's actions); and (b) train specific actions, in order to promote motor learning and 'drive' plasticity and effective functional motor performance (Eyre et al, 2014; Martin et al, 1999; Shepherd 2014).

Randomized controlled trial (RCT) data is beginning to indicate that infants with unilateral/hemiplegic cerebral palsy, who receive early Constraint Induced Movement Therapy (CIMT) have better hand function than controls short-term and probably substantially better hand function long-term (Eliasson et al, 2015). Population register data indicates that children with bilateral cerebral palsy, who receive regular surveillance and intervention have lower rates of hip displacement, contracture and scoliosis complications (Elkamil et al, 2011; Hägglund et al, 2005; Scrutton et al, 2001). Hip Surveillance guidelines can be found on the care pathways website [https://www.aacpdm.org/publications/care-pathways/hip-surveillance]. RCT data is also beginning to indicate that infants with any type and topography of cerebral palsy, who receive "GAME" (Goals – Activity – Motor Enrichment, which is an early, intense, enriched, task-specific, training-based interventions at home), have better motor and cognitive skills at 1-year,

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than those who received usual care (Morgan et al, 2016). Importantly, RCTs also suggest that, improvements are even better when training occurs at home (Novak et al, 2009; Rostami et al, 2012) because children learn best in supported natural settings, where training is personalized to their enjoyment – translating to more intense, specific and relevant practice. Task-specific, motor learning training-based early intervention (e.g. GAME and CIMT) are recommended as the new paradigm of care for infants with cerebral palsy as they induce neuroplasticity and produce functional gains (Morgan et al, 2016b). Larger replication studies are underway, meaning more evidence will inform our estimate in the confidence of the effects.

TARGET POPULATION:

Infants with cerebral palsy and their parents.

TARGET CLINICAL PROVIDERS:

Neurologists, pediatricians, neonatologists, pediatric rehabilitation specialists/physiatrists, general practitioners, neuro-radiologists, physiotherapists, occupational therapists, speech pathologists, nurses and early educators.

EARLY DETECTION STRATEGIES

Evidence indicates that there are two major pathways to accurate and early detection of cerebral palsy depending on the infant's age at the time of assessment using different tests in combination with the clinical examination.

1. **For infants *younger* than 5-months of age** (corrected for prematurity) known as the "Newborn Detected Risks" pathway: abnormal motor function detected as "absent fidgety" on Prechtl's General Movements Assessment (GMs) plus an abnormal brain Magnetic Resonance Imaging (MRI) indicating damage to the motor area/s accurately predicts cerebral palsy more than 95% of the time and is strongly recommended. The Test of Infant Motor Performance (TIMP) can also be used as it predicts cerebral palsy 61-90% of the time. NOTE: Each test has excellent sensitivity and specificity in isolation, but the pooled predictive power of three tests is even higher for an early accurate diagnosis of cerebral palsy. The combined predictive power of neuroimaging plus HINE plus absent fidgety GMs is a sensitivity and specificity value of 97.86% and 99.22% (PPV 98.56%, NPV 98.84%) (Morgan et al, 2019). Key Neuroimaging Evidence: PRE-TERM infants: Term equivalent age (TEA) (or as close as possible) MRI is most predictive of outcome (Reid et al, 2014). Where possible, use a 3 Tesla (3T) scanner to improve the ability to detect subtle lesions. Sequential cranial ultrasound (CUS) can also predict non-ambulatory cerebral palsy but may fail to detect subtle lesions commonly associated with diplegia. When an MRI is performed within a week after a presumed insult, diffusion weighted imaging (DWI) can be predictive of subsequent cystic evolution in the white matter (de Vries et al, 2015; Kwon et al, 2014; Woodward et al, 2006). TERM-BORN infants: MRI in the first week of life is recommended for infants born at term with suspected brain abnormalities. If the infant has had encephalopathy, conventional MR sequences may not show any signs of abnormality in the first 48-hours Diffusion weighted imaging (DWI) and apparent diffusion coefficient maps (ADC) are likely to detect the injury early. Waiting 3-5 days before imaging is recommended, to maximize identifying abnormal findings. Conventional T1 beyond the first week and DWI before the end of the first week may also allow examination of the posterior limb of the internal capsule (PLIC) and the descending corticospinal tracts at the level of the cerebral peduncles, which is highly predictive of permanent motor dysfunction (Cowan et al, 2005; Kirton et al, 2007). If myelination asymmetry can be visualized this is highly predictive of hemiplegic cerebral palsy (de Vries et al 2001).
2. **For infants *older* than 5-months of age** (corrected for prematurity) known as the "Infant Detected Risks" pathway: A Hammersmith Infant Neurological Evaluation (HINE) score lower than 73 (at 6, 9 or 12 months) (scored neurological clinical examination) plus an abnormal brain MRI indicating damage to the motor area/s accurately predicts cerebral palsy 90% of the time and is strongly recommended. The Developmental Assessment of Youth and Children (DAYC) (parent-report scored checklist) can also be used as it accurately predicts cerebral palsy 80% of the time. The Alberta Infant Motor Scale (AIMS) and the Neuro Sensory Motor Development Assessment (NSMDA) can be used as supplementary assessments for predicting an abnormal motor outcome, 86% and 82% predictive respectively. Parent concern is a valid reason to trigger formal diagnostic investigations and referral to early intervention, as eighty-six per cent of parents suspect their child has cerebral palsy before the clinical diagnosis is made (Baird et al, 2000). NOTE: High-quality early detection studies of lower-risk term-born infants without early discernable indicators of cerebral palsy do not exist in the literature, as these infants are more difficult to identify

and study very early. Therefore, the recommendations for early detection of cerebral palsy in infants older than 5-months are conditional (or weaker strength) recommendations based on best-available evidence, which is extrapolated from high-risk populations. We chose to make this extrapolation because despite the differing causal pathways to cerebral palsy, population data indicates that lower-risk cases have comparable type and topography cerebral palsy profiles to high-risk cases, but with more severe motor impairments. Key DAYC evidence: A large retrospective study of n=606 high-risk neonatal intensive care graduates (preterm <1500g or neonatal encephalopathy), found that a drop of 2 standard deviations in DAYC motor scores between 6-12 months is 89% predictive of cerebral palsy (Maitre et al, 2013).

In Low to Middle Income Contexts (LIMC) or where MRI is not safe, feasible or affordable, the most reliable alternatives are: the HINE (scored neurological clinical examination) and the DAYC (parent-report scored checklist) which accurately predicts cerebral palsy 90% and 80% of the time respectively. NOTE: In contexts where an MRI is not available, safe, feasible or affordable, then detection of cerebral palsy with "infant detectable risks" and older than 5-months of age but less than 24-months of age is still possible using standardized tools and should be carried out to enable access to early intervention. On the algorithm this care pathway, is referred to as option B. Early detection of risk of cerebral palsy in 5-24 months olds without an MRI is most accurately conducted using the: (a) Hammersmith Infant Neurological Evaluation (HINE) detects abnormal neurological dysfunction and is 90% predictive of cerebral palsy from 2-24 months of age. HINE scores at 6, 9 or 12 months, where: <73 indicates risk of cerebral palsy; and <40 indicates abnormal outcome, usually cerebral palsy; (b) Developmental Assessment of Young Children (DAYC) to quantify motor delay (89% predictive of cerebral palsy); and (c) Movement Assessment of Infants (MAI) to quantify motor delay (73% predictive of cerebral palsy in high-risk infants at 8 months of corrected age). Key evidence: A large prospective cohort study of high-risk infants (preterm or term with encephalopathy) were studied from birth until 12 months corrected age and the global HINE scores were found to predict cerebral palsy with >90% accuracy (Pizzardi et al, 2008). Systematic review evidence of tools to detect cerebral palsy, found moderate quality evidence that the MAI can detect cerebral palsy with 96% accuracy at 8-months post term age, in infants with high-risk for cerebral palsy (Spittle et al, 2008).

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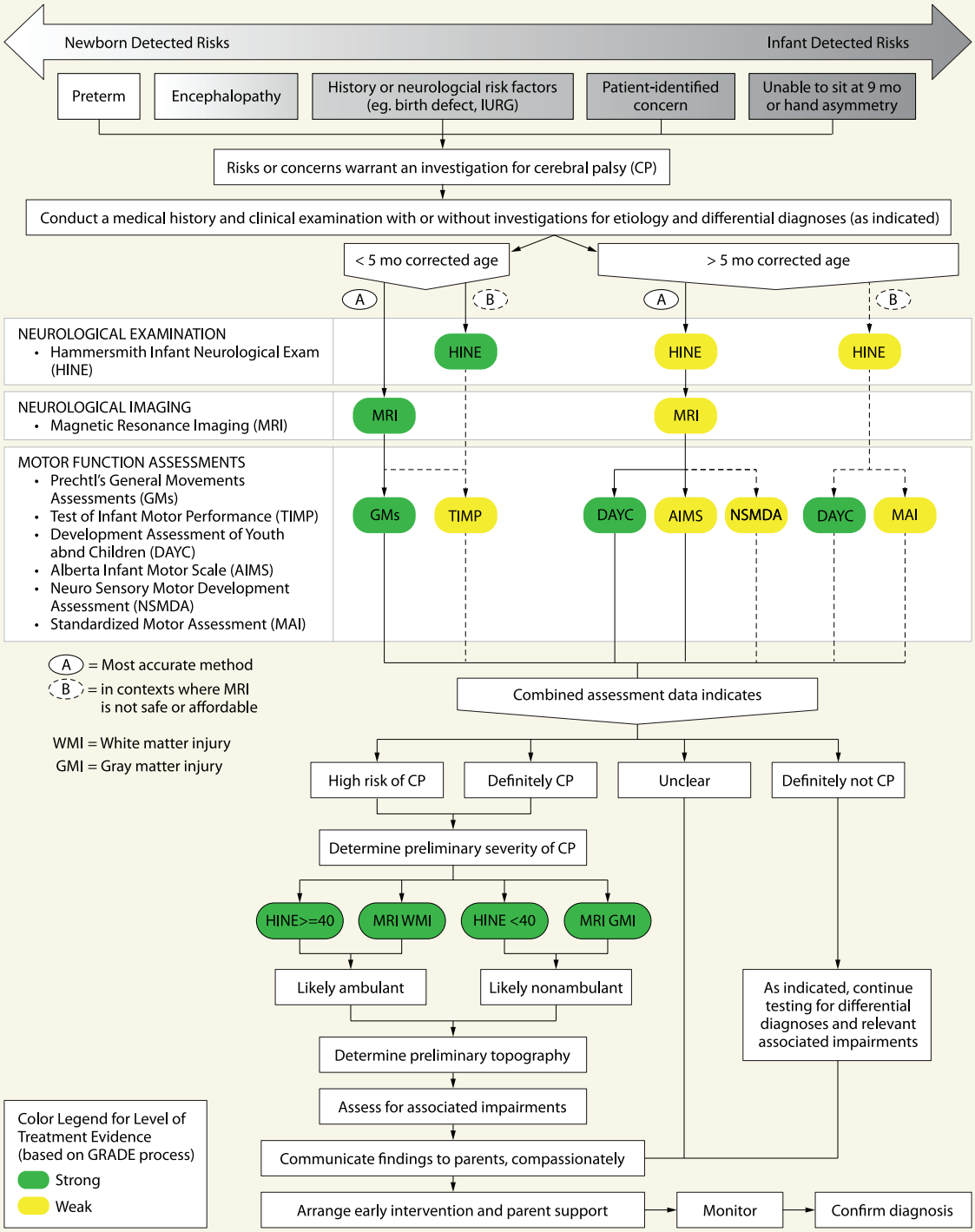
Flow Diagram for Evidence-Informed Care Pathway for Early Diagnosis of Cerebral Palsy



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Plain Language Summary

The early years are the most important for a child's brain development. Learning can be interrupted by brain injury in children with cerebral palsy. Early diagnosis of cerebral palsy enables: (1) children to receive specialist intervention when the greatest gains are possible from neuroplasticity; (2) prevention of complications; and (3) support to parents.

Unlike diabetes, no one test can be ordered, to conclusively diagnose cerebral palsy. Consequently, the diagnosis was historically made late between 12-24 months of age once it was clear that a child's movement such as walking or sitting was permanently delayed. Now an international clinical practice guideline shows that using 3 tests together in combination, enables early diagnosis of cerebral palsy at 12 weeks of age with over 95% accuracy. The 3 tests are: a brain scan (MRI) showing damage to the movement areas of the brain, plus a movement test where the child's movement is scored to be of low quality from video footage (General Movements Assessment), and a scored neurological test showing either asymmetries between the left and right or atypical postures (Hammersmith Infant Neurological Examination).

For some families, parents are the first to notice, "there is something wrong with my child". In children 5 months and older, screening for cerebral palsy should occur if the child cannot sit independently by 9 months of age or has an abnormally early hand dominance. MRI is not always safe or affordable in children aged between 2-12 months of age, because anaesthetic is required to help the child remain still in the scanner. An early diagnosis can still be made but will need to rely on the Hammersmith Examination and a parent completed checklist known as the Developmental Assessment of Young Children. No matter which tests are used, the aim of early diagnosis is to ensure early intervention, so that the child can live a healthy and included life.

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